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By Brad Christian McDowell, MD

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Dr McDowell is a Plastic Surgeon at the Denver Medical Office in CO. More of his photography can be viewed online at www.diversityofvision.com.

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TABLE OF CONTENTS

ORIGINAL RESEARCH & CONTRIBUTIONS

CME credits are available online at www.tpjcme.org. The mail-in CME form can be found on page 112.

SPECIAL REPORTS

REVIEW ARTICLES

CLINICAL MEDICINE

SOUL OF THE HEALER

CASE REPORTS

Contents continued on next page.

Contents continued from previous page.

NARRATIVE MEDICINE

ONLINE

More content is available at: www.thepermanentejournal.org.

ORIGINAL RESEARCH & CONTRIBUTIONS

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ORIGINAL RESEARCH & CONTRIBUTIONS

Ten-Year Trends in Preventive Service Use Before and After Prostate Cancer Diagnosis: A Comparison with Noncancer Controls

Lauren P Wallner, PhD, MPH; Jeffrey M Slezak, MS; Ronald K Loo, MD; Roshan Bastani, PhD; Steven J Jacobsen, MD, PhD

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ABSTRACT

Context: Few studies have assessed the longer-term quality of preventive care in prostate cancer (PCa) survivors.

Objective: To compare the rates of preventive services among PCa survivors five years before and after diagnosis, to men without PCa.

Design: Men enrolled in Kaiser Permanente Southern California with newly diagnosed PCa (2002-2008) were matched 1:1 to men without a PCa diagnosis on age, race, and timing of prostate-specific antigen test (N = 31,180). The use of preventive services, including colorectal cancer screening, diabetes tests, lipid panels, and influenza and pneumococcal vaccinations was assessed 5 years before and after diagnosis (or index date for controls).

Main Outcome Measures: Relative rates (RRs) of use were calculated for cases and controls separately and compared using Poisson regression, adjusting for comorbidities and outpatient utilization in 2014.

Results: Overall, the rates of preventive services were lower among men with PCa vs men without PCa. However, in the 5 years after diagnosis, rates of preventive service use for all services were greater among PCa survivors vs men without PCa (colorectal cancer: RR = 1.05, 95% confidence interval [CI] = 1.01-1.10; lipids: RR = 1.10, 95% CI = 1.08-1.11; hemoglobin A_{1C}: RR = 1.17, 95% CI = 1.14-1.19; glucose: RR = 1.24, 95% CI = 1.23-1.26; influenza vaccine: RR = 1.05, 95% CI = 1.03-1.07; pneumococcal vaccine: RR = 1.03, 95% CI = 0.97-1.09).

Conclusion: Delivery of preventive care improved after PCa diagnosis, with survivors receiving comparable preventive care to men without PCa during the five years following diagnosis.

INTRODUCTION

There are currently more than 15.5 million cancer survivors in the US, and it is estimated that the number of survivors will exceed 20 million by 2026.[1,2] Prostate cancer survivors now account for the largest proportion of male cancer survivors (3.3 million) and the second largest proportion of cancer survivors overall.[1] Prostate cancer is a largely survivable chronic condition for most men, with a 5-year survival rate of nearly 100%,[2] and most prostate cancer survivors are now older than age 65 years.[1] Thus, these survivors are at increased risk of the development of other diseases of aging because of their advancing age, potential treatment effects, and prolonged survival.[3,4]

Because most men with prostate cancer will die of causes other than the prostate cancer, the delivery of appropriate preventive services to prostate cancer survivors is particularly critical.[5,6] The US Preventive Services Task Force (USPSTF) recommends that aging men receive a variety of screening and preventive services.[7] However, the complex delivery of prostate cancer care, which involves multiple clinicians of varying specialties over time, may lead to an inadequate transition between treatment and survivorship. This, in turn, may result in less preventive care being delivered in the survivorship period. Although previous studies suggest that prostate cancer survivors receive comparable preventive care to disease-free controls after diagnosis,[8-12] most of these studies have focused solely on patients older than age 65 years, and only 2 studies have looked at preventive care beyond the first year after diagnosis.[10,13] In addition, little is known regarding the receipt of services before prostate cancer diagnosis as a source of comparison.

Therefore, the goal of this study was to compare the use of preventive health services for other comorbid diseases of aging in the five years before and after prostate cancer diagnosis among men with prostate cancer and noncancer controls in a multiethnic population of men in general medical practice settings.

METHODS

Study Population

Kaiser Permanente Southern California (KPSC) is an integrated health care system that provides comprehensive health services for approximately 4.4 million residents of Southern California via 14 hospitals, 222 medical offices, and more than 7000 physicians. The population served by KPSC is socioeconomically diverse and broadly representative of the racial/ethnic groups living in Southern California.[14] Members enroll through the Kaiser Foundation Health Plan for prepaid health care insurance, including pharmaceutical benefits. Diagnoses, treatments, and utilization of health services are linked through electronic medical records (EMRs).

Men were eligible for inclusion in this study if they received a diagnosis of prostate cancer between 2002 and 2008

Lauren P Wallner, PhD, MPH, is an Assistant Professor of Internal Medicine and Epidemiology at the University of Michigan in Ann Arbor, and an Adjunct Investigator at the Department of Research and Evaluation for Kaiser Permanente Southern California in Pasadena. E-mail: lwallner@med.umich.edu. **Jeffrey M Slezak, MS,** is the Research Manager of Biostatistics for the Department of Research and Evaluation for Kaiser Permanente Southern California in Pasadena. E-mail: jeff.m.slezak@kp.org. **Ronald K Loo, MD,** is Regional Assistant Medical Director for the Southern California Permanente Medical Group and Chair of the Kaiser Permanente Interregional Urology Chiefs. E-mail: ronald.k.loo@kp.org. **Roshan Bastani, PhD,** is a Professor of Health Management and Policy at the University of California, Los Angeles. E-mail: bastani@ucla.edu. **Steven J Jacobsen, MD, PhD,** is the Senior Director of Research in the Department of Research and Evaluation for Kaiser Permanente Southern California in Pasadena. E-mail: steven.j.jacobsen@kp.org.

(N = 17,296) and had record of a serum prostate-specific antigen (PSA) test within 6 months of diagnosis (N = 15,631). Men with missing membership length information (N = 15) or who had previously undergone a radical prostatectomy before their prostate cancer diagnosis (N = 26) were excluded, leaving 15,590 men eligible for inclusion. Men with prostate cancer were matched to men without prostate cancer 1:1 on age (within 1 year), race (non-Hispanic white, non-Hispanic black, non-Hispanic Asian/Pacific Islander, Hispanic, and other/unknown), and timing of PSA test (within 1 year). As a result, the total analytic sample size was 31,180 men. The Kaiser Permanente internal review board reviewed and approved this study; for this type of study, written informed consent was not required.

Prostate Cancer Diagnosis

Prostate cancer survivors were defined as men with a diagnosis of any stage of biopsy-confirmed prostate cancer from 2002 through 2008 who were still alive. They were identified through the KPSC cancer registry, which participates in the Surveillance, Epidemiology, and End Results (SEER) registry. The registry data are 99% complete for both inpatient and outpatient admissions for the diagnosis of new and prevalent cancers.[15]

Preventive Services

Trends in the use of preventive and health maintenance services for aging men were identified five years before and after prostate cancer diagnosis using electronic Health Plan files. The use of adult preventive services was then assessed by identifying the following testing as coded in the EMR: heart and vascular disease (total cholesterol, triglycerides, high-density lipoprotein cholesterol), colorectal cancer screening use (fecal occult blood test [FOBT] and/or sigmoidoscopy or colonoscopy), diabetes screening and monitoring (glucose testing and hemoglobin A_{1C} [HbA_{1C}] measurement), and pneumonia and influenza vaccination (seasonal).

Covariate Assessment

Age at prostate cancer diagnosis, race (non-Hispanic white, black, Hispanic, Asian, other), Health Plan membership length, and marital status were abstracted from the EMR. Medical histories, including previous diagnosis of comorbid conditions such as cardiovascular disease (including hypertension), diabetes, hyperlipidemia, and other cancers, were collected via electronic Health Plan files and on the basis of International Classification of Diseases, Ninth Revision, coding. The presence of comorbidities was also measured using a modified version of the Charlson Comorbidity Index (CCI).[16]

Statistical Analysis

In 2014, the distributions of demographic and clinical characteristics at the time of matching (prostate cancer diagnosis in cases) were compared between men with a diagnosis of prostate cancer and men without prostate cancer using χ^2 tests for association and 2-sided *t*-tests when appropriate. The rates of preventive service use per year were calculated in the

Table 1. Demographic and clinical characteristics of study sample (N = 31,180)

Characteristic	Men without prostate cancer (n = 15,590)	Men with prostate cancer (n = 15,590)	p value
Age at matching, mean (SD)	64.9 (9.51)	64.9 (9.51)	0.747
Race at matching, no. (%)			
Non-Hispanic white	8113 (52.0)	8113 (52.0)	> 0.99
Non-Hispanic black	2599 (16.7)	2599 (16.7)	
Non-Hispanic Asian/Pacific Islander	3026 (19.4)	3026 (19.4)	
Hispanic	931 (6.0)	931 (6.0)	
Other/unknown	921 (5.9)	921 (5.9)	
Charlson Comorbidity Index, no. (%)			
0	9407 (60.3)	10,518 (67.5)	< 0.0001
1	2992 (19.2)	2522 (16.2)	
≥ 2	3191 (20.5)	2550 (16.4)	
Utilization (outpatient visits/y), no. (%)			
Q1, 0-2	3038 (19.5)	3283 (21.1)	< 0.0001
Q2, 3-6	4473 (28.7)	4760 (30.5)	
Q3, 7-12	3842 (24.6)	3944 (25.3)	
Q4, ≥ 13	4237 (27.2)	3603 (23.1)	
Other characteristics			
PSA level (ng/mL), mean, median (SD)	2.8, 1.3 (16.12)	31.8, 7.0 (225.89)	< 0.0001
History of diabetes, no. (%)	3760 (24.1)	2847 (18.3)	< 0.0001
History of CVD, no. (%)	768 (4.9)	634 (4.1)	0.0003
History of hyperlipidemia, no. (%)	11,948 (76.6)	11,057 (70.9)	< 0.0001
History of other cancers, no. (%)	2181 (14.0)	2115 (13.6)	0.2782

CVD = cardiovascular disease; PSA = prostate-specific antigen; Q = quarter; SD = standard deviation.

5 years before and after prostate cancer diagnosis (or the corresponding index date for controls). They were calculated in 30-day intervals as the number of tests divided by the number of people who were eligible members at that time interval and then multiplied by 12. The annualized rates were calculated for cases and controls separately and compared within service type using Poisson regression.

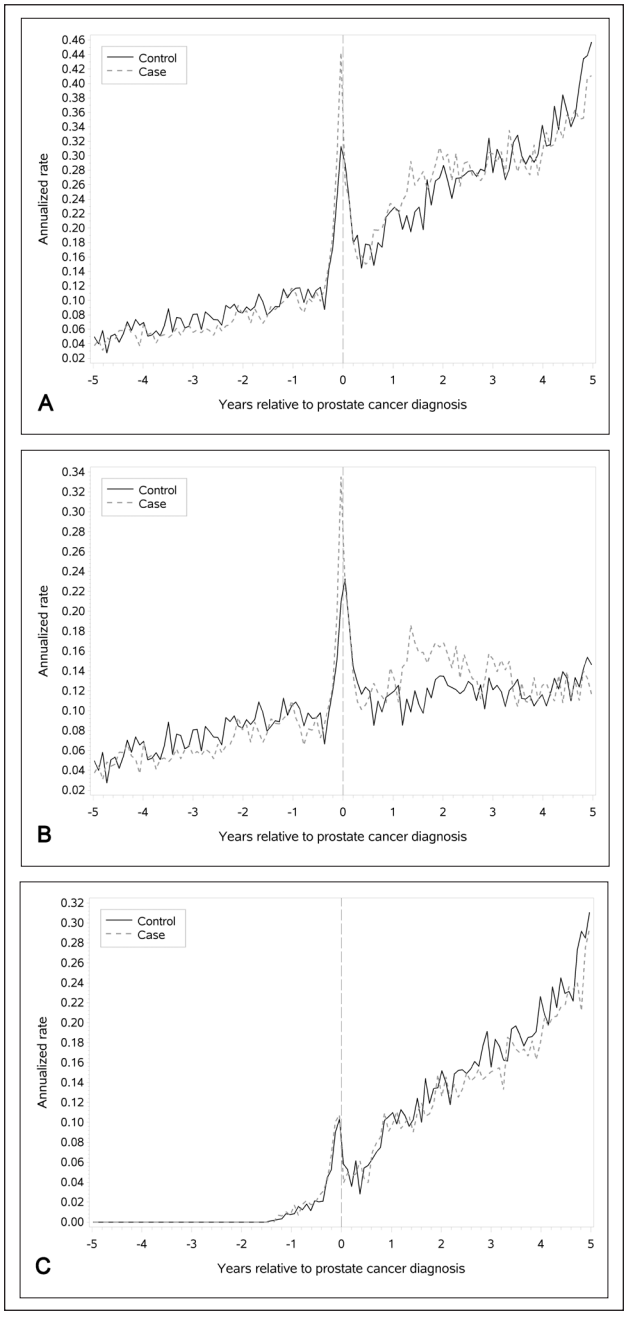

Figure 1. Rates of testing before and after diagnosis in prostate cancer cases diagnosed from 2002 to 2008 and matched controls: A. Any colorectal cancer screening; B. Fecal occult blood test and fecal immunochemical tests; C. Colonoscopy.

The relative rates (RRs) of use and 95% confidence intervals (CIs) were estimated comparing cases and controls throughout the entire period and comparing the use before and after diagnosis (regardless of case status) separately. In addition, an interaction term was fit to estimate the RR of preventive service use before and after prostate cancer diagnosis comparing cases and controls. All the models were adjusted for CCI and outpatient visit utilization. The models estimating the rates of HbA_{1C} use and lipid testing were further adjusted for the diagnosis of diabetes (HbA_{1C}), cardiovascular disease, and hyperlipidemia (lipid tests). Sensitivity analyses were run to assess the impact of removing all services within 90 days of diagnosis (or index date) in the rate calculations and adjusted models. All analyses used an α level of 0.05 to determine statistical significance and were performed using SAS 9.2 (SAS Institute Inc, Cary, NC).

RESULTS

Table 1 compares the demographic and clinical characteristics at time of matching between men with a prostate cancer diagnosis and men without prostate cancer. Age at matching ($p = 0.747$) and race ($p > 0.99$) were well balanced across groups. The median PSA level at matching was higher among men with prostate cancer (7.0 ng/mL) compared with men without prostate cancer (1.3 ng/mL; $p \leq 0.001$). Men with prostate cancer had fewer comorbidities compared with men without prostate cancer ($p < 0.001$) and were less likely to have a history of diabetes, cardiovascular disease, and hyperlipidemia (all $p < 0.001$; Table 1).

Figures 1 through 4 display the trends in the rates of each preventive service in the five years before and after diagnosis for cases and controls. For all services, the rates of use per year spiked right before prostate cancer diagnosis (or index date), most likely because these services were ordered at the same time the diagnostic PSA test was ordered. Rates of colonoscopy were notably highest among men with prostate cancer in the one to three years after diagnosis, whereas FOBT and fecal immunochemical tests (FIT) increased sharply with time after diagnosis (Figures 1B). Lipid panel test results remained stable over time, with a sharp peak just before prostate cancer diagnosis

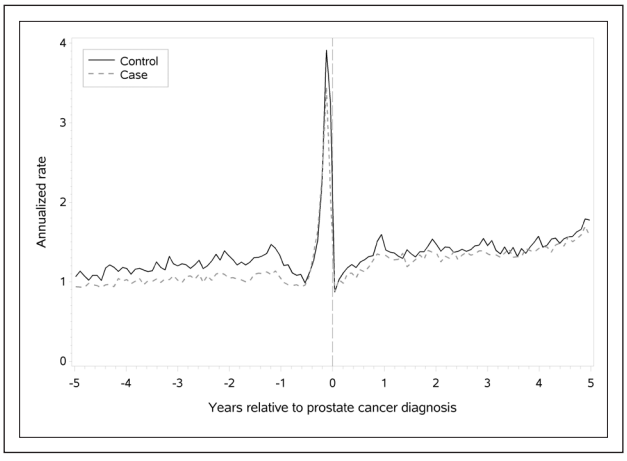

Figure 2. Rates of testing before and after diagnosis in prostate cancer cases diagnosed from 2002 to 2008 and matched controls: Lipid panel testing.

(or index date) (Figure 2). HbA_{1c} rates and glucose testing rates remained lower among cases throughout the study period compared with controls, with a more notable separation between rates among men with and without prostate cancer for HbA_{1C} testing. However, there were two peaks in glucose testing, one peak right before diagnosis and, interestingly, one in the first two months after diagnosis, potentially reflecting repeated testing among those with initially elevated levels (Figure 3). Influenza vaccination rates increased steadily during the study period and were higher among both groups after diagnosis. Finally, the pneumococcal vaccination rate remained stable over time and was equivalent between groups (Figure 4).

Men with a diagnosis of prostate cancer were 8% less likely to have a lipid test during the 10-year period compared with men without a prostate cancer diagnosis (adjusted RR = 0.91, 95% CI = 0.90-0.92) after adjustment for comorbidities, outpatient visit utilization, and diagnosis of cardiovascular disease and hyperlipidemia (Table 2, Column A). Men with prostate cancer were also 11% less likely to have an HbA_{1C} test and 12% less likely to have a glucose test than were men without prostate cancer after adjustment for diabetes diagnosis, CCI, and outpatient utilization (adjusted RR = 0.89, 95% CI = 0.88-0.91; RR = 0.88, 95% CI = 0.87-0.89; Table 2, Column A). The adjusted rates of colorectal cancer (CRC) screening were equivalent when groups were compared over the study period (RR = 0.99, 95% CI = 0.95-1.02). Although men with a diagnosis of prostate cancer were 3% less likely to have an annual influenza vaccine (adjusted RR = 0.97, 95% CI = 0.95-0.98), they were equally as likely to have a pneumococcal vaccine as men without prostate cancer after adjustment for CCI and outpatient utilization (Table 2, Column A).

Annual CRC screening rates were 2.75 times greater after diagnosis compared with before diagnosis, after adjustment for CCI and outpatient utilization (adjusted RR = 2.75, 95% CI = 2.67-2.84). When separated, FOBT/FIT was the biggest contributor to this trend: Use in the 5 years after diagnosis (or index date) was 15.2 times greater than use in the 5 years before diagnosis (adjusted RR = 15.2, 95% CI = 13.9-16.6). The rate of lipid panel testing was 8% greater in the 5 years after diagnosis (or index date) compared with before (adjusted RR = 1.08, 95% CI = 1.07-1.09). Testing for diabetes was higher in the 5 years

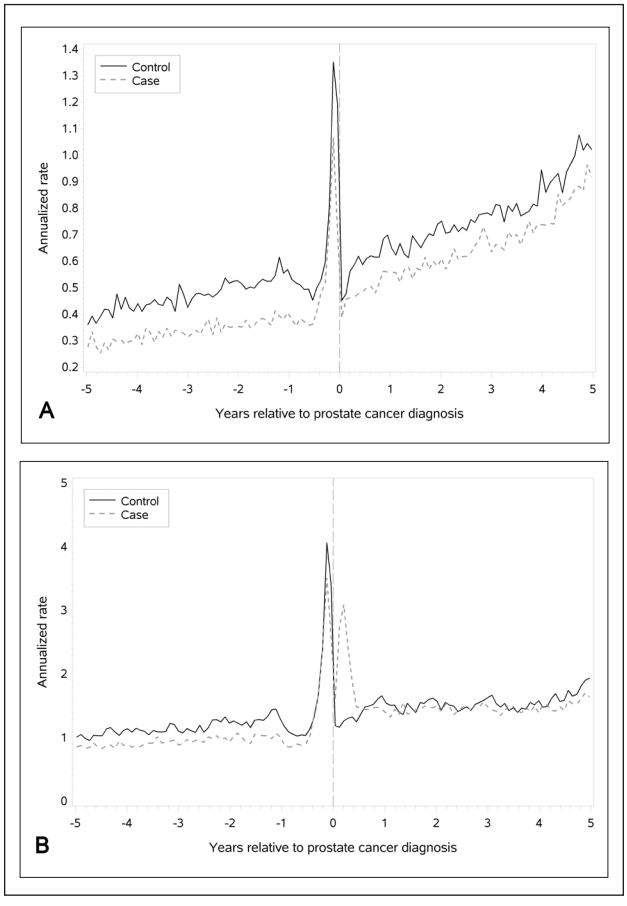

Figure 3. Rates of testing before and after diagnosis in prostate cancer cases diagnosed from 2002 to 2008 and matched controls: A. HbA_{1c} testing; B. Glucose.

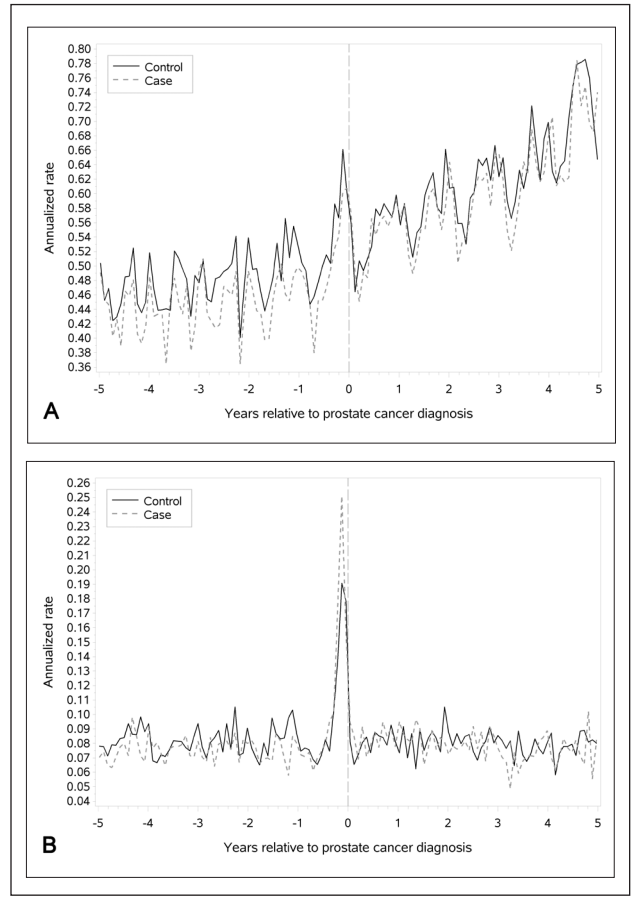

Figure 4. Rates of testing before and after diagnosis in prostate cancer cases diagnosed from 2002 to 2008 and matched controls: A. Influenza vaccinations; B. Pneumococcal vaccinations.

after diagnosis (or index date) compared with before diagnosis. Men were 45% more likely to have an HbA_{1C} test and 19% more likely to have a glucose test after diagnosis (or index date; HbA_{1C}: adjusted RR = 1.45, 95% CI = 1.43-1.47; glucose: adjusted RR = 1.19, 95% CI = 1.18-1.20) regardless of whether the men had a diagnosis of prostate cancer (Table 2, Column B).

The annual rates of CRC screening increased an additional 5% among men with prostate cancer compared with men without prostate cancer in the 5 years after diagnosis (adjusted RR = 1.05, 95% CI = 1.01-1.10). The rates of lipid testing after diagnosis or index date increased an additional 10% in men with prostate cancer relative to men without prostate cancer (adjusted RR = 1.10, 95% CI = 1.08-1.11). Rates of HbA_{1C} testing increased 17% and glucose testing increased 24% more in the men with prostate cancer after diagnosis relative to the men without prostate cancer, with the highest rate in the first 6 months after diagnosis (adjusted RR = 1.17, 95% CI = 1.14-1.19; RR = 1.24, 95% CI = 1.23-1.26). Although the rates of influenza vaccination increased 5% more after diagnosis in the men with prostate cancer compared with men without prostate cancer (adjusted RR = 1.05, 95% CI = 1.03-1.07), the trends in pneumococcal vaccination rates in the 5 years after diagnosis compared with before diagnosis were equivalent in both groups (adjusted RR = 1.03, 95% CI = 0.97-1.09; Table 2, Column C). These results remained unchanged when we removed services performed in the 90 days around the time of diagnosis or index date (results not shown).

DISCUSSION

This study evaluated the trends in preventive care in the five years before and after prostate cancer diagnosis and compared them with those in a population of men without a diagnosis of prostate cancer, to determine any care gaps in the delivery of preventive care to prostate cancer survivors in the period following diagnosis. Our results suggest that prostate cancer survivors received comparable preventive care in the five years after diagnosis compared with men without prostate cancer, particularly around the time that the PSA test was ordered that ultimately led to the diagnosis. In this integrated health care system, the diagnosis of prostate cancer seems to result in improved preventive care being delivered to survivors.

Our results suggest that colorectal cancer screening, lipid and diabetes testing, and influenza and pneumococcal vaccination were slightly greater among prostate cancer survivors in the five-year period after diagnosis; these findings are consistent, albeit more conservative, compared with prior studies in the SEER-Medicare database and in the United Kingdom.[10,13] Our findings expand on these results and suggest that despite increased use of colonoscopies among survivors and FOBT/FIT overall in more recent years, there remains room for improvement in the use of FOBT/FIT among men with prostate cancer after their diagnosis. Because patients with diagnosed prostate cancer who undergo treatment may be at increased risk of second primary cancers,[17,18] delivering appropriate screening for these cancers should be an important part of their survivorship care.

When we assessed the rates of preventive services use during the entire 10-year study period, the rates of screening and monitoring tests for diabetes (HbA_{1C} and glucose) were lower among men with prostate cancer compared with men without prostate cancer. Although fewer men with prostate cancer received a diagnosis of diabetes during the study period compared with men without prostate cancer (24% vs 18%), the difference in the rates of HbA_{1C} and glucose testing during the entire study period persisted after

Table 2. Adjusted relative rates (RR) and 95% confidence intervals (CI) comparing use of preventive services between prostate cancer cases and matched controls over 10-year study period (A), before and after diagnosis (or index date) overall (B), and before and after diagnosis (or index date) (C)[a]

	Adjusted RR (95% CI)		
Preventive service	A. Use in prostate cancer cases vs use in controls over entire study period	B. Use after prostate cancer diagnosis (or index date) vs use before diagnosis (or index date) overall	C. Use after prostate cancer diagnosis vs use before diagnosis compared between cases and controls
CRC screening			
Colonoscopy with or without FOBT/FIT	0.99 (0.95-1.02)	2.75 (2.67-2.84)	1.05 (1.01-1.10)
Colonoscopy only	0.96 (0.93-1.00)	1.45 (1.40-1.50)	1.18 (1.13-1.24)
FOBT/FIT only	1.27 (1.14-1.43)	15.2 (13.9-16.6)	0.79 (0.70-0.89)
Heart disease[b]			
Lipid panel	0.91 (0.90-0.92)	1.08 (1.07-1.09)	1.10 (1.08-1.11)
Diabetes[c]			
Hemoglobin A_{1c}	0.89 (0.88-0.91)	1.45 (1.43-1.47)	1.17 (1.14-1.19)
Glucose	0.88 (0.87-0.89)	1.19 (1.18-1.20)	1.24 (1.23-1.26)
Vaccinations			
Influenza	0.97 (0.95-0.98)	1.25 (1.23-1.27)	1.05 (1.03-1.07)
Pneumococcal	0.99 (0.96-1.03)	0.92 (0.89-0.96)	1.03 (0.97-1.09)

[a] Models were adjusted for Charlson Comorbidity Index and utilization (number of outpatient visits).
[b] Diagnosis of cardiovascular disease and/or hyperlipidemia was also included in the adjusted model.
[c] Diagnosis of diabetes also included in the adjusted model.
CRC = colorectal cancer; FOBT/FIT = fecal occult blood test/fecal immunochemical test.

adjustment for diabetes. However, the use of HbA_{1C} testing increased steadily during the study period, which in part may have mitigated the rate differences between groups, resulting in higher rates of the use of HbA_{1C} testing among men with prostate cancer after diagnosis. This is most likely the reflection of overall increasing the use of HbA_{1C} testing in clinical practice to monitor and screen for diabetes.

Previous studies have assessed a variety of factors associated with receiving preventive care after a cancer diagnosis.[12,19] It is possible that the high use of services in this cohort is related to higher utilization among men in whom cancer was once diagnosed, as shown in studies by Snyder and colleagues,[20-23] which focused on patients with colorectal cancer and breast cancer. The number of outpatient visits per year was high in this sample, with more than half of the sample with seven or more visits. However, when adjusting for utilization, the results remained largely unchanged. It is also possible that the high use of preventive services in this sample is because this is an entirely insured population who received care in an integrated system, where the use of preventive care is promoted widely regardless of clinician specialty. These reasons would align with the results from Robin Yabroff et al,[24] suggesting that access to care plays an important role in the use of preventive services among survivors, with use lowest among uninsured survivors and the highest use among those who are privately insured.

… access to care plays an important role in the use of preventive services among survivors, with use lowest among uninsured survivors and the highest use among those who are privately insured.

As a result of assessing the rates of preventive service granularly (30-day intervals), we found a noticeable and sharp increase in use of these preventive services just before or at prostate cancer diagnosis, suggesting that these services are ordered as part of a preventive panel along with the PSA test that ultimately led to the cancer diagnosis. We accounted for this increase in use, which was also evident among controls by matching on the timing of the PSA test that led to the cancer diagnosis in the case. We also performed sensitivity analyses that excluded the services used in the 90 days around the prostate cancer diagnosis/index date and found the results to be very similar. It is therefore possible that the increased use of services seen among cases in prior studies, particularly in the first year, may in part be driven by this sharp increase in use of preventive services around the time of PSA testing. However, the increased rates of use among prostate cancer survivors compared with men without prostate cancer in our study persisted even after excluding the services around the time of diagnosis, making this possibility less likely in this sample.

The increased rates of use after prostate cancer diagnosis (or index date) in this sample are most likely a result of a redesigned health care delivery model that was implemented during the study called Complete Care.[25] As part of this Complete Care model, several clinician-targeted and system-level interventions are in place to promote the use of preventive services among eligible members. These include a proactive office encounter tool embedded in the EMR that prompts the physician (regardless of specialty) to order appropriate preventive services, including the vaccinations and CRC screening tests in this study.[26] In addition, a successful CRC screening outreach program was launched during the study period to increase the use of FOBT/FIT among all age-eligible members,[27] which most likely caused the sharp increase in the use of these tests among both men with and without prostate cancer in this sample.

This study is unique in that it granularly assessed the use of preventive care services among prostate cancer survivors in a large, diverse cohort of men and compared it with noncancer controls. We assessed the use of preventive services both before and after diagnosis to get a better sense of how the quality of preventive care changed over time among survivors. It also included additional preventive services that were not assessed in prior studies, including pneumococcal vaccination and testing for diabetes. However, there are some potential limitations to consider. This analysis did not account for previous use of preventive services or whether men were due to receive these services. Because of varying schedules for these services, it is possible men may not have been due to receive the services in the period studied. In addition, we are unable to distinguish between testing done for screening vs maintenance or diagnostic purposes, as a proportion of the testing done may have been for the maintenance of already existing comorbidities or diagnostic in response to symptoms. However, adjustment for important comorbidities that would influence the use of these tests did not change our results. There are also system-level factors that are specific to this managed care organization that influenced the use of preventive services, which may limit the generalizability of these findings to other populations in which these interventions are not employed. However, our results support the notion that system interventions may play an important role in promoting the use of preventive services after cancer diagnosis.

CONCLUSION

In this integrated health care system, prostate cancer survivors received comparable preventive care for colorectal cancer, heart disease, diabetes, influenza, and pneumonia in the five years after diagnosis compared with men without a diagnosis of prostate cancer. These results provide reassurance that the quality of general preventive care is not diminished after a prostate cancer diagnosis. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. The Kaiser Permanente internal review board reviewed and approved this study.

Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

Author Contributions

Lauren P Wallner, PhD, contributed to project development and manuscript writing and editing; Steven J Jacobsen, MD, PhD, to project development and manuscript editing; Jeffrey M Slezak, MS, to data collection and data analysis; and Roshan Bastani, MD, and Ronald Loo, MD, to project development and manuscript editing.

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Social Cost of Sickness

The social cost of sickness is incalculable. The prevention of disease is for the most part a matter of education, the cost is moderate, the results certain and easily demonstrated.

— Haven Emerson, 1874-1957, American physician and public health official

CME credits available for this article — see page 112

ORIGINAL RESEARCH & CONTRIBUTIONS

Patient Perspectives on Communication with Primary Care Physicians about Chronic Low Back Pain

Sarah Evers, MPH; Clarissa Hsu, PhD; Karen J Sherman, PhD, MPH; Ben Balderson, PhD; Rene Hawkes; Georgie Brewer; Anne-Marie La Porte, MA; John Yeoman, MA, MHC; Dan Cherkin, PhD

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ABSTRACT

Objectives: Chronic low back pain (CLBP) is a common health problem with challenges for providing satisfactory care. This study was undertaken to identify opportunities to improve key aspects of physicians' communications with CLBP-affected patients.

Methods: A series of 3 focus groups, each with 7 to 11 patients with CLBP, were recruited from primary care settings and grouped by risk level of reduced function resulting from back pain, to elicit perspectives about interactions with their primary care physicians. Analysis of focus group transcripts used an iterative process based on a thematic approach and a priori concepts.

Results: A total of 28 patients participated in the focus groups. Patient comments about communicating with physicians around CLBP fit into themes of listening and empathy, validating pain experiences, conducting effective CLBP assessment, providing clear diagnosis and information, and collaboratively working on treatment. Patients shared that physicians can foster positive interactions with CLBP-affected patients by sharing personal experiences of chronic pain, being truthful about not having all the answers and being clear about how patients can benefit from referrals, reviewing the patient's previous treatments before beginning conversations about treatment options, providing follow-up instructions, giving patients a diagnosis beyond "chronic pain," and explaining the role of imaging in their care.

Conclusion: This study provides specific steps that physicians in the US can take to improve physician-patient interactions during primary care visits pertaining to CLBP. The findings could inform physician training, development of educational materials for patients, and future research.

INTRODUCTION

Chronic low back pain (CLBP) is a common and costly health problem in primary care. A study reviewing North Carolina data between 1996 and 2013 found that personal health care expenditures for low back pain in 2013 were greater than $86 billion.[1] Globally, low back pain causes more disability than any other condition.[2] Providing care for patients with CLBP is challenging, with few tools for diagnosing and treating it. The structural cause of the pain is often not identifiable,[3] and treatment options may not be effective.[4,5]

With these challenges, it is not surprising that many patients are dissatisfied with care provided for their CLBP.[6,7] Physicians tend to take a biomedical approach to problems such as CLBP that involve psychological and social factors. The physician's adherence to a strictly biomedical model can frustrate patients and result in visits that do not meet their needs. Research has found that patients with CLBP expect physicians to offer diagnostic tests, a diagnosis, information on prognosis, prescription medicines, and referrals.[8] Predictors of patient satisfaction with health care include feeling that one is treated with respect, listened to, and taken seriously.[9,10] Patient dissatisfaction is associated with feeling disrespected or distrusted by the physician and feeling that the physician dismissed symptoms as trivial or suspected drug seeking.

The quality of physician-patient communication is associated with patient satisfaction,[11] patient adherence to treatment plans,[12] and positive health outcomes.[13] Furthermore, the way physicians communicate with CLBP-affected patients can influence beliefs about their condition. Physician communication that is correctly interpreted can affect the patients' ability to understand the source and meaning of symptoms and prognostic expectations, whereas misinterpreted messages can result in amplified vigilance, guilt about not adhering to treatment plans, or frustration when plans fail.[14]

Improving physician-patient interactions regarding chronic pain has the potential to enhance the care experience of patients with CLBP. The aim of this article was to identify strategies to improve physician-patient communication surrounding CLBP and to shed light on opportunities for physicians to communicate with patients in ways that patients find supportive. Our findings help address knowledge gaps about communication and personalization of visits, specific characteristics of physician-patient interactions that make patients feel respected, and perspectives of US patients about communicating about back pain.

METHODS

Three focus groups were conducted in preparation for a larger project evaluating a risk-stratification strategy for improving

Sarah Evers, MPH, is a Research Associate at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: evers.s@ghc.org. **Clarissa Hsu, PhD,** is an Assistant Investigator at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: hsu.c@ghc.org. **Karen J Sherman, PhD, MPH,** is a Scientific Investigator at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: sherman.k@ghc.org. **Ben Balderson, PhD,** is a Research Associate at Kaiser Permanente Washington Health Research Institute and a Psychologist for Kaiser Permanente Washington-Behavioral Health in Seattle. E-mail: balderson.b@ghc.org. **Rene Hawkes** is a Project Manager at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: hawkes.r@ghc.org. **Georgie Brewer** is a Patient Partner at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: omelvenyg@gmail.com. **Anne-Marie La Porte, MA,** is a Patient Partner at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: laporte.a@ghc.org. **John Yeoman, MA, MHC,** is a Patient Partner at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: painchoices@yahoo.com. **Dan Cherkin, PhD,** is Emeritus Senior Scientific Investigator at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: cherkin.d@ghc.org

CLBP treatment in primary care. The analysis assessed differences in care experiences and perspectives of physician communication, if any, between patients with differing levels of biopsychosocial factors.[15] Our methods were consistent with rigorous criteria in qualitative research, as documented by the consolidated criteria for reporting qualitative research (COREQ) checklist for interview and focus groups.[16] The study design and materials were reviewed and approved by the institutional review board of Kaiser Permanente (KP) Washington Health Research Institute, Seattle, WA.

Selection and Recruitment of Participants

Focus groups were assembled to inform understanding of patient experiences in seeking treatment of CLBP. Patients were eligible if they had recently seen their primary care physician regarding CLBP, were from the central Puget Sound region of Washington State whose physician worked at one of KP's owned and operated clinics, were aged 18 years or older, and had a visit to a primary care physician in the previous week that resulted in a diagnosis code for nonspecified back pain. Study staff sent recruitment letters using patient information extracted from our administrative data system. Patients were excluded if they had diagnoses indicating specific reasons for back pain or had conditions that affected their ability to provide informed consent.

Potential participants were mailed an invitation letter two weeks after their visit for CLBP. The research team then contacted potential participants by telephone to determine eligibility. If the patient was eligible and willing to participate, the STarT Back Tool,[15] which recommends treatments on the basis of patient scores from a nine-item questionnaire, was administered. The tool categorizes patients by risk scores of the impact of pain on their physical and psychosocial functioning. High risk includes a risk of impaired psychosocial functioning, medium risk involves the risk of pain or dysfunction but no clinically significant psychosocial impairment, and low risk is less severe pain and no psychosocial risk. Potential participants were asked if they were willing and able to participate in focus groups and were recruited into these groups by their risk group. The recruitment process and sample sizes for each step are shown in Figure 1.

Focus Groups

Two qualitative researchers conducted 2-hour focus groups. The discussion guide was designed to elicit rich descriptions of the individual experiences of patients seeking treatment of CLBP, their interactions with physicians, and other issues germane to the larger research study (see Appendix, available at: www.thepermanentejournal.org/files/2017/16-177-Appendix.pdf). Three groups, one for each risk group, had a maximum of 12 participants each. Each participant received $100 for participating; a light meal was served during the focus group. A court reporter transcribed the discussions; transcripts were imported into qualitative analysis software (ATLAS.ti Version 6.2 for Microsoft Windows, Berlin, Germany). All participants provided informed consent.

Analysis

The analysis team consisted of two project team members (SE and CH), who conducted or were present at all three focus groups.

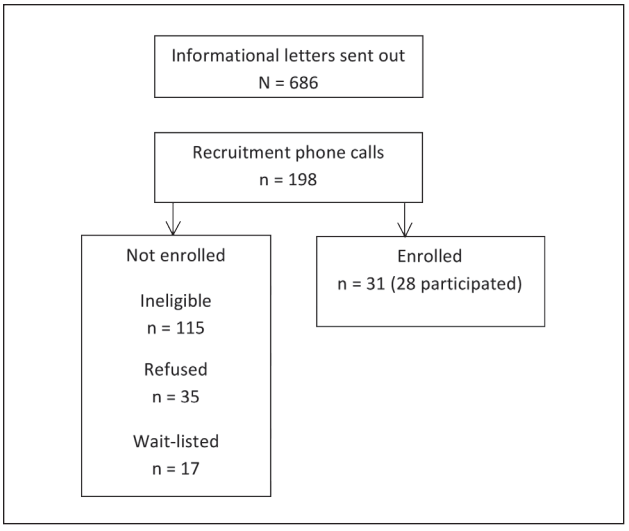

Figure 1. Focus group for patients with chronic low back pain: Recruitment process and sample sizes.

Using an iterative process based on a thematic analysis approach, the primary coder (SE) developed a code list on the basis of emergent themes that surfaced during transcript review and a priori concepts of interest. These concepts included patients' views of their interaction with their physicians; physician evaluation of their back pain; treatments they discussed or received; and expectations and factors related to patients feeling empowered, encouraged, and clear about next steps. This code list was reviewed and revised by the secondary coder (CH). Both analysts then coded one transcript using a draft code list and compared their coding. Codes were added and revised, and definitions were clarified on the basis of differences. After the process was repeated with a second transcript, the team believed that the code list captured the emergent issues raised by respondents. The final transcript was coded by the primary coder, who also reviewed the other transcripts to ensure consistency.

The analysis team discussed key themes of interest with other project members, prioritizing codes related to communication between physicians and patients about their CLBP. Prioritization was based

Table 1. Focus group participants' characteristics by risk group[a]

Characteristic	High (n = 10)	Medium (n = 11)	Low (n = 7)
Average age, years (range)	58 (36-79)	56 (25-82)	52 (26-84)
Sex, no. (%)			
Men	5 (50)	8 (73)	4 (57)
Women	5 (50)	3 (27)	3 (43)
Race, no. (%)			
White	6 (60)	8 (73)	4 (57)
Black	2 (20)	2 (18)	2 (29)
Asian	1 (10)	1 (9)	1 (14)
Unknown	1 (10)	0 (0)	0 (0)

[a] Risk group: Low, medium, or high risk for persistent, disabling, chronic lower back pain in primary care settings.

on the overall frequency of the codes and issues of most importance to the field from the perspective of our research team. We did not observe substantive differences among patients in different risk groups for this subset of codes, so results are presented for all groups.

To create a coding memo, the primary coder extracted data by code and reviewed the data for subthemes and insights. The coding memo went through iterations with feedback from the secondary coder. Other team members provided feedback on a near-final version of the coding memo. The final version was used to structure the findings.

RESULTS

Participant characteristics are summarized in Table 1 by risk group. Here we present findings from our coding memo in an order that corresponds to common stages of an office visit: Listening to concerns, and validation, assessment, diagnosis, and development of treatment plan.

Listening and Showing Empathy

Patients wished for an empathetic encounter with their physician—a visit that emphasized careful listening, getting to know the patient, and discovering what is important to them in their care and recovery. Patients described wanting their physician to try to know them and understand how pain uniquely affects their lives. Patients talked about how they did not think the physician cared about their unique experience when they felt they were rushed out of an office, or when they were not being closely listened to.

We had a doctor that we liked … and often we had to sit there and wait. But you know why we waited? Because he listened to each person, and we knew that when he came in, he was going to take his time with us. —Low-risk patient

Patients responded very well to physicians who connected with them by sharing their personal experiences with chronic pain. Patients described a belief that physicians who had not experienced chronic pain were unlikely to understand the patient's condition or be able to truly empathize with their situation.

[M]y doctor actually had a back injury, so I think she was more sympathetic. —Medium-risk patient

Validating Pain Experience and Belief that the Pain is Real

Patients shared a desire for physicians to validate their pain experience by imparting an understanding that the way each patient experiences and relates to pain was unique. Patients thought that physicians invalidated them, or did not believe the "realness" of their pain when they were viewed as "opioid seekers"; when a physician indicated that their pain was not as strong as the patient reported; when the physician suggested the patient "buck up"; or when the patient felt put in a "box" or category of other patients. One focus group participant noted that pain is not visible so physicians might not acknowledge it. Another described a physician who was helpful about diabetes but minimized the impact of back pain.

It's too bad you don't have something where you can poke a button, and it shows that you're having pain, because pain doesn't show. And I'm not sure that all doctors believe in it … . It very much hurt that the doctor doesn't believe that you have all this pain. And maybe he's never had pain like that. —High-risk patient

Performing Effective Assessment of Chronic Low Back Pain

Patients had opinions about the thoroughness or effectiveness of the back pain assessment done in their office visit. The concept of an effective assessment from the patient perspective included investigative necessities such as a physical examination or ordering an x-ray or magnetic resonance image. Patients believed that their visit was incomplete when physicians did not perform a physical examination of the affected areas, including touching/palpating painful areas. They also complained about physicians who did not ask them enough questions about their history of back pain or factors contributing to it.

I'm very frustrated. They hardly even touch you. —High-risk patient

Patients believed that imaging is critical for a definitive diagnosis. They were often dissatisfied when physicians did not order diagnostic tests. Evidence-based guidelines recommend not ordering imaging early in an episode of back pain. However, if imaging is ordered later in the course of treatment, patients may see this as a failure to provide a thorough assessment at the outset.

Finally one day, I went to her in tears, something is going on, and this is two years later. So finally she did an MRI [magnetic resonance image], and the results came back, and the doctor said, "Oh, there's one of your disks that [is] degenerating." —Low-risk patient

Providing a Clear Diagnosis and Information about Chronic Low Back Pain

Patients wanted physicians to give clear and specific diagnoses with information about what can be done to minimize future damage. They wanted to know when urgent care may be needed. Although the term *chronic pain* appears to be commonly used when talking with patients, it did not seem to help them understand their condition, in part because patients may view the term as a medical symptom rather than a diagnosis.

When I asked that question [about diagnosis], they said "Well, your condition is that you have CLBP." Well, yes, I know that. But what is it called? I know it's pain, I mean, do I have a slipped disk, a crushed disk? I want to know what caused it. And that's been since 2005; we're now [in] 2013. —High-risk patient

Patients worried that their CLBP could be an indication of more serious underlying problems such as kidney disease. In addition to wanting a clear diagnosis and a good sense of the problem, patients sought detailed information about their CLBP, including biological explanations of the cause and how the recommended treatment addresses it.

I like to know a lot of details, like a lot of details. [Quoting doctor] "Well, this is what could be happening, and this is what might help it. And physical therapy, I think that would loosen this up, and break up this particular tissue, or this is going to help." —Low-risk patient

Patients had an awareness and frustration with the difficulty of treating back pain. They recognized that physicians do not have all the answers and realized the difficulty of treating back pain; some appreciated when physicians acknowledged that lack of certainty of how best to help a patient. Patients expressed that

they liked when physicians were clear about the limits of their knowledge about CLBP and referred them to other physicians with more specialized knowledge.

I would have more respect for the doctor [if s/he were] to say, "I'm not qualified or experienced in that. Let me send you to this person that I know." —Medium-risk patient

Although patients appreciated physician referrals or recommendations to see physical therapists, they were dismayed if they thought that physicians referred them out of frustration or because they did not want to spend time addressing their needs.

I felt kind of shoved aside. "Do the physical therapy. Here, get out of my office" kind of thing. —Medium-risk patient

Working with the Patient to Develop a Treatment Plan

Patients had experience with a variety of evidence-based and complementary and alternative treatments of back pain. In general, patients were willing to try anything a physician thought could help relieve pain and were eager for their physician to offer options. Patients reported positive experiences with primary care physicians who reviewed and inquired about previous treatments before offering other options. There was a sense that this inquiry into treatment history made for a more effective and thoughtful plan for the future.

… patients with CLBP wanted a specific diagnosis other than "chronic pain," and they wanted an explanation for their pain.

She asked me, "What treatments have you done before for your back?" So that was important because she wanted to get my history. [She asked me,] "How have you responded to pain meds?" I said, "I don't respond well to them, and I need to be able to function to take care of my daughter." —Medium-risk patient

Patients wanted physicians to offer timely treatment of immediate pain relief and follow-up therapy. Patients were frustrated when they perceived physicians to not take steps to address immediate pain that severely limited function. They expressed the need to be assertive, or "steer" the physician toward a type of treatment or opportunity for follow-up. They identified a critical element of the treatment plan being clarity around when a patient should follow up with his/her physician, or when it might be appropriate to seek urgent or emergency care.

What I prefer to hear from my doctor is in many cases that you are going to get better, or if this happens, then you're probably in that bucket, and if this happens, then you should call me and we should take care of it. When this happens, do that. As opposed to [patient speaking for doctor], "Oh, we're hoping it will float in that direction, let's see what happens." —Low-risk patient

DISCUSSION

Our results highlight key aspects of care that are important to patients with CLBP and extend previous research from different health care contexts in other developed countries. A qualitative study from Australia looked at the partnership in care between physicians and patients and found that listening and demonstrating empathy was critical to the patient feeling part of a partnership. A mixed-methods study from Norway observed consultations between back pain specialists and patients and highlighted the importance that patients believe they are taken seriously. Also, a qualitative study from New Zealand found a clinician's language and messaging had an impact on attitudes and beliefs of people with CLBP.[9,14,17] Our study participants emphasized that physicians must let patients know that they believe their pain is real. Patients seek legitimization, yet may interpret some comments from physicians as implying that their pain is unimportant.[18] Themes from our focus groups suggest that an effective approach to CLBP care emphasizes empathy, builds a shared understanding of what CLBP is, and includes a discussion of previous treatments. Incorporating these specific elements into care may help patients feel heard and validate their experience of pain.

Similar to other studies, our patients with CLBP wanted a specific diagnosis other than "chronic pain," and they wanted an explanation for their pain.[18-20] Patients who seek a diagnosis and do not receive one may believe their physician did not take their concerns seriously. To further help patients understand their condition, physicians should consider discussing pain concepts such as the following: 1) gate control theory,[20] which offers a biological explanation of pain, including how nonpain sensory input "closes a gate" to relieve pain and why emotions influence pain perception; 2) pain centralization to help patients understand that the location of pain is not necessarily connected with a physical place in the body; and 3) pain central sensitization to explain how after an injury, the nervous system can enter into a persistent reactive state that continues even after an injury has healed.[20] Explanations of chronic pain can be brief and still build understanding between the patient and physician. Having a deeper understanding of chronic pain may increase adherence to treatment plans that require active participation.

Our results confirmed that patients often expect and demand imaging; some believe that identifying the cause of pain through imaging is required to guide treatment options. This desire for imaging is challenging for physicians, who may feel forced to accommodate these demands.[21,22] Similar to patient dissatisfaction with not receiving a diagnosis, we found that patients may think that physicians are not taking them seriously if they refuse to order imaging without an explanation. Talking a patient through the examination process may be a key strategy for overcoming patient wishes for imaging. A discussion point can include that imaging is not usually recommended early in an episode of back pain.[4,23] One reason is that imaging rarely identifies a clear structural cause for CLBP because of the high frequency of incidental imaging findings.[24] These nonrelevant findings can lead to harm such as misdiagnosis and inappropriate treatment. Physician-patient discussions should include articulating how and why serious diagnoses are ruled out and sharing the rationale for final conclusions. A patient request for imaging can be an educational opportunity and help the patient understand that the physician is fully considering the patient's condition.[25] These results highlight the importance of the development of a mutual treatment plan, including consideration of the treatments that a patient has already tried.

Patients with CLBP shared that if physicians were unable to explain the source of their pain, they nonetheless appreciated when physicians acknowledged their lack of understanding and referred them to others with more specialized knowledge. However,

referral must be done thoughtfully to avoid making patients feel dismissed.[10] Referrals were most appreciated when patients understood why the physician chose to refer the patient (ie, by explaining what they believe the referral may accomplish) and letting the patient know when it would be important to return for another visit and how the physician will follow-up with the patient.

A primary limitation of this study was the potential for self-selection bias. Compared with other patients with CLBP, participants may have been more concerned with the CLBP care they received or could have had more issues with their physician. All patients were from KP Washington, an integrated health care delivery system, and may have had experiences that are not generalizable to a fee-for-service setting. Nonetheless, our finding that patients reported common perspectives, regardless of their level of back-pain risk, suggests that our conclusions are applicable for a range of patients with CLBP.

CONCLUSION

This study adds new insights on aspects of physician-patient interactions around CLBP during primary care visits in the US. We learned that physicians can gain trust and foster a positive interaction with patients experiencing CLBP in the following ways: 1) listening and showing empathy, for example, sharing personal experiences of their own chronic pain; 2) admitting they do not have all the answers and being clear about how patients can benefit from referrals; 3) reviewing previous treatments before beginning a conversation about treatment options; 4) including follow-up instructions and letting patients know when it would be important to return for a visit; and 5) giving patients an explanation of their diagnosis beyond the label of "chronic pain," with an explanation for why imaging is needed or not needed. Findings from this current research have implications for training of physicians, developing educational materials, and planning future research. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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ORIGINAL RESEARCH & CONTRIBUTIONS

Use of Epidural Analgesia as an Adjunct in Elective Abdominal Wall Reconstruction: A Review of 4983 Cases

Efstathios Karamanos, MD; Sophie Dream, MD; Anthony Falvo, DO; Nathan Schmoekel, DO; Aamir Siddiqui, MD

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ABSTRACT

Context: Use of epidural analgesia in patients undergoing elective abdominal wall reconstruction is common.

Objective: To assess the impact of epidural analgesia in patients undergoing abdominal wall reconstruction.

Design: All patients who underwent elective ventral hernia repair from 2005 to 2014 were retrospectively identified. Patients were divided into two groups by the postoperative use of epidural analgesics as an adjunct analgesic method. Preoperative comorbidities, American Society of Anesthesiologists status, operative findings, postoperative pain management, and venothromboembolic prophylaxis were extracted from the database. Logistic regressions were performed to assess the impact of epidural use.

Main Outcome Measures: Severity of pain on postoperative days 1 and 2.

Results: During the study period, 4983 patients were identified. Of those, 237 patients (4.8%) had an epidural analgesic placed. After adjustment for differences between groups, use of epidural analgesia was associated with significantly lower rates of 30-day presentation to the Emergency Department (adjusted odds ratio [AOR] = 0.53, 95% confidence interval [CI] = 0.32-0.87, adjusted $p = 0.01$). Use of epidural analgesia resulted in higher odds of abscess development (AOR = 5.89, CI = 2.00-17.34, adjusted $p < 0.01$) and transfusion requirement (AOR = 2.92, CI = 1.34-6.40, adjusted $p < 0.01$). Use of epidural analgesia resulted in a significantly lower pain score on postoperative day 1 (3 vs 4, adjusted $p < 0.01$).

Conclusion: Use of epidural analgesia in patients undergoing abdominal wall reconstruction may result in longer hospital stay and higher incidence of complications while having no measurable positive clinical impact on pain control.

INTRODUCTION

Ventral hernias represent a challenging problem for the surgeon. Abdominal wall reconstruction for ventral hernias can result in lengthy hospitalizations, especially for recurrent hernias with substantial loss of domain.[1-5] These abdominal wall reconstructions can result in major postoperative complications with subsequent increases in hospital costs and morbidity. In the modern era of health care, quality is not only expected but also reportable. The focus on potentially preventable complications after major surgery has taken center stage not only for caregivers and patients but also administrators, regulators, and payers. In the context of quality control, pain management has become an area of concern. Depending on the physician's preference and the anticipated complexity of the surgery, many patients undergoing abdominal wall reconstruction are offered epidural analgesia as an adjunct to the traditional narcotic analgesia. The potential benefits of the use of epidural analgesia include more steady analgesia, limited exposure to opioids and their side effects, and better cooperation with mobility programs.

Several studies have favored the use of epidural analgesia in major abdominal surgeries. In a randomized controlled trial of 915 patients undergoing major surgery, Rigg et al,[6] in 2002, concluded that the use of epidural analgesics resulted in a significant decrease in pulmonary complications. However, the data on patients undergoing abdominal wall reconstruction are scant. The present study aims to assess the impact of the use of epidural analgesics as an adjunct to conventional analgesia in patients undergoing abdominal wall reconstruction for initial or recurrent ventral hernias in an elective setting. A multi-institution collaborative database was used to review outcomes.

METHODS

This retrospective study used the Michigan Surgical Quality Collaborative Database, a collaborative of 52 Michigan hospitals dedicated to overall surgical quality improvement, including better patient care and lower costs.[7] After institutional review board approval from Henry Ford Hospital, Detroit, MI, all patients undergoing elective ventral hernia repair, from January 2005 to December 2014, were identified using Current Procedural Terminology codes (49560: Repair initial incisional or ventral hernia; reducible and 49565: Repair recurrent incisional or ventral hernia; reducible).

All patients received intravenous anesthesia for induction that was subsequently maintained during the course of the case via an endotracheal tube. All patients received intravenous fluids for intraoperative resuscitation in the usual standard of care. The patients were divided into two groups on the basis of the use of epidural analgesia postoperatively. Patient variables extracted included age, sex, body mass index, alcohol use, tobacco abuse, functional status preoperatively, presence of comorbidities (diabetes, chronic obstructive pulmonary

Efstathios Karamanos, MD, is a Surgeon in the Division of Acute Care Surgery in the Department of Surgery at Henry Ford Hospital in Detroit, MI. E-mail: ekarama1@hfhs.org. **Sophie Dream, MD,** is a Surgeon at Henry Ford Hospital in Detroit, MI. E-mail: sdream1@hfhs.org. **Anthony Falvo, DO,** is a Surgeon at Henry Ford Hospital in Detroit, MI. E-mail: afalvo1@hfhs.org. **Nathan Schmoekel, DO,** is a Surgeon in the Division of Acute Care Surgery at Henry Ford Hospital in Detroit, MI. E-mail: nschmoeke2@hfhs.org. **Aamir Siddiqui, MD,** is a Plastic and Reconstructive Surgeon at Henry Ford Hospital in Detroit, MI. E-mail: asiddiq1@hfhs.org.

disease, sleep apnea, congestive heart failure, arrhythmias, coronary artery disease, hypertension, use of β-blockers or statins, peripheral vascular disease, deep vein thrombosis, and history of malignancy), American Society of Anesthesiologists (ASA) classification, and wound classification at the end of the surgery. To control for any confounding factors, the type of adjunct pain control was identified for the database (use of nerve block, infiltration of local anesthesia, use of intravenous or oral narcotics, and use of patient-controlled anesthesia) perioperatively and on postoperative day 1. The type of venothromboembolic prophylaxis was also identified.

Outcomes

The primary outcome included severity of pain on postoperative day 1 and postoperative day 2. A Likert-type pain scale was used to measure pain, with 0 being no pain and 10 being the worst pain the patient has experienced.[8] Secondary outcomes included presentation to the Emergency Department within 30 days, readmission and/or reoperation within 30 days, development of surgical site infection, myocardial infarction, need for transfusion, and development of postoperative deep vein thrombosis and pulmonary embolism.

Statistical Analysis

The patients were stratified into 2 cohorts: patients who had epidural analgesia as an adjunct vs patients who did not. The 2 groups were compared for differences between the baseline characteristics using Pearson χ^2 or Fisher exact test as appropriate for categorical variables. Continuous variables were examined for normality of distribution using the Shapiro-Wilk test. Parametric variables were compared between the 2 groups using the Student *t* test whereas nonparametric variables were compared using the Mann-Whitney U test. To assess the impact of the use of epidural analgesia in patients undergoing abdominal wall reconstruction, logistic regressions were used with the dependent variable being the use of epidural analgesia. Variables that differed at a $p < 0.05$ between the 2 groups were inserted in the logistic regressions. Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) were derived from the regressions. To assess the impact of the use of epidural analgesia on hospital length of stay and pain score on postoperative days 1 and 2, we used linear logistic regression, inserting variables that differed between the 2 groups at a $p < 0.05$. For assessment of the impact of epidural analgesia in patients with significant comorbidities, the study population was stratified into 2 groups by their ASA class (ASA 1/2 vs ASA 3/4). The same process as described above was repeated for the ASA classes. All analyses were performed using SPPS for Windows, Version 19 (IBM Corp, Armonk, NY).

RESULTS

During the study period, 11,324 patients underwent elective abdominal wall reconstruction for a ventral hernia. Of those, 4983 had documentation regarding the use of epidural analgesia as an adjunct and were subsequently included in the analysis. A total of 237 patients received epidural analgesia and 4746 patients did not. The mean age was 54.1 years, and 47% of the study population was male. The mean body mass index was 32 kg/m^2. The most common comorbidities included hypertension (53%), hyperlipidemia (31%), and a history of coronary artery

Table 1. Demographics and comorbidities of study population

Characteristic	Overall (N = 4983)	Epidural (n = 237)	No epidural (n = 4746)	p value
Age (years)	53.1 ± 4.2	52.4 ± 3.1	53.1 ± 4.7	0.41
Male sex, no. (%)	2316 (46.5)	96 (40.5)	2220 (46.8)	0.06
Body mass index (kg/m^2), mean ± SD	31.9 ± 7.6	32.7 ± 7.6	31.9 ± 7.6	0.09
Social history, no. (%)				
Alcohol abuse	138 (2.8)	6 (2.5)	132 (2.8)	0.82
Tobacco use	1229 (24.7)	63 (26.6)	1166 (24.6)	0.48
Functional status, no. (%)				
Independent	4880 (97.9)	232 (97.9)	4648 (97.9)	
Partially dependent	71 (1.5)	5 (2.1)	69 (1.5)	
Totally dependent	29 (0.5)	0 (0.0)	29 (0.7)	0.552
Comorbidities, no. (%)				
Diabetes	977 (19.6)	71 (30.0)	906 (19.1)	< 0.01
Chronic obstructive pulmonary disease	510 (10.2)	30 (12.7)	480 (10.1)	0.21
Sleep apnea	855 (17.1)	58 (24.5)	797 (16.8)	0.01
Congestive heart failure	17 (0.3)	1 (0.4)	16 (0.3)	0.56
History of arrhythmia	375 (7.5)	20 (8.4)	355 (7.5)	0.59
Coronary artery disease	690 (13.8)	24 (10.1)	666 (14.0)	0.09
Hypertension requiring medication	2632 (52.8)	146 (61.6)	2486 (52.4)	0.01
Beta-blocker	1222 (24.5)	71 (30.0)	1151 (24.3)	0.04
Statin	1526 (30.6)	88 (37.1)	1438 (30.3)	0.03
PVD	153 (3.1)	12 (5.1)	141 (3.0)	0.07
History of deep vein thrombosis	345 (6.9)	27 (11.4)	318 (6.7)	0.01
Malignancy	19 (0.4)	1 (0.4)	18 (0.4)	0.60
ASA classification, no. (%)				
1	278 (5.6)	3 (1.3)	275 (5.8)	
2	2391 (48.0)	103 (43.5)	2288 (48.2)	
3	2160 (43.3)	124 (52.3)	2036 (42.9)	
4	151 (3.0)	7 (3.0)	144 (3.0)	0.01
Wound classification at end of surgery, no. (%)				
Clean	4406 (88.4)	164 (69.2)	4242 (89.4)	
Clean/contaminated	424 (8.5)	59 (24.9)	365 (7.7)	
Contaminated	153 (3.1)	14 (5.9)	139 (2.9)	< 0.01

ASA = American Society of Anesthesiologists; PVD = peripheral vascular disease; SD = standard deviation.

disease (14%). Nearly all (98%) of the patients were functionally independent before surgery. Case classification was clean for 88% of the operations. The 2 groups are described in Table 1. Patients who received an epidural analgesic were significantly more likely to have more comorbidities, be assigned a higher ASA score, and have a higher incidence of contaminated wound classification at the end of the surgery (see Table 1). Patients who had an epidural analgesic placed were also more likely to undergo a repair of a recurrent hernia (38% vs 20%, p < 0.01). The reported extent of the adhesions was similar between the 2 groups (moderate adhesions: 20% vs 21%, p = 0.56; severe adhesions: 11% vs 9%, p = 0.89, Table 2).

Table 3 depicts the type of pain control administered to the study population perioperatively and postoperatively. Local anesthesia was infiltrated perioperatively in 60% of the patients. Those who received epidural analgesia as an adjunct had a significantly lower incidence of use of local anesthesia during the case (27% vs 61%, p < 0.01). On postoperative day 1, 38% of the patients received intravenous narcotics, 34% received oral narcotics, and 15% received nonsteroidal anti-inflammatory drugs. The use of intravenous narcotics, patient-controlled analgesia, and nonsteroidal anti-inflammatory drugs was significantly different between the 2 groups (52% vs 38%, 22% vs 15%, and 27% vs 14%, respectively).

The use of venothromboembolic prophylaxis is summarized in Table 4. Patients who did not receive an epidural analgesic were less likely to receive heparin perioperatively; however, postoperatively, patients given an epidural were less likely to receive heparin 3 times daily (43% vs 81%, p < 0.01). After adjusting for confounding factors, the use of epidural analgesia correlated with a significant decrease in 30-day presentation to the Emergency Department (AOR= 0.53, 95% CI = 0.32-0.87, adjusted p = 0.01). The use of epidural analgesia was linked with a higher probability of developing a deep/organ space infection and needing a blood transfusion (AOR = 5.89, 95% CI = 2.00-17.34, adjusted p < 0.01; and AOR = 2.92,

Table 2. Type of surgery

Type of surgery	Overall, no. (%) (N = 4983)	Epidural, no. (%) (n = 237)	No epidural, no. (%) (n = 4746)	p value
Repair initial incisional or ventral hernia (reducible)	3751 (75.3)	148 (62.4)	3603 (75.9)	
Repair recurrent incisional or ventral hernia (reducible)	1055 (21.2)	89 (37.6)	966 (20.4)	
Repair umbilical hernia, age ≥ 5 years (reducible)	177 (3.6)	0 (0.0)	177 (3.7)	< 0.01
Concurrent component separation	206 (4.1)	53 (22.4)	153 (3.2)	< 0.01

Table 3. Type of pain control

Type of pain control	Overall, no. (%) (N = 4983)	Epidural, no. (%) (n = 237)	No epidural, no. (%) (n = 4746)	p value
Perioperatively				
Nerve block	165 (3.3)	1 (0.4)	164 (3.5)	0.01
Local anesthesia infiltrated	2940 (59.0)	63 (26.6)	2877 (60.6)	< 0.01
Postoperative day 1				
Intravenous narcotics	1909 (38.4)	124 (52.3)	1785 (37.7)	< 0.01
Oral narcotics	1686 (33.9)	88 (37.1)	1598 (33.7)	0.28
Patient-controlled anesthesia	739 (14.9)	51 (21.5)	688 (14.5)	0.01
Nonsteroidal anti-inflammatory drugs	745 (15.0)	65 (27.4)	680 (14.4)	< 0.01
Local anesthesia infiltrated	58 (1.2)	5 (2.1)	53 (1.1)	0.20

Table 4. Venothromboembolic prophylaxis

Prophylaxis	Overall, no. (%) (N = 4983)	Epidural, no. (%) (n = 237)	No epidural, no. (%) (n = 4746)	p value
Perioperatively				
Heparin	952 (19.1)	89 (37.6)	863 (18.2)	< 0.01
Low-molecular-weight heparin	63 (1.3)	3 (1.3)	60 (1.3)	1.00
Sequential compression devices	4489 (90.1)	230 (97.0)	4259 (89.7)	< 0.01
Postoperatively				
Heparin 2x/d	421 (8.5)	101 (42.6)	320 (6.8)	< 0.01
Heparin 3x/d	1061 (21.3)	102 (43.0)	3854 (81.2)	< 0.01
Low-molecular-weight heparin	430 (8.6)	14 (5.9)	416 (8.8)	0.12
Sequential compression devices	3325 (66.7)	225 (94.9)	3100 (65.3)	< 0.01

95% CI = 1.34-6.40, adjusted p < 0.01, respectively, Tables 5 and 6). The use of epidural analgesia also resulted in a significantly longer length of stay after adjusting for confounding factors: 6.5 days vs 3.8 days; mean (95% CI) = 2.42 (1.81-3.03), as shown in Table 7. When the pain score was examined on postoperative day 1, a statistical but not clinically significant difference was identified (3 vs 4, see Table 7). This difference was diminished on postoperative day 2. When the patients were stratified on the basis of ASA class, no statistically significant differences were identified between patients who received an epidural analgesic vs those who did not (Table 8).

Table 5. Outcomes

Outcome	Overall, no. (%) (N = 4983)	Epidural, no. (%) (n = 237)	No epidural, no. (%) (n = 4746)	p value
Presentation to Emergency Department within 30 d	629 (12.6)	19 (9.0)	610 (12.8)	0.03
Readmission within 30 d	516 (10.3)	33 (13.9)	483 (10.2)	< 0.01
Reoperation within 30 d	368 (7.4)	20 (8.4)	348 (7.3)	0.53
Superficial surgical site infection	97 (1.9)	11 (4.6)	86 (1.8)	0.01
Deep surgical site infection	49 (1.0)	7 (3.0)	42 (0.9)	0.01
Deep/organ space infection	22 (0.4)	7 (3.0)	15 (0.3)	0.01
Urinary tract infection	17 (0.3)	4 (1.7)	13 (0.3)	< 0.01
Myocardial infarction	15 (0.3)	3 (1.3)	12 (0.3)	0.01
Need for transfusion	63 (1.3)	10 (4.2)	53 (1.1)	< 0.01
Postoperative deep vein thrombosis	1 (0.3)	2 (0.8)	14 (0.3)	0.15
Sepsis	36 (0.7)	6 (2.5)	30 (0.6)	< 0.01
Severe sepsis	32 (0.6)	6 (2.5)	26 (0.5)	< 0.01
Unplanned intubation	39 (0.8)	6 (2.5)	33 (0.7)	< 0.01
Pulmonary embolism	15 (0.3)	3 (1.3)	12 (0.3)	0.01
Pneumonia	52 (1.0)	6 (2.5)	46 (1.0)	0.02

Table 6. Adjusted outcomes[a]

Outcome	Adjusted odds ratio (95% confidence interval)	Adjusted p value
Presentation to Emergency Department within 30 d	0.53 (0.32-0.87)	0.01
Readmission within 30 d	1.16 (0.77-1.75)	0.49
Reoperation within 30 d	1.16 (0.70-1.92)	0.58
Superficial surgical site infection	1.67 (0.82-3.37)	0.16
Deep surgical site infection	2.29 (0.92-5.74)	0.08
Deep/organ space infection	5.89 (2.00-17.34)	< 0.01
Urinary tract infection	3.13 (0.82-12.00)	0.1
Myocardial infarction	2.30 (0.53-10.00)	0.27
Need for transfusion	2.92 (1.34-6.40)	< 0.01
Postoperative deep vein thrombosis	1.34 (0.25-7.05)	0.73
Sepsis	2.40 (0.85-6.76)	0.1
Severe sepsis	1.77 (0.60-5.20)	0.3
Unplanned intubation	1.48 (0.53-4.12)	0.46
Pulmonary embolism	3.91 (0.93-16.53)	0.06
Pneumonia	1.26 (0.47-3.37)	0.65

[a] Adjusting for diabetes, sleep apnea, hypertension requiring medication, β-blocker, statin, history of deep vein thrombosis, American Society of Anesthesiologists class, wound classification at the end of the surgery, type of surgery, type of analgesia, and type of perioperative venothromboembolic prophylaxis.

DISCUSSION

The present study suggests that the use of epidural analgesia is associated with a higher incidence of postoperative complications and an increased hospital length of stay. Although the use of epidural analgesia resulted in a statistically significant decrease in the postoperative pain levels on postoperative day 1, that finding may not be clinically significant. There was no difference in the pain level between the 2 groups on postoperative day 2. Both options presumably offer appropriate patient analgesia. This is, to our knowledge, one of the largest studies to evaluate the impact of epidural analgesia in patients undergoing abdominal wall reconstruction for ventral or incisional hernias.

The beneficial effects of epidural analgesia have been extensively studied in patients undergoing other major abdominal surgeries. A large body of research suggests that there is considerable procedure variation in the results of epidural analgesia. Even though most of the studies agree that the use of epidural analgesia may result in better pain control, there is a notable variation in the impact of epidural analgesia on other postoperative measures and outcomes. Park et al[9] studied a total of 1201 patients requiring analgesia for intraabdominal aortic, gastric, biliary, or colon operations. The study randomly assigned patients to receive an epidural analgesic vs not; the authors concluded that for the subgroup of patients undergoing abdominal aortic operations, the use of epidural resulted in a lower incidence of new-onset myocardial infarctions, cerebrovascular accidents, and respiratory failure. In a subsequent Cochrane database review of patients undergoing abdominal aortic surgery, Nishimori et al[10] concluded that epidural analgesia, when used as an adjunct to traditional opioid analgesia, results in better pain relief and decreases complications associated with the postoperative period. Similar to vascular surgery, the use of epidural analgesics has been shown to have beneficial effects in other surgical specialties. Literature on colorectal surgery strongly favors the use of epidural analgesics. Carli et al[11,12] studied 64 patients undergoing elective colon resection and found that the use of epidural analgesics was associated with better pain control,

Table 7. Pain management and length of stay[a]

Parameter	Overall (N = 4983)	Epidural analgesia (n = 237)	No epidural analgesia (n = 4746)	p value	mean (95% CI)	β	Adjusted p value
Length of stay (days)	4.0 ± 4.5	6.5 ± 5.3	3.8 ± 4.4	< 0.01	2.42 (1.81 to 3.03)	0.155	< 0.01
Pain score, median (range)							
Postoperative day 1	4 (0-10)	3 (0-10)	4 (0-10)	< 0.01	-1.15 (-1.59 to -0.70)	0.228	< 0.01
Postoperative day 2	3 (0-10)	2 (0-10)	3 (0-10)	0.01	-0.35 (-0.81 to 0.10)	0.231	0.13

[a] Adjusting for diabetes, sleep apnea, hypertension requiring medication, β-blocker, statin, history of deep vein thrombosis, American Society of Anesthesiologists class, wound classification at the end of the surgery, type of surgery, type of analgesia, and type of perioperative venothromboembolic prophylaxis.
CI = confidence interval.

earlier return of bowel function, and early out-of-bed mobilization compared with their counterparts. Results of a study by Fant et al[13] similarly suggested that thoracic epidural analgesia significantly improved the postoperative pain and pulmonary function for patients undergoing radical retropubic prostatectomy.

Several studies have advocated against the use of the epidural analgesic as an adjunct. A study by Jayr et al[14] in 1993 was unable to show a decrease in the incidence of postoperative pulmonary complications or the total hospital length of stay with a concurrent increase in the incidence of episodic systemic hypotension. The literature in cardiothoracic surgery remains equivocal on this subject. A randomized controlled trial in elective cardiac surgery showed no difference in hospital length of stay, quality of recovery, or morbidity between the patients who received epidural vs those who received traditional narcotics.[15] Similarly, O'Hara et al[16] studied 31 pediatric patients undergoing spinal fusion and found no differences in the use of narcotics, postoperative pain, time to oral intake, ambulation, return of bowel function, or total hospital length of stay between patients who received epidural analgesics and their counterparts.

In a study by Fischer et al,[17] 134 cases of patients undergoing abdominal wall reconstruction were retrospectively reviewed. In that study, epidural use was associated with a lower incidence of major surgical complications (19.7% vs 36.1%, p = 0.04) and medical complications, namely acute renal failure, postoperative arrhythmias, and septicemia (26.8% vs 54.1%, p = 0.001). However, the authors failed to show improved outcomes regarding wound complications. Interestingly, the article failed to show any benefits of the use of epidural analgesics in pulmonary

Table 8. Subgroup analysis stratified by American Society of Anesthesiologists (ASA) class[a]

Class	Epidural, no. (%)	No epidural, no. (%)	AOR (95% CI)	Adjusted p value
ASA Class 1/2[b]				
Presentation in Emergency Department within 30 d	7 (6.6)	332 (13.0)	0.45 (0.19-1.02)	0.06
Readmission within 30 d	10 (9.4)	236 (9.2)	1.07 (0.51-2.24)	0.86
Reoperation within 30 d	6 (5.7)	193 (7.5)	0.94 (0.38-2.36)	0.9
Superficial site infection	7 (6.6)	32 (1.2)	2.38 (0.80-7.08)	0.12
Deep site infection	2 (1.9)	15 (0.6)	4.18 (0.73-23.92)	0.11
Deep/organ space infection	3 (2.8)	8 (0.3)	8.35 (1.24-56.42)	0.03
Urinary tract infection	1 (0.9)	9 (0.4)	1.10 (0.08-14.82)	0.94
Transfusion	2 (1.9)	14 (0.5)	1.61 (0.28-9.43)	0.6
Deep vein thrombosis	0 (0.0)	3 (0.1)	NA	NA
Sepsis	1 (0.9)	6 (0.2)	2.96 (0.20-43.96)	0.43
Severe sepsis	1 (0.9)	6 (0.2)	2.14 (0.12-38.37)	0.61
Unplanned intubation	0 (0.0)	4 (0.2)	NA	NA
Pulmonary embolism	1 (0.9)	3 (0.1)	3.27 (0.09-113.54)	0.51
Pneumonia	1 (0.9)	10 (0.4)	1.49 (0.13-17.16)	0.75
ASA Class 3/4[c]				
Presentation in Emergency Department	12 (9.2)	278 (12.7)	0.70 (0.37-1.33)	0.27
Readmission within 30 d	23 (17.6)	247 (11.3)	1.32 (0.79-2.23)	0.29
Reoperation within 30 d	14 (10.7)	155 (7.1)	1.32 (0.70-2.49)	0.39
Superficial site infection	4 (3.1)	54 (2.5)	0.71 (0.23-2.21)	0.56
Deep site infection	5 (3.8)	27 (1.2)	2.07 (0.62-6.86)	0.24
Deep/organ space infection	4 (3.1)	7 (0.3)	9.96 (2.05-48.33)	< 0.01
Urinary tract infection	2 (1.5)	8 (0.4)	2.46 (0.56-10.88)	0.24
Transfusion	8 (6.1)	39 (1.8)	3.81 (1.53-9.51)	< 0.01
Deep vein thrombosis	2 (1.5)	11 (0.5)	0.91 (0.14-5.98)	0.92
Sepsis	5 (3.8)	24 (1.1)	2.48 (0.80-7.75)	0.12
Severe sepsis	5 (3.8)	20 (0.9)	2.14 (0.63-7.29)	0.23
Unplanned intubation	6 (4.6)	29 (1.3)	1.82 (0.62-5.37)	0.28
Pulmonary embolism	2 (1.5)	9 (0.4)	3.72 (0.50-27.94)	0.2
Pneumonia	5 (3.8)	36 (1.6)	1.33 (0.44-4.01)	0.62

[a] Adjusting for diabetes, sleep apnea, hypertension requiring medication, β-blocker, statin, history of deep vein thrombosis, ASA class, wound classification at the end of the surgery, type of surgery, type of analgesia, and type of perioperative venothromboembolic prophylaxis.
[b] For ASA class 1/2, Epidural n = 106 and No epidural n = 2563.
[c] For ASA class 3/4, Epidural n = 131 and No epidural n = 2183.
AOR = adjusted odds ratio; CI = confidence interval; NA = not available.

complications or postoperative ileus. It also needs to be noted that the patients who did not receive an epidural analgesic were 4 times more likely to have an ASA score of 4 (4.9% vs 1.4%), which adds to the possibility of selection bias. Our study included a vigorous analysis of a large population while adjusting for multiple confounding factors. Subgroup analyses were performed to evaluate the impact of epidural analgesics in patients with severe comorbidities based on the ASA classification. This analysis also failed to demonstrate any benefits over traditional narcotic analgesia.

In the present study, the use of epidural analgesia was associated with a statistically significant increase in the risk of developing deep/organ space infection. One potential explanation is that epidural analgesia may induce a suppression of the postoperative inflammatory cascade. It is possible that the higher infection rate is related to the higher incidence of contaminated wound class than to the presence of an epidural analgesic. Chen et al[18] studied 53 otherwise healthy individuals (ASA 1/2) undergoing colectomy for treatment of colon cancer and found that patients who received an epidural analgesic as an analgesic adjunct had a significantly lower increase in the lymphocyte count, including T-helper type 2 and regulatory lymphocytes. Similarly, C-reactive protein levels were significantly higher postoperatively for patients who did not receive an epidural analgesic. Decreased immune system vigilance induced by the use of epidural analgesia may potentially result in blunted immune activity and subsequent increased risk of infection.

There are several limitations to this study. This is a retrospective study, making it prone to all the limitations inherent to the nature of the design. Furthermore, despite having important information regarding the operative details, the size of the abdominal wall defect was not available. It is possible that patients with larger defects were more likely to receive an epidural analgesic, potentially skewing the results. The Michigan Surgical Quality Collaborative Database contains self-reported clinical data in predetermined fields. Although it is better than purely administrative data, it does limit one's ability to query the patient information. For example, it is unknown when different institutions were measuring the severity of the pain. This lack of consistency makes it difficult to compare the outcomes of this study with those of other published reports. Finally, the percentage of patients receiving an epidural analgesic was relatively low (5%), making the study potentially underpowered.

Strengths of the study include a large population, given that the Michigan Surgical Quality Collaborative Database represents the largest regional database in the US, and a robust multivariate analysis.

CONCLUSION

The present study showed that the use of epidural analgesia in patients undergoing abdominal wall reconstruction is associated with longer hospital lengths of stay and higher incidence of complications. The findings suggest there may be no superiority in the use of epidural analgesia for abdominal wall reconstruction. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Appropriate Interval for Imaging Follow-up of Small Simple Pancreatic Cysts

Jordan Menda; Maile E Yoon; Hyo-Chun Yoon, MD, PhD

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ABSTRACT

Context: The frequency at which patients should undergo follow-up imaging of small pancreatic cysts is problematic because different medical societies have different follow-up guidelines.

Objective: To determine whether short-term follow-up of small pancreatic cysts is necessary to detect pancreatic cancer or cystic neoplasia.

Design: We retrospectively reviewed all abdominal magnetic resonance imaging (MRI) studies obtained in a geographically isolated health maintenance organization between January 1, 2012, and December 31, 2014, looking for pancreatic cysts. For each patient with one or more simple cysts, we recorded the size of the largest cyst. For patients with cysts, all their other computed tomography and MRI studies were reviewed to determine any change in size or morphology. The electronic medical record of every patient who underwent MRI was reviewed to determine development of pancreatic cancer.

Main Outcome Measures: Change in cyst size on images.

Results: Of 1946 patients, 342 were found to have at least 1 pancreatic cyst. A total of 228 patients had additional imaging from which to determine rates of change. The mean rate (standard deviation) of change for these cysts was 0.1 ± 2.0 mm/y. None of those cysts measuring 2 cm or smaller on MRI grew more than 5 mm in 2 years.

Conclusion: Our data validate the clinical efficacy of obtaining follow-up imaging no sooner than 24 months after the initial detection of a simple pancreatic cyst 2 cm or smaller. Patients with cysts are more likely to have pancreatic cancer, but earlier follow-up imaging would not change their diagnosis of pancreatic cancer.

INTRODUCTION

The management of small pancreatic cysts is problematic. Small pancreatic cysts are a common finding in cross-sectional imaging of the abdomen, which is usually performed for reasons not related to pancreatic disease. Only a small percentage of these cysts have malignant potential. Different medical societies have different follow-up guidelines. The Fukuoka guidelines recommend that all cysts without nodularity or associated pancreatic duct dilation that measure between 1 cm and 2 cm in size be imaged every 6 to 12 months, whereas those less than 1 cm be imaged annually.[1] These guidelines make no recommendation to ever cease follow-up imaging. The American College of Radiology guidelines for pancreatic cysts recommend that all cysts less than 2 cm be imaged in 1 year, with no further follow-up if stable at that time.[2] The American Gastroenterology Association recommends that cysts less than 3 cm be imaged after 1 year and then every 2 years, twice, for a total of 5 years of follow-up imaging.[3]

A recent study by Brook et al[4] found that small pancreatic cysts in most patients remained stable during a median follow-up period of 2.2 years. However, 11% of these cysts demonstrated growth after an initial 1-year period of stability.[4] We hypothesized that small pancreatic cysts do not require frequent or early follow-up imaging because these cysts are rarely the precursor to aggressive cancer.

METHODS

This study was approved by our institutional review board with a waiver of informed consent because it was a data-only retrospective review with no patient interactions. The study was compliant with the Health Insurance Portability and Accountability Act. We define small simple pancreatic cysts as those cysts 2 cm or smaller in maximal diameter that are unilocular or have only thin septations. We reviewed all abdominal magnetic resonance imaging (MRI) studies between January 1, 2012, and December 31, 2014, for patients who belonged to a geographically isolated health maintenance organization. All clinical information for these patients was available in an integrated electronic medical record that included all patient encounters.

All MRIs were performed on a GE 1.5T using a body coil (GE Signa HD, GE Medical Corp, Milwaukee, WI) or on a Philips 1.5T or 3.0T using a body coil (Philips Intera 1.5T or Ingenia 3T, Philips Healthcare, Andover, MA). Although the exact sequences used for each study varied according to the original indication for the study, almost every study included an axial T2-weighted sequence through the pancreas with and/or without fat saturation as well as at least 1 coronal T2-weighted or contrast-enhanced sequence. For every abdominal MRI performed during the study period, which we call the index MRI, at least 2 of the study coauthors reviewed the images to look for the presence of pancreatic cysts. Solid and part-solid cystic masses were excluded. However, multiseptated cysts were included if there was no mural nodularity or localized wall thickening (ie, contained only a few thin septations).

Jordan Menda is a Student in the College of Arts and Sciences at the University of Southern California in Los Angeles. E-mail: jmenda@usc.edu. **Maile E Yoon** is a Student at Punahou School in Honolulu, HI. E-mail: myoon18@punahou.edu. **Hyo-Chun Yoon, MD, PhD,** is a Radiologist in the Department of Diagnostic Imaging at the Moanalua Medical Center in Honolulu, HI. E-mail: hyo-chun.yoon@kp.org.

For each patient with a cyst, the largest cyst diameter was measured in the transverse plane. Patients with pancreatic cysts less than or equal to 5 mm were included only if the cyst could be confirmed on both the axial and coronal imaging planes. For every patient with a cyst, all other computed tomography (CT) and MRI studies between July 1, 2001, and June 1, 2016, were also reviewed to determine if there was any change in the size of their cyst. We reviewed the images of these cross-sectional imaging studies only if there was at least 3 months separating the study from the index MRI.

For every patient, we collected data on their age, sex, latest physician visit, and any diagnoses related to the pancreas, including pancreatic cancer, as of June 1, 2016. For patients with a diagnosis of pancreatic cancer, we reviewed their electronic medical records for the circumstances around which the diagnosis was ascertained. For all patients with a pancreatic cyst, we reviewed their electronic medical records for any diagnosis of cystic neoplasia, including an intraductal papillary mucinous neoplasm, mucinous cystic neoplasia, or serous cystadenoma, and the circumstances around which any of these diagnoses were ascertained.

All statistical analysis was performed using Stata Version 11 (Stata Corp, College Station, TX).

RESULTS

We reviewed MRI studies for 1946 unique patients: 895 men and 1051 women. As shown in Table 1, the men in our study population were significantly older than the women, with an average age of 59.6 years vs 57.2 years. There were 342 patients whose index MRI demonstrated at least 1 pancreatic cyst, for an overall prevalence of 17.6%. Among these, 183 were women and 159 were men. There was no significant difference in mean age between the men and women who had cysts. Among all women, 14.8% were found to have a pancreatic cyst, and 15.7% of men had a pancreatic cyst, which was not a significant difference (χ^2, p = 0.84).

Older patients in our study were more likely to have cysts. We sorted patients using an age cutoff of 70 years. For both men and women, the prevalence of cysts was significantly higher in patients aged 70 years or older compared with those younger than age 70 years. Among men, the prevalence of cysts in those younger than age 70 years was 13.8% compared with 27.8% in the older patients (χ^2, p < 0.001). The disparity was even more marked in women: 10.8% younger than age 70 years had pancreatic cysts vs 30.3% in older women (χ^2, p ≤ 0.001).

The size distribution of the largest cyst in each patient is presented in Figure 1. Mean size was 10.7 ± 9.1 mm, with an interquartile range (IQR) of 5 mm to 12 mm. There were 40 patients who had a cyst larger than 20 mm on their index MRI (11.7% of all patients with cysts), whereas only 13 patients (3.8% of all patients with cysts) had a cyst greater than 30 mm in maximum diameter on their index MRI.

Among the 342 patients with at least 1 pancreatic cyst, 228 underwent additional CT or MRI studies at least 3 months before or after the index MRI for whom we could determine an annual rate of change. The average time between imaging studies was 40.7 ± 32.4 months (IQR = 18.5-59.6 months). The average annual rate of change was 0.1 ± 2.0 mm/y (IQR = 0.0-0.6 mm/y).

An additional 27 patients all had at least 1 CT study after their index MRI in which no corresponding cyst or mass in the pancreas could be identified. In all but 1 of these 27 patients, the cyst seen on index MRI was less than 10 mm. Therefore, it is uncertain whether the cyst was too small to visualize with CT or if the cyst had resolved. The former scenario is more probable because a cyst could be identified by CT in several patients with cysts larger than 10 mm. Only 1 patient among these 27 had a 12-mm pancreatic body cyst on index MRI that we could not identify on CT obtained 20 months later (Figure 2).

Table 1. Demographic characteristics of patients

Characteristic	All (N = 1946)	Men (n = 895)	Women (n = 1051)	p value
Age ± SD, y (95% CI)	58.4 ± 16.6 (48.7-69.6)	59.6 ± 16.0 (51.8-70.4)	57.2 ± 17.0 (46.8-68.9)	0.001
Total number of patients with cysts	342	183	159	0.63
Mean cyst size ± SD, mm (95% CI)	10.7 ± 9.1 (9.7-11.7)	10.6 ± 8.7 (9.3-12.0)	10.8 ± 9.5 (9.4-12.2)	0.86
Patients < 70 y with cysts	209	114	95	0.81
Patients ≥ 70 y with cysts	133	69	64	0.57

CI = confidence interval; SD = standard deviation.

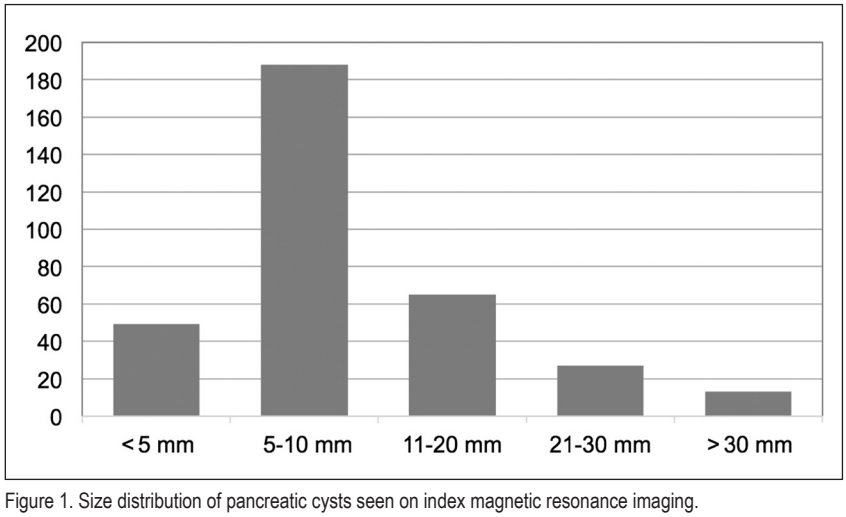

Figure 1. Size distribution of pancreatic cysts seen on index magnetic resonance imaging.

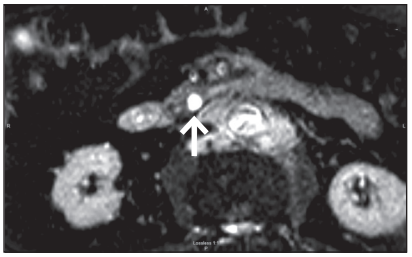

Figure 2A. Axial fat-saturated T2-weighted magnetic resonance image. The white arrow indicates a 1.2-cm simple cyst in the region of the uncinate process.

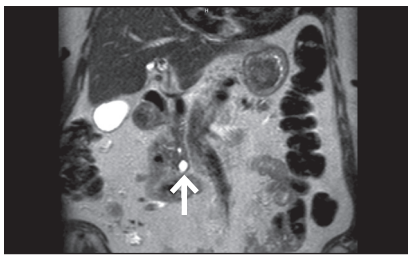

Figure 2B. Coronal T2-weighted magnetic resonance image demonstrating the same 1.2-cm pancreatic cyst.

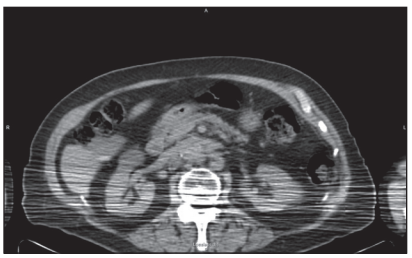

Figure 2C. Axial unenhanced computed tomography scan of the uncinate process performed 20 months after the images in Figures 2A and 2B were taken. This computed tomography scan does not show a low-attenuation lesion in the expected region of the cyst seen on previous magnetic resonance imaging.

Among the 189 patients with pancreatic cysts less than or equal to 20 mm who had additional imaging studies from which to calculate rates of change, the average annual rate of change was 0.07 ± 1.76 mm/y (95% CI = -0.18 to 0.32 mm/y).

Figure 3 plots the change in cyst size vs the duration of imaging follow-up for all 189 cysts that were 2 cm or less on index MRI. There was little change in size for most cysts. In fact, no cyst grew or shrank by more than 5 mm within 24 months after the index MRI. Only after 24 months did any cysts grow more than 5 mm. We found only 1 instance in which a cyst 20 mm or smaller became larger than 20 mm within 2 years of the index MRI. This occurred for a 74-year-old woman noted to have a 20-mm cyst in the head of her pancreas, main pancreatic duct dilation to 6 mm, and a separate pancreatic mass, which proved to be cancer diagnosed at the time of the index MRI. This cyst enlarged to 22 mm as measured on a contrast-enhanced CT scan 8 months later.

Finally, we analyzed the prevalence of pancreatic cancer in patients with cysts and those without cysts. Ten of the 342 patients with cysts (2.9%) had or subsequently received the diagnosis of pancreatic cancer, whereas 22 of the 1604 patients without cysts (1.4%) had or subsequently received the diagnosis of pancreatic cancer, resulting in a significantly higher prevalence of pancreatic cancer in those patients with pancreatic cysts compared with those without pancreatic cysts (χ^2, p = 0.04). Among the 10 patients with pancreatic cysts and cancer, 2 patients already carried a diagnosis of pancreatic cancer before their index MRI, whereas 7 others received their diagnosis of cancer within 6 weeks of their index MRI.

The 1 patient with a pancreatic cyst in whom the diagnosis of pancreatic cancer was determined after 6 weeks was a 77-year-old man with known pancreatic atrophy and multiple pancreatic body and tail cysts, which were stable on MRI studies performed in 2011 and 2013. He presented in June 2015 with jaundice and abdominal pain, for which he underwent an MRI. This imaging demonstrated massive biliary and pancreatic ductal dilation without evidence of a discrete mass. The patient underwent endoscopic retrograde cholangiopancreatography, which revealed a friable adenocarcinoma in the ampulla. Routine-interval MRI for this patient would have been of doubtful utility in the early detection of the ampullary lesion.

Among the 1604 patients without cysts, 18 of the 22 patients with cancer already carried the diagnosis of pancreatic cancer or were diagnosed with pancreatic cancer within 6 weeks of their index MRI. In our study, 1 of 332 patients with a pancreatic cyst and without an initial cancer diagnosis, and 4 of 1586 patients without a cyst and without an initial cancer diagnosis, received a diagnosis of pancreatic cancer after 6 weeks from their index MRI, which is not statistically significant (Fisher exact test, p = 0.99).

Among the 342 patients with a pancreatic cyst, a diagnosis of intraductal papillary mucinous neoplasm or mucinous cystic neoplasia was confirmed by a pancreatic endoscopic ultrasonogram with fluid sampling in 7 patients. In 6 of these patients, ultrasonography was performed shortly after the index MRI finding of a pancreatic cyst. In 1 patient,

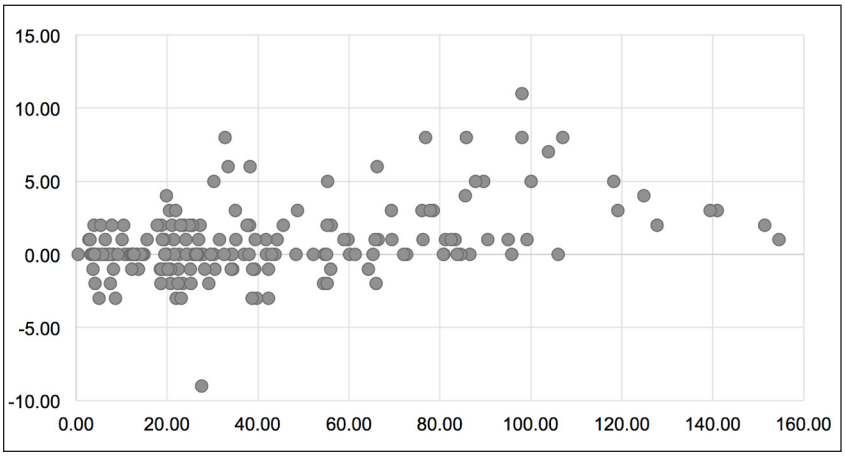

Figure 3. Plot of change in cyst size versus interval between imaging studies.[a]

[a] Vertical axis is change in cyst size (mm); horizontal axis is interval between imaging studies (months).

the ultrasound scan was obtained before the index MRI but was used to obtain a baseline for future follow-up. No patients had a diagnosis of an intraductal papillary mucinous neoplasm or mucinous cystic neoplasia during the clinical follow-up period in this patient cohort.

Four patients were found to have a pancreatic serous cystadenoma. One patient had a 5.1-cm cyst in the tail of the pancreas, and the diagnosis was made on the basis of the surgical specimen from distal pancreatectomy. Diagnosis for the remaining 3 patients was made on the basis of ultrasound fluid sampling. In 1 of these 3 patients, ultrasonography was performed 1 year after the index MRI but without interval imaging. The size reported on the ultrasonogram (1.8 cm) was similar to that measured on the index MRI (1.7 cm).

DISCUSSION

Pancreatic cysts are common, although estimates vary depending on the method of cross-sectional imaging. Laffan et al[5] estimated a prevalence of 2.6% for unsuspected pancreatic cysts in their study of 2832 consecutive contrast-enhanced CT scans of the abdomen. The prevalence is much higher when MRI is the modality used to evaluate cysts. In a 2015 study, de Oliveira et al[6] found an overall prevalence of 9.3% in their cohort of 2583 patients when their MRI reports were reviewed for the presence of cysts. In our patient population undergoing abdominal MRI, roughly 3 of every 20 patients had at least 1 cyst. Among our older patients, this rate increased to more than 1 in every 4 patients. Although these numbers are higher than those reported by the 2 studies mentioned earlier, they are similar to those reported by Lee et al,[7] who estimated a prevalence of 13.5% in 616 consecutive patients undergoing abdominal MRI. These authors also noted an increasing prevalence with older age. In both studies estimating the prevalence of pancreatic cysts using MRI,[6,7] patients aged 70 years and older demonstrated a much higher prevalence of cysts on MRI, with 30.7% of patients (65 of 212) having cysts in the study by de Oliveira et al[6] and 40.2% of patients (43 of 107) in the study by Lee et al.[7]

The characteristics of cysts are important to the risk of malignancy. In a prospective study of 114 patients with pancreatic cysts and pathologic correlation of the surgically resected specimen, Sahani et al[8] found that those associated with main pancreatic ductal dilation greater than 10 mm, mural nodularity, age older than 70 years, and cyst size larger than 3 cm correlated with aggressiveness of lesions, although only cyst size larger than 3 cm correlated with moderate or high-grade dysplasia vs low-grade dysplasia. Similarly, in a meta-analysis including 23 studies with a total of 1373 patients, Kim et al[9] found that presence of mural nodules, followed by main pancreatic duct dilation, thick septum or wall, cyst size larger than 3 cm, and publication bias adjustment were all significant predictors of malignancy, whereas multilocularity and multiplicity of the cystic lesions did not reveal a statistically significant association with malignancy. In our study, we limited our final analysis to pancreatic cysts with a size less than or equal to 2 cm and without mural nodularity or masslike component specifically for these reasons. However, these types of cysts account for most cysts seen on MRI. In both MRI studies on the prevalence of pancreatic cysts mentioned earlier, approximately 12% of cysts had mural nodularity or thickened septations.[6,7]

There have been relatively few studies on which to base our decisions for the management of these small pancreatic cysts, meaning those less than or equal to 2 cm. In 2005, Handrich et al[10] published their study of 49 patients with small (≤ 2 cm) pancreatic cysts and a minimum of 5 years' radiologic or 8 years' clinical follow-up. They found that among the 22 patients with follow-up imaging studies, 13 had cysts that were stable or smaller on follow-up, whereas 9 patients' cysts were larger. Among the 27 patients with only clinical follow-up, none showed symptoms of pancreatic disease. Of the 18 patients who died during the minimum 8-year follow-up period, none died of pancreatic causes, according to their medical records.

Das et al[11] performed a retrospective study of 150 patients with cysts 1 cm or larger to determine growth rates during a median follow-up of 32 months (IQR = 19-48 months). A total of 129 patients had cysts 3 cm or smaller, whereas only 21 patients had cysts greater than 3 cm. The authors found that only 5.6% of cysts smaller than or equal to 3 cm demonstrated any measurable growth, with an estimated median growth-free period of 103 months, whereas 44% of cysts larger than 3 cm demonstrated some growth, but even these had an estimated median growth-free period of 86 months.[11]

Most recently, Brook et al[4] performed a retrospective analysis of 259 subjects with small pancreatic cysts between 5 mm and 20 mm, with a minimum 6-month imaging follow-up. The median follow-up was 2.2 years, with an IQR of 1.2 to 3.9 years and a range of 0.5 to 11 years. The investigators found that cysts remained stable or shrank throughout the follow-up interval for 189 (73%) patients but grew larger for 70 (23%) patients. Among the 70 patients whose cysts grew, only 21 (30%) saw that growth occur during the first year; in the remaining patients, cyst growth occurred after at least 1 year of stability. The results from all of these studies suggest that early imaging may not be necessary for the follow-up of small cystic lesions of the pancreas.

In our patient population, the presence of pancreatic cysts was associated with an increased prevalence of pancreatic cancer. This finding concurs with the results of a recent large study of 2034 patients with pancreatic cysts and 6018 patients without pancreatic cysts in whom the presence of at least 1 pancreatic cystic lesion resulted in a 3-fold higher probability of pancreatic adenocarcinoma.[12]

A retrospective cohort study of adult patients with pancreatic cysts evident on medical record review found that patients could be stratified into low-, intermediate-, and high-risk categories on the basis of 4 cross-sectional imaging features: size, pancreatic duct dilation, septations with calcifications, and growth.[13] Patients with cysts 2 cm or less with no other suspicious imaging features have a very low probability of malignancy developing (≤ 0.6%), whereas these authors suggest that patients with cysts sized 1 cm to 3 cm that also have at least 1 suspicious imaging characteristic deserve close surveillance.[13] Finally, Matsubara et al[14] determined the relative risk of pancreatic cancer in patients with and without pancreatic cysts visualized on MRI and found that the presence of cysts was a

significant risk factor for cancer, especially those cysts larger than 10 mm.

Our data validate the clinical efficacy of obtaining follow-up imaging no sooner than 24 months after the initial detection of a simple pancreatic cyst 2 cm or smaller for our own patient population. Cysts larger than 2 cm may not require more frequent imaging, but given the small numbers of larger cysts in this study, it may be premature to assume that larger cysts may be treated as conservatively as the more prevalent small cysts. Cystic masses were specifically excluded from this analysis and should be treated differently from the small unilocular cysts or cysts with only thin septations evaluated in this study. Unfortunately, the best interval for follow-up and the duration of follow-up cannot be answered by our data. Patients who are undergoing routine surveillance for active cancer should continue to have regular imaging irrespective of small pancreatic cysts.

CONCLUSION

Small unilocular or thinly septated pancreatic cysts do not require short-term follow-up. Our data show that if follow-up is to succeed in detecting change, the imaging interval should be long rather than short because short-term follow-up can lead to a false sense of security if there has been no change. We recommend a follow-up imaging interval of no sooner than 24 months for patients with simple pancreatic cysts measuring 2 cm or less. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Tomorrow

The church and the law deal with the yesterdays of life; medicine deals with the tomorrows.

— William J Mayo, MD, 1861-1939, American physician and surgeon, one of the founders of the Mayo Clinic

Emotional Freedom Techniques to Treat Posttraumatic Stress Disorder in Veterans: Review of the Evidence, Survey of Practitioners, and Proposed Clinical Guidelines

Dawson Church, PhD; Sheri Stern, MS, CRNP, APRN-PMH; Elizabeth Boath, PhD; Antony Stewart, FFPH, FRSPH, MPH; David Feinstein, PhD; Morgan Clond, MD, PhD (Cand)

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ABSTRACT

Background: High prevalence rates of posttraumatic stress disorder (PTSD) in active military and veterans present a treatment challenge. Many PTSD studies have demonstrated the efficacy and safety of Emotional Freedom Techniques (EFT).

Objectives: To develop clinical best practice guidelines for the use of EFT to treat PTSD, on the basis of the published literature, practitioner experience, and typical case histories.

Methods: We surveyed 448 EFT practitioners to gather information on their experiences with PTSD treatment. This included their demographic profiles, prior training, professional settings, use of assessments, and PTSD treatment practices. We used their responses, with the research evidence base, to formulate clinical guidelines applying the "stepped care" treatment model used by the United Kingdom's National Institute for Health and Clinical Excellence.

Results: Most practitioners (63%) reported that even complex PTSD can be remediated in 10 or fewer EFT sessions. Some 65% of practitioners found that more than 60% of PTSD clients are fully rehabilitated, and 89% stated that less than 10% of clients make little or no progress. Practitioners combined EFT with a wide variety of other approaches, especially cognitive therapy. Practitioner responses, evidence from the literature, and the results of a meta-analysis were aggregated into a proposed clinical guideline.

Conclusion: We recommend a stepped care model, with 5 EFT therapy sessions for subclinical PTSD and 10 sessions for clinical PTSD, in addition to group therapy, online self-help resources, and social support. Clients who fail to respond should be referred for appropriate further care.

INTRODUCTION

A number of systematic reviews consider the evidence for Emotional Freedom Techniques (EFT) as an "evidence-based" practice.[1-3] Studies are typically evaluated using criteria published by the American Psychological Association's (APA's) Division 12 Task Force on Empirically Validated Treatments, hereafter abridged as "APA standards."[4-6] The APA standards amalgamate current scientific consensus to identify 7 "essential" criteria that must be present for a study to qualify: randomization, sample size sufficient to establish statistical significance, a clear definition of the treatment population, valid and reliable assessments, blind interview assignments, a treatment manual, and sufficient data to allow the study's statistical methods to be assessed for appropriateness.[1-3] A minimum of 2 randomized controlled trials (RCTs) are required for a therapeutic method to be deemed "efficacious."

When proposing its own standards, the US Food and Drug Administration contemporaneously set a similar standard of 2 RCTs for drug trials.[7] A systematic review searching the scientific literature until April 2012 found 51 studies of EFT and allied methods collectively referred to as energy psychology. It found that "Criteria for evidence-based treatments proposed by Division 12 of the American Psychological Association were also applied and found to be met for a number of conditions, including PTSD."[1]

A systematic review and meta-analysis of 7 studies of EFT for posttraumatic stress disorder (PTSD) was recently reported.[8] It used the Cohen difference, an appropriate effect size for the comparison between 2 means, in which 0.2 indicates a treatment effect, 0.5 indicates a moderate treatment effect, and 0.8 indicates a large treatment effect. The meta-analysis found a large treatment effect, with a *d* of 2.96 when EFT was compared with normal care. Compared with eye movement desensitization and reprocessing (EMDR) and cognitive behavior therapy (CBT), no significant treatment difference was found, indicating similarities in efficacy between the 3 treatments. Two other systematic reviews with meta-analyses, 1 for anxiety (14 RCTs) and 1 for depression (20 RCTs and within-subjects studies), found "large" treatment effect sizes of 1.23 and 1.31, respectively.[9,10] Authors of all 3 meta-analyses used the APA standards as their quality-control criteria when selecting studies for inclusion. An online database of EFT research lists more than 100 clinical trials (www.Research.EFTuniverse.com).

A psychophysiologic intervention, EFT draws from 2 established therapies: CBT and exposure therapy. It adds the novel component of somatic stimulation using acupuncture points ("acupoints"). Developed in the early 1990s, EFT is described

Dawson Church, PhD, is the Executive Director of the National Institute for Integrative Healthcare in Fulton, CA. E-mail: dawsonchurch@gmail.com. **Sheri Stern, MS, CRNP, APRN-PMH,** is a former Integrative Medicine Nurse in the Veterans Administration Maryland Health Care System in Reisterstown. E-mail: sherinp1@cs.com. **Elizabeth Boath, PhD,** is an Associate Professor in Health at Staffordshire University in Stoke-on-Trent, UK. E-mail: e.boath@staffs.ac.uk. **Antony Stewart, FFPH, FRSPH, MPH,** is a former Professor in Public Health at Staffordshire University in Stoke-on-Trent, UK. E-mail: antonystewart@hotmail.co.uk. **David Feinstein, PhD,** is the CEO of Innersource Energy Medicine in Ashland, OR. E-mail: df777@earthlink.net. **Morgan Clond, MD, PhD (Cand),** is a Medical Student at Ben-Gurion University of the Negev in Israel. E-mail: clondmorgan@gmail.com.

in subsequent editions of a standardized manual.[11,12] Clients are asked to assess the intensity of traumatic events before and after EFT using the Wolpe Subjective Units of Distress (SUD) measure,[13] an 11-point Likert scale ranging from 0 (no distress) to 10 (maximum distress). During a typical treatment session, clients recall a traumatic event and pair it with a statement of self-acceptance, such as "Even though I experienced [name of the event] I deeply and completely accept myself." They stimulate 7 acupuncture points with their fingertips (acupressure) by tapping on them or rubbing them while repeating the name of the event. If their SUD score is still high, they might describe the event in detail. An optional supplemental technique is called the 9 Gamut procedure and uses eye movements similar to those employed in EMDR. Often EFT is taught by therapists, physicians, nurses, and life coaches to patients as a method of self-care to use between treatment sessions. The method and typical applications are fully described elsewhere in the literature.[2,3]

To differentiate the acupressure component from the cognitive and exposure elements that EFT shares with other therapies, a meta-analysis examined six dismantling studies.[14] While retaining the cognitive and exposure parts of EFT, these six studies used control groups that either substituted an active treatment such as diaphragmatic breathing for acupressure or used pressure on sham acupoints. The meta-analysis found a large treatment difference between the groups that used authentic acupoints vs controls, indicating that acupressure is an active treatment ingredient in EFT's protocol and not merely an inert component.

Many studies conducted by independent research teams using a variety of different population samples, including veterans, adolescents, refugees, and disaster survivors, demonstrate the efficacy of acupressure stimulation as a treatment of PTSD.[15-23] In a typical RCT of veterans who met clinical criteria for PTSD (N = 59) and were assessed against a control group receiving treatment as usual (TAU), 86% of participants no longer met the criteria for PTSD after 6 sessions of EFT ($p < 0.0001$).[15] The military version of the Posttraumatic Stress Disorder Checklist (PCL-M),[24] a valid and reliable 17-item tool on which a score of 50 indicates the likelihood of a PTSD diagnosis, was used to assess symptoms. Mean PCL-M scores were 61.4 before treatment and 34.6 on posttreatment test. A replication of this study by an independent research team demonstrated similar results.[18]

A hospital in the United Kingdom's National Health Service conducted a study of a PTSD-positive outpatient population (N = 46) comparing EFT with EMDR and a waiting list with usual care.[17] They found both EFT and EMDR to remediate PTSD in a mean of 4 sessions ($p < 0.001$). An RCT of abused male adolescents (N = 16) used the Impact of Events Scale[25] to evaluate participant distress. Scores declined from 36 to 3 ($p < 0.001$) after a single EFT session.[16] Another RCT (N = 21) examined the impact of EFT on resiliency in veterans at risk of PTSD.[26] Six sessions produced a reduction in symptoms comparable to the results noted in a clinical population ($p < 0.0001$). Gains were maintained on follow-up in all 4 studies, whereas the wait-list participants did not improve.[16-18,26]

A systematic review of the literature includes 12 studies in which EFT demonstrated efficacy for a range of psychological conditions, such as PTSD, depression, and anxiety when delivered in the form of group therapy.[2] A written protocol called Borrowing Benefits, describing how to use EFT in groups, has been tested in both RCTs and outcomes studies.[12] In an uncontrolled study with veterans and their spouses, 218 participants were evaluated for PTSD symptoms before and after a 7-day retreat in which they used Borrowing Benefits and other EFT techniques.[27] Of the veterans, 83% exhibited clinical symptom levels on pretest, as did 29% of their spouses. On follow-up, only 28% of veterans and 4% of spouses still met the clinical cutoff ($p < 0.001$).[27] The Borrowing Benefits technique is described in detail in the EFT manual.[12] In a group, the practitioner works with one individual while witnesses self-apply EFT to their own personal issues. Studies of Borrowing Benefits find it efficacious for a wide variety of psychological conditions.[2]

Clinicians widely practice EFT and similar techniques. A recent survey critical of the method solicited responses from licensed psychotherapists using Listservs such as Acceptance and Commitment Therapy, the Society for a Science of Clinical Psychology, and the Association for Behavioral and Cognitive Therapies.[28] It found that 42% of therapists were using these modalities.

The Veterans Stress Project[29] is a charitable program of the National Institute for Integrative Healthcare that has served as a recruitment vehicle for several studies. Its Web site (www.StressProject.org) serves as a clearinghouse, allowing veterans to locate practitioners. The Veterans Stress Project also hosts an interactive virtual EFT coaching software program called Battle Tap and archives numerous testimonials from veterans who have used Battle Tap, individual therapy, and group EFT therapy to support their recovery from PTSD. These and other private and public initiatives pair veterans seeking treatment with practitioners offering EFT and similar therapeutic methods.

The objective of the current research was to develop clinical best practice guidelines for the use of EFT to treat PTSD. Toward that end, we evaluated practitioner experience and the published literature to arrive at a consensus statement.

METHODS

We undertook a survey of practitioners using EFT to treat PTSD (www.surveymonkey.com/s/GTZXD2B; SurveyMonkey, Palo Alto, CA). The goals of the survey were to develop a demographic profile of practitioners, to evaluate how EFT is used in professional settings, and to determine current practices for PTSD treatment. Drawing on the results, the evidence base, and case histories, we formulated clinical guidelines for the use of EFT in the treatment of veterans and military personnel, with the "stepped care" model used by the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom as our framework.

The invitation to complete the survey was extended in February 2014 by several US and United Kingdom organizations: the National Institute for Integrative Healthcare, the Association for Comprehensive Energy Psychology, and the Association for Meridian and Energy Therapies, as well as informal networks of practitioners. We received responses from 448 practitioners. The number of those responding to each question is indicated in Tables 1 to 5. Some survey questions allowed practitioners to

select more than 1 option. For example, a practitioner could select both "nurse" and "retired" or for professional settings both "private practice" and "medical center"; thus; the number of responses to these questions exceeded 448.

One item asked practitioners to estimate how many sessions were required to treat complex PTSD (C-PTSD). Although C-PTSD does not appear as a diagnosis separate from PTSD in current diagnostic manuals, C-PTSD has been the subject of a great deal of debate in the clinical community. It is scheduled to appear in the upcoming edition of the World Health Organization's (WHO) *International Statistical Classification of Diseases and Related Health Problems.*[30] Usually, C-PTSD is defined as repetitive and prolonged trauma, such as that which can occur in a war zone, in cases of child abuse, or in domestic violence situations. It is regarded as more difficult to treat than single-incident PTSD.

Table 1. Demographic characteristics of practitioners surveyed

Characteristic	Number (%)[a]
Age (n = 436)	
Mean years (range)	58 (22-85)
Sex (n = 439)	
Men	121 (27.6)
Women	318 (72.4)
Profession (n = 446)[b]	
LMHP	168 (37.7)
Medical professional	29 (6.5)
AMP	141 (31.6)
Life coach	86 (19.3)
Retired	18 (4.0)
Other	73 (16.4)
Setting (n = 444)[b]	
Private practice	375 (84.5)
Medical center	30 (6.8)
University	4 (0.9)
Medical school	1 (0.2)
Mental health	43 (9.7)
Social services	11 (2.5)
Corporation	11 (2.5)
Other	53 (11.9)
Education (n = 446)	
High school	11 (2.5)
Some college	67 (15.0)
Bachelor's degree	88 (19.7)
Master's degree	174 (39.0)
Doctorate	85 (19.1)
Postdoctorate	21 (4.7)
Years in practice (n = 433)	
1-5	62 (14.3)
6-10	80 (18.5)
11-20	116 (26.8)
21-30	79 (18.2)
31-40	69 (15.9)
≥ 41	27 (6.2)

[a] Data are number (%) except for Age.
[b] Practitioners were permitted to check more than 1 option in this category; thus, the total exceeds the number of respondents for this category.
AMP = alternative medicine practitioner; LMHP = licensed mental health professional.

RESULTS

Table 1 summarizes the demographic characteristics of the 448 respondents. Most respondents were either licensed mental health professionals (37.7%) or alternative medicine practitioners (31.6%). More than 62% held a master's degree or higher, and 84.5% reported practicing in a private practice setting. The percentage of practitioners with 10 or fewer years of experience was 32.8%, 11 to 20 years was 26.8%, 21 to 30 years was 18.2%, 31 to 40 years was 15.9%, and 41 or more years in practice was 6.2%. Respondents had a mean age of 58 years, with a range of 22 to 85 years, and 72.4% were women.

Table 2 profiles the course of treatment for PTSD-positive clients. The PTSD clients constituted more than 20% of the practice for 37.0% of practitioners and less than 10% for 39.9% of respondents. Nearly half the respondents (45.2%) reported having worked with more than 50 clients with PTSD, and 41.4% said they spend more than 5 hours per week treating PTSD. Estimates of the average number of sessions needed to successfully treat complex PTSD were in the 1 to 5 range for 25.7% of

Table 2. Clients with posttraumatic stress disorder (PTSD), and experience and expectations regarding treatment course

Factor	Number (%)
Percentage of clients with PTSD (n = 429)	
1-10	171 (39.9)
11-20	99 (23.1)
21-50	95 (22.1)
≥ 51	64 (14.9)
Number of clients with PTSD (n = 436)	
0-10	96 (22.0)
11-20	55 (12.6)
21-50	88 (20.2)
51-100	71 (16.3)
101-200	44 (10.1)
201-300	21 (4.8)
≥ 301	60 (13.8)
Hours per week treating PTSD (n = 430)	
1-5	252 (58.6)
6-10	106 (24.7)
11-20	47 (10.9)
≥ 21	25 (5.8)
Number of sessions needed, complex PTSD (n = 420)	
1-5	108 (25.7)
6-10	157 (37.3)
11-15	63 (15.0)
16-20	39 (9.3)
21-25	22 (5.2)
26-30	9 (2.1)
≥ 31	22 (5.2)

the practitioners and 6 to 10 sessions for an additional 37.3% of practitioners. These estimates of sessions required align with those in the published literature.[15-23]

Table 3 summarizes responses regarding the perceived prevalence of PTSD, the use of diagnostic scales, and referrals. According to the US National Institutes of Health, the prevalence of PTSD in the general adult population is 3.5%,[31] but 91.7% of our survey respondents believed that this estimate is too low; only 7.6% assessed it as accurate. When asked to estimate the true prevalence, answers varied widely, but the most common answers were 6% to 10% (24.1%), 11% to 15% (19.7%), and 16% to 20% (18.2%).

Table 3. Measuring posttraumatic stress disorder (PTSD) and referrals

Factor	Number (%)
Accuracy of 3.5% NIH estimate of PTSD prevalence (n = 432)	
Too high	3 (0.7)
Accurate	33 (7.6)
Too low	396 (91.7)
Estimate of true PTSD prevalence, % (n = 395)	
5	17 (4.3)
6-10	95 (24.1)
11-15	78 (19.7)
16-20	72 (18.2)
21-25	38 (9.6)
26-30	31 (7.8)
≥ 31	64 (16.2)
Use of assessments to record client progress (n = 430)	
Yes	126 (29.3)
No	304 (70.7)
Ten most commonly used assessments (n = 153)[a]	
PTSD Checklist	87 (56.9)
Life Events Checklist	56 (36.6)
PTSD Symptom Scale	47 (30.7)
Trauma Symptom Inventory	37 (24.2)
Impact of Event Scale	37 (24.2)
Detailed Assessment of Posttraumatic Stress	36 (23.5)
Clinician-Administered PTSD Scale	30 (19.6)
Acute Stress Disorder Interview	25 (16.3)
Impact of Event Scale-Revised	23 (15.0)
Posttraumatic Stress Diagnostic Scale	22 (14.4)
Percentage of clients who continued treatment in conjunction with another professional (n = 429)	
0-10	267 (62.1)
11-20	78 (18.1)
21-50	41 (9.5)
≥ 51	43 (10.0)
Stopped treatment and referred out, % (n = 424)	
0-10	390 (91.8)
11-20	20 (4.7)
21-50	7 (1.6)
≥ 51	7 (1.6)

[a] Practitioners were permitted to check more than 1 option in this category; thus, the total exceeds the number of respondents for this category.
NIH = National Institutes of Health.

Validated instruments to track client progress were used by 29.3% of respondents, which is consistent with other surveys of mental health professionals.[32] Of the 448 respondents, 153 reported which assessments they use. The PTSD Checklist (PCL) was the most common, used by 56.9%, followed by the Life Events Checklist (36.6%) and the PTSD Symptom Scale (30.7%).

Practitioners rarely terminated work with a client and referred that client to another practitioner. For 91.8% of respondents, this occurred with 10% or fewer of clients. Continuing treatment in conjunction with another professional was more common.

Table 4 summarizes the most used therapy techniques, both EFT and non-EFT. Regarding use of EFT, 43.6% indicated they use it 51% or more of the time during their therapy sessions, and 27.4% said they use EFT 21% to 50% of the time. The 3 most common non-EFT methods used are cognitive therapy (45.7% of practitioners surveyed), life coaching (39.8%), and EMDR (31%). In an open-ended question, the non-EFT techniques that respondents listed as most beneficial for treating PTSD were cognitive therapy (12.0%), EMDR (10.2%), and meditation (7.7%).

Table 5 summarizes respondents' evaluations of PTSD therapy outcomes. Full rehabilitation in more than 60% of their clients was reported by 64.7% of respondents, with full rehabilitation in 90% of their clients being reported by 22.1% of respondents. Clinical trials of EFT in treating PTSD[15-23] show higher success rates than those most frequently reported by the respondents. Most respondents (89.8%) reported that less than 10% of their clients make little or no progress with EFT. This is reflected in the low dropout rates typical of EFT treatment programs; in the 7 studies reported in the meta-analysis of EFT for PTSD, the mean dropout rate was under 10%.[8]

We now present two typical case studies of veterans who presented for treatment at Veterans Affairs facilities and exhibited positive outcomes.

Case Study 1: Vietnam Combat Memories

More than four decades after returning from service in Vietnam, a male veteran presented for treatment. His issues included complex medical problems, multiple addictions, broken relationships, intolerable mental and emotional symptoms, nightmares, and homelessness. As one component of a multidisciplinary evidence-based treatment regimen at the Veterans Affairs Medical Center, he chose to learn and practice EFT as an adjunct to individual psychotherapy and group therapy.

During one appointment, he chose to use EFT on three persistent Vietnam combat memories that induced hyperarousal, reexperiencing, and avoidance. In the first, he was faced with an approaching enemy unit. In the second, his unit was attacked and most of his "battle buddies" were killed. In the third, he witnessed another adolescent warrior's life-threatening wounds and emotional suffering.

Table 4. Emotional Freedom Techniques (EFT) and non-EFT techniques

Factor	Number (%)
Percentage of time spent using EFT vs other methods (n = 426)	
0-10	63 (14.8)
11-20	64 (15.0)
21-50	117 (27.4)
≥ 51	182 (42.6)
7 most common other methods used (n = 352)[a]	
Cognitive therapy	161 (45.7)
Life coaching	140 (39.8)
EMDR	109 (31.0)
Health coaching	84 (23.9)
Tapas Acupressure Technique (TAT)	84 (23.9)
Psychodynamic approaches	83 (23.6)
Thought Field Therapy (TFT)	78 (22.2)
7 non-EFT techniques considered most beneficial (n = 325)[b]	
Cognitive therapy	39 (12.0)
EMDR	33 (10.2)
Meditation	25 (7.7)
Mindfulness	19 (5.9)
Hypnosis	16 (4.9)
NLP	11 (3.4)
Active listening	9 (2.8)
10 most-trained-in EFT techniques (n = 416)[a]	
Full Basic Recipe	385 (92.5)
9 Gamut Procedure	363 (87.3)
Shortcut Basic Recipe	351 (84.4)
Tell the Story Technique	333 (80.0)
Movie Technique	330 (79.3)
Floor to Ceiling Eye Roll	327 (78.6)
Aspects (emotional, physical, visual, cognitive)	325 (78.1)
Reframing	321 (77.2)
Borrowing Benefits	301 (72.4)
Chasing the Pain	296 (71.2)
10 EFT techniques considered most beneficial (n = 400)[a]	
Full Basic Recipe	253 (63.3)
Movie Technique	251 (62.8)
Tell the Story Technique	238 (59.5)
Aspects (emotional, physical, visual, cognitive)	238 (59.5)
Reframing	215 (53.8)
Tearless Trauma Technique	192 (48.0)
9 Gamut Procedure	188 (47.0)
Shortcut Basic Recipe	183 (45.8)
Customized Setup Phrasing and Flowing Setup Statements	154 (38.5)
Sneaking Up on the Problem	143 (35.8)

[a] Practitioners were permitted to check more than 1 option in this category; thus, the total exceeds the number of respondents for this category.
[b] The "7 non-EFT techniques" question elicited a wide diversity of responses. Only the top 7 interventions are shown.
EMDR = Eye movement desensitization and reprocessing; NLP = neurolinguistic programming.

He provided an SUD score of 10 of 10 for the first 2 memories at the start of an hourlong appointment. After EFT, this fell to 0. He commented, "It's over. I'm home now. I'm safe." By the time he felt ready to apply EFT to the third memory, he reported distress already reduced to 3 and, after EFT, 0. He appeared animated and chose to retell the stories, sharing graphic details without any evidence or report of emotional distress. He demonstrated positive cognitive shifts, reframing his perception to reflect that his quick actions under fire did not reflect cowardice, as he had believed since the incident, but rather that he had quickly done exactly what he was trained to do; this saved his own life and the lives of others. He smiled and laughed and reported immense relief, energy, and joy. By the following appointment, he reported that he had not had a single nightmare about Vietnam that week, for the first time in more than 40 years.

He continues to experience sustained symptom relief. He now has spent three years in recovery from substance abuse, the longest period yet. Veterans Affairs clinicians are gradually weaning him off his psychotropic medications. He uses EFT independently between appointments for sustained smoking cessation, ongoing healthy weight loss, and stress management. He has found stable housing and renewed healthy relationships with his family. He wants clinicians and other veterans to know this: "I was in a fight for my life. Don't give up. Keep trying. EFT helped me to cope with life. It relaxes me and puts me in a place where I want to be: from the inside looking out, not the outside looking in. It's given me a positive perspective on life. I have my family back, my mind got clearer, and I have more confidence. It's lovely."

Case Study 2: Military Sexual Trauma

When he came for treatment, this veteran was experiencing intolerable emotional, mental, and physical symptoms. He had been numbing these by self-medicating with multiple illicit substances for more than 30 years. He was homeless, with broken relationships and medical problems. Although skeptical about EFT "because it gave me the impression of being silly," he decided to try it. He states, "After a few sessions, with practice, I began to notice how I was able to release the distress and fears caused by old and new painful emotions. … One of its advantages [is] that I can and would utilize it at home, in school, or on the job as a form of relaxation."

Table 5. Posttraumatic stress disorder outcomes

Outcome	Number (%)
Percentage of clients fully rehabilitated (n = 410)	
0-30	57 (13.9)
31-60	87 (21.2)
61-90	175 (42.6)
≥ 91	91 (22.1)
Percentage of clients who made little or no progress (n = 412)	
0-10	371 (89.8)
11-20	24 (5.8)
21-50	13 (3.1)
≥ 51	4 (1.0)

Initially, he was reluctant to address his experience with military sexual trauma using any psychotherapeutic modality. He had already dropped out of other evidence-based modalities before trying EFT, stating that sessions were like "experiencing it all over again." During one appointment, he chose to use EFT on his military sexual trauma experience, stating that it was blocking him from moving forward in his life. During the next four EFT appointments, he achieved resolution of his distressful symptoms. The positive effect persisted for the following year as he was weaned from his psychotropic medications.

During an EFT session, a defining moment occurred when he was stuck at a persistent level of emotional distress, a 5 to 6 on the SUD scale. He used EFT on a particular aspect of his sexual trauma experience, "the look on their faces." (For a discussion of "Aspects," see *The EFT Manual,* p 100[12]). Once his SUD score fell to 0, he stated: "It doesn't matter now. I don't have to live my life this way anymore. It's over. I know it happened, but I can think about it now without feeling those symptoms or wanting to go out and use [illegal substances]. I'm at peace now. I feel as if the weight of the world has been lifted off my shoulders." The clinician observed positive cognitive shifts, relaxed facial and body posture, and smiles in support of his comments.

This veteran has now achieved more than five years in recovery from substance abuse, his longest time ever. His PTSD symptoms are resolved. He is enjoying healthy relationships with family and friends. He is independent, living in his own apartment, attending classes with the goal of employment, and experiencing a positive quality of life. He continues to use acupuncture, meditation, and EFT. He wants clinicians and other veterans to know this: "These techniques have given me a new outlook on life and to see new possibilities in the hope of setting goals and to visualize stability in my life, free of tension. Most of all it has helped me to accept my faults, forgive myself and others, to make amends, and change my negative feelings and behaviors into positive ones, giving me a sense of peace, lots of joy, and much love and compassion for others."

… the symptoms of depression, anxiety, and other psychological conditions decline simultaneously after PTSD treatment.

Additional veteran case studies; letters from veterans, practitioners, and members of the US Congress; and transcripts from congressional testimony on EFT may be viewed at the Web site of the Veterans Stress Project (www.StressProject.org).[29]

DISCUSSION

On the basis of the studies outlined earlier, the results of the survey, and expert consensus, we propose the following treatment guidelines for using EFT for PTSD.

Proposed Treatment Guidelines

The NICE guidelines use a "stepped care" model that we believe is an appropriate framework for treating PTSD.[33] We also believe that the risk of PTSD should be mitigated using a proactive approach to develop resiliency. In the NICE model, the patient is offered the least intrusive potentially effective intervention first. If the patient does not benefit, or prefers not to continue, s/he is offered the next step. The NICE guidelines emphasize the importance of integrated care, because many mental health conditions share similar neural pathways. This position is reinforced by results of EFT studies, which show the symptoms of depression, anxiety, and other psychological conditions declining simultaneously after PTSD treatment.[2,34] A study of 216 health care workers tracked whether participants used EFT after the intervention period and found that those who used EFT afterward experienced greater symptom reductions than those who did not.[35] At the Warrior Combat Stress Reset Program at Fort Hood, TX, EFT has been used for many years, along with EMDR and other complementary therapies.[36] Fort Hood clinicians typically use EMDR during sessions while teaching EFT to patients as a method of managing stress between sessions. Practitioners typically recommend that clients use EFT between sessions as well as during them, and after courses of treatment have ended to manage the stress of daily life.[2,12] The following recommendations are based on NICE Guideline 26, titled "The Treatment of PTSD in Adults and Children in Primary and Secondary Care."[37]

The NICE Step 1 guideline advocates identification, assessment, psychoeducation, active monitoring, and referral for further assessment and interventions. In Step 1, the PCL or PCL-M is used to assess PTSD symptom levels, and further treatment is based on the cutoff scores. Although several cutoff points for the PCL-M have been evaluated, a score of 35 or greater indicates PTSD risk probability in a military population and is appropriate for Step 1.[38] Veterans Affairs guidelines describe a 10- to 20-point reduction in PCL scores as representing clinically significant change.[39] Although reduction of symptoms below a score of 50 results in a client falling below the cutoff for a PTSD diagnosis, we recommend a treatment goal of below 35 because this reduces the risk of delayed-onset PTSD. If indications of complex PTSD are apparent, a multimodal approach encompassing more than 10 sessions might be considered. These scores should be updated as subsequent versions of the PCL are implemented and validated. For other assessments, accepted cutoff scores for clinical and at-risk symptom levels can be substituted for those of the PCL.

NICE Step 2 guidelines for PTSD recommend treatment using Trauma-Focused Cognitive Behavior Therapy (TFCBT) or EMDR. These recommendations did not include EFT because most of the earlier referenced studies had not been published at the time the guidelines were developed. To make EFT available to a PTSD-positive population, we recommend an update of the guidelines based on currently published research. We propose that EFT be added to the recommended treatments based on the following criteria:

Subclinical Scores (35-49) in Initial Assessment

Treatment as usual plus A) 5 individual EFT therapy sessions and B) 1 instructional session on using the Battle Tap interactive online coach plus C) 3 Borrowing Benefits group therapy sessions. If members of the client's family are willing and able to attend Borrowing Benefits sessions, they should be invited.

Assessment 2: After the primary treatment program is complete, if symptom levels are persistently more than 34, A) 3 more sessions plus B) 1 additional Battle Tap instructional session.

Follow-up Assessment: 3 months after the final therapy session, if symptom levels are persistently above 34, monitor the client and perform regular follow-up assessments.

Clinical Scores (> 49) in Initial Assessment

Treatment as usual plus A) 10 individual EFT therapy sessions plus B) 2 sessions on using Battle Tap plus C) 5 Borrowing Benefits group sessions. If members of the client's family are willing and able to attend Borrowing Benefits sessions, they should be invited.

Assessment 2: After the primary treatment program is complete, if symptom levels are persistently above 40, A) 3 more individual therapy sessions plus B) 1 additional Battle Tap session plus C) 5 additional Borrowing Benefits group sessions.

Follow-up Assessment: 3 months after final therapy session, if clinical symptoms persist, escalate intervention to Steps 3 and 4 of the NICE guidelines, which advocate appropriate medication and intensive individual psychotherapy.

RISK MITIGATION FOR ACTIVE-DUTY WARRIORS

Instead of waiting until PTSD is diagnosed, we recommend a proactive approach using psychoeducation and Borrowing Benefits to mitigate the risk of development of symptoms in active-duty warriors. This has two components: the first applicable to the predeployment phase and the second in the postdeployment phase.

Predeployment Component: Independent of PCL-M assessment, three days of group EFT training using Borrowing Benefits as stress inoculation therapy, including an introduction to Battle Tap.

Postdeployment Component: Independent of PCL-M assessment, seven days of group EFT therapy using Borrowing Benefits and Battle Tap. Individual psychotherapy sessions as requested by participants.

CONCLUSION

According to published reports, systematic reviews of the published evidence, a meta-analysis of seven RCTs, and practitioner consensus, most cases of PTSD are remediated in ten EFT sessions or less. As a safe, efficacious, and easily learned self-help method, EFT should be offered to clients as an initial treatment option immediately after diagnosis. Group therapy involving family members may reinforce treatment effects through social support, and access to Battle Tap provides veterans and warriors with access to EFT at times and places of their own choosing. A structured evidence-based practice protocol should be widely disseminated to clinicians and institutions bearing the burden of PTSD treatment. For those patients who do not respond, appropriate medication and intensive individual psychotherapy is recommended, especially in cases of complex PTSD. ❖

Disclosure Statement

Dr Church is a stockholder in Energy Psychology Group, an organization providing training services and publications to medical and mental health professionals; he also receives income from presentations and publications related to the therapeutic method discussed. Dr Feinstein is the CEO of Innersource and Volunteer Executive Director of Energy Medical Institute.

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Solely for Good

Not for the self, not for the fulfillment of any worldly desire or gain, but solely for the good of suffering humanity, I will treat my patients and excel all.

— Charaka, ~6th-2nd century BCE, principle contributor to Ayruveda, author of *Charaka Samhita*

Induction with Infliximab and a Plant-Based Diet as First-Line (IPF) Therapy for Crohn Disease: A Single-Group Trial

Mitsuro Chiba, MD, PhD; Tsuyotoshi Tsuji, MD, PhD; Kunio Nakane, MD, PhD; Satoko Tsuda, MD; Hajime Ishii, MD, PhD; Hideo Ohno, MD; Kenta Watanabe, MD; Mai Ito, MD; Masafumi Komatsu, MD, PhD; Takeshi Sugawara, MD

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ABSTRACT

Background: Approximately 30% of patients with Crohn disease (CD) are unresponsive to biologics. No previous study has focused on a plant-based diet in an induction phase of CD treatment.

Objective: To investigate the remission rate of infliximab combined with a plant-based diet as first-line (IPF) therapy for CD.

Methods: This was a prospective single-group trial conducted at tertiary hospitals. Subjects included consecutive adults with a new diagnosis (n = 26), children with a new diagnosis (n = 11), and relapsing adults (n = 9) with CD who were naïve to treatment with biologics. Patients were admitted and administered a standard induction therapy with infliximab (5 mg/kg; 3 infusions at 0, 2, and 6 weeks). Additionally, they received a lacto-ovo-semivegetarian diet. The primary end point was remission, defined as the disappearance of active CD symptoms at week 6. Secondary end points were Crohn Disease Activity Index (CDAI) score, C-reactive protein (CRP) concentration, and mucosal healing.

Results: Two adults with a new diagnosis were withdrawn from the treatment protocol because of intestinal obstruction. The remission rates by the intention-to-treat and per-protocol analyses were 96% (44/46) and 100% (44/44), respectively. Mean CDAI score (314) on admission decreased to 63 at week 6 ($p < 0.0001$). Mean CRP level on admission (5.3 mg/dL) decreased to 0.2 ($p < 0.0001$). Mucosal healing was achieved in 46% (19/41) of cases.

Conclusion: IPF therapy can induce remission in most patients with CD who are naïve to biologics regardless of age or whether they have a new diagnosis or relapse.

(The study ID number is UMIN000019061, UMIN000020335: Registration at www.umin.ac.jp).

INTRODUCTION

The incidence and prevalence of inflammatory bowel disease (IBD) are increasing as the condition expands into new regions; consequently, IBD is now a global disease.[1]

Newly introduced biologics have revolutionized the treatment of various conditions, including malignant neoplasms, autoimmune diseases, and others.[2-4] Infliximab and adalimumab are monoclonal antitumor necrosis factor α antibodies that were introduced for IBD treatment and have effectively induced and maintained remission in Crohn disease (CD).[5-11] Therapy with biologics has popularized the concept of mucosal healing for IBD treatment.[12,13]

IBD is a polygenic disease triggered by environmental factors.[14] Despite the recognition that Westernization of lifestyle is a major IBD driver,[15,16] no countermeasures have been recommended against such lifestyle changes with the exception of nonsmoking for patients with CD.[17] Gut microflora may be the main environmental factor responsible for IBD[18]; further, diet influences gut microflora.[19,20]

IBD is prevalent in wealthy nations in which dietary Westernization has occurred.[21] Dietary Westernization is characterized by increased consumption of animal protein, animal fat, and sugar, with decreased consumption of grains. A consistent risk factor for IBD is the consumption of meat[22-26] and sweets,[24-26] whereas a preventive factor is the consumption of vegetables and fruits.[22,27] Consequently, we recognize from our clinical experience that IBD is highly associated with lifestyle and that it is mainly mediated by a Westernized diet. Additionally, diet-associated dysbiosis of the gut microflora seems to be the most relevant environmental factor in IBD.[18] Therefore, restoring and maintaining gut symbiosis with an adequate diet is fundamental for IBD treatment. We designed a semivegetarian diet (SVD), a type of plant-based diet (PBD), as therapy for IBD.[28] Since 2003, we have served the PBD to all inpatients with IBD at our center and found that PBD prevented CD relapse[28] and induced remission without medication in a subset of patients with mild ulcerative colitis.[29,30]

The Dietary Guidelines for Americans (US Department of Agriculture [USDA] Food Pattern) and dietary guidelines for chronic common diseases consistently recommend increased consumption of vegetables and fruits and decreased consumption of meats, processed meats

Mitsuro Chiba, MD, PhD, is the Chief of the Inflammatory Bowel Disease Section at Akita City Hospital in Japan. E-mail: mchiba@m2.gyao.ne.jp. **Tsuyotoshi Tsuji, MD, PhD,** is the Chief of the Gastrointestinal Endoscopy Section at Akita City Hospital in Japan. E-mail: ac070289@akita-city-hp.jp. **Kunio Nakane, MD, PhD,** is the Chief of the Gastroenterology Division at Akita City Hospital in Japan. E-mail: ac060950@akita-city-hp.jp. **Satoko Tsuda, MD,** is a Gastroenterologist at Akita City Hospital in Japan. E-mail: satokotsuda07@gmail.com. **Hajime Ishii, MD, PhD,** is a Gastroenterologist at Akita City Hospital in Japan. E-mail: acd00377@akita-city-hp.jp. **Hideo Ohno, MD,** is a Gastroenterologist at Akita City Hospital in Japan. E-mail: ac120502@akita-city-hp.jp. **Kenta Watanabe, MD,** is a Gastroenterologist at Akita City Hospital in Japan. E-mail: nabeken_9989@yahoo.co.jp. **Mai Ito, MD,** is a Gastroenterologist at Akita City Hospital in Japan. E-mail: pixmon1231@gmail.com. **Masafumi Komatsu, MD, PhD,** is a Gastroenterologist and the Director of Akita City Hospital, in Japan. E-mail: ac990892@akita-city-hp.jp. **Takeshi Sugawara, MD,** is a Gastroenterologist at Nakadori General Hospital in Japan. E-mail: nrp05157@nifty.com

and added sugars.[31,32] PBDs are listed as variations of USDA healthy eating patterns.[31] Epidemiologic studies provide convincing evidence that individuals who consume PBDs experience improved longevity and are less affected by common chronic diseases than those who eat omnivorous diets.[33,34]

Ideal treatment involves early commencement of therapy before irreversible damage occurs, namely during the window of opportunity.[35] This concept has been validated in rheumatoid arthritis treatment.[36-38] Current guidelines for CD limit the use of infliximab or adalimumab for patients who are unresponsive to conventional therapy.[17]

The natural history of CD usually is characterized by a disabling course; 10% to 15% of patients are relapse-free for the rest of their lives, however.[39-41] The current remission rate in CD with early use of infliximab is 64%.[8] This indicates that 30% to 40% of patients, even those treated early with infliximab, are likely to experience a disabling disease course after their first treatment. Reliable induction of remission is the first step toward improving the natural history of CD.

Our goal is a drastic enhancement of the relapse-free rate in CD—namely, induction of remission by incorporating three recently developed concepts in medicine (biologics, PBD, and window of opportunity), followed by maintenance of remission with a PBD rather than further use of biologics with or without immunosuppressants. We hypothesized that these modalities could enhance the relapse-free rate.

We designed the present trial to determine whether **i**nfliximab combined with a **P**BD as **f**irst-line (IPF) therapy could enhance the remission rate for patients with CD.

METHODS

Design and Settings

We designed a single-group, nonrandomized, open noncontrolled trial that was conducted at Nakadori General Hospital and Akita City Hospital, tertiary care facilities in northern Japan. The first author, MC, worked for the former facility between 2003 and 2012 and Akita City Hospital since 2013.

Patients

All patients with active symptom(s) regardless of their Crohn Disease Activity Index (CDAI) score[42] were advised to undergo hospitalization for potential IPF therapy. Between August 2003 and December 2015, 60 patients with active CD were admitted to the hospital (Figure 1). Subjects were tested for tuberculosis or hepatitis B infection[43]; no patient had a positive result. Patients previously treated with biologics or those taking prednisolone or azathioprine, which influence IPF efficacy, were excluded. Patients prescribed a partial elemental diet or 5-aminosalicylic acid were included.

Protocol: IPF Therapy

The protocol involved standard induction therapy with infliximab combined with an SVD.[28] Briefly, metronidazole 750 mg/d was administered after admission. Patients received a liquid infusion without meals during morphologic studies to assess clinical types and intestinal stenosis. Liquid infusion duration varied from 3 to 7 days depending on the extent of previous outpatient morphologic studies before admission. Infliximab (5 mg/kg) was infused at weeks 0, 2, and 6.[11] The PBD, which was initiated on the same day of the infusion, was a lacto-ovo-semivegetarian diet that included fish once a week and meat once every 2 weeks. Calories were gradually increased to a maximum of about 30 kcal per kg standard body weight. After about 1 month, metronidazole was switched to 5-aminosalicylic acids. After the third infusion of infliximab, patients were discharged. Patients who could not be admitted for the entire induction phase were discharged after the second infliximab infusion and readmitted for the third infusion.

IPF Therapy Efficacy

The primary end point was clinical remission at week 6 after the first infliximab infusion. Clinical remission was defined as the absence of active symptoms. Remission was assessed by the attending physician (MC). Secondary end points were normalization of C-reactive protein (CRP) concentration at week 6 and mucosal healing. CDAI also was evaluated. Patients were morphologically studied with colonoscopy and/or contrast barium enema before discharge. In this study, mucosal healing was defined as the absence of active findings of CD such as ulcer, aphthoid lesions, edema, redness, and bleeding. Symptoms and CDAI were

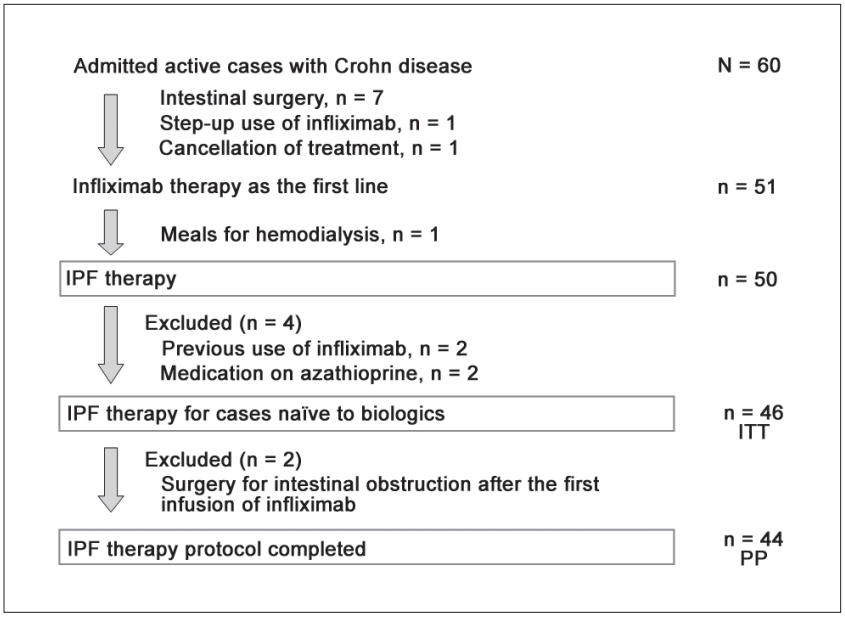

Figure 1. Enrollment of inpatients with active Crohn disease for IPF therapy.

IPF therapy = infliximab and plant-based diet as first-line therapy; ITT = intention to treat; PP = per protocol.

evaluated before and after infliximab therapy up to week 6.

Safety Evaluations

Vital signs, patient reports, findings during daily practitioner rounds, physical examinations, and weekly laboratory test findings were assessed to ensure safety.

Statistical Analysis

To evaluate differences of therapeutic effects among adults with a new diagnosis, children with a new diagnosis, and relapsed adults, the rates of remission, normalization of CRP concentration, and mucosal healing were assessed with a χ^2 test. CDAI score and CRP concentration were expressed as the mean plus or minus the standard deviation and median (interquartile range). To evaluate effects of treatment on CDAI and CRP, differences were first analyzed by repeated analysis of variance (ANOVA). If ANOVA results were statistically significant, data were analyzed using the post hoc Tukey-Kramer honestly significant difference test. A p value of 0.05 or lower indicated a statistically significant difference. Statistical analysis was performed using JMP 8 software (SAS Institute Inc, Cary, NC).

Ethical Considerations

For patients with strictures,[44] infliximab therapy poses risk for intestinal obstruction,[45-47] and the need for potential surgery was discussed. This protocol and the template informed consent forms were reviewed and approved by the Ethical Committee of Nakadori General Hospital and the Ethical Committee of Akita City Hospital (Protocol number 19-2003, 12-2013, 15-2015). The primary author/investigator (MC) obtained informed consent from all patients.

RESULTS

Patient Characteristics

Among 60 patients with active CD, 7 were indicated for intestinal surgery (Figure 1). Infliximab was used as a step-up approach for 1 patient. One patient cancelled medical treatment, and another patient on hemodialysis underwent standard first-line infliximab therapy; in that scenario, the patient required a diet for hemodialysis instead of a PBD. IPF therapy was administered to the remaining 50 patients. Two patients previously treated with infliximab and 2 patients receiving azathioprine were excluded. Forty-six patients who were naïve to biologics comprised the intention-to-treat subset and underwent IPF therapy. However, 2 patients with a new diagnosis (both men aged 21 years with stricture-type disease) developed intestinal obstruction after the first infusion of infliximab and underwent surgery. The 44 patients who completed the protocol (Figure 1) included 24 adults with a new diagnosis, 11 children ages 18 years and younger with a new diagnosis, and 9 relapsing

Table 1. Patient demographics and clinical characteristics

Characteristic	Total	New diagnosis		Relapsed
		Adults	Children[a]	Adults
Number of patients	44	24	11	9
Male/female	29/15	15/9	9/2	5/4
Age (y)				
Range	13-77	19-61	13-18	21-77
Mean ± SD	27.2 ± 13.7	30.0 ± 11.9	15.9 ± 1.8	33.6 ± 18.8
Median (IQR)	22.0 (18.3-30.8)	27.5 (21.0-35.0)	16.0 (15.0-17.0)	24.0 (21.5-43.5)
Disease duration (mo)				
Range	1-240	1-39	1-60	22-240
Mean ± SD	26.9 ± 45.1	8.8 ± 10.6	12.7 ± 17.2	92.8 ± 64.1
Median (IQR)	8.0 (3.0-33.3)	4.5 (2.0-11.5)	6.0 (3.0-18.0)	72.0 (57.0-122.5)
Location of lesion				
L1 Ileal	1	1	0	0
L2 Colonic	13	8	2	3
L3 Ileocolonic	30	15	9	6
L4 Isolated upper lesions	0	0	0	0
Behavior				
B1 Nonstricturing, nonpenetrating	33	18	10	5
B2 Stricturing	11	6	1	4
B3 Penetrating	0	0	0	0
Perianal disease modifier	31	16	10	5
Anal fistula	24	11	9	4
Anal skin tag	13	8	3	2
Current smoker	5	4	0	1
Previous segmental resection	3	0	0	3
CDAI score				
Range	52-834	52-834	144-472	88-679
Mean ± SD	314 ± 188	348 ± 214	270 ± 97	279 ± 200
Median (IQR)	270 (177-357)	296 (195-547)	278 (157-322)	225 (130-404)
< 150	8	4	1	3
150-220 mild-moderate	7	4	2	1
220-450 moderate-severe	19	9	7	3
> 450 severe/fulminant	10	7	1	2
C-reactive protein concentration (mg/dL)				
Mean ± SD	5.4 ± 4.9	5.4 ± 5.9	5.2 ± 3.5	5.6 ± 3.9
Median (IQR)	4.0 (1.6-7.5)	2.8 (1.2-7.1)	4.4 (2.4-8.6)	5.9 (2.8-7.4)

[a] Children = 18 years of age or younger.
CDAI = Crohn Disease Activity Index; IQR = interquartile range; SD = standard deviation.

adults. The demographic characteristics of our 44 patients are presented in Table 1. The mean disease duration for relapsing adults (92.8 months) was longer than the mean for adults with a new diagnosis (8.8 months) or the mean for children (12.7 months). More than 50% of patients in all groups had 1 or more perianal fistula(s) that were draining pus and/or anal tag(s). Five of 33 (15%) adults were smokers who stopped smoking after their admission. Eight patients had a CDAI score lower than 150 (quiescent stage); 7 had a score of 150 to 220 (mild-moderate); 19 scored 220 to 450 (moderate-severe); and 10 patients had a score higher than 450 (severe/fulminant).[44] Three relapsing adults were on partial elemental diet: 600, 900, and 1200 kcal/d, respectively. The same elemental diet was maintained during the first half of hospitalizations and was decreased by 300 kcal during the latter half of hospitalizations, while the amount of PBD was increased. Five patients were discharged after the second infliximab infusion and were readmitted for the third infusion. Sixteen of 44 patients in the present protocol also were described in a 2010 paper.[28]

Efficacy

The primary end point was remission. Two patients were withdrawn from the protocol because of intestinal obstruction. All remaining patients reported considerable improvement 1 week after the first infliximab infusion. Most patients had no symptoms between weeks 1 and 3. A CDAI score lower than 150 indicates remission in many studies.[42] The rate of CDAI scores lower than 150 among patients with baseline CDAI scores higher than 150 was 50% (18/36), 69% (25/36), 86% (30/35), 94% (31/33), 94% (31/33), and 100% (36/36) at weeks 1, 2, 3, 4, 5, and 6, respectively. Among patients with draining perianal fistulas, 24 experienced fistula closure within weeks 1 and 3. All 44 patients who completed the protocol achieved remission at week 6. Remission rates by intention-to-treat and per-protocol analysis were 96% and 100%, respectively (Table 2).

Secondary End Points

The mean CDAI score was significantly decreased from 314 before IPF therapy to 163 after the first infliximab infusion ($p < 0.0001$). The scores were further decreased chronologically: 115, 98, 82, 74, and 63 at weeks 2, 3, 4, 5, and 6, respectively (Table 3, Figure 2). Chronologic CDAI score changes were similar among the 3 groups (Table 3).

The mean CRP concentration decreased from 5.3 mg/dL before IPF therapy to 0.9 mg/dL after the first infliximab infusion ($p < 0.0001$). The CRP concentration (reference range, ≤ 0.3 mg/dL) was within defined limits (0.2 mg/dL) at week 2 and thereafter (Table 3, Figure 2). The chronologic CRP concentration changes were similar among the 3 groups (Table 3). Among adults with a new diagnosis,

Table 2. Rates of remission and normalization of C-reactive protein concentration and mucosal healing at week 6 after infliximab and a plant-based diet as first-line therapy

Subjects	N	Remission	CRP concentration	Mucosal healing
Total	46	96% (44/46) ITT, 100% (44/44) PP	84% (37/44)	46% (19/41)
Adults, new diagnosis	24	92% (24/26)[a] ITT, 100% (24/24) PP	92% (22/24)[b]	38% (9/24)[c]
Children, new diagnosis	11	100% (11/11)[a] ITT	82% (9/11)[b]	60% (6/10)[c]
Relapsed adults	9	100% (9/9)[a] ITT	67% (6/9)[b]	57% (4/7)[c]

[a] p value for comparison among the three groups (χ^2 test) = 0.3085.

[b] p value for comparison among the three groups (χ^2 test) = 0.2344.

[c] p value for comparison among the three groups (χ^2 test) = 0.3980.

CRP = C-reactive protein; ITT = intention to treat; PP = per protocol.

Table 3. CDAI score and CRP concentration changes during induction phase after IPF therapy

Subjects	Number of patients	Weeks after IPF therapy (mean ± SD)							p value (ANOVA)
		0	1	2	3	4	5	6	
CDAI score									
Total	44	314 ±189	163 ± 116	115 ± 89	98 ± 70	82 ± 45	74 ± 45	63 ± 32	< 0.0001
Adults, new diagnosis[a]	24	348 ± 214	171 ± 141	121 ± 104	93 ± 73	76 ± 50	65 ± 44	57 ± 30	< 0.0001
Children, new diagnosis[a]	11	270 ± 97	145 ± 76	108 ± 78	112 ± 86	84 ± 37	89 ± 52	71 ± 35	< 0.0001
Relapsed adults[a]	9	279 ± 200	162 ± 87	109 ± 58	99 ± 40	93 ± 38	78 ± 38	69 ± 35	< 0.0001
CRP concentration (mg/dL) (normal ≤ 0.3)									
Total	44	5.3 ± 5.0	0.9 ± 1.7	0.2 ± 0.2	0.1 ± 0.1	0.1 ± 0.2	0.1 ± 0.2	0.2 ± 0.2	< 0.0001
Adults, new diagnosis[b]	24	5.7 ± 5.9	0.8 ± 1.4	0.1 ± 0.2	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.2	< 0.0001
Children, new diagnosis[b]	11	5.2 ± 3.5	1.1 ± 2.8	0.1 ± 0.3	0.1 ± 0.1	0 ± 0.1	0.2 ± 0.3	0.2 ± 0.2	< 0.0001
Relapsed adults[b]	9	5.6 ± 3.9	0.8 ± 0.7	0.3 ± 0.3	0.1 ± 0.2	0.2 ± 0.3	0.2 ± 0.2	0.2 ± 0.3	< 0.0001

[a] p value for comparison among three groups (ANOVA) = 0.7949.

[b] p value for comparison among three groups (ANOVA) = 0.9263.

ANOVA = analysis of variance; CDAI = Crohn Disease Activity Index; CRP = C-reactive protein; IPF therapy = infliximab and a plant-based diet as first-line therapy; SD = standard deviation.

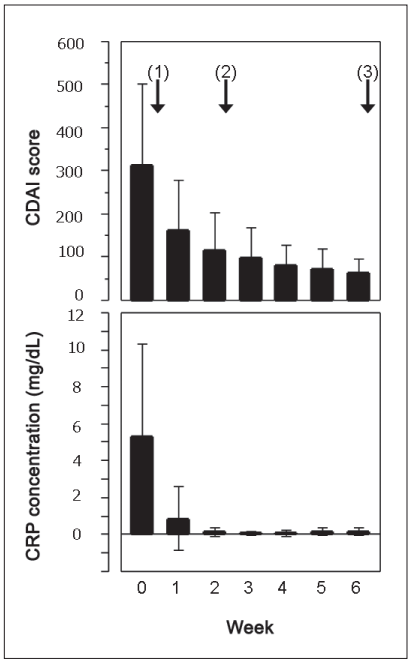

Figure 2. Change of CDAI score (upper panel) and CRP concentration (lower panel) before and after IPF therapy in 44 patients with CD. The solid bar denotes the mean and the thin line shows the standard deviation. Arrows with numbers in brackets indicate 3 infliximab infusions at weeks 0, 2, and 6. CDAI score and CRP concentration (mg/dL) (reference range ≤ 0.3) are presented in Table 3. All CDAI scores and CRP concentrations significantly decreased after IPF (analysis of variance $p < 0.0001$, Tukey-Kramer honestly significant difference test $p < 0.0001$).

CD = Crohn disease; CDAI = Crohn Disease Activity Index; CRP = C-reactive protein; IPF therapy = infliximab and a plant-based diet as first-line therapy.

CRP concentrations from weeks 2 to 6 remained stable (0.1 mg/dL). However, CRP concentration fluctuated within the reference range for the other 2 groups. The lowest concentration was 0 mg/dL at week 4 and 0.2 mg/dL at week 5 among children with a new diagnosis, and 0.1 mg/dL at week 3 and 0.2 mg/dL at week 4 among relapsing adults (Table 3). The rates of CRP normalization at week 6 were highest (92% [22/24]) among adults with a new diagnosis; intermediate (82% [9/11]) among children with a new diagnosis; and lowest (67% [6/9]) among relapsing adults, although the difference was nonsignificant ($p = 0.2344$) (Table 2). Normal CRP concentration was achieved by week 5 for 6 of 7 patients with abnormal CRP concentrations at week 6.

Three patients did not undergo morphologic assessment before discharge. Mucosal healing was achieved for 19 of 41 patients (46%) (Table 2).

Safety

Two patients were withdrawn from the protocol because of intestinal obstruction. Infusion reactions to infliximab were observed in two patients (eruptions with itching and vomiting). One child with a new diagnosis developed herpes zoster three weeks after completing IPF therapy. Metronidazole was withdrawn because of paresthesia (three patients) and leukocytopenia (one patient). 5-aminosalicylic acid was withdrawn because of mild pancreatitis (two patients), alanine aminotransferase elevation (one patient), and epigastralgia (one patient). All patients ate the PBD, and none experienced an adverse effect such as gaseous distress, abdominal discomfort, or diarrhea.

DISCUSSION

On the basis of the etiopathogenesis of IBD, we designed a PBD as a therapeutic diet for IBD.[28] To drastically improve the relapse-free rate associated with CD, the first step involves safe and reliable remission induction with initial treatment. Our study showed that IPF therapy can induce remission for most patients with CD regardless of age or new diagnosis or relapse status.

The CD population (Table 1) in this study reflects Japan's epidemiology. Male predominance is an Asian (including Japanese) characteristic related to CD.[48,49]

Clinical remission is far more important than clinical response in practice (the remission rate is lower than the response rate). In this study, the primary end point was induction of remission at week 6. Remission rates reported with infliximab or adalimumab are presented in Table 4.[5-10,50-52] In most of the studies reported, subjects had moderate to severe CD (CDAI 220-450),[42] but these studies did not include less severe (CDAI score < 220) or more severe (CDAI > 450) cases.[5-10,50,51] Our study, however, included cases involving all severity levels. Most patients with CD will experience a disabling course,[39-41] and even patients with mild CD experience relapse rates of 60% to 70% in a year.[53] Additionally, there is no way to predict which patients will have a disabling or relapse-free course.[39-41] If we attempt to improve the natural course of all patients with CD, we must study all patients with active CD regardless of severity. In this study, even if mild cases (CDAI score lower than 220 [n = 15]) were excluded, all 29 patients with CDAI scores higher than 220, including the 10 patients with severe/fulminant disease, achieved remission.

Patients who are naïve to biologics and those receiving infliximab combined with azathioprine achieved a higher remission rate with early use of biologics and had a better prognosis than those who began treatment at a later phase or those previously exposed to a biologic or infliximab alone.[8,50-52,54] One group of investigators evaluated remission rates under these conditions (early use of infliximab combined with azathioprine in biologics-naïve patients) by using a top-down approach; their patients achieved a remission rate of 64% at week 14.[8] So far, that is the highest remission rate reported for a large series (Table 4), demonstrating that 30% to 40% of patients with CD are nonresponders (primary nonresponders) to infliximab. As a result, many studies have been conducted to evaluate response predictors and primary nonresponders.[55-58] In our study, even though we included relapsed patients with a median disease duration of 6 years, all our patients achieved remission with IPF therapy. Therefore, disease duration of several years does not seem to be a critical factor for the induction of remission with IPF therapy. Our data show that most patients with CD who are naïve to biologics achieve remission with IPF therapy. Consequently, nonresponse to biologics seems to reflect the therapeutic modality chosen. Several factors may be involved in the successful induction of remission in our studies.

First, all patients in this study were admitted during IPF therapy. Although clinical remission could be obtained in a subset of patients after the first infusion of infliximab,[5] we considered that a certain period is needed for the recovery of morphologic changes in the intestine. Consequently, 3 inductive infusions of infliximab were given in 6 weeks[11] while

patients were hospitalized. However, mucosal healing was achieved only for 46% of patients (Table 2).

Patients' experience with a PBD, physician knowledge about IBD etiopathogenesis, and dietary guidance regarding PBD from a registered dietitian during hospitalization helped to ensure smooth PBD transitions from hospitals to homes after patient discharge. We confirmed a significantly higher PBD score (mean 25.0), indicating a higher adherence to a PBD[59] when compared with the mean base score of 6.4 in 24 patients with CD at approximately 6 years after discharge ($p = 0.0131$) (unpublished observation).

Hospitalization promotes smoking cessation, and smoking is prohibited in most hospitals in Japan. In our sample, 11% of patients (5/44) were smokers until admission, at which time they quit smoking; thus, all patients were considered nonsmokers. Smoking is a deteriorating factor in CD.[60,61] In other studies, the current smoking rate was as high as 43% (Table 4).[8-10] Hospitalization duration in our study was shorter than duration for

Table 4. Literature review: Induction of remission in Crohn disease

	Subjects							Outcomes	
Author	Inclusion criteria/ scores	Number of patients	CDAI score	CRP concentration (mg/dL)	Duration of disease	Current smoker, % (no.)	Regimen	Time of assessment	Remission rate (CDAI score < 150 unless otherwise specified), % (no.)
Targan et al, 1997[5]	CDAI 220-400	27	Mean 312	Mean 2.2	Mean 12.5 y	nd	IFX 5 mg/kg, single infusion	Wk 4	48.1 (13/27)
Mayer et al, 2001[6]	CDAI 220-400	385	Median 297	Median 0.8	Median 7.9 y	nd	IFX standard	Wk 6	38.4
Hyams et al, 2007[7]	Moderate to severe[a] Children, PCDAI > 30	112	Mean PCDAI 41	nd	Median 1.6 y	Unlikely	IFX standard and immuno-suppressant	Wk 10	58.9 (66/112)
D'Haens et al, 2008[8]	CDAI > 200, age ≥ 16 New diagnosis	67	Mean 330	Median 1.9	Median 2.0 wk from diagnosis	43 (28/65)	IFX standard and AZA	Wk 14	64 (42/65)
Colombel et al, 2010[50]	Moderate to severe[a] (Naïve to anti-TNF, AZA)	169	Mean 290	Median 1.0	Median 2.2 y	nd	IFX standard	Wk 6	30 (50/169)
		169			Median 2.2 y		IFX standard and AZA		33 (55/169)
Hanauer et al, 2006[9]	Moderate to severe[a] Naïve to anti-TNF	76	Mean 295	Mean 1.4 Median 0.9	nd	42 (32/76)	Adalimumab standard	Wk 4	36 (27/76)
Sandborn et al, 2007[10]	Moderate to severe[a] Previous IFX	159	Mean 313	Mean 1.9 Median 0.9	nd	35 (55/159)	Adalimumab standard	Wk 4	21 (34/159)
Watanabe et al, 2012[51]	Moderate to severe,[a] Japanese	33	Mean 301	Mean 2.2	Mean 11.0 y	nd	Adalimumab standard	Wk 4	33 (11/33)
	Naïve to anti-TNF	14							43 (6/14)
	Previous anti-TNF	19							26 (5/19)
Miyoshi et al, 2014[52]	Active, Japanese	45	Median HBI 6.5	Median 1.3	Median 8.0 y	nd	Adalimumab standard	Wk 4	62 (28/45)[b]
		12			≤ 3 y				92 (11/12)
		33			> 3 y				52 (17/33)
Present study	Active, Japanese (Naïve to anti-TNF)	44	Mean 314 Median 270	Mean 5.4 Median 4.0	Mean 26.9 mo Median 8.0 mo	11 (5/44)	IPF therapy	Wk 6	Clinical remission 96 (44/46) ITT 100 (44/44) PP

[a] Moderate to severe, CDAI 220-450.
[b] Harvey-Bradshaw index ≤ 4.
Adalimumab standard = adalimumab 160/80 mg at weeks 0 and 2; AZA = azathioprine; CDAI = Crohn Disease Activity Index; CRP = C-reactive protein; HBI = Harvey-Bradshaw index; IFX = infliximab; IFX standard = infliximab 5 mg/kg at weeks 0/2/6; IPF therapy = infliximab and a plant-based diet as first-line therapy; ITT = intention to treat; nd = not described; PCDAI = pediatric Crohn Disease Activity Index; PP = per protocol; TNF = tumor necrotizing factor.

a conventional elemental diet therapy in Japan, for which more than 6 weeks is required.[62]

PBD was initiated on the same day as the infliximab infusion and was provided throughout hospitalization. We previously reported the efficacy of PBD in preventing relapse in CD.[28] In the current study, all patients who completed the protocol achieved remission. Altogether, these findings indicate that PBD is effective during the active and quiescent CD stages.

Preventive factors for IBD (eating vegetables and fruits)[22,27] are recommended, and risk factors (eating meat and sweets)[22-26] are moderated; indeed, a PBD includes these preventive recommendations and risk moderating factors. Considering that the most important environmental factor in IBD is diet-associated gut microflora,[18] we hypothesized that an adequate diet is the basis for IBD treatment during both active and quiescent stages. On the basis of our results, a PBD is recommended for patients with IBD. To date, most studies evaluating induction of remission or prognosis have not devoted resources to diet during treatment. Omnivorous and conventional low-residue diets might reduce the efficacy of biologics.

Metronidazole was used during the first half of hospitalization and is effective in CD with or without perianal fistulas.[63,64] An antibiotic is used during the active stage to eliminate potentially pathogenic bacteria in the intestine.[65]

Clinicians strive to provide the best therapy on the basis of their experience; as a result of our 30-plus years' experience in treating CD, IPF became routine therapy for CD in 2003 when infliximab was introduced in Japan. The therapeutic approach we propose is comprehensive, and we consider that all factors are necessary for induction of remission, although the contribution of each factor varies. This is the first study in which close attention was paid to diet during induction treatment of CD. In the absence of a control diet, the efficacy of PBD for induction of remission could not be demonstrated. It appears, however, that a PBD plus infliximab was a major contributor to our study's success.

The Ministry of Health, Labour, and Welfare of Japan designated ulcerative colitis and CD as intractable diseases. Patients with intractable diseases are provided with public medical aid on registration at the Public Health Office, so physicians in Japan are able to provide the best treatments for patients with IBD with less concern about medical expenses. Therefore, its immediate applicability in other countries may be limited.

Preventive factors for IBD (eating vegetables and fruits) are recommended, and risk factors (eating meat and sweets) are moderated.

IPF therapy, which can induce remission for most patients with CD, offers several advantages over the current induction therapy. No serious adverse events occurred with IPF therapy. The rapid efficacy of infliximab enabled patients to eat dinner on the same day of infliximab treatment. Mean CDAI scores at baseline and weeks 1, 2, and 4 in patients treated with adalimumab were 313, 264, 232, and 226, respectively.[9] In contrast, patients treated with IPF therapy had mean CDAI scores of 314, 163, 115, and 82, respectively (Table 3, Figure 2). With IPF therapy, the mean CDAI score was 115 as early as week 2, which is lower than the cutoff score of 150 that is recognized as denoting remission.[42]

The main disadvantage associated with IPF therapy is that hospitalization is required. However, most of our patients who were dealing with chronic symptoms recognized that they needed treatment and accepted hospitalization. There is risk for intestinal obstruction after infliximab treatment.[45-47] Infliximab is thought to be effective for inflammatory stenosis and ineffective for fibrotic stricture,[66] but it is difficult to distinguish between inflammatory and fibrotic stricture.[67] In the absence of signs of obstruction, stricture per se is no longer regarded as a contraindication for infliximab therapy; patients still are regarded as reasonable candidates.[66,68] In this study, intestinal obstruction developed within two weeks after the first infliximab infusion for two patients. There is scant literature about early obstruction after infliximab treatment.[45-47] We speculate that infliximab is so swiftly effective in ulcer healing[69] that the healing process further narrows the stenotic site, resulting in intestinal obstruction. If obstruction is a result of infliximab efficacy, an obstruction could also occur in CD with stricture. When obstruction occurs, it can be immediately diagnosed and surgically treated because patients are in a hospital. We fully inform patients with stricture about intestinal obstruction risk. Apart from two IPF study withdrawals attributable to intestinal obstruction, there were no other withdrawals.

Our study had limitations. There was no control group, and the sample size was small. Nevertheless, we expect that large, controlled studies will be conducted to validate these results.

IPF therapy can induce remission for most patients with CD. Further study is required to determine how remission can be maintained in the long term. Normal CRP concentration is a good indicator of lasting remission, but CRP concentration outside of defined limits is a sign of forthcoming relapse.[59,70] Most adults in our study with a new diagnosis (92%) had a normal CRP concentration at week 6, as did children with a new diagnosis (82%) and relapsing adults (67%) (Table 2). About 50% of patients with newly diagnosed adult CD maintained long-term remission with a PBD without periodic maintenance infliximab therapy (the remission rate at 3 to 7 years was 58%, according to Kaplan-Meier analysis [unpublished observation]). Conversely, children and relapsing adults treated with PBD alone tended to relapse within 2 years. Out of 11 children and 9 relapsed adults, 9 and 4 patients experienced relapse, respectively (unpublished observation). IPF therapy should be provided to adults with a new CD diagnosis to help decrease relapse incidence.

CONCLUSION

IPF therapy can induce remission for most patients with CD regardless of age or new diagnosis or relapse status. ❖

Disclosure Statement

The authors have no conflicts of interest to disclose.

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Food

Everything in food works together to create health or disease.

— T Colin Campbell, MD, b 1934, American biochemist, author of *The China Study*

CME credits available for this article — see page 112

ORIGINAL RESEARCH & CONTRIBUTIONS

Special Report

Urgent Need for Improved Mental Health Care and a More Collaborative Model of Care

James Lake, MD; Mason Spain Turner, MD

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ABSTRACT

Current treatments and the dominant model of mental health care do not adequately address the complex challenges of mental illness, which accounts for roughly one-third of adult disability globally. These circumstances call for radical change in the paradigm and practices of mental health care, including improving standards of clinician training, developing new research methods, and re-envisioning current models of mental health care delivery. Because of its dominant position in the US health care marketplace and its commitment to research and innovation, Kaiser Permanente (KP) is strategically positioned to make important contributions that will shape the future of mental health care nationally and globally.

This article reviews challenges facing mental health care and proposes an agenda for developing a collaborative care model in primary care settings that incorporates conventional biomedical therapies and complementary and alternative medicine approaches. By moving beyond treatment delivery via telephone and secure video and providing earlier interventions through primary care clinics, KP is shifting the paradigm of mental health care to a collaborative care model focusing on prevention. Recommendations are to expand current practices to include integrative treatment strategies incorporating evidence-based biomedical and complementary and alternative medicine modalities that can be provided to patients using a collaborative care model. Recommendations also are made for an internal research program aimed at investigating the efficacy and cost-effectiveness of promising complementary and alternative medicine and integrative treatments addressing the complex needs of patients with severe psychiatric disorders, many of whom respond poorly to treatments available in KP mental health clinics.

INTRODUCTION

Existing models of care and available treatment approaches fail to adequately address the global crisis of mental health care. Mental illness accounts for about one-third of the world's disability caused by all adult health problems, resulting in enormous personal suffering and socioeconomic costs.[1] Severe mental health problems including major depressive disorder, bipolar disorder, schizophrenia, and substance use disorders affect all age groups and occur in all countries, including the US, Canada, the European Union countries, and other developed and developing countries. Mental illness is closely associated with poverty, wars, and other humanitarian disasters, and in some cases, leads to suicide, one of the most common causes of preventable death among adolescents and young adults. Mental illness is the pandemic of the 21st century and will be the next major global health challenge. Despite the increased availability of antidepressants during the past few decades, limited efficacy, safety issues, and high treatment costs have resulted in an enormous unmet need for treatment of depressed mood. It is estimated that 350 million individuals experience depression annually.[2] On average, it takes almost 10 years to obtain treatment after symptoms of depressed mood begin, and more than two-thirds of depressed individuals never receive adequate care.[3] Enormous psychological, social, and occupational costs are associated with depressed mood, which is the leading cause of disability in the US for individuals aged 15 to 44 years with annual losses in productivity in excess of $31 billion.[4]

Suicide is currently the second leading cause of death in 15 to 29 year olds, resulting in enormous social disruption and losses in productivity. Between 10 and 20 million depressed individuals attempt suicide every year and approximately 1 million complete suicide. In response to these alarming circumstances, in 2016 the World Health Organization declared depression to be the leading cause of disability worldwide.[5]

More than 85% of the world's population lives in 153 low- and middle-income countries.[2] Poverty is linked to a higher burden of mental illness, with variables such as education, food insecurity, housing, social class, socioeconomic status, and financial stress exhibiting a strong association.[6] Most of these countries allocate scarce financial resources to mental health care needs and have grossly inadequate professional mental health services. A recent comprehensive survey of European Union member countries found that 38.2% (approximately 165 million people) met criteria for a psychiatric disorder, with fewer than one-third receiving any treatment at all.[7] Disorders of the brain, including psychiatric disorders, were found to be the largest contributor to the all-cause morbidity burden as measured by disability-adjusted life years. In response to shared global concerns over the crisis in mental health

James Lake, MD, was a Staff Psychiatrist at the Oakland Medical Center in CA at the time this article was written, and is a founding member and former Chair of the American Psychiatric Association Caucus on Complementary and Alternative Medicine. He is the author of four books on integrative mental health care. E-mail: jameslakemd@gmail.com. **Mason Spain Turner, MD,** is the Director of Outpatient Mental Health and Addiction Medicine for Regional Mental Health Services for The Permanente Medical Group, the Chief of the Department of Psychiatry at the San Francisco Medical Center, and an Assistant Clinical Professor at the Univesity of California, San Francisco. E-mail: mason.turner@kp.org.

care, in 2012 the World Health Organization published "Mental Health Action Plan 2013-2020"[8] and set forth 4 major objectives:

- more effective leadership and governance for mental health
- the provision of comprehensive, integrated mental health and social care services in community-based settings
- implementation of strategies for promotion and prevention
- strengthened information systems, evidence, and research.

In developed countries, elderly individuals, minorities, low-income groups, uninsured persons, and residents of rural areas are less likely to receive adequate mental health care, and most people with severe mental health problems receive either no treatment or inadequate treatment of their disorders.[8]

In the US the situation is even worse in large metropolitan areas, where most of the Kaiser Permanente (KP) outpatient mental health clinics are located. For example, in the San Francisco Bay area where one of the authors (JL) worked as a staff psychiatrist at a large KP mental health clinic at the time this article was written, there is a large and growing gap between mental health care needs of the population and available resources. This gap is becoming ever wider in suburban, semirural, and rural areas throughout the US and is related to the fact that the medical subspecialty of psychiatry is one of the oldest workforces in medicine, with many psychiatrists nearing or past the age of retirement. Combined with increasing vacancies in psychiatry residency training programs, the staffing pipeline for psychiatrists is shrinking.[9] Relying exclusively on specialty mental health practitioners to solve the problem of improved access to mental health care is clearly not the best or most realistic approach. Training other health care practitioners in basic psychotherapy techniques and prescribing psychopharmacologic regimens for common psychiatric disorders will become an essential future strategy for expanding access to mental health care in the US and other developed countries.

In addition to limited access to mental health care caused by scarce mental health resources and financial hardship, social stigma associated with seeking specialty mental health services prevents many individuals with depressed mood or other severe mental illnesses from seeking and obtaining adequate care. A large percentage of KP members seeking care for a mental health problem have complex needs that are difficult to adequately address in the current model of care. We feel strongly that these circumstances define an agenda for further refining KP's existing model of care into a truly collaborative care model in which patients receive medical and mental health care in the same clinic setting.

"Integrated care" and "collaborative care" are models of care that refer to the same kind of health care delivery system and are used interchangeably. In this article, we use the term *collaborative care* to avoid confusion. The Agency for Healthcare Research and Quality defines *collaborative care* as "the care that results from a practice team of primary care and behavioral health clinicians, working together with patients and families, using a systematic and cost-effective approach to provide patient-centered care for a defined population. This care may address mental health and substance abuse conditions, health behaviors (including their contribution to chronic medical illnesses), life stressors and crises, stress-related physical symptoms, and ineffective patterns of health care utilization."[10]

Increasingly, small community-based mental health clinics are shifting the context in which mental health care takes place to services aimed at wellness and prevention in primary care settings. Starting from its existing care delivery system, KP is uniquely positioned to develop and implement a collaborative care model at the national level aimed at patient-centered care focusing on primary prevention and wellness. Implementing a program on this scale would allow research and academic study of the most effective means of primary prevention of mental illness, data that would be invaluable in designing effective programs in collaborative care settings. Leveraging collaborative care in primary care settings throughout geographic regions that KP already serves and providing individualized interventions that prioritize specialty mental health care for the most severely ill and impaired patients will improve both medical and psychiatric outcomes. The results will likely be more cost-effective solutions to complex mental health problems, reduced stigma associated with seeking mental health care, and enhanced overall health of the population.

Efficacy and Safety Concerns Affect Conventional Mental Health Care

Widely used treatments in the current model of conventional mental health care include psychotropic medications, psychotherapeutic techniques such as insight-oriented therapy and cognitive behavioral therapy, electroconvulsive therapy, and transcranial magnetic stimulation. Psychotropic medications comprise an important part of mental health care, especially for severe mental illness. Many individuals diagnosed with bipolar disorder, major depressive disorder, and schizophrenia depend on medications to function and be productive members of society. However, after decades of research and billions of dollars of industry funding, the evidence supporting pharmacologic treatments of major depressive disorder, bipolar disorder, and other psychiatric disorders is not compelling.[11-18] Recently KP expanded its range of mainstream treatments by establishing several ketamine clinics where patients with severe refractory depressed mood are being successfully treated using ketamine intravenous infusion therapy, resulting in improved quality of life and reduced disability. In fact, internal, nonpublished data from within KP demonstrate that ketamine infusion therapy is rapidly being shown to have superior efficacy to more traditional antidepressants, although some patients report improvements in mood of shorter duration. Expanding the reach of this important treatment intervention in both specialty care and primary care settings will be essential for alleviating symptoms associated with the most severe forms of depression.

In addition to concerns about their efficacy, many commonly prescribed psychotropic medications including antidepressants and antipsychotics are associated with serious adverse effects, including weight gain, increased risk of diabetes and heart disease, neurologic disorders, and sudden cardiac death.[19] Metabolic syndrome associated with weight gain and increased risk of diabetes and coronary artery disease is a well-documented adverse effect of antipsychotics and other psychotropic agents. Poor treatment

outcomes owing to limited efficacy of antidepressants, mood stabilizers, antipsychotics, and other psychotropic medications result in long-term impaired functioning, work absenteeism, and losses in productivity.[20-24]

In addition to concerns about efficacy and safety of conventional treatments, the current mainstream model of care is limited by disparities in the delivery of mental health services to different socioeconomic classes and the lack of integration of mental health services into primary care and other medical subspecialties.[25] The limitations of the mainstream model of care invite open-minded consideration of collaborative care models capable of more adequately addressing mental illness in primary care settings, taking into account complex medical, psychological, social, and cultural factors. Numerous studies show that collaborative care models reduce health care disparities in patients from different socioeconomic and ethnic backgrounds[26-29] and are more effective than conventional care models for treatment of depressed mood, anxiety disorders, bipolar disorder, and schizophrenia.[30-34] Practitioners and patients report high levels of satisfaction with the management of depressed mood in collaborative care settings[30,35] Finally, collaborative care is more cost-effective than usual care in all categories measured, including medication costs and inpatient, outpatient, and mental health specialty care,[36] as well as for the management of depressed patients with comorbid medical disorders,[37] severe anxiety disorders,[38] and serious chronic mental illness.[39-41]

Widespread use of CAM by patients who are concurrently receiving conventional treatments such as psychotropic medications and psychotherapy is driving a trend toward increasingly integrative mental health care in North America, Europe, Australia, and other world regions.

Increasing Use of Complementary and Alternative Treatments in Mental Health Care

In the context of the limitations of available conventional biomedical treatments, accumulating research findings are providing evidence for both safety and efficacy of select complementary and alternative (CAM) treatments of depressed mood, anxiety, and other mental health problems, including select pharmaceutical-grade natural products, lifestyle modifications (Lifestyle Medicine), mind-body approaches, and nonallopathic whole-system approaches such as traditional Chinese medicine and Ayurveda. Examples of natural supplements being investigated as nonpharmacologic therapies include S-adenosyl methionine for depressed mood; the adjunctive use of nutraceuticals (ie, botanicals and other natural product supplements) in combination with psychotropics such as omega-3 fatty acids, folic acid (especially its active form l-methyl-folinic acid), 5-hydroxytryptophan, and n-acetyl cysteine for mood disorders; a standardized extract of the herbal kava; and the amino acid l-theanine.[42] In addition to nutraceuticals, evidence is emerging in support of acupuncture for treatment of generalized anxiety and depressed mood, and of mindfulness training for improvement of negative symptoms of schizophrenia, anxiety, and mood disorders.[43] Lifestyle modifications such as regular exercise, healthy diet, sufficient sleep, and reducing alcohol and nicotine use also enhance mental and emotional well-being while reducing the relapse risk for many psychiatric disorders.[44]

The concept of a wellness-focused model of mental health care gained momentum in 2011 with publication of the UK Public Health White Paper emphasizing the fundamental importance of prevention and health improvement through lifestyle changes.[45] Large population surveys confirm that consumer use of CAM globally has remained high and in some countries has steadily increased[46]; however, estimates of CAM use vary significantly with respect to how CAM is defined. In this broad context uses of CAM to treat mental illness are growing rapidly. Survey findings suggest that 43% of patients with an anxiety disorder[47] and 53% of depressed[48] individuals use 1 or more CAM treatments. Individuals with severe mental illnesses who use CAM therapies to treat their symptoms feel strongly that such nonpharmacologic treatments improve their physical, emotional, cognitive, social, and spiritual functioning; reduce the severity of their symptoms; and enhance overall wellness.[49] Widespread use of CAM by patients who are concurrently receiving conventional treatments such as psychotropic medications and psychotherapy is driving a trend toward increasingly integrative mental health care in North America, Europe, Australia, and other world regions. Findings of a survey published by the Bravewell Collaborative[50] support that integrative treatment strategies incorporating pharmaceuticals and evidence-based CAM therapies are often beneficial for common medical and psychiatric disorders, and this survey highlights depressed mood and anxiety as among the top 5 health concerns for which CAM and integrative approaches are most beneficial.

Although it is estimated that more than 50% of all individuals with a diagnosis of mood or anxiety disorder use CAM therapies to manage their symptoms, few disclose CAM use to their psychiatrist, family physician, or other conventional health care practitioner.[51] To complicate matters, many widely used CAM therapies are supported by limited research evidence. Relatively few CAM therapies have been substantiated by consistent positive findings from large, well-designed, placebo-controlled studies. Furthermore, most CAM therapies are limited by incomplete knowledge of mechanisms of action, small study sizes, inconsistent research findings, and—in some cases—safety concerns. Patients who use nutraceuticals or other CAM therapies not supported by strong research place themselves at risk of disappointing outcomes or potentially serious safety problems[52] when such therapies are used in combination with pharmacologic agents.

Emerging Paradigms of Integrative Medicine and Integrative Mental Health Care

High prevalence rates and unmet treatment needs of patients with severe mental illnesses in both developed and less developed countries underscore the inadequacies of both conventional biomedical and CAM treatments and the limitations of current models of mental health care. These circumstances define an urgent agenda for developing more effective, safer, and more affordable integrative

treatment strategies incorporating evidence-based conventional biomedical and CAM modalities and establishing a more integrated model of mental health care delivery in which medical and mental health problems are addressed in a single clinic.

Increasing acceptance of CAM therapies in the US and other economically developed world regions is the result of scientific advances, social trends, and the availability of safe, affordable nonpharmacologic treatments.[42,44,47] Biomedicine is evolving in response to increasing openness to nonallopathic systems of medicine among conventionally trained physicians in the context of growing patient demands for a variety of treatment choices that are not presently included in the dominant model of mental health care, as well as more individualized health care.[21] The result has been the emergence of integrative medicine in response both to patients' needs, practitioners' changing perspectives, and the limitations of the current model of care. Integrative medicine affirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by research evidence, and goes beyond the limitations of biomedicine or CAM by incorporating diverse treatment approaches with the goals of achieving optimal wellness, preventing relapse, and improving outcomes.[53] Integrative mental health care is an important offshoot of integrative medicine that focuses on the whole person rather than a particular disorder. Like integrative medicine, integrative mental health care emphasizes wellness and healthy lifestyle choices while addressing the range of complex biological, psychological, cultural, economic, and spiritual or religious factors that affect general well-being and mental health. As such, integrative mental health care is an evidence-based, research-driven paradigm that acknowledges the legitimacy of conventional and CAM treatments and recommends specific treatment combinations supported by research findings. (For a more detailed discussion of the history, conceptual foundations, and methods of integrative mental health care, see the article by Lake et al.[54]) We believe that incorporating conventional and CAM therapies that are supported by robust research evidence into KP's existing integrated model of care will address the limitations of currently available treatments, improve outcomes, increase patient satisfaction, and reduce costs.

Need for a Broader Research Agenda in Psychiatry

In addition to the need for a broader range of treatment choices that is inclusive of evidence-based CAM therapies, psychiatry urgently needs a more eclectic research agenda that includes studies on promising CAM and integrative approaches using modern research methods. For decades, conventional psychiatric research has emphasized the development of novel pharmaceuticals and, to a much lesser extent, the role of psychotherapy. Although both treatment modalities are often effective in reducing suffering and disability associated with mental illness, both approaches are resource intensive. Broadening research priorities in psychiatry to include investigations of CAM and integrative approaches will help elucidate the multifactorial causes of psychiatric disorders at the level of social, cultural, psychological, and biological factors. It also will provide a framework for developing individualized treatment protocols addressing complex causes of symptoms on the basis of each unique patient's response to multimodal treatments. More affordable treatment approaches are also urgently needed. Recent studies have reported positive findings for a variety of nonresource-intensive CAM interventions, including the role of lifestyle changes on mental and emotional well-being, mind-body therapies, and select natural product supplements.[55]

As previously noted, a large percentage of patients with a diagnosed psychiatric disorder receive medications while concurrently using one or more CAM treatments. Recent research findings support that select natural products are safe and effective adjuvants when used in combination with antidepressants or other psychotropic medications.[56] Most studies on conventional biomedical treatments and CAM treatments employ randomized controlled trial designs that examine single interventions in artificial populations that are not representative of the diversity and complex medical and mental health problems of real-world populations. Few rigorously designed, well-powered studies have been done on more complex integrative approaches that combine multiple therapeutic modalities. Important advances will take place in psychiatric research and mental health care delivery when formal research methods are developed that permit rigorous evaluation of complicated patients receiving complex interventions involving multiple therapeutic modalities (which more accurately reflects how patients seek care) to treat real-world clinical populations.

Future clinical trials could examine individually tailored, multiple-component interventions using both quantitative outcome measures (eg, laboratory tests and validated psychometric scales) and qualitative measures (eg, subjective perceptions of improved functioning and placebo and nocebo effects). For example, a controlled trial on patients with diagnosed major depressive disorder could compare "treatment as usual" with a multimodal treatment protocol using a decision-tree algorithm employing specific combinations of evidence-based conventional and CAM modalities. A future research agenda that encompasses CAM treatment modalities will also help clarify the roles of genetic and biochemical individuality, ethnicity, family history, and culture in the pathogenesis of mental illness. Along these lines, Hoenders et al[57] recently reported the advantages of an innovative research method that uses single-subject time series analysis to examine dynamic real-time relationships between symptom and treatment variables and interactions between treatment modalities in a patient receiving integrative treatment for anxiety. Findings of this "N-of-1" study revealed complex interrelationships between the patient's symptoms and responses to treatment, positive feedback loops between lifestyle behaviors and outcomes, and differential effects of different treatment variables that would potentially have gone unnoticed in conventional group study designs. Future studies investigating CAM or integrative treatments would ideally use standardized forms of high-quality natural product supplements or other nonpharmacologic treatment approaches substantiated by strong data on both safety and efficacy. Other important future research areas should include

- investigating mechanisms of action of single CAM treatments or complex integrative protocols using advanced pharmacogenomic, epigenetic, and neuroimaging approaches

- studies of the impact of lifestyle modification (eg, diet, exercise, and stress management) on mental health aimed both at prevention and treatment
- studies of interactions between specific pharmaceuticals and CAM therapies aimed at elucidating potentially beneficial synergistic effects or potentially dangerous adverse effects as well as toxic or potentially unsafe interactions.

Cost-effectiveness Considerations

Findings from economic modeling research support that although treatment strategies that incorporate CAM and conventional biomedical treatment modalities may initially be costly, downstream savings can be achieved when such integrative strategies yield positive long-term outcomes.[58,59] Systematic reviews of economic modeling studies on comparative cost-effectiveness of conventional vs CAM or integrative treatments of many medical and psychiatric disorders support that CAM or integrative treatment is cost-effective and may result in cost savings in some cases.[60] It has been argued that higher upfront costs of CAM or integrative health care may be offset by improved work productivity and increased future quality adjusted life years.[59] In the same vein, a study done in Australia[61] estimated that switching depressed individuals from a conventional antidepressant to St John's wort (*Hypericum perforatum*) could result in a potential savings of AU$50 million per annum. The use of economic modeling to estimate cost-effectiveness differences between conventional biomedical treatments, CAM, and integrative treatment protocols warrants further exploration especially when comparing the equivalent efficacy of CAM treatments with conventional biomedical treatments. As noted earlier, collaborative care is more cost-effective than usual care in terms of medication costs and inpatient, outpatient, and mental health specialty care.[36] KP is strategically positioned to pursue research on cost-effectiveness in health care delivery that may lead to a more cost-effective collaborative model of mental health care.

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Developing Clinical Guidelines for Integrative Mental Health Care

The implementation of CAM and integrative approaches in clinical settings is highly varied and idiosyncratic, reflecting differences in personal values and perspectives of practitioners, and disparate goals and priorities of training programs and clinics or hospitals where integrative approaches are employed. Results of a survey of integrative clinics and training programs suggest that integrative medicine is evolving into a coherent set of values and a consistent model of care delivery and clinical therapeutics, as evidenced by an increase in the peer-reviewed journal literature and a trend toward increasing numbers of affiliations between integrative centers and hospitals, health care systems, and medical and nursing schools.[50] Integrative mental health care is a strongly collaborative enterprise that fosters cooperation among practitioners from disparate backgrounds and between patients and practitioners.

A 2012 survey of integrative centers found that integrative approaches are perceived as successful when used to treat both medical and mental health conditions.[50] Respondents identified consultative care as the most widely used model of integrative medicine in the US today. In this collaborative care model, integrative clinicians work closely with the patient's primary care physician to develop individualized treatment plans. The next most frequently used collaborative care model (in centers surveyed) is comprehensive care in which an expert clinician manages a specific medical condition throughout the course of treatment. Finally, increasing numbers of integrative centers are using a primary care model in which family medicine physicians, internal medicine physicians, and nurses collaborate to provide medical and mental health care as needed throughout the patient's life span. In all these models, a flexible patient-centered approach was perceived as a major strength of integrative medicine and mental health care compared with conventional models of care. In all collaborative care models, comprehensive clinical assessment of each patient was regarded as the crucial first step to ensure a valid diagnostic formulation. In all centers, surveyed treatment approaches were considered only after a thorough review of published research evidence supporting their use for a specific medical or psychiatric condition and taking into account risks of adverse effects, cost, and availability. It is important that 55% of survey respondents reported that depression and anxiety were successfully treated at their clinics using integrative therapies. Along these lines, Hoenders et al[62] have developed guidelines for integrative mental health care using algorithms to identify optimal treatment protocols for common psychiatric disorders. Future innovations in mental health care should incorporate evidence-based integrative protocols employing a flexible, patient-centered collaborative care model with the goal of more effectively and more cost-effectively addressing complex medical and psychiatric disorders that respond poorly to available conventional treatments and the usual model of care.

The clinical practice of integrative mental health care in the US and other developed countries will spread rapidly and evolve to a very high standard following the establishment of consensus-driven clinical guidelines. Such guidelines will provide a template for deriving safe, effective, and cost-effective assessment and treatment approaches on the basis of the best available research evidence on efficacy and safety for both conventional and CAM therapies.

Ideally, integrative guidelines should cover

- structure and content of a rigorous integrative clinical evaluation

- selection and interpretation of diagnostic modalities
- overarching treatment protocols that address efficacy, safety, and ethical concerns
- selection and prescription (or recommendations) of multimodal therapeutic interventions
- assessment of therapeutic efficacy using standardized outcome measures
- structure of the therapeutic relationship and appropriate follow-up.

Diagnostic formulations based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) do not provide an adequate framework when one approaches patient care from an integrative perspective; however, clinical practice guidelines based on DSM-V diagnostic categories provide a practical template for interdisciplinary collaboration in assessment and treatment planning. Clinical guidelines employing DSM-V categories and methods also provide a framework for developing economic models that can be used to evaluate the cost-effectiveness of specific integrative approaches.

Need for Integrative Training Programs for Mental Health Care Practitioners

In the US and other developed countries, there are essentially two parallel systems of education as well as clinical care: 1) conventional training programs in psychiatry and the allied mental health fields and 2) CAM-related training programs in naturopathy, herbal medicine, and traditional Chinese medicine. Conventional allopathic medical training programs—including psychiatry residency training programs and MA or PhD psychology programs—include limited coverage of CAM or integrative approaches outlined in this article. Similarly, most CAM training programs offer limited or no opportunities for education, training, and research in the basic sciences, including biochemistry, psychology, pathophysiology, pharmacology, and neuroanatomy (except for naturopathic medicine, which provides rigorous education in these areas). Successful implementation of interdisciplinary education and training programs needed to foster competent integrative clinicians will require a high level of cooperation between academic centers, professional societies, and clinicians across disciplines. The successful implementation of a residency program in integrative medicine has demonstrated that it is possible to develop a rigorous training program in integrative medicine and import it into traditional residency curricula on a large scale.[63] At the KP Oakland Medical Center in CA, planning is ongoing for a unique psychiatry residency training program that will emphasize integrative mental health care. In addition to residency and other postgraduate training programs, Web-based education will play an increasing role in the training of future integrative practitioners.

Given the diversity of factors driving the emerging field of integrative medicine and integrative mental health care as well as the broad range of interests and perspectives of postgraduate training programs in family medicine, psychiatry, psychology, and allied health fields, it is likely that disparate postgraduate training programs will emphasize different areas of specialization. After completing formal training, many family physicians and psychiatrists seek out continuing education and mentorship opportunities in areas such as mind-body medicine, including mindfulness-based stress reduction, pain medicine, palliative care, biofeedback, or hypnotherapy, whereas others procure training in acupuncture or in prescribing nutraceuticals. In the same way that conventional residency training programs in family medicine and psychiatry currently incorporate training in specialized clinical areas, we envision that residency training programs in family medicine and psychiatry will increasingly emphasize integrative mental health care by including validated CAM approaches in their curricula.

Advancing a Kaiser Permanente Agenda for Innovation in Mental Health Care

The alarming statistics reviewed in this article suggest that most people with mental illness in the US and globally probably receive inadequate care, and widely used conventional biomedical treatments and CAM treatments have limited efficacy against depression, bipolar disorder, schizophrenia, and other psychiatric disorders. Survey findings confirm that integrative mental health care using both conventional and CAM treatments is currently being practiced by many mental health professionals and pursued by our patients and the public at large.[21,50,53] However, as noted in this article, the implementation of collaborative models of care in primary care clinics is limited by the absence of consensus on research priorities and clinical practice guidelines, few residency training programs addressing CAM and integrative medicine, the paucity of reliable safety and efficacy information on many CAM and integrative modalities, and limited involvement of relevant government agencies in shaping health care policy reform. Together, these circumstances define an urgent agenda for KP and other health care delivery organizations to proactively address the limitations of the current model of mental health care delivery and conventional pharmacologic treatments of mental illness.

As previously described, given the philosophy of whole-person care that KP embodies, the tradition of translating research into clinical applications and operational improvements in care delivery, and the wealth of data available to our clinicians regarding the total health of the patient, KP is uniquely positioned to lead and innovate in the field of integrative medicine and to improve mental health care for the populations and communities we serve. Concentrating on areas where there are fewer mental health clinicians, such as rural or semi-rural service areas, while prioritizing the development of collaborative models of care in primary care clinics will permit KP to reach a larger population of patients in need. In this process, flexible and innovative technologies that allow for self-care and psychoeducation about illness will be crucial (psychoeducation is a term used to denote training in self-care for patients who are receiving mental health care).

CONCLUSION

Currently available conventional biomedical treatments, CAM treatments, and the dominant model of care used in the US and other world regions fail to adequately address the complex biological, social, cultural, and spiritual dimensions of mental illness. These circumstances define an urgent agenda for broadening the current paradigm of mental health care to include evidence-based

integrative treatments incorporating conventional and CAM modalities and implementing a collaborative care model on a large scale in primary care settings aimed at wellness, prevention, and treatment of specific psychiatric disorders. Accumulating research evidence supports that lifestyle modifications including changes in diet and exercise, mindfulness meditation and mind-body practices, and select natural products are beneficial, safe, and affordable interventions for many common mental health problems that can be safely combined with pharmacologic and psychotherapeutic interventions and can easily be incorporated into mainstream mental health models of care. In this article, we have argued that doing so will probably result in improved outcomes, enhanced patient satisfaction, and more cost-effective care over the long term.

Because of its strong research base and commitment to innovation, KP is positioned to transform mental health care. We offer this article as a work in progress to invite dialogue, debate, and consensus building among KP physicians and allied health care practitioners and administrators on novel collaborative models of care delivery, with the goal of achieving safer, more effective, and more cost-effective mental health care. We hope this article will guide future policy discussions within KP and stimulate internal research programs on promising CAM and integrative treatment approaches addressing mental illness in complex patient populations. A collaborative model of care incorporating conventional biomedical treatments and evidence-based CAM treatments will result in a broader range of choices addressing common psychiatric disorders while providing patients with practical, affordable resources for optimal wellness and relapse prevention. We believe that innovations taking place in KP will translate into improved mental health care in the US and potentially on a global level. Through KP's commitment to the communities we serve and to alleviating suffering for our members and those outside our walls, KP is illuminating a path forward in expanding mental health care for all global citizens. ❖

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Disorder

A mental disorder is a medical disorder.

— Spitzer RL, Klein DF, editors. *Critical Issues in Psychiatric Diagnosis*. New York, NY: Raven Press, 1978

Enchanted
photograph

Sapna Reddy, MD

Fog rolling through Yosemite Valley at sunrise.

Dr Reddy is a Radiologist at the Walnut Creek Medical Center in CA and is pursuing a dual career as a landscape/nature photographer. More of her work can be seen at www.sapnareddy.com.

Special Report

Minimizing Medical Radiation Exposure by Incorporating a New Radiation "Vital Sign" into the Electronic Medical Record: Quality of Care and Patient Safety

Jonathan Lukoff, MD, FAAP, FABPM; Jaime Olmos, ScD

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ABSTRACT

There is a clearly perceived and imminent need to decrease unnecessary and detrimental exposure to medical ionizing radiation. We propose a new radiation "vital sign" that incorporates cumulative radiation exposure to create a risk score on the basis of an individualized assessment of potential harm from additional exposure to medical radiation. We propose to then tie the risk score to real-time, evidence-based, clinical decision support for procedures that use ionizing radiation. Additionally, we offer recommendations that minimize unnecessary or low-yield uses. Preference is given to approaches and modalities that use less or no ionizing radiation and that are medically appropriate, acceptable to, and safer for patients.

INTRODUCTION

The risks of radiation are substantial and varied.[1] It is generally accepted that any exposure to radiation carries some risk. The most commonly accepted paradigm is the linear no-threshold model, which assumes that the long-term, biological damage caused by ionizing radiation is directly proportional to the dose.[2] Still, some experts believe that there is insufficient evidence of any carcinogenic risk at low levels (< 50 mSv) of ionizing radiation exposure.[3] Even if their hypothesis is correct, there are medical procedures and combinations of multiple procedures that exceed these postulated thresholds for risk.[4] Also, each individual and organ has a variable threshold susceptibility based on many factors, which we discuss in this article. The physicians' precept to "first do no harm" must presume that all radiation has the potential for adverse effects.

Glossary of Radiation Terms

Air kerma: Air kerma (kinetic energy released per unit mass) is of importance in the practical calibration of fluoroscopy instruments. It is used for the traceable calibration of gamma instrument metrology facilities using a "free air" ion chamber to measure air kerma. Conversion coefficients from air kerma in gray (one joule of energy in the form of ionizing radiation per kilogram of matter) to equivalent dose in sieverts (see *Sievert*) are published in the International Commission on Radiologic Protection (ICRP) report 74 from 1996 (www.icrp.org/publication.asp?id=ICRP Publication 74).

Effective dose: The International Commission on Radiological Protection adopted the term effective dose (ED). The ED is based on the energy deposited in biologic tissue by ionizing radiation. It takes into account the type of radiation and the sensitivity of the tissue exposed. The ED is a measure of overall whole-body radiation risk, which enables comparison of doses received in different tissues and organs of the body. It is measured in sievert units (see *Sievert*). Acute ED radiation of 250 mSv is known to cause immediate harmful biological effects. An acute dose of 3000 mSv will cause death to 50% of a population exposed within 30 days, and 100 mSv is statistically associated with an increased risk of cancer. Besides medical radiation, humans are regularly exposed to "background radiation" from natural sources. On average, a person in the US receives an ED of about 3 mSv per year from naturally occurring radioactive materials and cosmic radiation from outer space.

Sievert: The standard unit in the International System of Units (SI) of the equivalent dose of the biological effect of one joule of x-rays per kilogram of recipient mass.

Side effects of radiation include acute radiation sickness,[5] increased incidence of cancer,[1,2,6] ophthalmic damage,[7,8] chromosome aberrations,[9] birth defects,[5] immune system dysfunction, hematopoietic system disease,[1] gastrointestinal system disorders,[1] dermal injury,[10] nervous system damage,[1,5] growth retardation,[5] miscarriage,[5] organ and glandular injury,[11] premature menopause, stroke,[1] and cardiovascular disease.[1,12,13] (Irradiation induces a sustained vascular endothelial cell dysfunction. Such impairment is known to lead to occlusive artery disease and may be an important risk factor for cardiovascular diseases.[13]) The levels of radiation exposure that health care practitioners now order and administer can potentially induce any number of these adverse health effects.

Scope of the Problem

Sodickson and colleagues[14] studied a cohort of 31,462 patients at a tertiary medical center who underwent diagnostic computed tomography (CT) in 2007. They had undergone 190,712 CT examinations during the prior 22 years. One-third of patients underwent 5 or more CT studies during their lifetime, and 5% received 22 to 132 studies. Fifteen percent received an estimated cumulative effective dose (see Sidebar: Glossary of Radiation Terms) exceeding 100 mSv, with 4% of those receiving a cumulative effective dose between 250 and 1375 mSv. Doses in excess of 100 mSv are in the realm in which there is convincing epidemiologic evidence of increased cancer risk.

In 2010, the Food and Drug Administration's (FDA's) Center for Devices and Radiological Health launched an initiative to reduce unnecessary radiation exposure

Jonathan Lukoff, MD, FAAP, FABPM, is a retired Pediatrician and Informatician from the Southern California Permanente Medical Group and The Permanente Federation in CA. E-mail: lukoff.jy@gmail.com.
Jaime Olmos, ScD, is a retired Nuclear Engineer from the San Onofre Nuclear Generating Station in Pendleton, CA. E-mail: xaguarqft@gmail.com.

from medical imaging.[15] These efforts were in response to increasing exposure to ionizing radiation from medical imaging as highlighted in the National Council on Radiation Protection and Measurements Report No. 160[16] and safety concerns highlighted in the FDA's safety investigation on CT brain perfusion scans.[17] The FDA proposed the use of alternative diagnostic procedures, such as ultrasonography and magnetic resonance imaging (MRI), and reducing radiation exposure to medical imaging—limited examinations, dose optimization with adaptive statistical iterative reconstruction,[17] better collimation, protection of noninvolved or more highly susceptible anatomical areas, and medically acceptable delays (risks related to total dose exposure are time-interval dependent) including watchful waiting. Clearly, the medical community has been less than successful at implementing many of these concepts to achieve the goal of minimal but necessary medical radiation exposure.[14,18] For example:

1. Protocols are not always followed[19]
2. Not all equipment is state of the art or optimized[14,20]
3. Alternative investigative means may not be available or used[21]
4. Testing may simply be unnecessary in up to one-third of CT scans.[20]

Berrington de González et al[22] calculated that: "When we combined the age- and sex-specific annual frequencies with the estimated risk per 10,000 scans, it was estimated that, overall, approximately 29,000 (95% [upper limit], 15,000-45,000) future cancers could be related to the number of CT scans performed in the US in 2007."

The 29,000 future cancers were estimated using the specific distribution of CT scans done in the US in 2007. Because the number of diagnostic CT scans has been increasing at a rate of 6.5% per year (estimates are that 62 million CT scans were performed in 2006[6] and 85 million in 2011[23]), we could easily double those projections by now. According to the International Commission on Radiological Protection, an independent international organization with the mission to help prevent cancer and other diseases and the effects associated with exposure to ionizing radiation,[24] almost 1 in 4 persons have had a recent CT test or nuclear medicine procedure, and the use of CT now accounts for at least 50% of the collective dose from all imaging procedures. Prolonged fluoroscopic examinations (often those with other procedures) can expose patients to particularly high doses of radiation.

Efforts to Limit Radiation Exposure

Given these data and projections, it is critical that the medical community develop more effective methods to limit medical ionizing radiation procedures to medically indicated situations, and only when alternative, safer approaches will not suffice. Current concepts to achieve this include the following: Education for all stakeholders in the principles of radiation safety, appropriate utilization of imaging to minimize any associated radiation risk, standardization of radiation dose data to be archived during imaging for its ultimate use in benchmarking good practice, and the identification of alternative imaging of patients who may have reached or potentially will reach threshold levels of estimated exposure from diagnostic imaging. These concepts, important as they are, have been repeatedly recommended in scientific articles for many years, yet they have not been successfully implemented on a large scale.

In 2007, the American College of Radiology (ACR) created a white paper[25] stating: "There is increasing international and federal interest in, and scrutiny of, radiation dose from imaging procedures. Although there has been recent widespread interest in patient safety issues, the possible hazards associated with radiation exposure generally have not been brought into clear focus by the public or members of the medical community other than radiologists." They proposed accreditation programs, practice guidelines and technical standards, Appropriateness Criteria, a dose index registry, and educational programs. Routine reviews of patients were recommended, as were detailed imaging histories to alert radiologists that such alternatives should be considered. They charged technologists with the responsibility for determining the need for additional radiation safety actions before instituting radiation exposure. This included identification of high-risk patients and body parts, individualized shielding, more focused collimation, and lower-dose examinations. The ACR concluded that although the benefits of diagnostic imaging are immense, the rapid growth of CT and nuclear medicine studies since the early 1990s could result in an increased incidence of radiation-related cancer. The ACR went on to propose standardizing and archiving radiation dose data for use in benchmarking best practices, with the goals of identifying threshold levels of estimated exposure from diagnostic imaging and proposing alternative imaging for these patients. The College did not, however, create a method to actualize its proposals. We are proposing a method to take these proposals and implement them on a large scale.

Sodickson et al[14] identified methods to reduce the dose of each examination, including technical developments (eg, automated tube current modulation, beam filtration, and adaptive collimation), imaging parameter selection (decreasing tube potential, tube current, or both), protocol modifications (reducing duplicate coverage regions and multiple-pass scanning), and utilization of standardized reference dose levels. Measures to reduce CT utilization include adoption of broadly applicable imaging algorithms and recommendations

Conservative Prescribing of Radiologic Procedures[26]

1. Think beyond studies that use ionizing radiation.
2. Practice more strategic ordering. Use evidence-based protocols/decision support/best practices. Order sets or forced functions can increase compliance. Built-in suggestions for alternative nonradiologic approaches can add to success. Involve radiologists in the decision tree. Ensure necessity of the imaging study.
3. Maintain heightened vigilance/concern regarding adverse effects.
4. Approach new indications for x-rays cautiously and skeptically.
5. Work with patients for a more deliberative shared agenda.
6. Consider longer-term broader effects (benefits vs risks), with ionizing radiation as a known adverse event.
7. Keep up to date by maintaining your continuing education and regularly updating your protocols with minimization of medical radiation exposure as a stated goal.

to use nonionizing imaging alternatives or no imaging at all. In addition, Sodickson et al[14] identified the requirement to include cumulative radiation exposure to accurately evaluate a patient's risk owing to further diagnostic radiation procedures. They also suggested using real-time clinical decision support. Their proposals presage our ideas recommending a radiation "vital sign" that is based on an individual's cumulative radiation exposure modified by his or her specific radiation-related risk factors and tied to real-time clinical decision support.

Schiff and coworkers[26] developed principles of conservative prescribing, which we have conceptually adapted to radiologic procedures, while adding a proposed seventh principle (see Sidebar: Conservative Prescribing of Radiologic Procedures).

Chassin et al[27] proposed relevant criteria for accountability measures in the process of medical care. Wachter[28] added accountability measures to those of Chassin and colleagues (see Sidebar: Accountability Measures) but noted that feedback leads only to modest change. Transparency ("disseminating the results of quality measures to key stakeholders") is the new norm. Chassin et al also discussed how to improve the quality of care.

We propose to systematically investigate ways to minimize exposure to ionizing radiation while maintaining high-quality medical care (see Sidebar: Minimization of Radiologic Imaging Exposure).

Each patient's full medical record and all medical procedures (completed and ordered) should be available digitally at any time on demand. The technologies available to process electronic medical records (EMRs), transmissions, and coding include: Health Level Seven (HL-7), the standardized protocols for clinical information and administrative data transfers; Digital Imaging and Communications in Medicine (DICOM), a document architecture for exchanging radiologic information and imaging; Current Procedural Terminology (CPT) and International Classification of Diseases (ICD) codes; and Systematized Nomenclature of Medicine (SNOMED), a subtype hierarchy of medical terms supported by defining relationships on the basis of description logic.

The DICOM-Structured Reporting (DICOM-SR)[29] standard is an approach that allows for structured medical imaging data to be electronically transmitted and integrated into HL-7 and thereby into EMRs. These digital standards enable advanced chart-based functions that search the record for patient exposure and the data for patient risk profiles, and allow for the insertion of advice. As Wachter[28] states in his pioneering book, *Understanding Patient Safety,* "innovative methods for screening caregiver notes, lab results and medication orders … will generate new and useful information. More and more of the work will involve real-time surveillance systems, with automatic 'just-in-time' feedback …" or, in other words, "real-time clinical decision support."

Our Proposal: A Method to Achieve Excellence in Radiation Ordering

We propose to harness the power of EMRs that use formats such as the DICOM-SR for radiation dose events and HL-7 so that we can create effective clinician and patient awareness of each patient's cumulative radiation dose, anticipate future exposures for patients with chronic diseases, and assess individualized risk from proposed exposure. Real-time clinical decision support will offer advice on alternative approaches. To accomplish this, we propose a new method: The radiation "vital sign" that is a risk score. The radiation vital sign will document all previous exposures to ionized radiation and create an individualized risk-specific assessment on the basis of the factors we discuss later in this article. Ideally, the radiation vital sign will be linked to clinical decision support that proposes medically appropriate and validated approaches based on evidence-based clinical practice guidelines[30] for each medical procedure that exposes a patient to ionizing radiation. Certain symptoms or diagnoses (especially chronic diseases) will trigger likelihood cascades to prevent accumulated radiation risks.

Not all known risks of radiation are well quantified or even identified. This field of study has the potential to advance with artificial intelligence (AI) or machine learning. Newer designs for "deep" learning (eg, the IBM Watson computing system AI combined with sophisticated analytic software and brute force computing power,[31] and Google's probabilistic neural networks,[32] in which AI grows from the data rather than from the rules) look promising to advance personalized medicine. Describing Google's networks, Lewis-Krauss[32] writes: "The simplest description of a neural network is that it's a machine that makes classifications or predictions based on its ability to discover

Accountability Measures[27,28]

1. There is strong evidence that the care process improves outcomes.
2. Documentation exists that the evidence-based care process has been provided.
3. The measurement is fairly direct.
4. There are no unintended consequences.
5. Improvement in medical care is promoted and supported.

Minimization of Radiologic Imaging Exposure

1. Ordered radiologic examinations are justified by evidence-based medicine, and nonradiologic alternatives are considered and strongly encouraged. The Agency for Heathcare Research and Quality's national guideline clearinghouse is a public resource for summaries of evidence-based clinical practice guidelines that would be an excellent starting point.[27]
2. Radiation exposures are minimized by well-accepted radiologic standards for exposure during each specific examination, and preference is given for nonradiologic approaches.
3. Radiation exposure from each ordered examination is clearly documented during the ordering process and considered in light of the documented cumulative radiation exposure. This is presented to the clinician as a new radiation "vital sign."
4. Each patient is uniquely considered for his/her risk of exposure to radiation, accounting for his/her age; medical, genetic, and family history (precision medicine); and previous cumulative radiation exposure.
5. A risk profile is developed to assess the individual risk for each level of new exposure, which is clearly documented with each examination ordered. Alternative strategies are increasingly forcefully recommended as the risk level or potential risks are increased.

patterns in data. With one layer, you could find only simple patterns; with more than one, you could look for patterns of patterns."

Automated repetitive systems such as what we propose have been shown to be far more effective than other measures to induce and maintain change.[33] Existing strategies to decrease medical radiation exposure have fallen short on a national level. Adding a radiation vital sign to the EMR—a personal risk assessment tied to evidence-based, patient-specific advice—will be far more likely to create an effective routine[34,35] that will decrease exposure to ionizing radiation. It can be time-consuming and problematic for clinicians to deal with warnings and computer-generated alternatives. However, incorporation of accepted medical imaging protocols based on patient history, symptoms, and/or diagnoses, or based on tests ordered (appropriate indications/risk-benefit analysis) would ensure that clinicians have the latest guidelines at their fingertips and that they evaluate patient safety whenever ordering medical ionizing radiation exposure. This would require a major effort to create buy-in because it causes delays, but clinical decision support provided contemporaneously with clinical decision making is achievable and often becomes invaluable.[33-37]

The National Research Council's Biological Effects of Ionizing Radiation VII (BEIR VII) *Health Risks from Exposure to Low Levels of Ionizing Radiation*[1] report in 2006 planned to do the following:

> 1) [D]evelop appropriate risk models for all cancer sites and other outcomes for which there are adequate data to support a quantitative estimate of risk, including benign disease and genetic effects; 2) provide examples of specific risk calculations based on the models and explain the appropriate use of the risk models; 3) describe and define the limitations and uncertainties of the risk models and their results; 4) discuss the role and effect of modifying factors, including host (such as individual susceptibility and variability, age, and sex), environment (such as altitude and ultraviolet radiation), and lifestyle (such as smoking history and alcohol consumption) factors; and 5) identify critical gaps in knowledge that should be filled by future research.

Thus, medical exposure to ionizing radiation should be tracked and monitored.

Tracking the radiation dose delivered to patients for medical purposes is gathering increasing attention from professional societies and regulatory groups. Publications include European directive Euratom 97/43,[38] the ACR dose white paper,[25] and Japanese regulations.[39] Ideally, we will be able to accomplish the patient-specific and quality of care measures of radiation exposure elucidated in the Sidebar: Radiation Exposure Tracking Guidelines.[40]

Although standards exist, such dose tracking has not been widely deployed because of the following:

- difficulty coordinating the roles of the different equipment involved (which actors should do what)
- difficulty coordinating tracking across multiple departments and multiple institutions
- the need to converge on one of the available standard approaches.

In our review of the literature, we found that many approaches have seen some success at decreasing medical ionizing radiation exposure. We have used these in the formulation of our proposal with the hope that their ideas and localized efforts can be broadened to the entire medical community. Patients with chronic medical conditions are at increased risk of radiation overexposure.[41] Lin[3] reviewed the risks of medical imaging and encouraged clinicians to play a role in prevention by referring their patients only to facilities that used reduced exposure methods as well as by ordering fewer tests, noting that "all imaging tests, particularly those with potential patient harm, be performed only when indicated." He also reviewed methods and equipment by which radiologists could decrease radiation doses.

Some authors have focused on radiation exposure in patients with specific medical conditions. Smookler et al[42] wrote: "Clinicians should recognize that increased radiation exposure puts patients with spina bifida and hydrocephalus at higher risk for cancer. The population of children and adults with spina bifida and hydrocephalus should be surveyed for incidence of cancer." Smookler has, since 2009, been involved in a successful program to decrease medical radiation exposure in patients with spina bifida by increasing awareness of the substantial imaging radiation exposure by head CT at his institution and in his subspecialty, and by including the radiation dose as part of the radiologist's report while encouraging a switch to First post-contrast Acquisition SubTracted (FAST) MRI (Gregory L Smookler, MD; personal communication, 2016 Aug 22).[a] However, some studies have found that evidence-based change is less effective in the long run than clinical decision support.[43]

Massachusetts General Hospital[44] achieved significantly decreased exposure, reducing its dose levels for CT examinations by 30% to 95% over National Council on Radiation Protection reference levels. The hospital customized its CT examinations for each patient on the basis of multiple factors, including weight, age, and history. Techniques to minimize radiation exposure included employing radiation-free alternatives such as ultrasonography and MRI. Massachusetts General Hospital actively maintains its equipment to ensure patient safety and takes advantage of technology advances by upgrading and replacing equipment expeditiously. Minimizing radiation exposure for all patients is a key guideline, especially for children. Multiple safeguards were put in place to prevent accidental exposure, and hospital personnel committed to continually strive to improve the protocols that govern each type of scan, with the goal of exposing patients to less radiation while obtaining not the best images but, rather, those of sufficient quality for accurate diagnoses.

Radiation Exposure Tracking Guidelines[40]

1. View a patient's history of cumulative radiation exposure.
2. View the organ-specific dose that a patient received from each previous examination.
3. Determine whether a given patient dose exceeds the maximum guidelines or is otherwise an outlier requiring investigation and action.
4. Compute the population "dose profile" for a certain hospital or region.
5. Compute the population dose profile for a certain disease.
6. Compare dose profiles against other sites/regions, local policy targets, or standards of practice.

Table 1. Risk ranking of radiation vital sign

Rank	Risk
1	very low significance
2	low significance
3	significant
4	high significance
5	very high significance[a]

[a] Patients with elevated likelihood of excessive exposure because of chronic medical conditions may be preventively given a high score.

Fetterly et al[45] introduced a philosophy of radiation safety that they successfully implemented through a collection of sustained practice and x-ray system changes for invasive cardiovascular procedures. These led to a significant 40% decrease in the radiation dose administered to patients. These practices included the following: "intra procedure radiation dose announcements; reporting of procedures for which the air-kerma exceeded 6000 mGy, including procedure air-kerma in the clinical report; and establishing compulsory radiation safety training for fellows. Technical changes included establishing standard x-ray imaging protocols, increased use of x-ray beam spectral filters, reducing the detector target dose for fluoroscopy and acquisition imaging, and reducing the fluoroscopy frame rate to 7.5 per sec."[45] (For an explanation of air kerma, see Sidebar: Glossary of Radiation Terms.)

The FDA recommends that criteria be developed and implemented to use radiologic procedures appropriately.[14] The FDA recommendations include advising the health care professional community to develop and adopt criteria for appropriate use of CT, fluoroscopy, nuclear medicine, and other procedures that use these techniques. Building on the efforts of various professional organizations, including the ACR and the American College of Cardiology, the FDA recommends that the health care professional community continue to develop and adopt appropriate use criteria for CT, fluoroscopy, and nuclear medicine procedures. In addition, the FDA encourages incorporation of electronic decision support tools for ordering imaging procedures to improve quality and consistency in clinical decision making.

From the professional experience of one of the authors (JL), some examples come to mind. The diagnosis of pneumonia rarely needs a CT scan; a plain film will do.[46] Few neonates need a routine daily chest x-ray film. Not every patient receiving high-frequency ventilation needs a chest x-ray to be obtained every four hours as is often the standard of care. Not every patient seeing an orthopedic surgeon needs a radiograph before his or her clinical examination. These routines, and many more, must be reexamined and reimagined.

Vital signs are measures of the status of the body's life-sustaining functions. There are four main vital signs: body temperature, blood pressure, pulse (heart rate), and breathing rate.[47] Additional vital signs have been proposed and used. A "fifth" vital sign may refer to a few different parameters. Pain is considered a standard fifth vital sign in some organizations such as the US Department of Veterans Affairs.[48] Other suggested fifth vital signs include menstrual cycle,[49] Glasgow Coma Scale,[50] pulse oximetry,[51] and others. Tysinger[52] identified that increased patient complexity in health care has led to greater efforts to identify early deterioration and adverse events. Key components of these efforts include timely vital sign collection and review as an early warning system. Tysinger notes that vital signs are intended to anticipate and prevent adverse outcomes.[52]

Radiation Vital Sign Risk Factors

1. patient's age
2. gestation of pregnancy
3. genetics
4. patient's sex
5. body mass index
6. smoking status and history
7. medical history, especially chronic disorders, with prematurity and malignancy included, creating an at-risk category (renal and cardiovascular disorders may also put patients at risk of excessive exposure)

8a. cumulative exposure
8b. time intervals between exposures (time intervals decrease at least some risks of exposure)

9. proposed imaging exposure
10. occupational and dwelling (radon) exposure[14]
11. specific organ exposure[21]
12. alcohol consumption

On the basis of that premise, it is our opinion that the traditional measures of a person's vital signs can be expanded to include a radiation "vital sign" that measures the risk from a patient's past and potential radiation exposure.

PROPOSED RADIATION VITAL SIGN

Our proposal for a new and universal radiation vital sign is intended to create clinician awareness of each patient's risk (an early warning system) owing to one's cumulative radiation exposure assessed relative to one's known sensitivity factors for harm from additional radiation exposure and, in conjunction with clinical decision support, offer medically appropriate alternatives. Each person's cumulative radiation exposure and known medical history will be combined to create the radiation vital sign.

The factors that are currently known to affect risk caused by radiation exposure are listed in the Sidebar: Radiation Vital Sign Risk Factors. Incorporation of these 12 radiation vital sign risk factors, and other risk factors as they may be identified, will require an extensive method involving acquisition and analysis of an ample patient radiation exposure and outcomes database, as well as use of sophisticated statistical analysis techniques. However, the initial scoring system could be based on the few well-studied risk parameters, including cumulative radiation exposure, patient age and pregnancy status, and the anticipatory medical history of chronic disorders that are known to engender repeated studies.

The radiation vital sign will be individualized and developed to dovetail with real-time clinical decision support to minimize radiation to "as low as reasonably achievable consistent with obtaining the required diagnostic information."[38]

We propose that the overall risk score for the radiation vital sign be ranked according to the categories listed in Table 1. The incorporation of the radiation vital sign's risk factors into an overall risk score will present several challenges. Most factors that contribute to the malignancy risks of radiation exposure have been identified, but nonmalignant side effects have not been well monitored or quantified. Although the risk of cancer is better studied, it still needs more in-depth study.

RADIATION VITAL SIGN RISK FACTORS

Several risk factors that are included in the radiation vital sign are discussed here as they pertain to the risk of cancer.

Cumulative Radiation Exposure

Wiest et al[53] reported that 30% of their patients in 2001 had more than 3 CT examinations mentioned in their medical histories, 7% had more than 5 examinations, and 4% had more than 9. They found that cumulative radiation exposure was sufficient to add, incrementally, to baseline cancer risk in their cohort. Although most patients accrue low radiation-induced cancer risks, a subgroup is at higher risk because of recurrent CT imaging. Although CT represents only 15% of imaging procedures, it accounts for approximately half of the collective medical radiation dose owing to the relatively high dose per examination and its frequent use.[3] This was corroborated by Sodickson et al.[14]

Patient's Age and Sex

Statkiewicz Sherer and colleagues,[54] using BEIR VII,[1] calculated that the same radiation dose in the first year of life for boys produces 3 or 4 times the cancer risk as radiation exposure between the ages of 20 and 50 years. They reported: "For girls the difference is six to eight times. For children in general, the risk is approximately three times." Studies of cancer in children after exposure in utero or in early life indicate that radiation-induced cancers can occur at low doses.[1] For example, the Oxford Survey of Childhood Cancer[55] found a 40% increase in the cancer rate among children up to age 15 years. This increase was detected at radiation doses ranging from 10 to 20 mSv.

Authors of a 2009 study performed in adults reported the following:[20p2083]

> *The corresponding [lifetime attributable risks] of cancer were also higher than typically reported and markedly variable by study type, patient, and hospital. For example, it is commonly reported that a CT scan may be associated with an increase in the risk of cancer of approximately 1 in 2000. Based on the highest effective dose we observed, a 20-year-old women [sic] who underwent a CT for [evaluation of] suspected pulmonary embolism, a CT coronary angiography or a multiphase abdomen and pelvis CT scan could have an associated increased risk of developing cancer of as high as 1 in 80. The risks declined substantially with age and were lower for men, so radiation-associated cancer risks are of particular concern for younger, female patients.*

Dwelling (Radon) Exposure and Smoking History

Approximately 157,400 people died of lung cancer (from all causes, including smoking and radon exposure) in the US in 1995.[56] Of the 95,400 men who died of lung cancer, about 95% were probably smokers at some point ("ever-smokers"); of the 62,000 women, approximately 90% were probably ever-smokers.[55] On the basis of 2 models, the BEIR VI committee[56] estimated that

> *… about 1 in 10 or 1 in 7 of all lung-cancer deaths—amounting to central estimates of about 15,400 or 21,800 per year in the United States—can be attributed to radon among ever-smokers and never smokers together. The number of radon-related lung-cancer deaths resulting from that analysis could be as low as 3,000 or as high as 33,000 each year. Most of the radon-related lungcancers occur among ever-smokers, and, because of synergism between smoking and radon, many of the cancers in ever-smokers could be prevented by either tobacco control or reduction of radon exposure. The committee's best estimate is that among the 11,000 lung-cancer deaths each year in never-smokers, 2,100 or 2,900, depending on the model used, are radon-related lung cancers.*

Clearly, if exposure to radon is synergistic with smoking in causing cancer, medical radiation exposure should be as well.

IMPLEMENTATION OF A RADIATION VITAL SIGN

We propose that this new life-sustaining radiation vital sign be viewed alongside all other vital signs documented in the medical chart. To increase visibility and awareness, the radiation vital sign could be color coded, highlighted, or scripted differently and could demarcate certain predetermined patient-appropriate limits. We propose that this new vital sign be tied in with automated warnings whenever additional radiologic studies are being ordered; evidence-based alternate strategies with the lowest medically appropriate radiation exposure possible will be proposed. A focus on high-dose procedures or frequently repeated procedures would be the traditional and most targeted approach. However, with this functionality built into the EMR, the radiation vital sign could easily encompass all patients and all ionizing radiation exposures.

CREATION OF A RADIATION VITAL SIGN RISK SCORE

Our proposed universal radiation vital sign uses the power of standards for EMRs to potentially allow us to enhance clinician awareness of radiation exposure and risk and to offer safer alternatives. The American Society of Radiologic Technologists created an online x-ray risk calculator (http://xrayrisk.com). This risk calculator is a progenitor to our concept, but it is limited to evaluating only the risk incurred for a proposed radiation study. The only risk factors it takes into account are the patient's age and sex. The calculator is therefore severely limited because it does not include the dose accumulated by a patient from previous tests or other known risk factors. However, it does offer a stepping-stone to actualizing our concept.

Although we have identified the known important factors necessary to perform an accurate risk evaluation, the design and implementation of a vital sign risk score is beyond the scope of this article. Creation of a radiation vital sign risk score will entail a major effort involving statistical quantification of the known contributing factors, programming to allow retrieval of necessary information from the EMR, and population of the EMR with the score. Real-time clinical decision support will require a similar effort.

All medical procedures (and treatments) must be "appropriate."[57]

The risk of ionizing radiation must be balanced against the benefits of any examination ordered. There are many clear and undisputed benefits to modern radiologic examinations, and there has been an explosion in the use of these tests.[58] Many authors have argued that they are now frequently overused.[19,59] According to Brenner et al,[6] "if it is true that about one third of all CT scans are not justified by medical need, and

it appears to be likely, perhaps 20 million adults and, crucially, more than 1 million children per year in the United States are being irradiated unnecessarily."

Our goal is to create an implementable method that maximizes appropriate use of procedures that expose patients to ionizing radiation by informing patients and clinicians of their individualized risk profile. We aim to accomplish this via a radiation vital sign tied into clinical decision support that attempts to provide optimal medical care with the minimal additional risk clinically acceptable. This can be accomplished through minimizing unnecessary or low-yield exposures to ionizing radiation by looking to all other modalities and approaches that would utilize less or no ionizing radiation as long as the results are medically acceptable and patient approved.

… with this functionality built into the EMR, the radiation vital sign could easily encompass all patients and all ionizing radiation exposures.

DISCUSSION

We have documented that radiation exposure is known to cause cancer and a variety of other medical maladies. We also documented that current medical diagnostic testing exposes patients to sufficient quantities of radiation to be of concern for iatrogenic side effects. We reviewed the literature that shows our concerns have been extensively documented and that recommendations to decrease use of medical ionizing radiation have been promulgated, with limited local successes but little effect nationally, while documenting the unrelenting increased use of radiologic testing. Yet, we also argue that alternative, safer, and medically useful approaches are available and would result in a 20% to 50% decrease in medical radiologic testing. This could potentially avert 20,000 to 50,000 induced cancers per year as well as other radiation-induced side effects.

We therefore have proposed a new method to implement the accepted advice to decrease use of medical ionizing radiation exposure, especially to CT, positron emission tomography, and fluoroscopy. Our proposed new radiation vital sign could be an effective safety measure to reduce medical ionizing radiation usage. It will document each patient's individual risk-adjusted score for potential radiation damage on the basis of previous cumulative exposure to ionizing radiation and likely additional exposure, modified by an individualized risk assessment based on our current understanding of quantifiable risks.

We propose anticipatory guidance for patients who are identified as high risk (pregnant, premature) or likely to require repeated examinations because of their medical diagnoses (hydrocephalus, spina bifida, cancer, renal disorders, etc). This information will then be factored against any proposed new exposure to medical ionizing radiation in the context of state-of-the-art computerized medical decision making and advanced AI. Alternative approaches to testing include watchful waiting, repeated clinical examinations, MRI, ultrasound, elastography, reduced-exposure radiologic examinations, and even exploratory surgery.

All tests should potentially improve patient care more than they create risks for the individual. We propose that there be a new paradigm that values exposing patients to less ionizing radiation and commits to 24-hour availability of FAST MRIs (with anesthesia as needed) and high-resolution ultrasound. Our old paradigm rationed imaging technologies that are non-radiologic more than CT scans because of cost, time, and detail without regard to necessity of that detail or risk of exposure to ionizing radiation.

CONCLUSION

To accomplish our goals, it will be necessary to improve our measurements of patients' radiation exposure from radiologic procedures; we need accurate standardized measurements to assess and communicate risk. We must then integrate those measurements and relevant patient data into a risk assessment that can be used to generate our new radiation vital sign. That radiation vital sign will then initiate a computer-generated, patient-specific, best practice/minimalist exposure set of recommendations to present to clinicians and patients. ❖

[a] Clinical Assistant Professor of Pediatrics; University of Southern California Keck School of Medicine and Children's Hospital, Los Angeles, CA.

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Mabel Dodge Luhan's House
photograph

Usha Tatini, MD

This image of the historic Mabel Dodge Luhan house was taken during the annual Taos Writing and Wellness Retreat for Health Professionals in New Mexico.

Dr Tatini is Medical Director at An Oasis of Healing in Mesa, AZ.

Painted Windows
photograph

April M Day, MD

Painted by DH Lawrence, these bathroom windows at the historic Mabel Dodge Luhan house in Taos, NM, provide both privacy and whimsy.

Dr Day is a Physician at the Baylor Scott & White Medical Center in Garland, TX.

Special Report

Perspective on Publishing Quality Improvement Efforts

Michael Kanter, MD; Patrick T Courneya, MD

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ABSTRACT

Quality improvement (QI) activities are critical to achieve the Triple Aim and to the Institute of Medicine's six "Aims for Quality Improvement": Safe, Effective, Patient-Centered, Timely, Efficient, and Equitable. These QI activities are essential to create a learning health care system. Academic publishing is critical to foster continuous QI and sharing, and yet it tends to favor more traditional research articles. Publishing QI activities has great value, encourages greater rigor, and helps facilitate greater willingness to share improvement opportunities.

Quality improvement (QI) activities are critical to achieve the Triple Aim and to the Institute of Medicine's six "Aims for Quality Improvement": Safe, Effective, Timely, Patient-Centered, Efficient, and Equitable.[1] These QI activities are essential to create a learning health care system,[2] yet it is highly inefficient for each health care system to learn on its own without being informed by the experience of others. Academic publishing is critical to foster continuous QI and sharing. Although fields such as applied research and delivery science are emerging areas of inquiry, there is still a paucity of journals that publish QI activities and instead favor the more traditional research articles.

A challenge to those wanting to learn from prior quality efforts is getting good information about what was tried and what were the outcomes. Kaiser Permanente (KP) has a long history of discussing quality and performance improvement in national forums, first through Total Quality Management conferences, and since 2003, in what we currently know as the KP National Quality Conference. These meetings have always been designed with the intent to spread successful practices and learnings. Although successful, these meetings leave no permanent record of what was presented. Furthermore, quality leaders who cannot attend the meetings don't have an easy way to access the learnings and don't have a good way to assess the evidence behind the QI activities.

Often QI activities are undertaken in a Medical Center. After some evaluation is done, an attempt is made to spread the results through word of mouth using physician "champions" or other engaged clinicians. Then we wonder why best practices spread slowly. When looking at whether a QI project might be suitable for spread, one should critically examine the methodology. QI projects may be highly context dependent[3] and thus not readily transferable. Because these occur outside of an experimental setting, there is a high risk of bias as compared with research studies.[4] Because spread of a QI study may incur costs and command some organizational attention, one should be aware of how a QI project has been evaluated.[5] Because randomization is usually not practical, QI studies may be conducted using a before-after design, time series, or stepped wedge design with greater potential for bias in the first and least in the latter.[6] In some cases statistical adjustments may control for confounding variables in observational studies.[7] Additional attention should be paid to data quality, whether the correct unit of analysis was used, and was followed-up long enough.[7]

Given the above, it behooves organizations that sponsor quality meetings to attempt to have presentations that describe the rigor of their studies and to encourage eventual publication. In trying to think through ways to better spread quality learnings, we enlisted *The Permanente Journal* to publish the abstracts of presentations from the KP National Quality Conference. There are many benefits to publishing these abstracts including 1) creating a permanent record of the quality projects, 2) forming a means of communicating both positive and negative outcomes from QI activities, 3) promoting more scientific rigor in designing and presenting QI activities, and 4) providing additional motivation for quality projects to be written and presented. Ideally, after going through the process of creating an abstract of publishable quality, authors would be encouraged to subsequently submit their work for publication in a peer-reviewed journal such as *The Permanente Journal*.

The 2017 KP National Quality Conference centered around the Institute of Medicine's "Six Aims for Quality Improvement," which our organization has adopted as our National Clinical Quality Strategy. In the spirit of continual improvement and striving to achieve these aims in everything we do, we hope that publishing the abstracts from this conference will encourage greater rigor and help facilitate greater willingness to share improvement opportunities both within and outside our organization. Perhaps this will also open the door to more academic publishing of QI projects. There is great value to learning from each other's improvement attempts—even those that do not achieve their intended outcomes or do not stick. ❖

Disclosure Statement

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Michael Kanter, MD, is the Executive Vice President and Chief Quality Officer of The Permanente Federation in Oakland, CA. E-mail: michael.h.kanter@kp.org. **Patrick T Courneya, MD,** is the former Health Plan Medical Director for HealthPartners in Minneapolis, MN. He is the current Executive Vice President and Chief Medical Officer for National Health Plan and Hospitals Quality at Kaiser Permanente in Oakland, CA. E-mail: patrick.t.courneya@kp.org.

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Abstracts from the Kaiser Permanente 2017 National Quality Conference

Abstract by discipline	
Discipline	**Abstract #**
Cardiology	2, 16
Care Management Institute	24
Emergency Medicine	20, 13
Head and Neck Surgery	17
Infectious Disease	6, 12, 18
Nephrology	2, 16
Neurology	20
OB/Gyn	4
Oncology	25
Orthopedics	23
Pain Management	15
Palliative care	25
Pediatrics	17
Pharmacy	17, 19
Primary Care	7, 8, 10, 14
Unit-Based Teams	21, 22
Urgent Care	13

Abstracts by conditions studied	
Condition	**Abstract #**
Chronic pain	15
Depression	8
Diabetes	1, 10, 14
Domestic violence	4
End-stage renal disease	17
Hepatitis C	12
Heart disease	20
Hospital-acquired pneumonia	18
Infections	6
Obesity	1, 23
Osteoarthritis	23
Stroke	16
Tonsillitis	17

BEHAVIORAL HEALTH AND WELL-BEING

From Northern California

1. Health Achieved Through Lifestyle Transformation (HALT): The Power of Lifestyle to Reverse Chronic Disease

Rajiv Misquitta, MD, FACP; Rachel Kitazono, PsyD; Lisa Edwards, RD, MBA

DOI: https://doi.org/10.7812/TPP/17-140-01

Objective: To assess the effectiveness of a multidisciplinary lifestyle program on improving health metrics related to heart disease and diabetes using existing resources at Kaiser Permanente South Sacramento.

Design: We sought out patients with diabetes or coronary artery disease for participation. Patients initially engaged in an 8-week lifestyle program that focused on a low-fat, whole-foods, plant-based diet; exercise; and stress reduction. The program was later expanded to a 20-week evidence-based behavioral change program along with weekly follow-up classes. This program was led by a physician. Health educators taught the classes with psychologist support. Cooking demonstrations were included in the classes. We surveyed outcomes from 4 cohorts of patients.

Main Outcome Measures: We collected data from the electronic medical record on weight, lipids, blood pressure, diabetes control (hemoglobin A_{1c} [HbA_{1c}]) and exercise. We also collected survey data on dietary compliance using a food frequency survey and mental health measures using the short form (SF-20) survey.

Results: Program attendance in all 4 cohorts ranged from 78% to 92%. Average minimum weight loss at 6 months was approximately 16 lbs. For cohort 1, average weight loss at 1 year was 24 lbs. In all cohorts, there was a trend towards reduction in blood pressure, low-density lipoprotein cholesterol, HbA_{1c}, role functioning, body pain, health perceptions, physical functioning, and reduction of medications for diabetes. Spousal participation in the program was a predictor of success. Three patients fully reversed their diabetes.

Conclusion: This is an example of a successful, multidisciplinary program focused on behavior modification that has the potential to reduce medication costs, improve quality metrics for heart disease and diabetes, and reduce obesity and associated sequelae. HALT uses existing resources that are readily available. We have demonstrated the reversal of diabetes in some patients, a feat that cannot be done with medications.

From Northern California and the Care Management Institute

2. Incorporating Life Care Planning into Specialty Care Populations

Matthew Handley, MD; Melissa Stern, MBA

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Though most people say they are willing to discuss end of life and agree that documenting their wishes is important, only a very small number actually do. When the process is done well, it has the power to produce a written plan that accurately represents the individual's preferences and thoroughly prepares others to make health care decisions consistent with these preferences. Life Care Planning is a National Quality Initiative driven by the six aims to deliver care that is patient-centered, effective, efficient, equitable, timely, and safe. It is currently being implemented in five Regions with a sixth to begin before year-end. This presentation describes an evidenced-based approach for ensuring that patients facing a life-threatening illness align the care given to their personal values and wishes and demonstrates how to integrate the methodology into "normal routine" care within the Nephrology and Cardiology specialties, which serve as examples of how it may be applied to any specialty. Making these decisions is difficult and the implications for not making them can have significant impact on patients, their families, and practitioners. This evidenced-based approach ensures patients are supported and guided in an unbiased and nonjudgmental way.

From Program Offices and Southern California

3. Cultural Medicine: Speaking Up at Kaiser Permanente

Grace Balbuena; Vanessa Benavides, JD; Quristin Coleman; Kathy Gerwig; Linda Leavell, RN, PhD

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Introduction: A "speaking-up" environment is one in which people feel valued and respected, have a say in their jobs, are comfortable voicing opinions, can speak up about problems, and action is taken on their input. When people speak up, we learn about issues and hazards as well as opportunities to innovate and improve.

Methods: Analysis of the 2014 through 2016 People Pulse results identified correlations between speaking up and business outcomes. Practices that correlate to improved speaking up were also identified through People Pulse, focus groups of employees, and interviews with managers.

Results: Departments that score well on the People Pulse Speaking Up Index have 58% fewer workplace safety injuries, 41% fewer lost work days, and 14% lower patient mortality rates. But the Index shows that a speaking-up environment is not fully present across Kaiser Permanente. We score 9% below "best-in-class" benchmarks. Barriers to speaking up include: Lack of management follow through on ideas or concerns, fear of retaliation, exclusion behaviors, and lack of trust.

Discussion: A proven practice for improving speaking-up environments is Direct Report Rounding. These are short, private discussions between a manager and an employee that occur on a monthly or other regular schedule. Information on how to conduct this practice is available at: http://kpnet.kp.org/qrrm/service2/COE/roundings.html.

A second proven practice is involving employees in their work. The Food and Nutrition Services Department at the Los Angeles Medical Center achieved an 11% improvement in their Index in one year. They initiated a "respect" campaign that included team-building activities and bringing family and social traditions into the workplace.

Conclusion: Great health care is inherently built on significant trust. Creating a speaking-up environment links to our ability to fulfill our mission.

From Northern and Southern California

4. Transforming the Health Care Response to Intimate Partner Violence

Brigid McCaw, MD, MS, MPH; Lyn Yasumura, MD; Tracy Flanagan, MD

DOI: https://doi.org/10.7812/TPP/17-140-04

Introduction: Intimate partner violence (IPV) is common and is associated with many health problems and increased health care utilization. Health care interventions can improve patient safety and outcomes, and the US Preventive Services Task Force recommends routine IPV screening for women.

Kaiser Permanente (KP) is the national leader in the health care response to IPV. Using an innovative systems model approach, performance improvement methodology, health information technology, and implementation science has resulted in significant and sustained improvement in addressing IPV.

Methods: The systems model includes four components: Supportive environment, clinician inquiry and brief intervention, referral to on-site behavioral health services, and community partnerships. Clinical workflows, training, and electronic health records (EHR) tools facilitate evaluation and referral. Quarterly reported metrics support performance improvement. Physician champions lead facility-based teams using a step-wise approach to implementation.

Results: As the systems model has been fully implemented in Medical Centers across KP Northern California (KPNC), there has been a 27-fold increase in IPV identification. As part of a 2010 strategic partnership between the KPNC IPV Champions and OB/Gyn Chiefs, IPV identification rate was added to the Womens Health Quality Dashboard, catalyzing rapid spread of best practices and significantly increasing IPV identification.

Discussion: In 2007, KP Interregional Family Violence Prevention (FVP) Physician Leaders adopted the systems model approach; developed clinical training, workflows and referral pathways; designed EHR tools; and created patient resource information, facilitating the implementation in other KP Regions.

In 2016, this group partnered with the Interregional (IR) OB/Gyn Chiefs. A common metric, IPV identification rate, was chosen to track progress across the Regions, and the IR OB/Gyn Chiefs selected improving IPV identification and response as a quality improvement initiative.

Conclusion: An interregional FVP leadership group has facilitated the spread of a successful KPNC approach to improving IPV identification and clinical care across KP. Now, a partnership with the IR Ob/Gyn Chiefs and the use of a programwide metric will advance the work further.

CARE MANAGEMENT

From the Northwest

5. Proactive Risk Assessment Using Simulation to Optimize the Institute for Healthcare Improvement Framework and Improve Safety

Georgina Ottaviano, BSN, RN-BC; Huy Huu Nguyen, BSN, RN, CHSE

DOI: https://doi.org/10.7812/TPP/17-140-05

Introduction: Proactively analyzing risk by using analytical tools such as the Failure Modes Effects Analysis (FMEA), rather than using retrospective analyses such as Root Cause Analysis and peer review, is becoming more prevalent in health care management. Simulation is proving to be an effective method to proactively probe for failure points and to identify strategies to mitigate risk. Applying the Institute for Healthcare Improvement (IHI) FMEA tool to multidisciplinary simulation scenarios taking place in the actual clinical setting has proven effective in our organization for proactively identifying patient safety risk and developing accountable action plans designed to improve outcomes. This approach has provided guidance in determining where educational efforts and process improvement plans would best be focused.

Methods: Multidisciplinary teams of stakeholders initially met to review objectives, introduce and score the IHI tool, and schedule the simulation(s). The simulation was conducted in-situ using a high-fidelity patient simulator. The stakeholders then met to discuss and rescore the FMEA, and identify action items.

Results: Participants and leaders scored the process as valuable, because it proactively identified potential areas of risk and vulnerability. This method was also effective in prioritizing and focusing education and training based on the FMEA scoring, leading to efficient use of valuable education resources.

Conclusion: Using medical simulation in this manner can be an effective tool for teams to identify and mitigate vulnerabilities proactively. This process can be applied to all areas of a health care organization.

From Southern California

6. Benchmarking Inpatient Antimicrobial Use: Is Risk-Adjustment Possible?

Kalvin C Yu, MD; Elizabeth Moisan, MS; Gunter Rieg, MD

DOI: https://doi.org/10.7812/TPP/17-140-06

Introduction: Antibiotic overuse has become a worldwide concern. *Clostridium difficile* and drug-resistant bacteria are of increasing clinical importance. California state law requires antimicrobials stewardship programs (ASPs) for all acute care facilities. We describe a risk-adjusted antibiotic exposure ratio that may help facilitate benchmarking of antimicrobial use.

Methods: The study included members admitted to 35 Kaiser Permanente Southern and Northern California hospitals in 24 consecutive months. Potential predictive variables were assessed using linear regression models. Ratios of risk-adjusted antibiotic consumption were calculated comparing: A) a gold standard consisting of all available antibiotic use risk factors and B) a simplified "Encounter Ratio" using only the most significant factors.

Results: Diagnosis-related groups, infection present on admission, patient class, and unit type were the major predictors of antibiotic use. Aside from history of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci for anti-MRSA drugs, additional clinical and comorbidity information did not improve the model. Analyses demonstrated high fit between the Encounter Ratio and the gold standard.

Discussion: Metrics of antibiotic use differ when using raw consumption data compared with a risk-adjusted model. The Encounter Ratio model we developed helps analyze consumption data in a risk-adjusted fashion that takes into account the types of patients seen at each facility. This type of metric may therefore better inform ASP operations.

Conclusion: Risk-adjustment of antibiotic use using observed to expected ratios is possible. Diagnosis-related groups, infection present on admission, unit type, and patient class are major determinants of our Encounter Model and are information data sets that can potentially be applied to other hospitals in the nation.

From the Northwest and Colorado

7. Supportive Care for Complex Needs—Kaiser Permanente Care Team Management Models

Tracy Ellen Lippard, MD; Stacey Moret, MOT, OTR/L; Michelle Wong, MPH, MPP

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Introduction: Responding to the needs of patients with complex needs is currently inadequate. Patients with complex needs suffer from medical comorbidities, functional limitations, and unmet social needs.

Methods: Kaiser Permanente (KP) Colorado's Primary Care Plus (PC+) followed a strict eligibility criteria to capture high-need, high-cost members older than age 65 years (or age 18-64 years on Medicare). The evaluation design was a prospective matched control study assessing cost and utilization of members from a single clinic at 12 months of enrollment. KP Northwest's (KPNW's) Team-Based Care (TBC) evaluation design was a retrospective matched control study that compared members 12 months pre-enrollment and 23 months postenrollment. A secondary assessment sampled members enrolled in TBC for 12 months between summer 2014 and summer 2015.

Results: In Colorado, office visit costs were 21% higher among PC+ participants compared with the control group; however this cost was more than offset by inpatient costs that were 75% lower among participants. In contrast to PC+, KPNW's TBC did not show a significant difference in cost and utilization (ie, operating cost per patient per month, admits per 1000 patients, average length of stay, inpatient cost per patient per month, Emergency Department [ED] visits per 1000, and ED visits per member).

Discussion: Early assessment evaluations of both programs reported high satisfaction among clinicians, staff, members, and caregivers. In addition, among the initial group of PC+ program participants, 104 members had 21 important pharmacy interven-

tions (ie, alendronate starts) within the first 6 months of enrollment compared with zero in the matched control group of 108 patients. The PC+ intervention group also saw an increase of specialty palliative care/hospice touches from 8% to 55%.

Conclusion: Initial findings from PC+ and TBC indicate that holistic, interdisciplinary focus on what matters most to high-cost, high-need members and their caregivers, with proactive outreaches and improved access to someone who knows them well, can yield benefits across the quadruple aim.

From Colorado

8. Depression Care Management from Implementation to Expansion: "No More Wasted Years"

Jennifer Stamps, MBA, RN, CPHQ; Ann Wells, MD; James Hardee, MD

DOI: https://doi.org/10.7812/TPP/17-140-08

Introduction: With limited resources in specialty Behavioral Health, we sought creative solutions to provide care for the growing population of patients with depression. Implementing a Depression Care Management (DCM) program was the first step in standardizing the criteria for the diagnosis of depression, decreasing treatment variability, assuring adequate monitoring of symptoms, and assessing for remission or relapse. In addition to enrolling "typical" Primary Care patients with newly diagnosed depression, we also reached out and enrolled more vulnerable populations with depression, such as Medicare members, postpartum women, adolescents, and those with multiple comorbid medical conditions.

Objective: To assess the effectiveness of a DCM program consisting of Registered Nurse Care Coordinators using proactive telephone and e-mail (kp.org) outreach to monitor and manage medications for patients recently started on an antidepressant. The patient health questionnaire-9 (PHQ-9) depression score was tracked, and standardized outreach and treatment protocols were followed.

Methods: A retrospective analysis was conducted using 908 patients enrolled in DCM, from January 2012 through August 2014, and a comparison group of 5468 patients. Outcomes were controlled for age, sex, health status, line of business, number of Behavioral Health visits, and baseline PHQ-9 score.

A financial analysis of the DCM program was completed in 2015 (based on 2012 through 2014 enrollments).

Results: Despite starting with similarly elevated PHQ-9 depression scores at baseline, within 3 months of enrollment, DCM participants' PHQ-9 scores were *lower* than the comparison group (adjusted mean score of 4.7 versus 9.4, respectively). The depression symptom improvement was sustained over time, and there was significant gratitude expressed by DCM enrollees for the thoughtful and thorough care. In addition, patients enrolled in DCM were screened for bipolar disorder, substance abuse, and suicidality—and referred appropriately when needed.

With the top and bottom 5% "outliers" excluded, the total per member per month (PMPM) costs were affected with an average of $62 PMPM savings for the 12 months post-DCM enrollment compared with a matched comparison group of depressed patients not enrolled in DCM.

Conclusion: DCM, using evidenced-based protocols in a virtual, telephonic setting is highly effective in reducing PHQ-9 scores, improving patient symptoms, and controlling costs for patients with depression. The clinical outcomes of this DCM program are seen quickly and remain sustained over time.

From Southern California

9. Engaging Kaiser Permanente's Business Side in Community Health Promotion Using a Data Visualization and Hotspot Mapping Tool

Dana Barnes, MPH; Samika Ramirez, MHA; Jeffrey Reynoso, DrPH

DOI: https://doi.org/10.7812/TPP/17-140-09

Introduction: Since its inception in the 1940s as one of the US's first prepaid health plans, Kaiser Permanente (KP) has had built-in incentives to invest in wellness and prevention among members. Recent efforts have expanded this prevention focus beyond the clinical sphere into social determinants of health and community-level health promotion—ie, "Total Health." Along with individual risk factor data, a member's zip code can be an informative proxy for disease risk, socioeconomic context, resource availability, and environmental barriers. Therefore, having actionable zip code-level data about both medical and nonmedical measures of Total Health is crucial for quantifying which efforts are most needed and where.

Methods: In 2016, the KP Southern California (KPSC) Region began piloting the Total Health Action Tool (THAT)—a data visualization and hotspot mapping tool that integrates zip code-level enterprise data with zip code-level external data. THAT is a set of resources on an internal intranet site that includes raw data as well as interactive dashboards. Through simple point-and-click, users can customize to any desired geography and subject matter.

Results: In the first six months post-"go live," KPSC developed three signature use cases in which THAT has been applied in both clinical and nonclinical functions: In facility planning (assessing the "Total Health" needs of the zip codes in a new facility's catchment to guide service planning), in clinical program planning (identifying highest-need zip codes for targeted intervention), and in procurement (prioritizing businesses and contractors located in high-unemployment/low-income zip codes).

Discussion: Among the three signature use cases, the recurring themes that illuminated the value of this tool were that: 1) it has helped users objectively identify areas of need, quantify potential impact, and justify the business case for upstream place-based interventions; 2) health promotion efforts have primarily targeted vulnerable communities in the service area; and 3) it has helped users reduce data bottlenecks which, before, may have hindered data-driven decision making. The next step for THAT, through 2017, is to continue gathering KPSC-user feedback to improve the tool's functionality and to expand the metric library. Then, in 2018 and beyond, the lessons from the KPSC pilot will be used to inform how to enhance the tool and to spread this resource across all KP Regions.

From Program Offices and Southern California

10. Consistent, Efficient, and Effective A_{1C} Management to Goal: Novel Approaches from Kaiser Permanente Kern County, San Diego, and Northern California

R James Dudl, MD; Todd Martin, X; Benjamin Ha, MD; Richard Dlott, MD

DOI: https://doi.org/10.7812/TPP/17-140-10

Introduction: New Kaiser Permanente (KP) data show delaying A_{1C} lowering from > 8% to < 7% by 1 year resulted in a 58% higher microvascular disease risk; however, KP Regions, except Northern California (NC) are not yet above HEDIS 90th percentile for the A_{1C} < 8% metric.

Methods: A population-based care program design promoted appropriate treatment of patients with high A_{1C}s: in Kern County (KC) > 5.7%, in NC > 8%, and in San Diego (SD) 7% to 8%. KC ensured patients with an A_{1C} > 5.7% received prediabetes/diabetes education and follow-up A_{1C}s to monitor prediabetes or diabetes status or to confirm its new diagnosis. NC and SD used processes with an accountable clinician to ensure timely, verified treatment intensification and automated A_{1C} follow-up for every patient with A_{1C} above goal. Clinician-level reporting was sent to managers to support performance improvement. All 3 program locations used similar diabetes "Treat-to-Target" protocols.

Results: KC's population with diabetes increased by 11.9% vs Southern California's of 8.1% during 1 year. SD increased A_{1C} < 7 from 40.2% to 45.3% in 6 months. NC achieved > 90th percentile and led all KP Regions for HEDIS A_{1C} < 8%.

Conclusion: Four features: Moving to a population-based approach, fixing clinician responsibility, promoting timely treatment intensification, and automating A_{1C} follow-up orders were associated with the programs' successes.

From Program Offices and Southern California

11. Fundamentals of Evidence-Based Care: How to Find, Evaluate, and Use Evidence in Your Quality Journey

Helen Wu, PhD; Craig Robbins, MD, MPH, FAAFP; Qiana Amos, MPH; Mary E White, MLS

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The term "evidence based" is a common catchphrase that suggests an intervention or practice is backed by science and thus proven to work. The promise of evidence-based care is not always realized, however, because of substantial variation in how evidence is defined, identified, evaluated, and applied. We addressed these discrepancies in a multifaceted, minicourse format that outlined how to build a strong evidence-based foundation for quality improvement (QI) within the Plan phase of a Plan-Do-Study-Act (PDSA) cycle. First, we established a common definition of "evidence-based": The integration of best research evidence with clinical expertise and patient values. Core principles include the use of systematic, a priori methods, in contrast with nonsystematic approaches. Then, we described information resources for finding evidence, including PubMed, Cochrane, UpToDate, and DynaMed. The evidence quality in all these resources is mixed, and users should be aware of the limitations. Next, we reviewed A Measurement Tool to Assess Systematic Reviews (AMSTAR) and the Appraisal of Guidelines for Research and Evaluation (AGREE II), tools with accepted frameworks for critically appraising systematic reviews and clinical practice guidelines, respectively. Kaiser Permanente's National Guideline Program uses these tools to evaluate the credibility of such resources, which often have important gaps and limitations. Finally, we shared insights about translating evidence into action, describing ways to assess the overall strength and relevance of a body of evidence and the need to implement interventions in a manner that balances local adaptation with fidelity to the evidence.

From Mid-Atlantic

12. Streamlining Screening to Treatment: The Hepatitis C Care Cascade in the Mid-Atlantic Region

Carla V Rodriguez, PhD; M Cabell Jonas, PhD; Kevin B Rubenstein, MS; Yan Sun, MS; Michael Horberg, MD; Bernadette Loftus, MD

DOI: https://doi.org/10.7812/TPP/17-140-12

Introduction: In 2015, the Mid-Atlantic Permanente Medical Group implemented a hepatitis C virus (HCV) care cascade (pathway) to identify patients with HCV and close care gaps. We describe this pathway and evaluate whether HCV antibody screening has increased since its implementation. We also describe changes in confirmatory testing, genotyping, and patient follow-up over time.

Methods: The pathway included an automated screening alert for patients without evidence of a prior HCV antibody (Ab) test, reflex testing (HCV RNA, hepatitis B surface antigen, and HIV Ab) on stored samples of those patients testing HCV Ab positive, and coordinators to assist patients and to support clinical workflow. We used electronic health record data to retrospectively compare screening among patients visiting during a ten-month period before the pathway was implemented and a ten-month period since the pathway began. We followed each cohort for an additional six months to measure differences in HCV Ab, HCV RNA, HCV genotyping, and follow-up visits with gastroenterology or infectious diseases. We used a proportional hazards model to compare the time to HCV antibody screening across cohorts, adjusting for race, age, sex, neighborhood median income, medical specialty, number of visits in the prior year, patient address, and payer type. We describe proportions of patients receiving care measures downstream from the antibody result.

Results: The adjusted screening rate during the pathway era was 2.89 (95% CI 2.83-2.95) times higher than it was pre-intervention. Measures downstream from the antibody test also improved: HCV RNA confirmatory testing increased from 85% to 93% ($p < 0.001$); genotyping from 82% to 87% ($p < 0.05$); and specialty follow-up from 85%-94% ($p < 0.001$).

Discussion: HCV screening and subsequent care measures have increased since the implementation of the HCV care pathway.

From Southern California

13. Branding Urgent Care: A Journey in Shifting Acute Outpatient Care Away from the Emergency Department

David Glass, PhD; Kathy Kigerl, RN, MN; John Shohfi, MD; Michael Neri, Jr, MD

DOI: https://doi.org/10.7812/TPP/17-140-13

Introduction: The Urgent Care Strategic Workgroup engaged in a four-year journey (2012 to 2016) to reposition and rebrand urgent care at Kaiser Permanente in Southern California. The mission is to provide convenient services for patients who perceive symptoms as needing urgent attention and do not want to inappropriately use the Emergency Department (ED). The "overuse" or "misuse" of the ED is a longstanding issue inside and outside of Kaiser Permanente.

Methods: In a qualitative study in 2012, the Workgroup found that members were often confused about the location, hours, and services of urgent care. Those going to the ED in low-acuity situations often sought guidance and were directed to go to the ED either indirectly (eg, lack of appointments in primary care) or directly.

The Workgroup, building on these insights, made the following interventions:

1. Standardized urgent care clinics across the Region in terms of services provided and more closely aligned hours of operation (through the development of a "playbook" and a certification process)
2. Implemented a marketing campaign on urgent care
3. Cobranded Urgent Care and ED signage on campuses to make the choice more obvious to patients at the point of service.

Results: Eighty percent of Southern California Kaiser Permanente members are now aware of the location and services at Urgent Care. After 4 years, low acuity visits to the ED dropped 32% whereas urgent care increased by 39%.

Discussion: Members are often confused about the appropriate place to seek care in nonlife-threatening but acute situations in which they are in a great deal of pain. It is possible to brand urgent care, lower the confusion, and substitute urgent care visits for low-acuity ED visits.

From Northern California

14. Prospective Calling for Spanish-Speaking Diabetic Patient Pilot to Improve Failed to Keep Appointment Rate

Lily T Nguyen, PharmD, BCPS, CDE; Erica T Chen, PharmD, BCACP, CDE; Sue Colby, RN, BSN, MPA-HSA; Meena Pai, MD; Annabelle Zabal, RN, BSN, CPC

DOI: https://doi.org/10.7812/TPP/17-140-14

Introduction: Disparity in health care, particularly diabetes control, continues to exist between the Spanish- and English-speaking populations. In 2016, there was a 7.5% disparity among patients who had an A_{1C} less than 9% at Kaiser Permanente San Jose. One of the barriers that may contribute to this disparity is the 40% rate among Spanish-speaking patients with diabetes who failed to keep appointments (FTKA) with the bilingual diabetes pharmacist. In this study, we looked to see if prospective calling of these patients could help improve the FTKA rate by 20%.

Methods: Between August 24, 2016 and September 30, 2016, patients with appointments to discuss diabetes control with a Spanish-speaking diabetes pharmacist received an appointment reminder phone call from the bilingual program assistant one business day before the appointment. Patients who did not keep their appointments received follow-up phone calls to rebook the appointment and to identify patient-specific barriers that contributed to the missed appointment.

Results: The FTKA rate decreased to 18% after process implementation. Additionally, those who received a live call instead of a voicemail reminder had a 9% FTKA rate vs 29% for those who received a voicemail. Additionally, 6 weeks after the project ended, the number of patients with an $A_{1C} < 9\%$ increased by 2%. Patient-reported barriers for missing their appointments were primarily related to work or family issues.

Discussion: Prospective calling appeared to decrease the FTKA rate, decrease time to A_{1C} control, and increase access to the diabetes pharmacist. There were several keys to success including a direct line for patients to call, consistent staffing for prospective calling, and the establishment of a relationship between clinicians and patients. Further study is required to continue to evaluate other solutions.

From Colorado

15. Applying the Stepped Care Model to Chronic Pain Management

Heidi Clune, MD; William Gersch, PharmD; Laurence Hren, MBA

DOI: https://doi.org/10.7812/TPP/17-140-15

Introduction: Chronic pain management requires a resource-intensive multidisciplinary approach. At Kaiser Permanente Colorado (KPCO), the Integrated Pain Service (IPS) needed to devise a system that increased access to pain specialists to improve patient safety and chronic pain management throughout the Region, using a limited number of fulltime employees.

Methods: KPCO implemented a stepped-care model for chronic pain management to direct members to more intensive resource interventions using a risk stratification model to predict the risk of an opioid-related overdose.

Results: This approach also increased access to pain specialists from about 3500 members at a limited number of clinics to all 15,000 chronic opioid therapy members and to any member with a chronic pain concern at KPCO. In addition to improved access, the implementation of the stepped-care model resulted in 421 chart reviews in a 1-year period, a greater volume than IPS was able to manage previously. The stepped-care model also resulted in a 41% decrease in overall opioid dose, a 33% reduction in concurrent opioid and benzodiazepine prescribing, a 40% improvement in urine drug screen monitoring, and a 16% reduction in the number of high-risk chronic opioid therapy members. There was also a favorable impact on health care utilization with a 25% reduction in per member per month cost, driven mainly by a reduction in ambulatory care appointments, inpatient hospitalizations, and emergency room visits.

Discussion: The implementation of the stepped care model for chronic pain management at KPCO improved access and member safety while decreasing health care utilization and remaining full-time equivalent neutral.

PERFORMANCE IMPROVEMENT

From Northern California

16. Optimal Starts for End-Stage Renal Disease

Philip Madvig, MD; Joanna Mroz, MPH

DOI: https://doi.org/10.7812/TPP/17-140-16

Methods: Beginning in 2010, Kaiser Permanente Northern California (KPNC) underwent a performance improvement effort to increase the rate of optimal starts for new end-stage renal disease (ESRD) patients. Optimal starts are defined as patients who begin renal replacement therapy by one of these modalities: Peritoneal dialysis, home hemodialysis with permanent vascular access, in-center hemodialysis with permanent vascular access, or preemptive kidney transplantation. Optimal starts are associated with improved clinical, quality of life, and financial outcomes. The performance improvement approach included sequential implementation of several initiatives: Educational programs on peritoneal dialysis were developed and presented for nephrologists and renal case managers; a training program in peritoneal dialysis catheter insertion was provided for general surgeons; an ESRD tracking system was built within the KPNC electronic medical record (HealthConnect); regional leadership conducted site visits to each Medical Center; Medical Center performance was published monthly on the Region's quality report card; and "playbooks" (standardized process guides) were created for optimal hemodialysis and peritoneal dialysis practices.

Results: Optimal Start performance improved from 39% in 2010 to 67% in 2015, and has remained high since.

Discussion: A multifaceted performance-improvement approach resulted in marked improvement in care for ESRD patients. Significant leadership effort and cultural change was needed as well as specific educational and training and information technology improvements. Efforts are underway to extend this work to all Kaiser Permanente Regions.

From the Northwest and Colorado

17. Achieving Spread and Breaking Down Silos: From Managing Tonsillectomy Pain to Reducing Pediatric Narcotic Usage

Anna H Grosz, MD; Greg Berman, MD

DOI: https://doi.org/10.7812/TPP/17-140-17

Introduction: In August 2012, the US Food and Drug Administration recommended against codeine use after tonsillectomy in children. The Head and Neck Surgery (HNS) Department at Kaiser Permanente (KP) Northwest (KPNW) implemented this recommendation, then helped other KP Regions and other groups within KPNW do the same.

Methods: Electronic medical records (EMR) tools and opioid reduction protocols were shared with HNS leaders in other Regions and with KPNW surgical services, pediatrics, and pharmacy committees. EMR tools included order sets, smart groups, restriction locators, alternative alerts, and patient instructions.

Results: From 2012 to 2016, KP HNS reduced opioid prescriptions after tonsillectomy in children younger than age 7 years from 79% to 8% in KPNW, 88% to 11% in KP Colorado, 83% to 9% in KP Hawaii, 81% to 52% in KP Northern California, and 62% to 22% in KP Southern California with no increased complications. KPNW surgical services reduced codeine prescriptions per surgical case in children younger than age 7 years from 14% to 0% and in children age 8 to 14 from 19% to 3%. Overall opioid use in KPNW pediatric surgeries went from 17% to 8% per surgical case in children younger than age 7 years and stayed around 40% to 50% for children age 8 to 14 years. Total KPNW pediatric codeine prescriptions in children younger than age 7 years decreased from 924 to 56 and in children age 8 to 14 from 1712 to 288. KPNW pediatric opioid prescriptions in children younger than age 7 years decreased from 1212 to 378 and in children age 8 to 14 years from 2703 to 1173.

Discussion: The US has an opioid epidemic. Children and teens may be exposed to opioids after a surgery or injury and are overlooked in opioid work. We have demonstrated effective tools to reduce codeine and other opioid use in children. EMR tools and methods can be used broadly to fight opioid overuse in children and adults.

Conclusion: KP is uniquely positioned to test and to implement successful opioid reduction protocols such as this. This project highlights the benefits of using EMR tools, breaking down silos, and sharing best practices within a large health care organization across multiple specialties and geographic locations.

From Northern California

18. The ROUTE to Reducing Patient Harm: Preventing Hospital Acquired Pneumonia in Northern California

David Witt, MD, FIDSA; Donna Patey, RN, CNS

DOI: https://doi.org/10.7812/TPP/17-140-18

Background: A mortality review of hospitalized patients undertaken in 2008 identified hospital acquired pneumonia (HAP) as the most common hospital-acquired infection and a significant contributor to disability and death in Northern California Kaiser Permanente Medical Centers. A subsequent review performed in 2012 showed that patients with HAP had longer hospital lengths of stay (an average of two weeks), were more likely to be discharged to skilled nursing facilities instead of home, and were six times more likely to die in the hospital.

Methods: Literature was reviewed, and the best-performing units were visited to build a bundle of evidence-based interventions that were implemented across nonintensive care unit adult care with the

goal of preventing HAP. The bundle elements are: **R: Respiratory** (incentive spirometer use) **and Reduced Sedation, O: Oral Care** (preoperative and twice-a-Chlorhexidine mouthwash and tooth brushing), **U: Up** (head of bed elevated 30 degrees, out of bed for meals, ambulating 20 feet or more twice a day), **T: Tube Care** (gastric feeding), and **E: Education.** An operational definition for HAP was introduced to measure outcomes along with implementation and process measures. Process measures reported were ambulation, sedation use (specifically benzodiazepines), and preoperative chlorhexidine oral rinse use.

Results: A 66% decrease in HAP incidence rates was noted across the Region: The rate decreased from 7.1/1000 to 2.4/1000 patient admissions between 2011 to 2016. Twice a day ambulation demonstrated a 138% increase in frequency from 2013 to 2016. During that time, an estimated 308 deaths were avoided and 22,944 patient days were saved by preventing 1648 HAP cases. This saved the organization approximately $72,640,704.

Discussion: Identifying patients at risk for HAP, providing standardized physician's orders for prevention strategies, and facilitating documentation supported consistent and reliable bundle implementation and led to profound patient benefits. Other tools, such as a daily ambulation report, helped managers on medical/surgical/telemetry units recognize patients who did not have elements of the bundle in place.

Conclusion: A targeted multidisciplinary approach can significantly reduce HAP in acute care hospitals.

From Northern California

19. The Sacramento Medical Center Discharge Prescription Improvement Process

Jimmy Munteanu, PharmD; Linda Yee, PharmD; Dan B Dong, PharmD; Jeff Mierczynski, PharmD; Qui Nguyen, PharmD

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Introduction: In June of 2016, the Morse Discharge Pharmacy was confronted with a number of complaints from patients and nursing staff regarding delays in discharging patients caused by delays in filling medication orders. Discharge medication orders for 30% to 40% of the patients were not processed within the regional standard of 1 hour.

Methods: The pharmacy team initiated an improvement project to track the time and the process to fill discharge medications. An updated Discharge Tracker Log Sheet was developed and officially implemented into the daily workflow on July 8, 2016. Prescription processing times for every hospital discharge were tracked and delays were documented. Common trends were identified and addressed with key stakeholders from various departments involved in the discharge process. Workflow challenges were acknowledged at the daily safety and operations briefings and resolved among the appropriate stakeholders. This process was implemented, repeated, and fine-tuned on a daily basis, resulting in significant and positive outcomes within the first month.

Results: Monthly average processing times for discharge medications ranged from 51 to 62 minutes per patient for the months of January 2016 through June 2016. Within the first month of implementing the improvement project, the monthly average processing time decreased to 34 minutes in July. By the third month, the average processing time was 28 minutes and each subsequent monthly average was maintained under 30 minutes. The percentage of discharge orders with processing times greater than 1 hour decreased from 30%-40% to 15% within the first month and was steadily maintained at ≤ 10% by the third Month.

Discussion: Pharmacy processing times were significantly reduced by identifying recurrent issues through the use of a simple tracking tool and promptly addressing them with key stakeholders. Noteworthy achievements and partnerships were established throughout the process with minimal cost impact on the department and high impact for patients.

From Northern California

20. Time is Brain: Redesigning Stroke Care at Kaiser Permanente Northern California

Jeffrey G Klingman, MD

DOI: https://doi.org/10.7812/TPP/17-140-20

Introduction: Stroke is the number one cause of adult disability. Reduction of time of arrival to the emergency room to administration of alteplase has been shown to reduce mortality and morbidity, and reduce poststroke disability. Endovascular stroke treatment has also been shown to dramatically improve outcomes in patients with large vessel occlusion in a time-senisitve manner, necessitating rapid identification of large vessel occlusion and rapid transfer after alteplase treatment. In 2015, Kaiser Permanente (KP) Northern California (KPNC) redesigned acute stroke treatment at all 21 hospitals to facilitate very rapid alteplase treatment and rapid identification and transfer of patients for endovascular stroke therapy.

Methods: The stroke alert process was redesigned with the introduction of initial evaluation of all acute stroke patients by teleneurologists as well as significant workflow changes. Changes include prenotification of the teleneurologist, rapid assessment, immediate ordering of critical care ambulance service when a large vessel occlusion is suspected, ordering of alteplase before computed tomography, administration of alteplase in the scanner after a safety check, and performance of computed tomography angiogram immediately after starting intravenous alteplase infusion. Systematic simulation work in partnership with local Medical Centers completed the culture change required.

Results: After implementation, median door-to-needle time was reduced from 61 minutes to 39 minutes. The complication rate of symptomatic intracerebral hemorrhage is 4.2%, pre-implementation rate of 4.5%. National averages are 4% to 6%.

Discussion: KP leads the nation in stroke care. The national average for door-to-needle in 30 minutes or less is 17%; KPNC was 63% for June 2017. All KPNC Medical Centers have received the highest stroke award from the American Heart Association. Multiple patients have received alteplase with positive outcomes, enabling return to a fulfilling life vs years in a nursing home.

From Northern California

21. Rome was not Built in a Day: Creating a System of Support and Structure for Unit-Based Teams to Thrive

Lisa Sperduto; Delmy Deloa; Delilah Jimenez; Kia Vue, MS; Ryan Darke, MHA, FACHE

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In the workshop, "Rome was not built in a day," participants learned how the Roseville Medical Center built a culture of continuous improvement through performance improvement and Unit-Based Team (UBT) integration, and how Redwood City Women's Health Team drove frontline improvement. Roseville increased their percentage of high-performing UBTs (Levels 4 and 5) from 9% to 75%, by using 3 foundational interventions: 1) joint (The Permanente Medical Group and Kaiser Foundation Hospitals and Health Plan) senior leadership and frontline labor leader engagement, 2) strategy integration in partnership with the performance-improvement program, and 3) communication via visual boards.

Roseville used existing structures (Local Resource Network [LRN] and Labor Management Partnership [LMP] Steering Committee [LMPSC]) to create support for UBTs. LMPSC leaders "adopted" teams to assist struggling teams, and the LRN provided oversight to hold sponsors and teams accountable. "Super Sponsors," labor and management high performers, are trained to coach targeted teams, and sponsor forums are held to help build trust among UBTs and to learn from one another across the service area.

Implementation of visual boards allowed teams to huddle daily or weekly without disrupting the work environment. Visual boards facilitated real-time problem solving, brainstorming, visual management, and communication flow.

Associate Improvement Advisor training was required of all Level 5 coleads, as was equipping frontline employees with tools to lead continuous improvement and to mentor other teams; training included SMART goals, Rapid Improvement Model, and UBT Tracker.

Teamwork was key to improvement and to making patient care a priority. The Redwood City Team provided details of how communication within their UBT (including medical assistants and clinicians) drove improvement. Their primary goal was to have patients walk out the office feeling like they were family and knowing they had received exceptional care. The biggest improvement was their use of senior medical assistants to help both staff and patients. Senior medical assistants also helped with problem-solving and brainstorming new ideas. An additional key is how staff-led UBT and staff meetings helped implement ideas and achieve department goals.

From Southern California and Program Offices

22. Improvement is a Mindset, not a Department

Lynn M Garofalo-Wright, MD

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There is no such thing as perfect. Leaders are reminded of this daily: stoplight dashboards flash red on metrics not meeting goals, tightening margins call for greater affordability, and regulators visit often to scrutinize our safety. Although many of our regional offices and service areas have departments called "Performance Improvement" (PI) or "Quality Improvement" (QI), the responsibility to design systems that optimally deliver safe, affordable care does not reside with them alone.

In companies that are the best at continuously improving, employees from the frontline to the "C-suite" have a role in identifying and in addressing improvement opportunities. We are no different in Kaiser Permanente. Each of our unit-based teams is responsible for improving service, safety, quality, and affordability in their departments. Managers are responsible for leading improvement within or across multiple departments. Labor and management leaders serve as sponsors for larger, strategic initiatives.

The PI/QI boot camp was created for the emerging leader who is new to the world of improvement or who is seeking a refresher. It provides participants with basic concepts and tools to: Differentiate problems from symptoms, identify improvement opportunities, design systems around the patient, test system changes quickly using Plan-Do-Study-Act cycles, implement controls that make it easy to do the right thing (and hard to do the wrong thing), and use data to interpret variation and drive improvement.

Ultimately, it is incumbent upon all of us to understand these basics because PI and QI are not just departments, they are a state of mind.

To learn more, contact your local PI leader.

From Georgia and Program Offices

23. Taking Total Joint Replacement Surgery and Care to the Next Level

Violeta Rabrenovich, MHA; Kate Koplan, MD

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Introduction: With the evolution of new medical technologies, treatments, and care delivery models, both clinicians and patients frequently face the challenge of understanding and adopting the complex scientific evidence in the self-care or care delivery process. At Kaiser Permanente (KP), Total Joint Care Teams have been innovating and improving quality outcomes and affordability of care for years. Recent innovations have led to shifting total joint recovery from the hospital to home. Patients who are engaged in selecting their recovery pathway and are reliably given the care in these programs report greater satisfaction with experience and sustained or improved quality outcomes. KP's aim is to accelerate adoption of these patient-centered models of care that demonstrate significant value to an individual patient, to practitioners, and to the organization.

Methods: KP's Total Joint Care Teams and leaders collaborate across the program in an innovative and methodical approach to spread the National Total Joint Replacement Initiative (NTJRI). At the national level, an interregional multidisciplinary team of clinical and administrative experts (eg, orthopedics, anesthesiology, perioperative nursing and management, performance improvement, analytics, and communications) collaborates to design, spread, and implement clinical improvement efforts. The following are some highlights of our approach: 1) ongoing evaluation of opportunities for improvement and a methodical process to address these opportunities; 2)

sharing of reliable performance data in a transparent and collaborative way; 3) systematic communication to support spread and to engage clinical teams; 4) carefully designed learning sessions to support each Region's learning objectives; 5) applying performance improvement methodology.

Results: On the basis of regional feedback and performance data, the NTJRI team initiated several interventions: 1) developed a spread guidebook with successful practices; 2) completed a baseline analysis of patient and clinician satisfaction and shared results with KP Regions for appropriate actions; 3) created a methodology and tool to assist Regions in calculating the value of this program; and 4) incorporated shared decision making into care delivery practices.

Conclusion: The KP NTJRI leads a process that emphasizes a person-centered approach to care delivery to accelerate spread and adoption of successful practices at KP.

From Program Offices

24. To Spread or Not to Spread: That is the Question …That Evaluation Can Answer

Jim Bellows, PhD; Ana Jackson, PhD; Courtnee Hamity, PhD; Margaret Wang, PhD; Lunarosa Peralta, MPH; Care Management Institute, Center for Evaluation & Analytics

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Introduction: Program evaluation informs decisions at each stage of Kaiser Permanente's (KP's) Accelerating Learning and Spread (XLS) model. The objective of this minicourse was to guide participants in using the right evaluation tools and methods at the right time to optimize KP programs and make evidence-informed decisions about scale and spread.

Methods: The Care Management Institute's Evaluation team developed and shared a framework for Evaluation for XLS, informed by KP Colorado's framework in a *National Academy of Medicine* discussion paper. The framework includes the "5 Rights" of program evaluation: Right People, Right Questions, Right Design, Right Data, and Right Analysis and Interpretation. We also designed an Evaluation for XLS Roadmap workbook and SharePoint site to guide participants in program evaluation planning and execution throughout a program's life cycle.

Results: Using case studies involving recent KP Voh's Awards winners, participants, ranging from improvement advisors, evaluators, researchers, analysts, program champions, and sponsors, worked in inter-role groups to apply the roadmap to common evaluation challenges. After course completion, participants were given the evaluation roadmap to continue strengthening their developmental or impact-evaluation efforts.

Discussion: Participants learned how to identify questions, methods, tools, and resources to help inform program optimization and decision making. Moving forward, courses that align evaluation methods with the XLS model will contribute to augmenting evaluation capacity at KP by ensuring widespread access to evaluation resources, consultation, and peer review within the organization. All minicourse materials can be found at: https://sites.sp.kp.org/teams/coltqilt/XLS/SitePages/Learning%20and%20Evaluation.aspx.

From The Care Management Institute

25. Current State and Next Steps for Specialty Palliative Care

Wui-Leong Koh, MD; Daniel Johnson, MD, FAAHPM

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Introduction: Despite growing evidence that demonstrates the many benefits of Specialty Palliative Care (SPC), access to high-quality, specialty-level support across inpatient and outpatient settings remains highly variable. Most Regions lack a standardized approach to the identification and assessment of seriously ill members with the highest risk of having unmet physical, emotional, practical, and/or spiritual needs. Even in Regions with more consistent access to SPC services, referrals to specialty support are variable and often late during the course of illness.

Methods: The SPC National Quality Initiative (NQI) aims to transform the way Kaiser Permanente delivers high-quality palliative care support. The National Permanente Quality Leadership, in partnership with the Care Management Institute and regional SPC Leadership, have created an initial roadmap to guide NQI design and implementation.

Results: To date, the National Permanente Quality Leadership has endorsed a six-step framework to facilitate the successful spread of high-quality, integrated SPC support: 1) invest in partnership; 2) agree upon high-risk patient population; 3) negotiate expectations, team staffing, and work flows; 4) incorporate standardized patient-family needs assessment; 5) triage and titrate support on the basis of needs; and 6) measure outcomes, learn, and spread. Initially, this framework will guide efforts to integrate SPC support for patients with serious cancer.

Discussion: The SPC NQI aims to ensure more systematic SPC support for high-risk populations. The NQI will accelerate inter-regional learning, scale, and spread by exposing SPC gaps and opportunities, driving investments in SPC services across settings, leveraging critical partnerships, and standardizing care delivery and quality measurement.

REVIEW ARTICLE

Knee Osteoarthritis: A Primer

Michelle J Lespasio, DNP, JD, ANP; Nicolas S Piuzzi, MD; M Elaine Husni, MD, MPH; George F Muschler, MD; AJ Guarino, PhD; Michael A Mont, MD

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ABSTRACT

The purpose of this article is to provide a synopsis of the current medical understanding of knee osteoarthritis. We describe the prevalence, causes and associated risk factors, symptoms, diagnosis and classification, and treatment options. A quiz serves to assist readers in their understanding of the presented material.

INTRODUCTION

Please see the Sidebar: Quiz to Assess Knowledge of Knee Osteoarthritis (True/False/Depends) with Answers.

Osteoarthritis (OA), also known as degenerative joint disease, primary OA, wear-and-tear arthritis, or age-related arthritis, is a leading cause of disability in the US and worldwide.[1] Clinicians use the word *arthritis* to mean inflammation of the joints. In public health sectors, arthritis is a blanket term used to refer to more than 100 rheumatic diseases and conditions that affect the joints, the tissues surrounding the joints, and other connective tissue. Discussion of all these conditions is beyond the scope of this primer, and we will focus on primary OA of the knee.

OA is the most common joint disorder in the US.[2] The number of people affected with symptomatic knee OA is likely to increase because of the aging of the population and the obesity epidemic.[3]

Knee OA affects the 3 compartments of the knee joint (medial, lateral, and patellofemoral joint) and usually develops slowly over 10 to 15 years, interfering with daily life activities.[4] Traditionally, it was interpreted as a "wear-and-tear" of the articular cartilage disease only because of aging and not related to inflammation. Although the disease pathophysiology is still poorly understood and is under investigation, it is accepted that knee OA is multifactorial in origin. Whereas both inflammatory and biomechanical whole-organ disease processes play an important role, knee OA is also influenced by a combination of factors, including family history, age, obesity, diabetes, synovitis, systemic inflammatory mediators, innate immunity, lower limb alignment (genu valgum and genu varum), joint shape and dysplasia, trauma, and inflammation by metabolic syndromes.[5-12] Regardless of the underlying mechanism, OA implies articular cartilage damage, bony osteophyte formation, and sclerosis of the subchondral bone, and in advanced cases, subchondral cyst formation can be seen pathologically.

Risk factors related to the development of knee OA may be divided into nonmodifiable and modifiable. Nonmodifiable risk factors include hereditary (genetic mutations that may predispose an individual to the development of OA of the knee) and congenital (inherited abnormalities in the shape of the bone that surround the knee joint) factors. Modifiable risk factors can be targeted for treatment. The most common modifiable risk factor in the US is overweight; every pound (0.45 kg) of weight gained adds 2 lbs to 4 lbs (0.9-1.8 kg) of extra pressure on one's

Quiz to Assess Knowledge of Knee Osteoarthritis (True/False/Depends) with Answers:

1. **Surgery is required to treat knee osteoarthritis (OA).**
   Answer: *Depends.* Although surgery is not performed for most patients, surgery is necessary for those with severe pain or joint damage.
2. **Knee OA may occur by wearing high heels.**
   Answer: *Depends.* Long exposure to wearing high heels does, in fact, generate altered forces at the knee when walking, which may predispose to degenerative changes in the joint and increase the risk of OA.
3. **There is an association between weather and knee OA.**
   Answer: *Depends.* Rainy climates do not cause OA, but those with OA may have increased pain during rainy weather.
4. **Knee OA will limit one's ability to exercise.**
   Answer: *Depends.* One will need to avoid high-impact exercise but should maintain a low-impact exercise routine.
5. **One is more likely to develop knee OA if a parent had knee OA.**
   Answer: *Depends.* One is at a higher risk of OA with a family history, but development is avoidable through a healthy lifestyle.
6. **For every pound of weight gained, there is an equal amount of pound pressure on the knees.**
   Answer: *False.* A 1-lb (0.45 kg) increase in weight equals approximately 2 lbs to 4 lbs (0.9 to 1.8 kg) of pressure on the knees.
7. **Knee OA is a serious health problem.**
   Answer: *True*. Arthritis is the most common cause of disability in the US, affecting about 1 in every 5 US adults and their families. The economic burden is also large, with estimated costs of more than $188 billion a year: $108 billion in lost wages and $80 billion in medical care.
8. **Knee OA is a normal consequence of aging.**
   Answer: *False.* Even though knee OA is associated with aging, it is not a normal consequence of it.

Michelle J Lespasio, DNP, JD, ANP, is an Assistant Professor and Adult Nurse Practitioner in Orthopedic Surgery at the Boston Medical Center in MA. E-mail: michelle.lespasio@bmc.org. **Nicolas S Piuzzi, MD,** is an Orthopedic Regenerative Medicine and Cellular Therapy Fellow at the Cleveland Clinic in OH. E-mail: piuzzin@ccf.org. **M Elaine Husni, MD, MPH,** is a Rheumatologist and Immunologist and Director of the Arthritis & Musculoskeletal Treatment Center in the Department of Rheumatologic and Immunologic Disease at the Cleveland Clinic in OH. E-mail: husnie@ccf.org. **George F Muschler, MD,** is a Professor of Orthopedic Surgery, Director of the Regenerative Medicine Laboratory, and Attending Physician at the Cleveland Clinic in OH. E-mail: muschlg@ccf.org. **AJ Guarino, PhD,** is a Professor of Biostatistics formerly at Massachusetts General Hospital Institute of Health Professions in Boston and currently at New England College of Optometry in Boston. E-mail: ajguarino@gmail.com. **Michael A Mont, MD,** is the Chairman of Orthopedic Surgery at the Cleveland Clinic in OH. E-mail: montm@ccf.org.

knees. Excess weight increases joint loading, resulting in deleterious effects on weight-bearing joints, and contributes with negative effects related to inflammation.

The diagnosis relies on the history and physical examination findings and is often confirmed with x-rays. Laboratory tests are usually reserved to rule out other diagnoses. Modern treatments focus on improving function and quality of life. They now range beyond nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen for mild arthritis to braces, physical therapy, weight loss, transcutaneous electrical nerve stimulation (TENS) units, and intra-articular cellular injections. The definitive treatment of severe arthritis remains one of the many types of surgeries.

PREVALENCE

Knee OA affects most adults aged 65 or older, with a prevalence in the US of 33.6% (12.4 million).[2] Women have a greater prevalence (42.1%) than do men (31.2%).[4] Women with radiographic knee OA are more likely to have symptoms than men, and African Americans generally report more knee and hip symptoms than do whites.[13] Strenuous physical activity, especially activities requiring kneeling, knee-bending, squatting, and prolonged standing, as well as knee trauma and injury have also been linked to a high prevalence of symptomatic knee OA.[3]

Knee OA has a higher prevalence rate compared with other types of OA.[14] The incidence of knee OA increases both with age and with longer lifetime and higher average weight of the population, particularly in obese women.[15]

CAUSES AND RISK FACTORS

Previously OA was thought to be a normal consequence of aging and the mechanical consequence of "wear and tear," thereby leading to the term *degenerative* joint disease. However, it is now realized that OA results from a multifactorial, complex interplay of constitutional and mechanical factors, including joint integrity, genetic predisposition, local inflammation, mechanical forces, and cellular and biochemical processes.[5-12] Knee OA is closely associated with age, as radiographic evidence of OA occurs in most people by age 65 years and in more than 75% of people older than age 75 years.[16] Although there are many associations and mechanisms that are not well understood, it has been reported that there is a higher prevalence of OA among elderly women.[16]

There are three compartments in the knee: 1) the medial tibiofemoral compartment, which joins the medial tibial plateau to the medial femoral condyle; 2) the lateral tibiofemoral compartment, which joins the lateral tibial plateau to the lateral femoral condyle; and 3) the patellofemoral joint, which joins the kneecap to the femur. These three compartments work together to form a modified hinge joint that allows the knee to bend and straighten, and to rotate slightly from side to side. Excess weight on the knee can adversely affect the functional capacity of the knee joint.

An association between obesity (body mass index) and the prevalence and incidence of knee OA has been consistently demonstrated in several cross-sectional and longitudinal studies.[17] Although excess weight increases joint loading, resulting in deleterious effects on weight-bearing joints, this is not the only factor involved in the relationship between OA and obesity. Obesity increases the risk of knee OA by multiple mechanisms: Increased joint loading; changes in body composition, with negative effects related to inflammation; and behavioral factors, such as diminished physical activity and subsequent loss of protective muscle strength.[18] Furthermore, it is expected that the prevalence of obesity is unlikely to decline and will probably increase the incidence of knee OA and the demand for knee arthroplasty.[19]

SYMPTOMS OF KNEE OSTEOARTHRITIS

Knee symptoms can vary depending on the cause of the problem. The most common symptom of knee OA is pain around the knee joint. Pain can be dull, sharp, constant, or intermittent (off and on). Pain can vary from mild to agonizing. Range of motion can be decreased. The practitioner may hear grinding or popping sounds and may report muscle weakness. Swelling, locking, and giving way of the knee are common problematic symptoms. These disabilities, mainly related to pain, are usually manifested by difficulty in walking, climbing stairs, performing household chores, and sitting upright and have a negative psychological impact, all of which can lead to a decreased quality of life.[20]

Knee pain can develop slowly and worsen over time (most common), or pain can have a sudden onset. Pain and stiffness in the morning, after sitting, or after prolonged rest are most common. Over time, painful symptoms may occur more frequently, including during rest or at night. Typically, pain flares up with vigorous activity. Joint pain and stiffness after sitting or prolonged rest typically loosen up in less than 30 minutes, known as gelling.

DIAGNOSIS AND CLASSIFICATION

The classification and diagnosis of knee OA should begin with a review of the different types of knee OA. OA of the knee has traditionally been classified by etiology into either idiopathic (ie, primary) or secondary forms. Idiopathic OA of the knee is usually localized but can be generalized if knee OA involves three or more joint sites. Knee OA can also be classified by anatomic involvement by the chief joint involved.

Before the practitioner makes a clinical diagnosis of idiopathic knee OA, secondary underlying disorders should be considered and excluded. Secondary conditions of the knee that may enhance the risk of knee OA should be examined carefully. These conditions include trauma, congenital or developmental disorders, calcium pyrophosphate dihydrate deposition disease, and other bone and joint disorders such as osteonecrosis, rheumatoid arthritis, gouty arthritis, septic arthritis, and Paget disease of the bone.[21] Of all secondary OA, posttraumatic OA, caused by previous fractures of the distal femur and proximal tibia, constitutes the plurality of causes but accounts for only 12% of symptomatic OA.[22] A clinical diagnosis of knee OA is supported by the presence of typical symptoms, physical examination findings, laboratory results, and imaging features. No single clinical feature is absolutely sensitive or specific. Generally, the more features that are present, the more likely the diagnosis.

When diagnosing knee OA, the health care practitioner should initially ask questions directed to chronic health conditions, history of known injury or trauma, previous surgery, medications, occupation, and symptoms (eg, pain level and location, morning stiffness). After the history evaluation, a focused physical examination should be conducted. Each patient should be examined for the presence of an effusion, loss of range

of motion, and loss of smooth mechanical movement. The examination should assess for tenderness to palpation of the joint, crepitus (a grating sensation inside the joint) with movement, pain when pressure is placed on the joint, ability to ambulate (with description of any problems with ambulation), as well as signs of injury to muscles, tendons, and ligaments surrounding the joint. In addition, the examination should describe passive range of motion (assisted) and active (self-directed) range of motion of the affected joint.

Goldberg[23] recommends the following as a common approach to the examination of all joints:

- Make sure the area is well exposed—no clothing covering either side. Patient gowns come in handy
- Carefully inspect the joint or joints in question. Are there signs of inflammation or injury (swelling, redness, warmth)? Deformity? Because many joints are symmetrical, compare it with the opposite side
- Understand normal functional anatomy. What does this joint normally do?
- Observe the joint while the patient attempts to perform normal activity. What can't the patient do? What specifically limits him/her? Was there a discrete event (eg, trauma) that caused this? If so, what was the mechanism of injury?
- Palpate the joint in question. Is there warmth? Point tenderness? If so, over what anatomic structures?
- Assess the range of motion, both active (patient moves it) and passive (you move it). If active range of motion is limited, determine causes of pain
- Perform strength and neurovascular assessments
- Perform specific provocative maneuvers related to pathology occurring in that joint (Goldberg[23] presents some for each joint)
- In the setting of acute injury and pain, it is often very difficult to assess a joint because the patient "protects" the affected area, limiting movement and thus your examination. It helps to examine the unaffected side first. This will help to set the patient at ease and will help the physician to gain a sense of the patient's normal range of motion.

Radiologic evaluation may be used to make a diagnosis of knee OA. The American College of Rheumatology, however, suggests that a clinician can make a secure diagnosis of knee OA without radiologic evidence. X-rays may be used to assess the condition of the joint, to reveal the presence, or lack thereof, of fractures, dislocations, and joint space narrowing (JSN). JSN occurs as cartilage is lost, and the joint space between the bone narrows. X-rays of an arthritic knee or hip may show a narrowing of the joint space because of cartilage loss, changes in the bone, and formation of bone spurs (osteophytes) caused by bone remodeling.

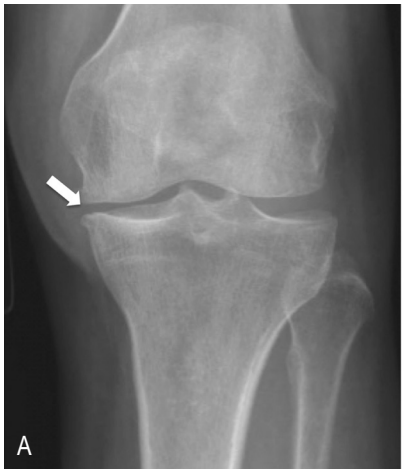

Figure 1A. Anterior-posterior (AP) radiograph of a left knee with mild osteoarthritis (OA; Kellgren and Lawrence Grade 1). The arrow indicates doubtful joint space narrowing and possible osteophytic lipping.

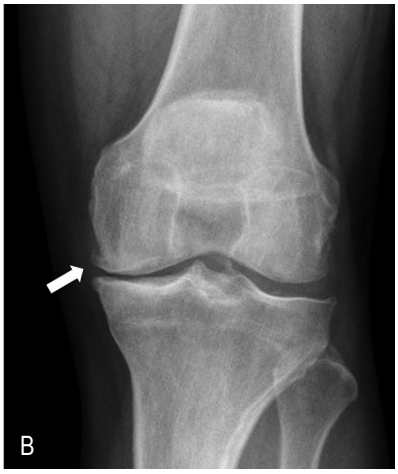

Figure 1B. AP radiograph of a left knee with moderate OA (Kellgren and Lawrence Grade 2). The arrow indicates definite osteophytes and possible joint space narrowing.

The most frequent radiographic grading system is described by Kellgren and Lawrence.[24] In this system, Grade 1 is characterized by doubtful JSN and possible osteophytic lipping (Figure 1A); Grade 2, by definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph (Figure 1B); Grade 3, by multiple osteophytes, definite JSN, sclerosis, and possible bony deformity (Figure 2A); and Grade 4, by large osteophytes, marked JSN, severe sclerosis, and definite bony deformity (Figure 2B).

Other imaging studies, such as magnetic resonance imaging, computed tomography, or a bone scan, although usually not required, may be needed to rule out other conditions of the bone and soft tissues of the joint.

Blood tests may be ordered to help determine what kind of arthritis a patient has and especially to rule out secondary causes. Among others, these are some of the common initial studies ordered: complete blood cell count with differential, erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor titers, and evaluation of synovial fluid. When the diagnosis of primary OA is made, these tests would be expected to be within normal limits, whereas patients with other types of rheumatologic conditions would have abnormal results of laboratory tests (eg, elevated erythrocyte sedimentation rate, elevated C-reactive protein concentration).

A diagnosis of knee OA can be reached only with clinical findings or with a combination of clinical and radiographic findings. There are multiple classification systems for OA. The European League Against Rheumatism recommended the use of 3 symptoms (persistent pain, limited morning stiffness, and reduced function) and 3 signs (crepitus, restricted range of motion, and bony enlargement) for making the diagnosis of knee OA. As more factors are present, the likelihood of having a diagnosis of OA increases. When all 6 signs and symptoms are present, the probability of seeing OA on radiographs is 99%.[25]

One of the clinical classification criteria most frequently used is the one developed by the American College of Rheumatology.[26,27] These criteria start with the presence of knee pain plus specific characteristics. The number of characteristics associated with knee pain varies depending on whether a diagnosis is being made using clinical criteria only, using clinical and radiographic criteria, or using clinical and laboratory criteria, as follows:

- **Clinical:** *Knee pain* for most days of the prior month, in addition to *at least 3* of the following:
  1. crepitus on active joint motion
  2. morning stiffness less than 30 minutes' duration
  3. age older than 50 years
  4. bony enlargement of the knee on examination
  5. bony tenderness of the knee on examination
  6. no palpable warmth.
- **Clinical plus radiographic:** *Knee pain* for most days of the prior month, plus radiographic evidence of osteophytes on joint margins in addition to 1 of the following:
  1. crepitus on active motion
  2. morning stiffness less than 30 minutes' duration
  3. age older than 50 years.
- **Clinical plus laboratory:** *Knee pain* for most days of the prior month, in addition to *at least 5* of the following:
  1. crepitus on active joint motion
  2. morning stiffness less than 30 minutes' duration
  3. age older than 50 years
  4. bony tenderness to palpation
  5. bony enlargement
  6. no palpable warmth
  7. erythrocyte sedimentation rate below 40 mm/h
  8. rheumatoid factor less than 1:40
  9. synovial fluid consistent with OA (white blood cell count < 2000/μL).

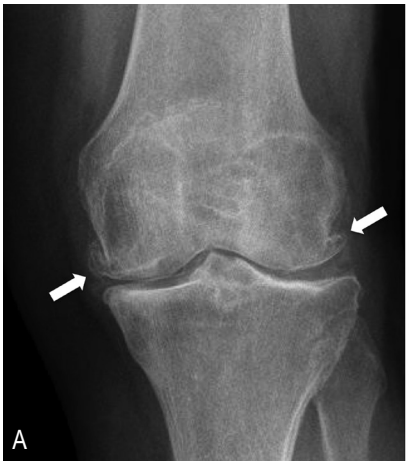

Figure 2A. Anterior-posterior (AP) radiograph of a left knee with moderate to severe osteoarthritis (OA; Kellgren and Lawrence Grade 3). The arrows indicate multiple osteophytes, definite joint space narrowing, sclerosis, and possible bony deformity.

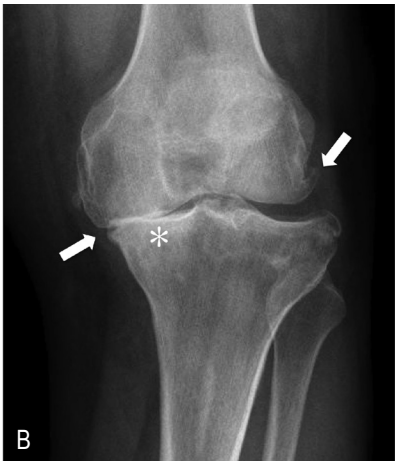

Figure 2B. AP radiograph of a left knee with severe OA (Kellgren and Lawrence Grade 4), showing large osteophytes (downward arrow at right), marked joint space narrowing (upward arrow at left), severe bone sclerosis (asterisk), and definite bony deformity in medial tibial plateau.

TREATMENT OPTIONS

Treatment designed for knee OA should aim to relieve pain, improve function, and limit disabilities. Knee OA treatment is usually driven by the patient's symptoms and the potential to improve quality of life. Nonoperative treatments of knee OA are often useful for patients with Kellgren and Lawrence Grades 1 to 3 (Figures 1 and 2A), which are "early" stages of OA. However, surgical treatments are generally needed to cure or ameliorate advanced stages of knee OA (Grade 4; Figure 2B).[28,29]

Nonsurgical Options

Nonoperative treatments constitute the initial approach for patients who consult for the first time with knee pain and signs of knee OA. There are multiple therapeutic options, and many times a patient needs to try multiple approaches until finding the most suitable therapy. Heat and cold treatments are effective pain relief methods. Heat treatments enhance circulation and soothe stiff joints and tired muscles, whereas cold treatments slow circulation, which reduces swelling, thus alleviating acute pain. The patient may need to experiment with heat and cold therapies to determine which is more effective to treat his/her specific symptoms.[30]

Treatment may include but is not limited to one or more of a large list of options: modifying the intensity of the activities performed, weight loss, muscle strengthening exercises, orthotics, osteopathic treatment, application of ice or heat, pharmaceutical treatment including NSAIDs, and viscosupplementation with hyaluronic acid injections, corticosteroid injections, glucosamine, and platelet-rich plasma (PRP). PRP is derived from a sample of the patient's own blood and then injected directly into the affected knee joint to reduce pain, improve joint function, and possibly repair the cartilage.[29,31] Quite often, an initial and more "simple" approach is to recognize triggers that aggravate symptoms and minimize those activities causing symptoms (eg, climbing stairs). Avoiding high-impact activities (eg, jogging) and switching to lower-impact activities (eg, swimming or cycling) may diminish stress on the knee and improve the symptoms. Exercise and/or other physical activity is recommended for improving pain and functional status in people with knee OA.[32] Specific exercises can increase range of motion and flexibility and strengthen muscles in the knee. Many times, an individualized exercise program combined with effective behavioral strategies aimed at weight loss may be most beneficial for reducing pain in overweight patients. Both can be difficult, especially in patients who find it difficult to exercise because of their painful joints.

Weight Loss

Addressing one specific modifiable risk factor for knee OA is fundamental to successful management. Weight loss not only reduces the risk of incident knee OA but, in established disease, also reduces symptoms, improves function, and may reduce disease progression.[18] Although weight loss approaches in knee OA are beyond the scope of this article, we cannot emphasize enough that weight loss must be encouraged at all available opportunities for appropriate patient care. There is some evidence suggesting that nonpharmacologic management strategies are underused by physicians in both primary and secondary care.[33,34] Close collaboration among physicians and other health care professionals from various clinical and research spectrums within the health care system may provide the most effective solutions to these issues.

Electrical Stimulation and Assistive Devices

Four nonoperative, noninvasive treatment modalities were identified in a recent systematic review of the literature to have a significant effect on the reduction of pain in knee OA. Those modalities identified included TENS, neuromuscular electrical stimulation, insoles, and bracing. Of note, most of the studies reviewed had less than a 6-month follow-up.[35] An easily affordable electrical stimulator (costs vary and can range from $20 on up) may be useful for treating knee OA,[35] particularly in patients who are unable to perform an exercise program. TENS uses low-voltage electrical current to produce pain relief. This therapy uses a small, battery-powered machine that is connected to electrodes (wires that conduct electrical current) from the machine to the skin. The electrodes are often placed on the area of pain (eg, around the knee), creating a circuit of electrical impulses that travels along nerve fibers. The electrical current generates a sensation that is thought to block the pain signal from the nerve to where it is perceived in the brain as pain.

Neuromuscular electrical stimulation also involves the use of a device that transmits an electrical impulse to the skin over selected muscle groups. Neuromuscular electrical stimulation is intended to strengthen or maintain muscle mass of the treated muscles. Electrical stimulation placed on the quadriceps muscle may ease pain and strengthen the quadriceps muscles supporting the knee. It also may delay the need for total knee replacement.

Using assistive devices such as a cane, wearing shock-absorbing shoes or inserts, or wearing a knee brace or sleeve can help relieve symptoms. Assistive devices or walking aids, such as a cane or crutch, can reduce pain in patients with knee OA.[36] Patients should be given instructions in the optimal use of an assistive device in the contralateral hand.[36] Although evidence is fairly inconclusive,[37] braces placed over the knee often assist with mobility and function; patients may find them especially helpful in arthritis located on either part of the knee. The rationale of an "unloader" brace is to shift weight away from the affected portion of the knee, whereas a "support" brace helps support the entire knee load.[38] The aim with the use of a brace is to reduce symptoms, improve gait mechanics, and correct knee malalignment.[39] Pneumatic unloader bracing with extension assists have been shown to strengthen the muscles around the knee.[40] Additional research is required because the optimal choice for an orthosis remains unclear, and long-term implications for their effectiveness remain undefined.[37]

Medications

Use of various medications such as NSAIDs (eg, ibuprofen, naproxen, diclofenac, or aspirin) at therapeutic doses can often be helpful. A recent network meta-analysis concluded that diclofenac, 150 mg/d, is the most effective NSAID available in terms of improving both pain and function.[41] Caution and attention must be focused on avoiding excessive use of these medications. In addition, consideration of all known safety information and individual patient comorbidities is imperative when the health care practitioner is selecting any of these medications for a patient.

Intra-articular Knee Injections

Intra-articular injections into the knee are an appealing option for patients because they present a low risk of harm while providing potential pain reduction and improvement in physical function. Intra-articular injections are a particularly tempting viable option in younger patients with less severe disease. Most reported intra-articular knee injections may be segregated into three groups (see Sidebar: Intra-articular Knee Injection Treatments).

Surgical Options

Surgery is indicated and should be considered when a patient is refractory to conservative, nonoperative treatment modalities have been tried for a reasonable period (at least three months), and quality of life is notably compromised. Surgical options for knee OA include multiple techniques: arthroscopy, cartilage repair, osteotomies, and knee replacement (partial and total knee arthroplasties).[42,43] Multiple variables are taken into consideration and must be evaluated when determining which of these procedures is the most appropriate for a specific patient. The location and extent or severity of knee OA along with patient comorbidities and risk factors must be contemplated for any surgical candidate.[43]

The role of arthroscopy in knee OA is controversial. Arthroscopic lavage and débridement do not alter OA disease progression in the knee, and the benefits seen from these interventions are limited in time and by inconsistency of results.[44,45] Nevertheless, knee arthroscopy may be used for any new onset of mechanical symptoms if desired, with understanding of its limitations.

If OA is limited to only one compartment of the knee joint, surgical techniques involving unicompartmental knee arthroplasty or unloading osteotomy may be considered. The goal of an osteotomy is to transfer the weight load from the damaged compartment to undamaged areas, delaying the need for joint arthroplasty. This procedure should be considered in young and active patients.[46,47] An alternative in between osteotomy and total knee arthroplasty (TKA) is partial knee arthroplasty. In select patients with isolated medial, lateral, or patella-femoral OA, unicompartmental knee arthroplasty or patella-femoral replacement can be successful alternatives.[42,43,48,49]

Nonetheless, for patients with severe and advanced knee OA, TKA may be the only option to resolve the pain and improve function. Today, TKA has become a safe and cost-effective treatment that provides 90% to 95% pain relief and has a 1% to 2% complication rate.[49] With the surgical techniques and surgeon skills available today, more than 90% of the patient population undergoing a TKA will continue to report satisfactory results 20 years after the surgery.[49]

CONCLUSION

Knee OA is a degenerative joint disease and one of the leading causes of disability in the US and worldwide. Although disease pathophysiology is still poorly understood and is under current investigation, it is accepted that knee OA is multifactorial in origin. Multiple risk factors related to the development of knee OA are described as either nonmodifiable or modifiable. Nonmodifiable risk factors are those that are hereditary (genetic mutations that may predispose an individual to the development OA of the knee) or congenital (inherited abnormalities in the shape of the bone that surround the knee joint). Modifiable risk factors are those that can be targeted for treatment (eg, obesity) and are therefore adjustable.

Treatment designed for knee OA should be aimed at relieving pain, improving

function, and limiting disabilities. It must focus on relieving symptoms and improving quality of life for patients. Nonoperative treatments (ie, conservative management) are the initial approach for patients who consult for the first time with knee pain and signs of knee OA. These may include modification of physical activities, weight loss for the patient with excess weight, engaging in muscle strengthening exercises, use of orthotics, application of cold or heat, pharmaceutical treatment such as NSAIDs, noninvasive electrical stimulation techniques, bracing, and intra-articular injection therapies. When nonoperative treatment fails and a patient's quality of life becomes notably compromised, surgery should be considered. Surgical options for knee OA may include knee arthroscopy, cartilage repair, osteotomies, and knee replacement (partial and total knee arthroplasties). ❖

Disclosure Statement

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Intra-articular Knee Injection Treatments

1. **Viscosupplementation with hyaluronic acid (HA):** Injection into the knee with HA (similar to the main component in cartilage) has been reported to provide temporary pain relief for up to three months. Evidence to date on use of HA has been contradictory, and recommendations regarding its use remain inconclusive.[1,2] Currently, the American Academy of Orthopaedic Surgeons does not recommend using hyaluronic acid for patients with symptomatic end-stage osteoarthritis (OA) of the knee. There are no existing data that any of the HA injections will cause regression of osteophytes, subchondral bone remodeling, or regeneration of cartilage and meniscus in patients with substantial, irreversible bone and cartilage damage. Further investigations are required to determine whether high-molecular-weight and cross-linked preparations of HA have superior efficacy compared with other HA preparations or other currently available treatments. In addition, studies involving long-term outcomes of efficacy, safety, and economic cost-benefit analyses are needed.[2] Because of the paucity of data supporting the effectiveness of HA injections to justify their cost, careful patient selection and decreasing the use of HA among patients with end-stage knee OA may represent a substantial cost reduction without negatively affecting the quality of health care.[3]
2. **Intra-articular corticosteroids:** Intra-articular injections of corticosteroids have long been used to try to relieve symptoms from knee OA, but studies addressing their efficacy have been contradictory. The American Academy of Orthopaedic Surgeons guidelines for nonoperative treatment options for patients with OA of the knee do not recommend for or against the use of intra-articular corticosteroids into the knee.[1] Furthermore, a recent Cochrane systematic review concluded that clinically important benefits of one to six weeks remain unclear because of the overall quality of the studies, the heterogeneity between trials, and presence of small-study effects.[4]
3. **Biologics:** Biologic injections include cell-based therapies and platelet-rich plasma (PRP).

   a. Cell-based therapies: Cell-based therapies for knee OA are in development stages. A recent systematic review suggested that intra-articular cellular injections for OA and focal cartilage defects in the human knee had positive results and seemed safe. However, improvement in patient symptoms was modest and a placebo effect could not be disregarded. The overall quality of the literature was poor; therefore, accurate assessment and optimization of these therapies will require further research.[5] Most of the studies analyzed reported on the use of autologous cellular therapies. Bone marrow-derived cells were the source chosen more often, followed by adipose-derived cells and blood stem cells.

   b. Platelet-rich plasma: Multiple studies and systematic reviews have reported on the use of intra-articular PRP for the treatment of knee OA.[6-14] Initial observations support an inference that PRP appears to be safe. Although some transient pain or swelling has been reported after its use, these symptoms typically resolve within two to three days, and no long-term side effects have been reported. Use of PRP, especially a lower leukocyte concentration known as leukocyte-poor PRP, showed improved results compared with HA and placebo, showing beneficial effects of amelioration in pain and improvement in function about two months after application and lasting up to a year.[9,15-17] On the basis of the current evidence, although PRP injections have been demonstrated to more effectively reduce pain and improve overall physical function compared with control studies, the quality of evidence is lacking, and further research is required to establish the efficacy of using PRP as a treatment option.

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REVIEW ARTICLE

Defecation-Specific Behavior in Children with Functional Defecation Issues: A Systematic Review

Isabelle Beaudry-Bellefeuille, MSc; Debbie Booth, M App Sci; Shelly J Lane, PhD, OTR/L, FAOTA, PhD

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ABSTRACT

Context: Atypical defecation habits are common and distressing for children and families and can have a major impact on quality of life. Often, no underlying factor can be identified, and the defecation disorder is considered functional. Current interventions are not successful for up to 50% of children. We suggest this high failure rate may be caused by lack of consistency in descriptors of behavioral indicators for functional defecation problems. Most investigations and descriptors focus on general behavior. There are fewer reports concerning defecation-specific behaviors.

Objective: To develop a thorough inventory of defecation-specific behaviors, providing a more informed foundation for assessment and intervention.

Design: A systematic review of six common databases was performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations. Reference lists of retained articles were screened for additional studies.

Main Outcome Measures: Content analysis was used to classify defecation-specific behaviors into 17 categories.

Results: Our search yielded 2677 articles; 98 peer-reviewed publications were retained for full-text review, and 67 articles were included in the final qualitative synthesis. Although there is inconsistency in reported diagnostic criteria, stool withholding and manifesting pain on defecation are the most commonly reported defecation-specific behaviors. In the studies that included children with autism or attention-deficit/hyperactivity disorder, the defecation-specific behaviors were not unique to the diagnostic group.

Conclusion: Consistent use of established diagnostic criteria, along with use of behaviors identified through this review, lay a foundation for more effective interventions.

INTRODUCTION

Atypical defecation habits are a common and distressing condition for children and families and can have a major impact on quality of life.[1,2] Given that they can be so impactful, appropriate and clear identification of problematic defecation behaviors is crucial. Research looking at behaviors associated with functional defecation concerns has taken 2 approaches. The most frequent has been to examine *general behavioral concerns;* considerably less common has been research concentrating on *defecation-specific behaviors*. However, both general and defecation-specific behavioral concerns are thought to play an important role in the development and in the persistence of constipation.[3] A deeper understanding of the behaviors reflective of actual toileting and defecation problems could provide greater insight into the unique manifestations of functional defecation disorders and thus a better foundation for treatment. Because approximately 25% to 50% of children do not fully recover from functional defecation disorders despite medical management and therapeutic strategies,[3,4] reconsidering our understanding of these disorders is imperative.

When referring to gastrointestinal disorders, the term *functional* is used to describe conditions that cannot be linked to a single discrete underlying biological etiology and are the result of the interaction between psychosocial factors and altered gut physiology via the brain-gut axis.[5] The Rome Foundation diagnostic criteria are considered a gold standard for identification of functional gastrointestinal disorders.[4,5] In the case of childhood functional defecation disorders, the clinical manifestations typically result from an interaction of physiologic, social, and behavioral processes.[1,2] As such, once organic pathology has been ruled out, clinicians are often faced with myriad simultaneous and interdependent behaviors that cannot be easily teased apart, described, or classified. For example, the clinician must evaluate the impact of the caregiver's behavior on the child's gastrointestinal tract processes (eg, punishment for involuntary fecal incontinence, unrealistic expectations), the child's response to the caregiver (eg, stubbornness, toileting refusal), the impact of gastrointestinal processes on the child's behavior (eg, painful defecation), and the impact of the child's behavior on the gastrointestinal processes (eg, voluntary stool withholding). Enhancing our understanding of these specific behavioral elements could help optimize outcomes.

The behaviors of children with atypical toileting habits is a longstanding subject of study and continues to be a central issue of debate.[6] Most reports focus on otherwise healthy children and general behavior using measures such as the Child Behavior Checklist.[7] Although most studies indicate a higher incidence of general behavioral issues in these children,[8-14] others fail to find this difference.[15-17]

Several reports exist concerning the elevated incidence of defecation issues in children with a diagnosis of autism spectrum

Isabelle Beaudry-Bellefeuille, MSc, is a PhD Candidate at the University of Newcastle School of Health Sciences in Callaghan, New South Wales, Australia. E-mail: isabelle.beaudrybellefeuille@uon.edu.au. **Debbie Booth, M App Sci,** is a Senior Librarian at the University of Newcastle in Callaghan, New South Wales, Australia. E-mail: debbie.booth@newcastle.edu.au. **Shelly J Lane, PhD, OTR/L, FAOTA, PhD,** is a Professor of Occupational Therapy at the University of Newcastle School of Health Sciences in Callaghan, New South Wales, Australia. E-mail: shelly.lane@newcastle.edu.au.

disorder (ASD)[18-20] or attention-deficit/hyperactivity disorder (ADHD),[21,22] but studies addressing the behaviors of children with these comorbidities are scarce. A few studies have specifically looked at the general behavior of children with autism and toileting issues. For instance, Peeters et al[23] report an association between mixed bowel symptoms and rigid-compulsive behaviors in children with ASD. Other studies point to a relationship between maladaptive behaviors and gastrointestinal issues in this population.[24,25] Studies dealing with the behavioral characteristics of children with ADHD and toileting issues were not found.

There are few reports concerning the defecation-specific behaviors of children with constipation, fecal incontinence, and/or stool toileting refusal. One older study compared children with encopresis and asymptomatic siblings and nonsiblings.[26] Using an automated telephone survey system, caregivers reported that children with encopresis voluntarily went to the toilet the same number of times each day as did controls. However, caregivers also reported a significantly greater amount of pain associated with defecation among children with encopresis. Cox et al[27] provided some early guidance for distinguishing between defecation-specific behaviors and generic behavioral concerns (eg, noncompliant to toileting instructions vs generally noncompliant) in children with encopresis using the Virginia Encopresis-Constipation Apperception Test. On the basis of this tool, both children with encopresis and their mothers reported more bowel-specific problems, but not more generic behavior problems, compared with controls.[27] Burket et al[9] added the dimension of stubbornness to the study of behavior in children with defecation issues, and differentiated between specific and generic toileting stubbornness. Together these studies suggest that general behavior concerns and bowel-related behavior concerns can be differentiated and that bowel-related concerns may be more useful in defining the problem.

Concomitantly with consideration of behavior and stubbornness, research has also focused on physical factors, such as pain, as contributing to functional defecation issues. Pain on defecation as well as stool withholding to avoid pain have been identified as problematic in children with chronic functional constipation and fecal incontinence; these behaviors also differentiate children with and without functional defecation disorders. Dehghani et al[28] identified painful defecation and stool withholding behavior in almost all of the 222 children with constipation studied. Kammacher Guerreiro et al[29] came to similar conclusions in a retrospective study of 270 children with functional constipation, reporting that among the most frequent complaints were pain during defecation and stool retention. Borowitz and colleagues[26] found that defecation-related pain was also common in children with encopresis.

Despite these insights, no review and synthesis of the reported defecation-specific behaviors and other concerns associated with functional defecation disorders could be found in the literature, making it challenging to comprehensively characterize these children and to clearly delineate behaviors indicating a need for specific intervention. Importantly, although toileting concerns have been identified in children with ASD and ADHD, it is unclear whether these are specific to the diagnosis or consistent with behaviors seen in children without these additional diagnoses. The aim of this review was to develop a thorough inventory of reported defecation-specific behaviors and to document their frequency, providing a more informed foundation for assessment and intervention. Although there is a large body of literature addressing *behavioral treatment approaches* for children with defecation issues,[30-33] a thorough summary of this literature is beyond the scope of this review.

The objectives, inclusion criteria, and methods of analysis for this review were specified in advance and documented in a protocol registered with the PROSPERO database (registration number CRD42016039436).

METHODS

Answers to the following questions were sought: *In children with functional defecation issues (constipation, fecal incontinence, encopresis, stool toileting refusal), which defecation-specific behaviors have been identified, and to what extent?* Considering the descriptive nature of the inquiry, the PEO (population, exposure, outcome) model for systematic review was used to formulate the research question.[34] The elements of the PEO question are as follows: 1) population: children age 0 to 18 years; 2) exposure: functional defecation issues (constipation, fecal incontinence, encopresis, stool toileting refusal); and 3) outcome or themes: defecation-specific behaviors.

Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[35,36] was used to guide the systematic review. An electronic database search of the Cumulative Index to Nursing & Allied Health Literature (CINAHL), Embase, PsycINFO, MEDLINE, The Cochrane Library, and

Table 1. MEDLINE search strategy, August 6, 2016

Number	Search terms	Results
1	Constipation	20,452
2	Fecal incontinence	9493
3	Faecal incontinence	1578
4	Elimination disorder*	66
5	Dysfunctional elimination syndrome	46
6	Encopresis	793
7	Toileting	687
8	Stool toileting refusal	15
9	Soiling	1426
10	Defecation	9591
11	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	36,433
12	Behaviour	139,611
13	Behavior	833,960
14	12 or 13	934,250
15	11 and 14	2516
16	Limit 15 to humans	1555
17	Limit 16 to "all child (0 to 18 years)"	707
18	Limit 17 to (English or French or Spanish)	655

Scopus was conducted to retrieve relevant articles for the literature review. Key terms used for the advanced search were: *behavior, behaviour, constipation, fecal incontinence, faecal incontinence, elimination disorder*, dysfunctional elimination syndrome, encopresis, toileting, stool toileting refusal, soiling,* and *defecation.* The table of contents of all issues of the *Journal of Pediatric Gastroenterology and Nutrition* was also reviewed using the same terms. The search strategy and the chosen keywords were developed and revised by the first (IBB) and second (DB) authors; DB is an experienced librarian.

Data Selection

Included articles met the following criteria: Addressed functional (not organic) defecation issues; described defecation-specific (not generic) behavioral concerns; focused on children ages 0 to 18 years; were published in English, Spanish, or French with an English abstract (IBB is fluent in these languages); appeared in a peer-reviewed journal; and were at any level of evidence. Given that the incidence of defecation issues is higher in children with ASD[18-20] and/or ADHD,[21,22] studies that included children with these diagnoses were also included in the review, but studies focused on children with other diagnoses were not. Given that no other review of this type has been identified, the search included all articles since the inception date of each database through August 2016. Articles were excluded if they addressed organic defecation issues, focused on generic behaviors, included subjects older than age 18 years, were review articles, or discussed the same study sample as another previous publication. Reference lists of included studies were reviewed for relevant publications. Table 1 illustrates an example of the search strategy, and Figure 1 illustrates the PRISMA flow diagram of searched results.

The first two authors identified search terms and strategy; the first author performed the initial comprehensive literature search and filtered for duplicates. After duplicates were removed, IBB and the third author (SJL) screened each study title and abstract for potential relevance. When disagreement was identified between reviewers, the full text of the article was retrieved; disagreements were again considered and discussed until consensus was reached. If disagreements had persisted, a third reviewer would have been consulted to determine final inclusion, but this was not necessary. The reviewers kept a log of all reviewed abstracts with reasons for inclusion or exclusion of articles. The full text of articles included in the final selection was reviewed by the first author. A data extraction table was used to organize the information extracted from each of the selected citations (see Table 2, available online at: www.thepermanentejournal.org/files/2017/17-047-Table2.pdf).

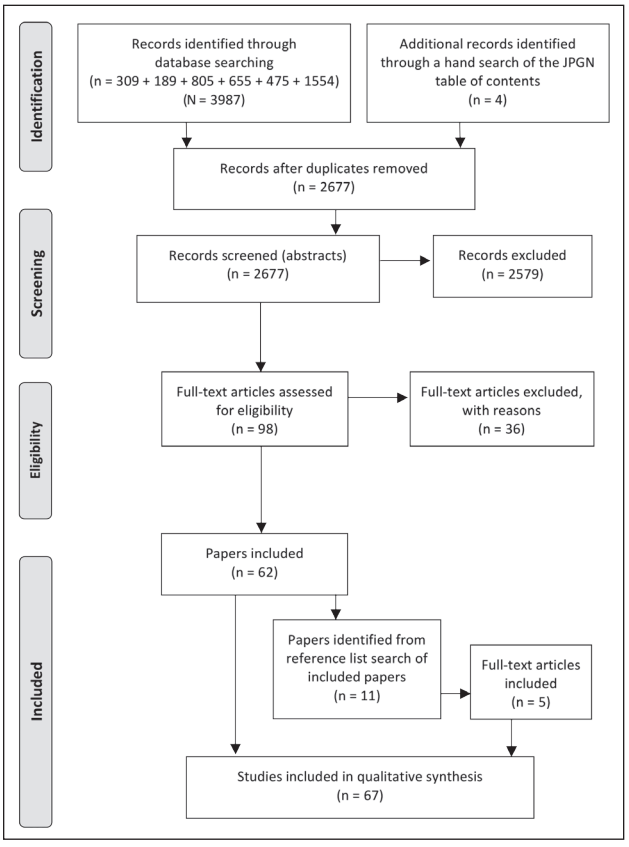

Figure 1. PRISMA 2009 flow diagram for all sources searched (August 2016).

JPGN = Journal of Pediatric Gastroenterology and Nutrition; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Data Analysis

The descriptive nature of this inquiry supports using conventional content analysis.[37,38] This approach made it possible to distill words into content-specific categories and enabled us to identify and to categorize the behaviors. Engaging in content analysis enabled the investigators to immerse themselves in the data and develop categories; here we used the process of abstraction to develop mutually exclusive categories of defecation-specific behaviors. The PDF (portable document format) files of the eligible studies were imported into qualitative data analysis software (NVivo, version 11; QSR International Pty Ltd, Doncaster, Victoria, Australia) to facilitate this analysis. No preconceived categories were established. The categories emerged from the data through repeated reading of the narrative descriptions of behavior, with the link to toileting and defecation driving the creation of the final classifications.

RESULTS

Our search yielded 3991 citations. After eliminating duplicates, we screened titles, abstracts, and keywords of 2677 citations. We excluded 2579 citations that did not match our research question; largely these citations focused on hygiene behavior relative to toileting and stool disposal in developing countries. DB was consulted on the possibility of narrowing the search; however, this would have involved the risk of missing citations relevant to the research question and was therefore dismissed. Ninety-eight peer-reviewed publications were retained for full-text review. After full-text review, 36 articles were excluded as follows: Behaviors not defecation specific (n = 21), sample/study is described in another publication

(n = 5), concomitant diagnosis other than ASD or ADHD (n = 6), subjects outside the age range (n = 1), defecation issues are not functional (n = 1), article is a review (n = 1), and article is not peer reviewed (n = 1). From the reference lists of the resulting 62 articles, 5 additional articles were identified. A total of 67 articles published between 1953 and 2016, representing 18 countries worldwide, were included in the final content analysis.

Because most of the citations belonged to observational studies, the Joanna Briggs Institute (JBI) evidence ranking system was chosen.[39] The JBI is a nonprofit research organization at the University of Adelaide in Australia whose approach to evidence-based health care considers the feasibility, appropriateness, meaningfulness, and effectiveness of health care practices. This system offers detailed subcategories for observational studies, differentiating it from other systems, which are less specific for this type of research. For example, the JBI system categorizes observational analytic designs (Level 3) and observational descriptive studies (Level 4) into a total of 9 subcategories. According to the JBI system, 7 citations were Level 1 studies,[40-46] 3 were Level 2 studies,[27,47,48] 12 were classified at Level 3,[15,24,49-58] 35 belonged to Level 4,[9,26,28,59-90] and 10 were expert opinions classified at Level 5.[91-100] (Details of subcategories can be found in Table 2, available online at: www.thepermanentejournal.org/files/2017/17-047-Table2.pdf.)

Defecation behaviors were described as part of the characterization of the samples in multiple studies.[a] An additional 18 studies, specifically aimed at identifying clinical features of children with functional defecation issues, described toileting-specific behaviors as part of the results section of the article.[b] The remaining 12 articles included the description of toileting and defecation behaviors as expert clinical observations[91-100] or in the discussion section of the article.[64,70]

Toileting and Defecation Behaviors

Narrative descriptions of reported defecation behaviors were classified by IBB into preliminary categories using common themes. Credibility and dependability of these themes were established through discussion between IBB and SJL. This iterative process allowed us to refine categories and create groupings that would fully capture the subtle differences in the behaviors described in the literature.[37] For example, some children are described as always refusing to sit on the toilet, whereas others manifest refusal of the toilet only for defecation, and some refuse to use the toilet only when outside their home; each of these variations of toilet refusal was categorized separately. Another example of this effort relates to resisting the urge to defecate. Stool withholding is often mentioned as a common behavior; however, some authors additionally describe retentive posturing and movement as a means to avoid defecation. As such, stool withholding alone and retentive efforts accompanied by specific postures or movements have been categorized separately.

Furthermore, to offer an accurate summary of the narrative description of children's behavior, we chose to consider as part of the behavioral categories all types of responses and manifestations of psychological or emotional distress, such as fear or anxiety. This decision was based on the following definition of *behavior:* "anything that an organism does involving action and response to stimulation; the response of an individual, group, or species to its environment."[101]

A total of 17 behavioral categories were established, with defecation-related manifestations of pain and stool withholding behavior being the most frequently reported defecation-specific behaviors in children with functional defecation disorders. Different types of toilet refusal behaviors are also frequently reported. Table 3 shows the number of articles that reference each of the 17 established behavioral categories.

Table 3. Defecation-specific behaviors identified in the literature

Behavior	Number of articles referencing/ describing the behavior
Manifests pain or fear of pain on defecation or urge to defecate	40
Withholds stool/avoidance of defecation/resists the urge to defecate	39
Refuses to defecate in toilet (accepts to urinate in toilet)/stool toileting refusal	16
Refuses to sit on toilet/manifests fear or anxiety in relation to sitting on toilet (in all contexts, even at home)	16
Retentive posturing/moves in a particular way when urge to defecate	12
Asks for/waits for/prefers a diaper or pull-up to defecate	11
Refuses/is reluctant to use school toilet or to use a variety of toilets (accepts toilet at home)	9
Hides to defecate or on urge to defecate, refuses to defecate in presence of others	9
Straining/prolonged time needed to have a bowel movement	9
Denies incontinence/hides soiled underwear	6
Does not manifest sensation of urge to defecate/denies or ignores urge to defecate	6
Defecates in a specific place other than toilet after being toilet trained	5
Not upset by soiling/does not notice incontinence	4
Manifests fear/resistance of wiping after a bowel movement/soiling	3
Manifests fear of flushing toilet	2
Manifests aversion to smell of feces	1
Manifests fear of feces	1

Clear classifications based on defecation diagnosis could not be made; a review of the retained publications shows that the identified categories of defecation behaviors are seen across studies and do not appear to be exclusive to any particular gastrointestinal diagnosis or defecation disorder. Thus, we could not explore the relationship between specific defecation disorders and defecation-specific behaviors because 1) diversity of diagnostic criteria across studies makes it difficult to clearly classify articles according to specific defecation disorders and 2) several articles refer to samples that group together children with different defecation issues or with more than one diagnosis.

Concomitant Diagnosis of Autism Spectrum Disorder

Among the articles retained from the systematic review, six articles include children with a diagnosis of autism.[24,65,70,76,83,84] The behaviors of these children are similar to those of children with defecation issues without any concomitant diagnosis; manifestations of pain in relation to defecation, stool withholding behavior, and all variants of toilet refusal are common. Table 4 shows the number of articles describing children with autism that reference the established behavioral categories.

Concomitant Diagnosis of Attention-Deficit/Hyperactivity Disorder

Among the articles retained from the systematic review, four included children with a diagnosis of ADHD.[26,53,70,82] Once again, manifestations of pain in relation to defecation and stool withholding behavior are the most commonly reported defecation-specific behaviors. Table 4 shows the number of articles describing children with ADHD that reference the established behavioral categories.

DISCUSSION

To our knowledge, this is the first systematic review concerning defecation-specific behavior in children with functional defecation issues. Our search strategy included three languages (English, French, Spanish), six databases from their inception through 2016, the table of contents of the *Journal of Pediatric Gastroenterology and Nutrition*, and the reference lists of all included articles. Content analysis was used to determine behavioral categories, which were determined to be both credible and dependable.

The key findings of this study were: The identification of 17 unique categories of defecation-specific behaviors and delineation of the frequency of reporting for each. Our findings support and extend previous work in this area.[9,26,27] These categories can now provide researchers and clinicians with a foundation for a clearer identification of, and differentiation between, functional defecation disorders. To date, there has been no consensus on how to assess, classify, or address these behaviors. Given that current long-term success rates using conventional treatment regimens remain limited,[3,4] there is an urgent need for consistency in the description of defecation-specific concerns to enable optimal classification and lay the foundation for focused interventions. We suggest that the descriptors identified in this review are a place to begin.

These findings move us beyond simply identifying a defecation-related behavior in broad, superficial terms, in a way that parallels previous research,[51,63] which guided clarification of fecal soiling. We now consider retentive and nonretentive fecal incontinence as very different conditions that require different treatment approaches. Such may be the case with other defecation-related behaviors, which once clarified and described in greater detail, could lead to better treatment.

Further analysis of each of the identified defecation-specific behavioral categories in this review may be needed to broaden our comprehension of the psychoemotional factors related to the observable behaviors common to children with functional defecation disorders. For instance, a behavior such as *stool toileting refusal* is not unique to a specific defecation disorder and is often described as a disorder in itself[15,52,73,99] or in association with other concomitant diagnoses[c] or temperamental characteristics.[9,80] The most frequently reported associations with this common childhood behavior are constipation and painful defecation.[d] However, encopresis,[44,45,51,83,92,98] sensory overresponsivity,[59,76,84] anxiety,[89,95,99] difficult temperament,[9,80] autism,[65,76,83] and oppositional defiant disorder[86] have also been linked to stool toileting refusal. Differentiating subgroups in the group with this common behavior may be necessary to provide clearer direction for treatment.

Diagnostic Criteria

In addition to inviting researchers to deepen our understanding of common toileting behaviors in children with functional defecation issues, this review also summons a reflection on

Table 4. Number of articles that document toileting and defecation-specific behaviors in children with defecation disorders and a concomitant diagnosis of autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD).

	Number of references	
Defecation-specific behaviors	ASD	ADHD
Pain	2	2
Withhold	3	2
Refuse toilet	3	0
Stool toileting refusal	1	0
Posture	0	0
Diaper	2	0
Hide	2	0
Refuse school toilet	2	0
Straining	0	0
Deny fecal incontinence	0	0
Deny urge	0	1
Not feel fecal incontinence	0	0
Place	2	0
Wiping	1	0
Flushing	1	0
Smell	0	0
Fear feces	0	0

diagnostic criteria. The Rome Foundation's diagnostic criteria are the most frequently cited in this review,[c] but others such as the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for encopresis[47,63,76,91,99] or the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition description of constipation[50] are also cited. However, it is noteworthy that most articles in this review (n = 52) do not reference any standardized diagnostic criteria. In many cases, researchers develop their own questionnaires and/or criteria using definitions found in the literature. This variability in diagnostic criteria makes it difficult to comprehensively appraise the research. Future studies should aim to use internationally accepted diagnostic criteria, such as Rome IV, for diagnosis, and develop surveys or questionnaires that tap into the 17 defecation-specific behaviors identified in this study to clarify the link between specific behaviors and functional defecation disorders.

It is also necessary to consider a deeper understanding of toileting behavior in relation to diagnosis. For example, the DSM-V criteria for encopresis, the second most frequently cited diagnostic criterion in this review, includes the repeated passage of feces into inappropriate places, either voluntarily or involuntarily. Considering this definition more closely, if a child *voluntarily* chooses to defecate in an unorthodox place, can we consider this child to have the same diagnosis as the child who *involuntarily* defecates in his clothing? If a child feels the urge to defecate, momentarily withholds stool, voluntarily goes to a specific place, although it may not be a socially acceptable one, and then proceeds to defecate, does s/he not possess all the elements of continence? The only problem is where the child chooses to defecate. The questions might be why is the child not able to accept the socially acceptable place, what are the features of this chosen place that the child is seeking, and what features of the socially acceptable place is he avoiding? On the other hand, the child who involuntarily defecates in his clothing shows none of the elements of continence. Considering voluntary and involuntary defecation together, simply because it is not in the toilet, does not make sense as we strive to ameliorate our understanding of functional defecation disorders.

Limitations

Although we saw including all levels of evidence as essential to answering the question posed in this review, the inclusion of weaker study designs may be seen as a limitation. However, given the intent of this investigation to produce a broad inventory of defecation-specific behaviors associated with functional defecation concerns, the broad inclusion of literature was appropriate. A second limitation is the restriction of diagnostic conditions to ASD and ADHD. However, defecation concerns are highly common in these two high-frequency diagnostic groups, making this choice logical. We acknowledge that conventional content analysis, a qualitative data analysis method, is open to subjectivity and represents a third limitation of this review. However, we have endeavored to establish rigor through the use of qualitative software and establishment of credibility and dependability of data. Finally, we are aware that a simple tally does not represent an in-depth analysis of results; however, given that the goal of this review was to develop an inventory of defecation-specific behaviors, this method provides a valid means by which to report our results.

CONCLUSION

Our review delineated 17 unique behaviors that have been identified as characterizing functional defecation concerns. We also identified a lack of consensus, fueled partly by the differences in diagnostic criteria but also in relation to assessment and classification of defecation-specific behaviors. Furthermore, this review found that defecation-specific behaviors overlap across functional defecation disorders and, on the basis of the limited evidence available, that the defecation behaviors of children with autism or ADHD are not unique to their diagnostic group. Moving forward, we suggest that we look at defecation-specific behaviors, rather than more general behaviors, in defining issues specifically related to defecation concerns. This work provides some guidelines for characterization that go beyond that of current diagnostic guidelines or existing assessment tools in looking at the context of behaviors. ❖

[a] References 40-50,52-54,56,57,59-61,63,66,68,72,73,75,78,79-85,89-90.
[b] References 9,15,24,26,27,28,51,55,58,62,65,67,69,71,74,77,78,86.
[c] References 44,45,50,51,57,65,76,83,98.
[d] References 15,51,52,56,71,89,92,95,99.
[e] References 28,62,70,77,78,82,85,86,94.

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Author Contributions

Isabelle Beaudry-Bellefeuille conducted the systematic review and wrote the manuscript.

Debbie Booth assisted Isabelle Beaudry-Bellefeuille in the literature search.

Shelly J Lane reviewed all included abstracts and reviewed and edited each draft of the manuscript.

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Ganoderma Applanatum
etching on fungus

David Moiel, MD

From the artist: "After supplying trail treats (food) to Pacific Crest Trail thru-hikers on Park Ridge, we descended to Russell Lake, capturing Mt Jefferson's midday reflection in the lake. I etched this image on an artist's conk, *Ganoderma applanatum.* The mycelium of this shelf mushroom produce enzymes that accelerate brown rot in dead trees. Medicinal teas have also been created from its inedible flesh."

Dr Moiel is a retired Surgeon from the Northwest Permanente Medical Group.

Image Diagnosis: Yellow Palms and Soles: Look Beyond the Eyes and Think Beyond Hyperbilirubinemia

Puneet Chhabra, MBBS, MD, DM; Deepak K Bhasin, MD, DM, FASGE, AGAF, FAMS

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CASE PRESENTATION

A 57-year-old man with diabetes presented to our clinic with 3 months of yellowish discoloration of his palms and soles. For the previous 5 years he had been on treatment for type 2 diabetes with metformin 500 mg twice daily. He denied history of jaundice, pruritus, loss of appetite, nausea, or any other symptom. He had not recently consumed carotene-rich foods such as carrots, spinach, lettuce, broccoli, or winter squash. On examination there was no icterus. Both of his palms (Figure 1) and soles (Figure 2) showed yellowish discoloration. Laboratory tests revealed a total bilirubin of 1.5 mg/dL, aspartate transaminase 36 IU/mL, alanine transaminase 40 IU/mL, thyroid stimulating hormone 2.01 IU/mL, and serum creatinine 1.4 mg/dL. Beta carotene levels were 64 mcg/dL (9-52 mcg/dL). The patient's fasting blood sugar was 183 mg/dL, and his hemoglobin A_{1C} (glycosylated hemoglobin) was 8.5%. We referred him to an endocrinologist for diabetes control. The endocrinologist changed the patient's medications to a combination of metformin, sitagliptin, glimepiride, and pioglitazone. After 16 weeks of treatment, our patient's hemoglobin A_{1C} was 6.7%, and the yellowish discoloration had almost disappeared from his soles and had been reduced by 75% in his palms.

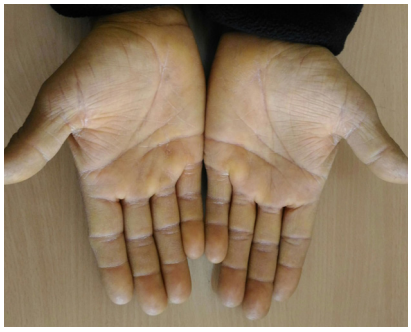

Figure 1. Yellowish discoloration of both palms.

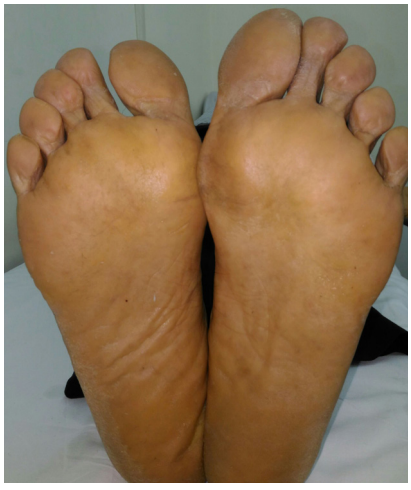

Figure 2. Yellowish discoloration of both soles.

DISCUSSION

Our patient's yellow palms and soles were attributed to diabetes mellitus. Other causes of yellow palms and soles, like carotenemia[1] caused by ingestion of nutritional supplements, hypothyroidism,[2] and renal[2] and hepatic failure, were ruled out. Yellow palms and soles in diabetes are caused by impaired metabolism of carotene in the liver. The exact frequency of this phenomenon is unknown, but approximately 10% of patients with diabetes and elevated carotene levels have yellowish discoloration of the skin.[2] Excessive blood glucose levels impair the liver's ability to convert carotene to vitamin A.[3,4] Another postulation is that proteins that have high turnover time, like dermal collagen, undergo glycosylation and give a yellowish hue to the skin.[5] Yellowish discoloration is visualized most clearly at the palms and soles because the abundance of sweat glands, minimal interference by melanocyte pigment, and the presence of a thick, horny layer of skin causes maximal accumulation of carotene at these sites.[6] ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Puneet Chhabra, MBBS, MD, DM, is a Gastroenterologist at Fortis Hospital Mohali in Punjab, India. E-mail: puneet.pgi@gmail.com. **Deepak K Bhasin, MD, DM, FASGE, AGAF, FAMS,** is the Director of Gastroenterology and Hepatology at Fortis Hospital Mohali in Punjab, India. E-mail: deepakkbhasin@gmail.com.

Left Ventricular Noncompaction Cardiomyopathy and Recurrent Polymorphic Ventricular Tachycardia: A Case Report and Literature Review

Oluwaseun A Akinseye, MD, MPH; Uzoma N Ibebuogu, MD, FACC, FSCAI; Sunil K Jha, MD, MRCP, FACC, FHRS

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ABSTRACT

Introduction: Noncompaction cardiomyopathy is a rare phenotype of cardiomyopathy associated with severe cardiac arrhythmia and thromboembolic complications.

Case Presentation: A 55-year-old woman presented with frank pulmonary edema and received a diagnosis of noncompaction cardiomyopathy.

Discussion: Left ventricular noncompaction cardiomyopathy is increasingly being diagnosed because of advances in imaging modalities. It is important to differentiate this new phenotype of cardiomyopathy from others because its diagnosis, management, and prognosis differ. We reviewed the literature and summarized the diagnostic criteria, associated complications, initial and long-term management, and the recommendation for family screening.

INTRODUCTION

Noncompaction of the left ventricular (LV) myocardium is caused by arrest in embryonic endomyocardial morphogenesis. It is rare and can occur in association with congenital heart diseases and neuromuscular disorders, and as part of genetic syndromes.[1]

Noncompaction cardiomyopathy has an incidence of about 0.05% in the adult population.[2] It is characterized by numerous and prominent trabeculations and intertrabecular recesses that extend between the LV cavity and subendocardium without any communication with the coronary circulation.[3]

We report a case of LV noncompaction cardiomyopathy (LVNC) in a woman who presented with frank pulmonary edema. Additionally, we conducted a review of the literature on the clinical presentation, diagnosis, and management of this rare entity.

CASE PRESENTATION

Presenting Concerns

A 55-year-old African American woman with a medical history of hypertension presented with progressive shortness of breath, cough with copious pink frothy sputum, and chest pain that started on the day of presentation. Her blood pressure was 168/104 mmHg, heart rate was 132/min, respiratory rate was 38/min, and oxygen saturation level was 88% on room air. On physical examination, she was dyspneic at rest, with bilateral coarse crackles; bilateral pitting pedal edema was noted.

Results of laboratory studies revealed an N-terminal pro-brain-type natriuretic peptide level of 5911 pg/mL, a troponin level of 0.022 ng/mL that peaked at 2.360 ng/mL, and a lactic acid level of 14.7 mmol/L. A chest x-ray and a chest computed tomography (CT) scan that was performed to evaluate for pulmonary embolism showed bilateral pulmonary edema. An electrocardiogram revealed a new left bundle branch block (LBBB), and QTc was 442 milliseconds. A transthoracic echocardiogram showed a severely enlarged LV (Figure 1) with a left ventricular ejection fraction (LVEF) of 30% to 35%, severe posterolateral eccentric mitral regurgitation, and moderate to severe aortic regurgitation. The transesophageal echocardiogram revealed severe aortic regurgitation, moderate mitral regurgitation,

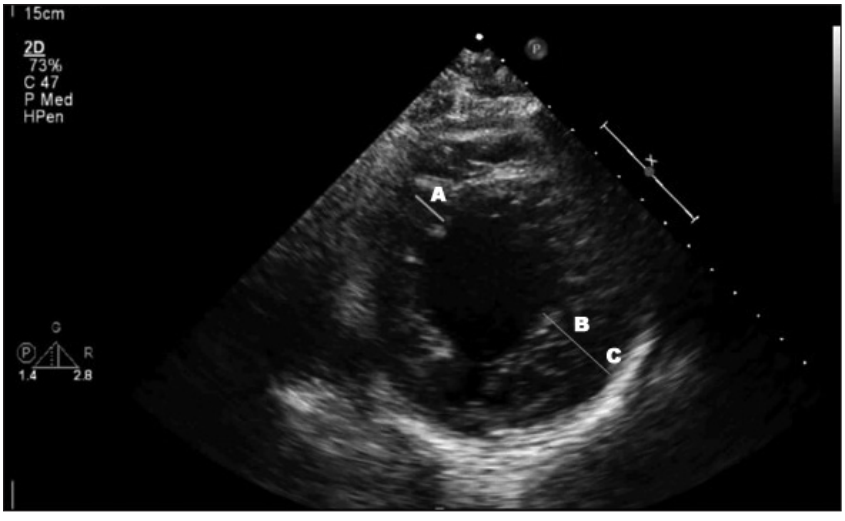

Figure 1. Parasternal short-axis view of transthoracic echocardiogram with measurement of wall thickness showing A) normal nonaffected wall, B) noncompacted subendocardial layer, and C) thinner and compacted subepicardial layer. Ratio of B:A is greater than 2.

Oluwaseun A Akinseye, MD, MPH, is a Cardiology Fellow at the University of Tennessee Health Science Center College of Medicine in Memphis. E-mail: akinseyeo@gmail.com. **Uzoma N Ibebuogu, MD, FACC, FSCAI,** is an Associate Professor of Cardiovascular Diseases at the University of Tennesse Health Science Center College of Medicine in Memphis. E-mail: uibebuog@uthsc.edu. **Sunil K Jha, MD, MRCP, FACC, FHRS,** is an Assistant Professor of Cardiovascular Diseases at the University of Tennessee Health Science Center College of Medicine in Memphis. E-mail: sjha1@uthsc.edu.

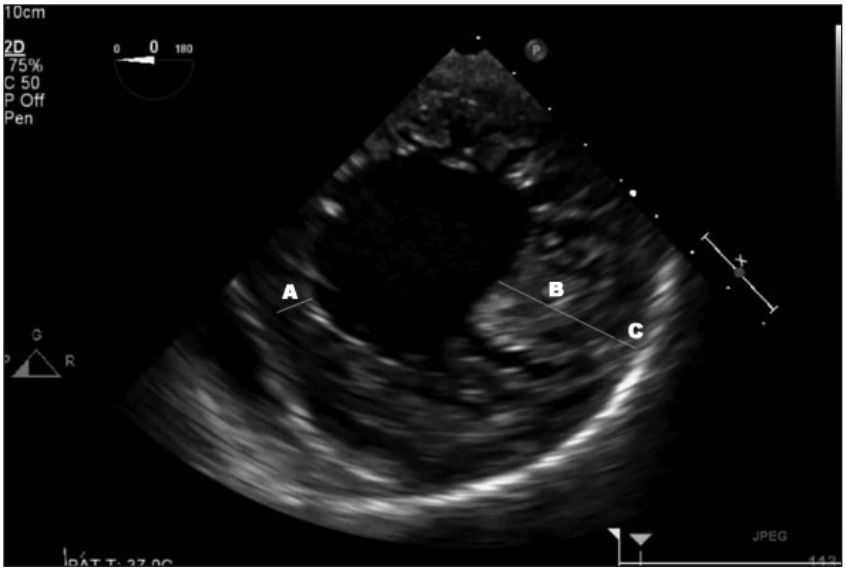

Figure 2. Transesophageal echocardiogram with wall thickness measurement showing A) normal nonaffected wall, B) noncompacted subendocardial layer, and C) thinner and compacted subepicardial layer. Ratio of B:A is greater than 2.

and an endocardial wall that was highly suggestive of an LVNC (Figure 2). Findings of left-sided cardiac catheterization revealed normal coronary arteries and a congenital right-sided aortic arch without aneurysmal dilation, which was also confirmed on the chest CT scan.

Therapeutic Intervention and Treatment

The patient was emergently intubated on presentation because of impending respiratory failure. She was started on an intravenous regimen of furosemide, 40 mg every 12 hours, and other supportive managements, including anticoagulation with heparin infusion and clopidogrel, 75 mg daily, because of an elevated troponin level and a new LBBB, but these treatments were discontinued after the coronary angiogram revealed normal coronary arteries. The patient improved greatly the next day and was extubated. Therapy with metoprolol, 12.5 mg twice daily, and ramipril, 5 mg daily, was started. A wearable defibrillator was provided in anticipation of future evaluation for cardiac resynchronization therapy with defibrillator if the LVEF remained low.

Follow-up and Outcomes

The patient's symptoms improved substantially, and she was discharged with prescribed guideline-directed medical therapy for heart failure as well as outpatient follow-up for evaluation of her severe aortic regurgitation. On the basis of the transesophageal echocardiogram finding of possible LVNC, cardiac magnetic resonance imaging (MRI) was performed after her discharge, which confirmed LVNC of the LV apex that was best appreciated on the short-axis image (Figure 3). The compacted myocardium was 7.1 mm, whereas the noncompacted myocardium was 21 mm, resulting in a noncompacted-to-compacted ratio of approximately 3.0.

Approximately 3 weeks after discharge, the patient presented with complaints of being shocked by her wearable defibrillator. An electrocardiogram showed sinus rhythm at 89/min, an isolated premature ventricular contraction, LBBB, QRS duration of 185 milliseconds, and QTc of 510 milliseconds. Polymorphic ventricular tachycardia (VT; torsades de pointes), which was appropriately treated with the application of 150 J from the wearable defibrillator, was noted on analysis of the device results. Laboratory studies revealed a serum potassium level of 2.6 mmol/L and a magnesium level of 1.8 mmol/L. Her electrolyte levels were repleted. She was subsequently started on anticoagulation therapy because of an elevated risk of systemic thromboembolism associated with LVNC.

The patient subsequently underwent aortic valve replacement with a 19-mm aortic valve bioprosthesis (Trifecta, St Jude Medical Inc, St Paul, MN) and a mitral valve repair and annuloplasty using a 25-mm flexible adjustable annuloplasty ring (Attune, St Jude Medical Inc, St Paul, MN). After surgery, polymorphic VT developed with subsequent ventricular fibrillation arrest, requiring defibrillation and amiodarone therapy. She achieved return of spontaneous circulation after several rounds of cardiopulmonary resuscitation. She subsequently had a long and complicated hospital course, including another sternotomy with resection of the anterior leaflet of the mitral valve and replacement of the valve with a 25-mm porcine aortic valve bioprosthesis (Epic, St Jude Medical Inc, St Paul, MN) for severe treatment of mitral regurgitation.

The patient's clinical status gradually improved, and she was enrolled in cardiac rehabilitation with plans for outpatient implantation of a biventricular implantable cardioverter-defibrillator (ICD).

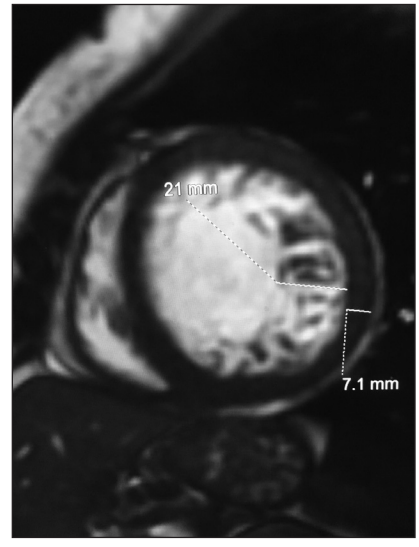

Figure 3. Cardiac magnetic resonance image showing short-axis of left ventricular apical myocardium. Compacted myocardium was 7.1 mm (bottom dashed line), and the noncompacted myocardium was 21 mm (top dashed line), resulting in a noncompacted-to-compacted ratio of approximately 3.0.

However, one day during her hospital stay, she had a cardiac arrest secondary to ventricular fibrillation, from which she could not be resuscitated (Table 1).

DISCUSSION

LVNC is a rare clinical entity that was first described in 1969 by Feldt et al after the discovery of a biventricular spongy myocardium with complete situs inversus in a 3-month-old female infant.[4,5] However, there has been an increase in awareness and growing interest since the first isolated LVNC case and 2 case series published in 1984[6] and 1990,[3] respectively. Its true prevalence is unknown, but it varies from 0.014% to 0.24% depending on the patient population being studied.[7,8] The condition can occur in association with congenital heart diseases,[1] as noted in this patient, who was also found to have a congenital right-sided aortic arch (Table 1).

LVNC has no predilection for a specific age group. Cases have been diagnosed in utero[9] and as late as age 94 years.[10] It appears to be more common in males than females.[3,7,11] There is considerable variability in the genetic patterns and the phenotypical and clinical presentations. Both familial and sporadic forms have been described.[11] The familial type is more common in the pediatric age group compared with adults and follows an X-linked, autosomal-dominant, or mitochondrial inheritance pattern.[11,12] During the fifth and eighth week of embryonic development of the normal heart, the myocardium is compacted

Table 1. Timeline of the case

Date	Relevant medical history and interventions		
	Summaries from initial and follow-up visits	Diagnostic testing	Interventions
November 25, 2016	A 55-year-old African American woman with a history of hypertension and smoking 1-2 cigarettes per d for 10 years presented with progressive shortness of breath, cough with copious pink frothy sputum, and chest pain that started on the day of presentation. Initial diagnostic assessment was acute respiratory failure because of acute pulmonary edema and new-onset congestive heart failure. History also included 1-2 glasses of wine twice a week and paternal diabetes mellitus.	**Laboratory and imaging studies** (Nov 25): NT pro-BNP, 5911 pg/mL; troponin, 0.022 ng/mL that peaked at 2.360 ng/mL **ECG:** New LBBB; QTc, 442 milliseconds **CT of chest:** Bilateral pulmonary edema, right-sided aortic arch **Transthoracic echocardiography** (Nov 28): LVEF, 30%-35%; moderate to severe aortic regurgitation, severe mitral regurgitation **Transesophageal echocardiography** (Nov 29): LVEF, 25%-30%; severe aortic regurgitation, moderate mitral regurgitation, endocardial wall highly suggestive of left ventricular noncompaction **Cardiac catheterization** (Nov 30): No substantial coronary artery disease	Patient was emergently intubated and started on intravenous diuresis. Guideline-directed medical therapy for heart failure (β-blocker and ACE inhibitor) was gradually introduced once acute pulmonary edema resolved. She was subsequently extubated. A low-salt, low-fat diet was started. Smoking cessation counseling was initiated. A wearable defibrillator was provided before her discharge on December 2, 2016.
December 23, 2016	Outpatient tests	**Cardiac MRI**: Showed left ventricular noncompaction	
December 25, 2016	Patient presented with syncope and subsequent shock from her wearable defibrillator.	**Wearable defibrillator interrogation** (Dec 25): Polymorphic ventricular tachycardia	Serum electrolyte levels were corrected. Wearable defibrillator was continued in anticipation of CRT-D implantation if LVEF remained low after 3 months of optimal medical therapy for heart failure. Anticoagulation therapy was started because of increased risk of thromboembolism with noncompaction diagnosed on cardiac MRI. Patient was discharged home on December 27, 2016.
January 30, 2017	Patient presented for aortic valve replacement and mitral valve repair. She had a prolonged and complicated hospital course because of acute respiratory failure requiring mechanical ventilator support.		Aortic valve replacement and mitral valve repair (February 20). Mitral valve replacement (March 10). Cardiac rehabilitation was initiated, and her clinical status improved.
March 26, 2017	Sudden cardiac arrest developed because of ventricular fibrillation, and she could not be resuscitated.		

ACE = angiotensin-converting enzyme; CRT-D = cardiac resynchronization therapy with defibrillator; CT = computed tomography; ECG = electrocardiography; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; MRI = magnetic resonance imaging; NT pro-BNP = N-terminal pro-brain-type natriuretic peptide.

and the coronary arteries are formed.[13] An arrest of the endomyocardial morphogenesis at this stage is thought to be the basis for myocardial noncompaction. This theory, however, was challenged by Bleyl et al,[14] who reported 3 cases without myocardial noncompaction on intrauterine echocardiograms but later were diagnosed with LVNC.

The clinical presentation of LVNC varies widely. Patients may remain asymptomatic for years, although symptoms can develop as early as childhood. Symptomatic presentation includes LV systolic and diastolic dysfunction, heart failure, arrhythmias, thromboembolic events, and sudden cardiac death.[15,16] In the systematic review conducted by Bhatia et al,[15] the most common symptom prompting referral was shortness of breath (63%), and approximately 30% of patients had New York Heart Association Class III or IV congestive heart failure with a mean LVEF of 36%. In the study, heart failure was the most common cause of morbidity, and 15 patients were subsequently referred for heart transplant. In addition, most arrhythmias in patients with LVNC were VT and atrial fibrillation,[15] with the prevalence of VT approaching 40%, and sudden cardiac death resulting in more than 55% of LVNC-related deaths. These presentations were also encountered in our patient. She presented with florid heart failure, and her LVEF was approximately 30%. Before her readmission, she had an episode of torsades de pointes, which was appropriately treated with the application of 150 J from the wearable defibrillator. Given the polymorphic nature of the VT and prolonged QTc, the event was thought to be triggered by electrolyte abnormality rather than a primary VT. However, it is known that LVNC may provide a pro-arrhythmogenic substrate for development of VT because the continuity between the endocardium and the deep intertrabecular recesses creates a pathway for reentrant circuits.[7] A substantial number of patients will also experience systemic thromboembolism.[15]

The diagnosis of LVNC is based on the LV morphology. An echocardiogram is the test of choice for initial evaluation. Several diagnostic criteria are widely accepted for diagnosing noncompacted myocardium. The most extensive echocardiographic criteria were proposed by Jenni et al.[17] The criteria include 1) an excessively thickened LV wall presenting with 2 layers of differing structure; 2) a noncompacted-to-compacted wall thickness ratio greater than 2:1 at end-systole; 3) communication of the deep intertrabecular recesses with the ventricular cavity, identified by color Doppler echocardiography; 4) absence of coexisting cardiac abnormalities; and 5) presence of multiple prominent trabeculations. In their proposal, Chin et al[3] focused on the LV free wall at end-diastole in parasternal short-axis and apical views. Noncompaction is likely when the ratio of the distance from the epicardial surface to the trough of the trabecular recess and the distance from the epicardial surface to the peak of trabeculation is 0.5 or less. The presence of at least 3 different LV apical hypertrabeculations in a single imaging plane is also a diagnostic criterion proposed by Stöllberger and Finsterer.[8] The authors further modified this criterion to include a 2-layered myocardium with a ratio of noncompacted to compacted myocardium greater than 2.0 at end-diastole. There are, however, several pitfalls with these echocardiographic parameters that are worth mentioning. It has been shown that about 68% of healthy hearts have prominent LV trabeculations,[18] and these trabeculations can also be observed in hypertrophied hearts resulting from dilated, valvular, or hypertensive cardiomyopathy.[7] In fact, LV trabeculations can be a normal finding in athletes and African Americans.[19] In a study by Kohli et al,[20] 8% of healthy blacks in the control group and 24% of patients with heart failure in an outpatient general cardiology clinic fulfilled at least 1 or more of the criteria listed earlier. Careful assessment and use of these echocardiographic parameters is therefore warranted to prevent overdiagnosis.

New echocardiographic parameters are presently being considered to aid in the diagnosis of LVNC. Bellavia et al[21] showed that there was a reduction in systolic strain, strain rate, and displacement in patients with LVNC independent of the LVEF. These techniques provide additional qualitative and objective assessment of LVNC.

Cardiac MRI, as reported in our case, is a useful diagnostic tool for LVNC. It is particularly important when echocardiographic findings are equivocal or there is inability to obtain a good-quality echocardiogram. It is also useful for assessing the severity of LVNC with the identification and quantification of the degree of fibrosis with delayed gadolinium enhancement.[22] There are proposed criteria for diagnosis of noncompaction using cardiac MRI. Petersen et al[23] studied 7 patients with a clinical diagnosis of LVNC and found that a ratio between the noncompacted and compacted myocardium greater than 2.3 measured at end-diastole accurately diagnosed LVNC. Although this approach has an 86% sensitivity and 99% specificity in individuals with suspected cardiac disease,[24] a sizable number of patients (43%) in the MESA (Multi-Ethnic Study of Atherosclerosis)[25] study without cardiac disease or hypertension met this cutoff point in at least 1 segment of the LV, suggesting that the specificity of this proposal is low in patients at low risk of LVNC. Another proposal by Jacquier et al[26] is the calculation of LV trabecular mass using steady-state precision short-axis views. An LV trabecular mass greater than 20% of the total LV mass is suggestive of LVNC; however, this approach has been shown to have poor interobserver variability.[24] CT angiography can be used when cardiac MRI is contraindicated or when echocardiographic findings are inconclusive. It also provides the benefit of assessing coronary arteries[24]; however, there is presently no consensus on specific criteria for diagnosing LVNC with CT angiography.

Symptomatic patients with LV systolic dysfunction and heart failure are treated conventionally according to American College of Cardiology/American Heart Association guideline-directed medical therapy. This includes the use of diuretics, β-blockers, and angiotensin-converting enzyme inhibitors. Addition of an aldosterone antagonist and digitalis may also be considered. Cardiac resynchronization therapy with or without ICD should be considered for symptomatic patients with New York Health Association Classes II, III, and IV, with LVEF of 35% or less despite optimal medical therapy,

and QRS duration longer than 120 milliseconds in those patients with LBBB QRS morphology and 150 milliseconds or longer in non-LBBB QRS morphology. There has been reported improvement in functional capacity, LVEF and dimensions, and brain-type natriuretic peptide with the use of cardiac resynchronization therapy in LVNC cardiomyopathy.[27,28]

Although there is lack of solid evidence on the impact of appropriate therapy on the progression of noncompaction and improvement of LVEF, regression of LVNC has been reported in selected patients receiving appropriate therapy.[29,30] A retrospective study evaluating the effect of β-blocker therapy in LVNC showed significant reduction in LV mass at one year compared with an increase in LV mass noted in patients not receiving a β-blocker; however, the LVEF was unchanged at one year.[31] A case of significant improvement in LVEF with aggressive medical therapy (β-blocker, angiotensin-converting enzyme inhibitor, and furosemide) at one year was reported by Lin et al.[32]

According to the American College of Cardiology/American Heart Association guidelines on device-based therapy for cardiac rhythm abnormalities,[33] there are sufficient observational data to indicate that placement of an ICD as a strategy to reduce the risk of sudden death is a reasonable clinical strategy in patients with LVNC. Implantation of an ICD should follow the general guidelines for primary and secondary prevention. In addition, ICD implantation is required if VTs are recorded, and in patients with normal systolic function or delayed gadolinium enhancement on cardiac MRI if an additional risk factor such as family history of sudden cardiac death, nonsustained VT, or previous syncope is present.[4]

Medically, the treatment of ventricular arrhythmia in LVNC is the same as with other patients.[11] Routine anticoagulation therapy with warfarin has been recommended because of the increased risk of systemic thromboembolism in these patients. There is need for close long-term follow-up, and it is recommended that all first-degree relatives of affected patients undergo clinical screening for LVNC.[34]

CONCLUSION

LVNC is an increasingly recognized condition because of the ubiquity of echocardiography. Patients may remain asymptomatic or present with symptoms ranging from congestive heart failure and abnormal valvular function to ventricular arrhythmias, systemic thromboembolism, and sudden cardiac death, with no predilection for a certain age group. Diagnosis is essential because of the need for aggressive treatment, close follow-up, and clinical screening of all first-degree relatives of affected patients. Echocardiography is the imaging modality of choice. However, cardiac MRI and CT imaging are increasingly becoming acceptable diagnostic tools. A noncompacted-to-compacted myocardium ratio of greater than 2 at end-systole on echocardiogram is the most commonly used diagnostic criterion, and the ratio of noncompacted to compacted myocardium greater than 2.3 at end-diastole on cardiac MRI is suggestive of LVNC.

The treatment strategy includes a combination of guideline-directed medical therapy for the treatment of heart failure and cardiac arrhythmias, and prevention of systemic thromboembolism. Once the condition is diagnosed, aggressive medical management is required, including long-term anticoagulation therapy, because of increased risk of thromboembolism. In patients with normal systolic function, the occurrence of sudden cardiac death, nonsustained VT, or syncope should prompt immediate consideration for an ICD. Clinical screening of all first-degree relatives of affected patients is also recommended. Prospective studies are needed to improve the management and clinical outcome of this patient population. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Tough Organ

The heart is a tough organ: A marvelous mechanism that, mostly without repairs, will give valiant pumping service up to a hundred years.

— Willis John Potts, MD, 1895-1968, American Surgeon

Sunrise at Tunnel View
photograph

Jorge Ramirez, MD

This image was taken at Yosemite National Park in CA in early February. Watching the beauty of the Yosemite Valley come out of the darkness, with Half Dome, El Capitan, and Bridalveil Fall illuminated by soft, gentle light, can be a very moving experience.

Dr Ramirez is a Family Physician and Chief of the Department of Family Medicine at the Downey Medical Center in CA. More of his photographs can be viewed at www.picturesandhealth.com.

Bilateral Large Pneumothoraxes Following Implantable Cardioverter-Defibrillator Generator Change: A Case Report of an Uncommon Event Complicating a Common Procedure

Ritin Bomb, MD, FACC; Sunil K Jha, MD, MRCP, FACC, FHRS

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ABSTRACT

Introduction: A bilateral large spontaneous pneumothorax to our knowledge has never been reported after a device implantation. We report an unusual case of a patient developing spontaneous bilateral large pneumothoraxes after an implantable cardioverter-defibrillator generator and lead revision without evidence of any obvious traumatic cardiac injury.

Case Presentation: A 79-year-old white man was scheduled for implantable cardioverter-defibrillator generator change and addition of an atrial lead. Approximately one hour after the procedure, he suddenly went into respiratory distress with profuse sweating, and pallor with falling oxygen saturation and blood pressure. Chest x-ray showed bilateral large pneumothoraxes.

Discussion: In our literature search, we found no reports of large bilateral pneumothorax in the absence of any traumatic cardiac or lung injury. Rupture of bilateral pleura during subclavian access or presence of pleuropleural communication or a right atrial microperforation could be possible causes.

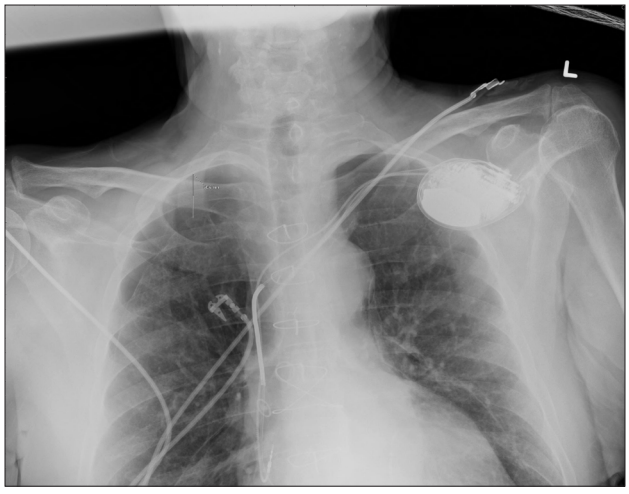

Figure 1. An initial right-sided 3-cm pneumothorax that developed 1 hour after an implantable cardioverter-defibrillator generator change.

INTRODUCTION

Pneumothorax following device implantation through subclavian venous access is uncommon and occurs during 1% to 2% of procedures with experienced operators.[1] Most commonly, pneumothorax occurs on the ipsilateral side and is associated with venous puncture. Pneumothorax may be detected during a procedure or within 24 hours of implantation. Unlike ipsilateral pneumothorax, contralateral pneumothorax may be caused by perforation of the cardiac wall, pericardium, and pleura.[2,3] We know of only one reported case of bilateral pneumothoraxes following device implantation with no apparent cause.[4] In the literature, bilateral spontaneous pneumothoraxes have been documented as "buffalo chest syndrome" with the cause hypothesized as congenital pleuropleural communication.[5,6] In all cases, the pneumothorax was reported several days after the procedure. We conducted an extensive literature review using Google Scholar, Ovid, and MEDLINE/PubMed. The search included the MeSH terms *pneumothorax, bilateral pneumothorax, pacemaker implantation, subclavian puncture, pericardial effusion, cardiac trauma,* and *pleural injury* and dated back to January 1, 1975. To our knowledge, no cases of large bilateral spontaneous pneumothoraxes have been reported. In this report, we describe the trajectory of a patient who developed spontaneous bilateral pneumothoraxes following an implantable cardioverter-defibrillator (ICD) generator change with atrial lead insertion and no direct evidence of traumatic cardiac injury.

CASE PRESENTATION

A 79-year-old white man with a history of coronary artery bypass graft surgery, severe ischemic cardiomyopathy (left ventricular ejection fraction, 30% to 35%), hypertension, diabetes mellitus, and paroxysmal atrial tachyarrhythmia was scheduled for an ICD generator change and addition of an atrial lead. His original ICD was implanted in 2005, with a single ventricular lead. The patient was a former smoker and had no known pulmonary history. He underwent an uneventful generator change and atrial lead placement through left subclavian access. Both atrial lead and existing right ventricular lead measurements were noted as normal before closure. There was a transient drop in blood pressure during the procedure from 130/90 mmHg to 100/70 mmHg. To rule out possible cardiac injury, an echocardiogram was performed in the laboratory before recovery, and there was no evidence of pericardial effusion.

Ritin Bomb, MD, FACC, is a Cardiologist at the University of Tennessee Health Science Center College of Medicine in Memphis. E-mail: ritinbomb@gmail.com. **Sunil K Jha, MD, MRCP, FACC, FHRS,** is an Assistant Professor of Cardiovascular Diseases at the University of Tennessee Health Science Center in Memphis. E-mail: sjha1@uthsc.edu.

The ICD generator was a Medtronic Evera XT DR Model DDBB1D1 (Medtronic, Inc, Minneapolis, MN) with a pacing mode AAIR with a default to DDDR if needed at a lower pacing rate of 60 beats per minute. The newly inserted atrial lead was a Medtronic active fixation Model 5076-45 cm ([Medtronic, Inc, Minneapolis, MN] right atrial P-wave 2.3 mV, right atrial pacing threshold 1.6 V at 0.5 milliseconds, and lead impedance 1030 ohms). The high-voltage right ventricular lead implanted in 2005 was a Medtronic 6944 Sprint Quattro ([Medtronic, Inc, Minneapolis, MN] R-wave 15.9 mV, pacing threshold 0.7 V at 0.5 milliseconds, and lead impedance 921 ohms).

After the procedure, the patient was comfortable. About 1 hour later, he went into respiratory distress with profuse sweating and pallor. His vitals were noted as pulse, 78/min regular; blood pressure, 130/88 mmHg; and respiratory rate, 18/min with pulse oximeter oxygen saturation at 98% on room air. A chest x-ray (CXR) showed a right apical pneumothorax about 3 cm in size (Figure 1). The patient's distress continued, with falling oxygen saturation and blood pressure levels. His vitals deteriorated to pulse, 100/min regular; blood pressure, 100/60 mmHg; respiratory rate, 25/min; and pulse oximeter oxygen saturation, 92% on 5 L oxygen. A clinical evaluation suggested bilateral pneumothoraxes. A repeat CXR revealed bilateral large pneumothoraxes (Figure 2). A tension pneumothorax was imminent, and we opted for immediate insertion of bilateral chest tubes. The patient immediately improved; however, it should be noted that in the setting of suspected tension pneumothorax, a needle decompression typically is performed before a CXR. A repeat CXR showed full expansion of the patient's lungs (Figure 3). He was discharged after 3 days. No subsequent pneumothorax was noted before the discharge and upon 2-week follow-up. Throughout the course of hospital stay during the procedure and postprocedure, the device was interrogated multiple times, and there was no evidence of lead malposition or atrium perforation.

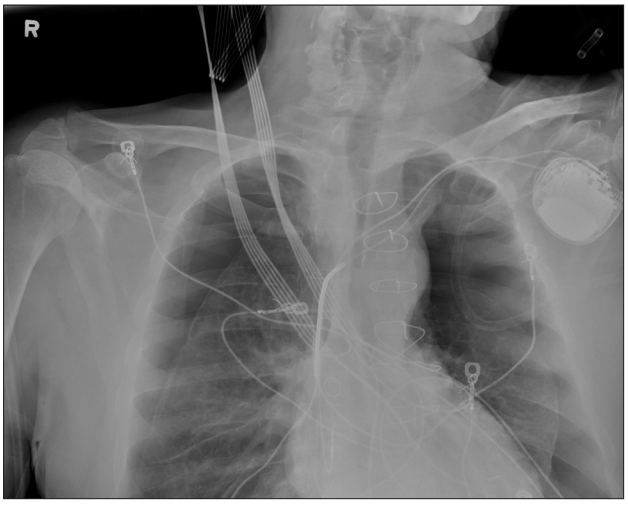

Figure 2. Bilateral tension pneumothoraxes.

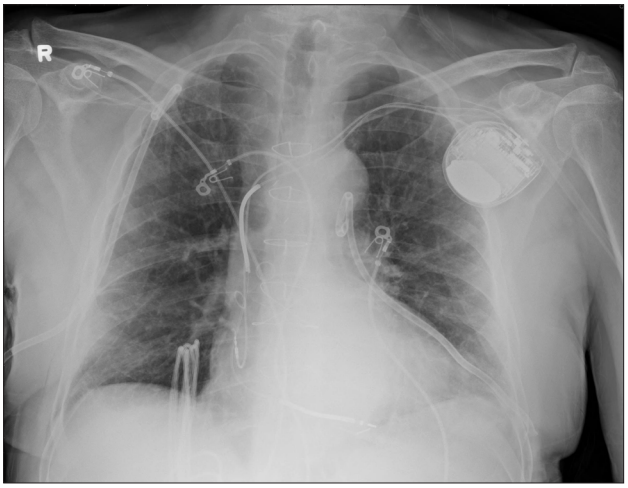

Figure 3. Pneumothorax resolution.

DISCUSSION

This case is unique because it is the first of its kind to involve large bilateral pneumothoraxes and no traumatic cardiac or lung injury. There was no direct evidence of atrial perforation or lead misplacement. So why did this patient develop bilateral large pneumothoraxes?

In 2015, Rali and Manyam[4] described a likely case of possible buffalo chest syndrome after ICD placement. This patient developed contralateral pneumothoraxes necessitating surgical intervention four days after ICD placement. The authors suspected pleuropleural communication because the contralateral pneumothorax developed after ipsilateral chest tube clamping. The authors referred to a "buffalo chest" as a single pleural space with no anatomical separation of the two hemithoraxes, as seen in an American buffalo or bison. In humans, the pleural cavities are separated, but a pleuropleural communication may result from intrathoracic procedures that lead to "iatrogenic buffalo chest." Two similar cases had been reported. Both patients in these reports were noted to have contralateral pneumothoraxes following an atrial rupture and misplaced atrial leads.[7,8] In both of these cases, subclavian access could be obtained only after multiple attempts. In our patient, subclavian access was obtained without difficulty. There was a ventricular lead in place, and an atrial lead accompanied the ventricular lead. The atrial lead postprocedure remained in place with no changes in threshold and impedance. There was no direct evidence of atrial perforation. There also was no evidence of pericardial effusion, ruling out hemopericardium.

Several potential causes may have played a part in our case. The left-sided pneumothorax can be explained by a possible pleural rupture during subclavian access or atrial lead placement. Although we obtained subclavian access without difficulty, a pleural rupture can never be ruled out. However, the contralateral pneumothorax cause remained a mystery; pleuropleural communication may have been the trigger as previously reported. Another possible etiology is a right atrial microperforation. A common finding in all the reported cases (including ours) was use of an active fixation atrial lead. Although we did not see any obvious

atrial perforation, a microperforation remains a remote possibility. Bullae that spontaneously ruptured may have been another possible cause. Because our patient improved after placement of chest tubes and did not develop a secondary pneumothorax, a computed tomography scan was not performed.

We successfully prevented the catastrophic outcomes associated with contralateral pneumothorax. The option to confirm this diagnosis by performing an urgent radiograph has been suggested for self-ventilating patients in high-dependency settings such as resuscitation rooms in the presence of a physician who can perform urgent decompression if necessary.[9] ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

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Difficult to Overrate

It would be difficult to overrate the value, as guides to practice, of the signs which declare themselves through the medium of the lungs in every case of unsound heart.

— Peter Mere Latham, MD, 1789-1875, British physician and medical educator, physician extraordinary to Queen Victoria

Deadly Sphenoid Fungus—Isolated Sphenoid Invasive Fungal Rhinosinusitis: A Case Report

Jason E Gilde, MD; Christopher C Xiao, MD; Victoria A Epstein, MD; Jonathan Liang, MD

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ABSTRACT

Introduction: Acute invasive fungal rhinosinusitis (AIFRS) is a potentially fatal infection, usually affecting immunocompromised patients. Isolated sphenoid sinus involvement is rare and has been reported in only a few cases. We discuss the clinical characteristics, histopathologic features, and differential diagnosis of AIFRS of the sphenoid sinus.

Case Presentation: A 57-year-old man with a history of refractory non-Hodgkin lymphoma and neutropenia presented with a 1-week duration of left-sided headache and ipsilateral cheek paresthesia. Nasal endoscopy showed mucoid drainage from the sphenoethmoidal recess. Magnetic resonance imaging demonstrated left sphenoid mucosal thickening and enhancement along the adjacent skull base. The patient underwent endoscopic sinus surgery with extended sphenoidotomy and débridement. The lateral wall and recess of the left sphenoid sinus demonstrated pale mucosa and fungal debris. Pathologic analysis demonstrated necrotic tissue and fungal hyphae with angioinvasion. Microbiology studies isolated *Aspergillus fumigatus*. The right maxillary sinus contained a synchronous fungal ball, which was removed during surgery; there was no evidence of tissue necrosis or invasive fungus in the maxillary sinus. He was treated with long-term voriconazole therapy, and 6-month follow-up showed disease resolution.

Discussion: AIFRS should be considered in the differential diagnosis of immunocompromised patients with nonspecific sinonasal symptoms. Usually, AIFRS is diffuse with multiple sinus involvement; however, isolated sphenoid AIFRS can occur. This is one of the few cases of AIFRS demonstrating isolated sphenoid involvement and is thought to be the first case showing a synchronous noninvasive fungal ball of another sinus cavity. Prompt recognition and surgical treatment may be curative and lifesaving.

INTRODUCTION

Acute invasive fungal rhinosinusitis (AIFRS) is a rare and often deadly infection that occurs primarily in immunocompromised patients. The incidence of AIFRS reported in the literature in immunocompromised patients is about 2%, with the most susceptible group being patients with hematologic diseases.[1] Other frequently affected patient groups are those with immunosuppression related to hematologic malignancy, bone marrow transplantation, poorly controlled diabetes, acquired immunodeficiency syndrome, immunosuppressive medications, and chemotherapy.[2]

AIFRS is most frequently caused by the *Aspergillus* and *Mucor* species. Studies have found a higher predisposition to aspergilli among patients with hematologic malignancies and to Mucoraceae among patients with diabetes mellitus.[2-5] Patients typically present with acute onset of signs and symptoms of sinusitis, with the most frequent symptoms reported being fever, nasal obstruction, headache, and purulent rhinorrhea with nasal crusting.[3] Pathophysiologically, the disease is characterized by fungal invasion into sinus tissue with frequent extension into adjacent structures. Treatment involves timely medical and surgical therapy. Surgical débridement of necrotic tissues is important in patients with AIFRS to reduce the fungal burden and to potentiate antifungal therapy. Short-term mortality ranges from approximately 20% to 80% across studies, largely dependent on extent of disease and recovery of immunologic function.[2,4,6,7]

CASE PRESENTATION

Presenting Concerns

A 57-year-old man presented initially to the Emergency Department with a medical history of chemotherapy-refractory diffuse large B-cell lymphoma, neutropenia, prior myocardial infarction after coronary artery bypass grafting in 2007, congestive heart failure, cardiomyopathy, and coronary artery disease with approximately a 1-week duration of left-sided headache centered along the left cheek and extending to the temple. The patient was then referred for a computed tomography (CT) scan that was initially read as sphenoid opacification without bony erosion. At the Head and Neck Surgery Clinic visit 2 days later, he affirmed he had numbness and swelling of his left cheek. He denied having nasal congestion, rhinorrhea, vision changes, fevers, chills, weight loss, and fatigue. His surgical history included laser trabeculoplasty in 2009 but no prior sinonasal procedures.

Examination revealed asymmetric pupils, larger on the left eye, with the rest of the ocular examination findings within normal limits. Nasal endoscopy in the clinic revealed bilateral inferior turbinate bogginess without lesions or erythema, no nasal polyps, and mild translucent white mucous drainage from the sphenoethmoidal recesses bilaterally.

Prompt CT and magnetic resonance imaging (MRI) were completed. Notable CT findings included mucosal thickening of the left sphenoid sinus and right osteomeatal unit obstruction by a soft-tissue density (Figure 1). Notable MRI findings included T2-weighted hypointense

Jason E Gilde, MD, is an Otolaryngology and Head and Neck Surgery Resident at the Oakland Medical Center in CA. E-mail: jason.gilde@gmail.com. **Christopher C Xiao, MD,** is an Otolaryngology and Head and Neck Surgery Resident at the Oakland Medical Center in CA. E-mail: chrisxiao@gmail.com. **Victoria A Epstein, MD,** is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: vepstein@gmail.com. **Jonathan Liang, MD,** is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: jonathan.liang@kp.org.

material in the left sphenoid sinus with abnormal thickening and enhancement along the foramen rotundum and the medial aspect of the left middle cranial fossa, eliciting concern for invasive fungal sinusitis with mild perineural/intracranial extension. Apparent T2 prolongation and enhancement of the left inferior rectus muscle and surrounding fat was favored to be artifactual (Figure 2). Chronic mucoperiosteal thickening of the right maxillary sinus with T2 hypointense and T1 hyperintense material, which was unchanged from a prior image in 2011, was thought to be compatible with proteinaceous/inspissated secretions.

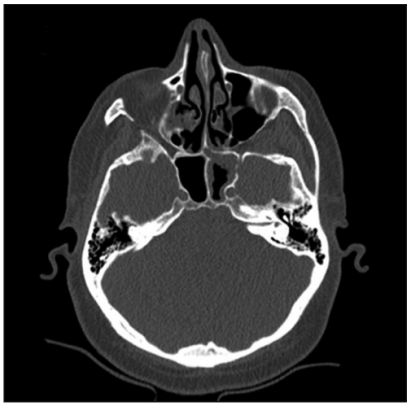

Figure 1. Computed tomography scan, axial view, without contrast enhancement. Mucosal thickening of the left sphenoid sinus is apparent. Possible dehiscence is demonstrated along the lateral wall of left sphenoid sinus.

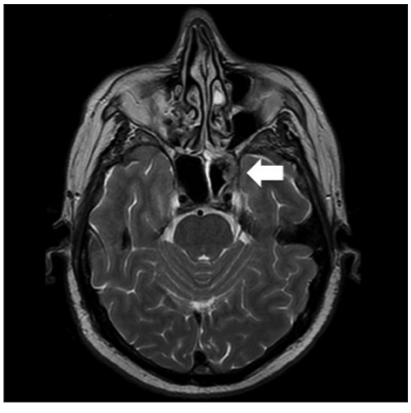

Figure 2. Magnetic resonance image, T2 weighted, axial view, with intravenous contrast enhancement. Hypointense signal is seen in the left sphenoid sinus with abnormal enhancement and thickening along the foramen rotundum and medial left middle cranial fossa (arrow).

Therapeutic Intervention and Treatment

The patient was admitted to the hospital that evening for intravenous (IV) antifungal therapy. Initial laboratory study results were remarkable only for neutropenia.

Endoscopic sinus surgery was performed the next morning. Procedures included left extended endoscopic sphenoidotomy, right endoscopic maxillary antrostomy, and right endoscopic anterior ethmoidectomy. Notable operative findings included left sphenoid with evidence of yellow-white necrotic tissue and fungal debris in the lateral wall and lateral recess of the sphenoid sinus (Figure 3). Intraoperative frozen section revealed fungal debris and necrotic tissue with submucosal presence of hyphae, consistent with invasive fungal sinusitis. On the right side, there was no evidence of invasive fungal sinusitis; well-perfused tissue was seen around a fungal ball in the right maxillary sinus, which was completely removed.

Final histopathologic analysis revealed sphenoid sinus contents consistent with acute invasive fungal sinusitis and numerous hyphae in the mucosal tissue, confirmed by positive Gomori methenamine silver nitrate stain, as well as necrosis (Figures 4A and 4B). Later, final microbiology culture isolated *Aspergillus fumigatus*. On postoperative day 1, filgrastim (Neupogen, Amgen, Thousand Oaks, CA) was started to address neutropenia after clearance by an oncologist.

Follow-up and Outcomes

On postoperative day 6, the patient was taken back to the operating room for a second look after follow-up MRI revealed possible residual left sphenoid sinus opacification. During the operative procedure, the left sphenoid lateral wall showed improved appearance of the mucosa and lacked eschar. The right maxillary sinus demonstrated a widened opening, with a thick granular appearance of the mucosa on the posterior wall. The maxillary sinus tested negative for fungal invasion on frozen sections.

The patient was discharged on hospital day 10. As an outpatient, he received IV voriconazole, 200 mg every 8 hours for 30 days, and then voriconazole orally, 200 mg every 12 hours for an additional 2 months. During the course of the next 3 months, he returned to clinic for repeated examinations and débridements.

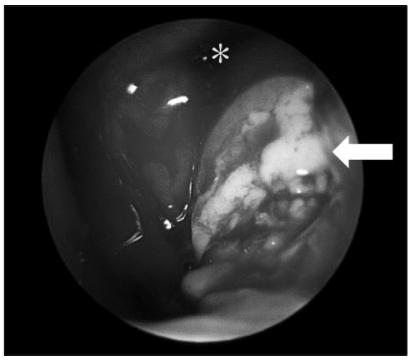

Figure 3. Intraoperative view of left sphenoid sinus, showing lateral wall (arrow) and opticocarotid recess (asterisk) with mucopurulence and tissue necrosis.

Follow-up MRI 1 month after discharge revealed substantial interval improvement with resolution of T2 hypointense fungal material in the left sphenoid sinus and in the region of foramen rotundum and bilateral maxillary and resolution of T1 hyperintensity in the right maxillary sinus.

At his six-month outpatient follow-up examination, nasal endoscopy revealed a healthy sphenoid sinus with a patent os and no evidence of recurrent sinus disease. The case timeline appears in Figure 5.

DISCUSSION

AIFRS is a rare disease, occurring in only about 2% of immunocompromised patients. The most susceptible group reported in the literature has been patients with hematologic malignancies. Valera et al[3] reported neutropenia, either caused by aplastic anemia or secondary to chemotherapy for hematologic malignancy, as the main cause of AIFRS (62%), a finding in agreement with other studies.[8,9] Regarding isolated sphenoid disease, as demonstrated in our patient, the rarity is increased. Of all sinus infections, the estimated incidence of sphenoid sinusitis is 2.7%. Isolated sphenoid sinusitis can be bacterial or fungal. Fungal sinusitis represents approximately 15% to 20% in all cases and is classified as noninvasive, invasive indolent, and fulminant. Only a few cases of sphenoid sinus aspergillosis have been reported in the published literature. Lee et al,[10] in 2009, reported that

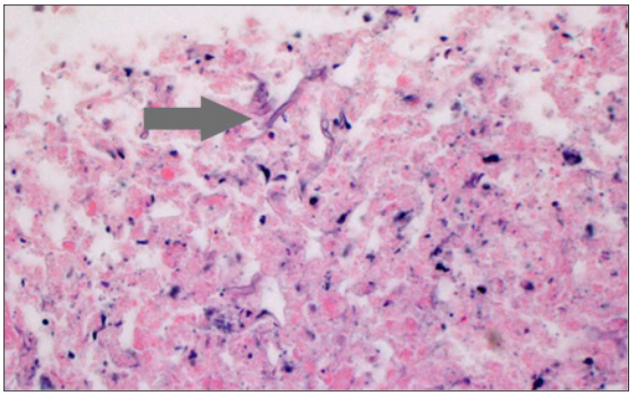

Figure 4A. Histopathologic specimen, hematoxylin-eosin stain, showing fungal hyphae (arrow) and necrotic tissue with submucosal presence.

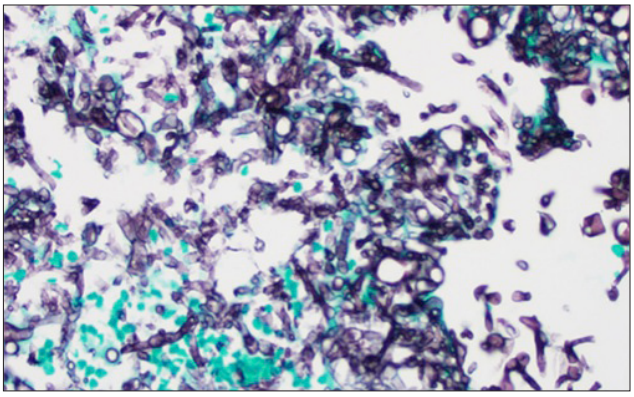

Figure 4B. Histopathologic specimen, Gomori methenamine silver nitrate stain, showing fungal elements stained black with sharp margins and a cleared center, against a light-green tissue background.

50 cases of noninvasive sphenoid aspergilloma were published since 1950. However, only a few cases of AIFRS of the sphenoid have been reported.[6,10]

The causative organism in our patient was *Aspergillus,* which, along with Mucoraceae, are the cause in most cases of AIFRS. *Aspergillus* has a predisposition for patients with hematologic malignancies, whereas Mucoraceae species tend to occur more often in patients with uncontrolled diabetes.[2,3,5] Both fungi are saprophytes, found worldwide in dust, decomposed substances, soil, and fruits, as well as in the throats, nasal cavities, and feces of healthy individuals. In immunocompromised patients, these fungi can be angioinvasive, resulting in thrombosis and ischemia of the nasal mucosa. The fungi can rapidly spread and invade paranasal structures, including the orbit and brain. Mucormycosis-causing species primarily invade the nose, lungs, and gastrointestinal tract, whereas *Aspergillus* species primarily invade the lungs and later spread to other organs.[4] *Rhizopus* has also been identified as a common causative organism in some cases, although its prevalence ranges greatly, between 0% and 26% in the series in the literature,[3,11,12] and was not reported in a 2013 meta-analysis of 398 patients by Turner et al.[13] Recently, dematiaceous fungi have now been recognized as causal organisms of AIFRS. Dematiaceous fungi are environmental pathogens, characterized by melanin in their cell wall. In 2010, Derber et al[14] reported that since 1987, there have been 14 published cases of invasive sinonasal infection caused by dematiaceous fungi in immunocompromised individuals.

For identification of patients with AIFRS, the history and physical examination findings are of paramount importance. Demographically, AIFRS tends to occur in the fifth decade of life and in female patients.[2,6,10,15] Patients traditionally present with signs and symptoms of sinusitis but may also display orbital and central nervous system signs and symptoms. For example, in the series of 32 patients described by Valera et al,[3] the most frequent symptoms reported were fever, nasal obstruction, headache, and purulent rhinorrhea with nasal crusting. Of these symptoms, headache has been cited as the most common presenting factor.[6,10,16,17] Clinical signs may include nasal discharge, epistaxis, orbital disorders (including oculomotor restriction and decreased visual acuity), and dysesthesia of the maxillary division of the trigeminal nerve. Posterior nasal discharge, although nonspecific, is frequently described. Be wary, however, of blood-streaked nasal discharge because this is considered a more specific indicator of AIFRS. Bleeding is related to either irritation of the sinus mucosa by the fungal infection or, at a more advanced stage, bone destruction of the sinus wall.[6] On nasal endoscopy, the most common signs seen are characteristic necrotic avascular and black crusts, granular serosanguinous rhinorrhea, septal perforation, and occasionally, visible hyphae.[4]

Additionally, the medical history will nearly always include an immunocompromised state, because it is the greatest risk factor for AIFRS. Monroe et al[2] reported that approximately one-fourth of the patients with AIFRS had more than one cause of immunosuppression.[2] AIFRS of a nonimmunocompromised patient is exceedingly rare. Lee et al[10] examined four cases of acute invasive sphenoid sinusitis and found one patient without a history of immunosuppression, and the others having either diabetes or multiple myeloma. In addition, any factor inducing decreased aeration of the sphenoid sinus has been classically described to constitute a risk factor for the development of fungal disease. For example, the presence of polyps on nasal endoscopy may contribute to obstruction of the ostium of the sphenoid sinus.

Our patient presented with headache but, interestingly, did not report other sinus complaints. Salient clinical findings included ipsilateral cheek paresthesia and pupil dilation, suggesting dysfunction of the maxillary division of the trigeminal nerve and oculomotor nerve, respectively. Nasal endoscopy revealed only mild, partially clear, white drainage from the sphenoethmoidal recess but no characteristic necrosis. The history of refractory diffuse large B-cell lymphoma aroused our suspicion for AIFRS, particularly when we considered the cranial nerve deficits and the risk of intracranial extension with AIFRS. It is critical, therefore, to keep AIFRS on the differential in immunosuppressed patients with both specific and nonspecific findings.

The distribution of disease in our patient was relatively unique. Valera et al[3] found a predominance of unilateral disease with bone erosion, with diffuse sinus involvement less common, orbital involvement being uncommon, and only a single case of intracranial extension. Sphenoid sinus involvement is less common than maxillary or ethmoid involvement, and isolated sphenoid disease is even rarer.[3] Moreover, simultaneous mycetoma has not been reported in the prior literature. The presence of the mycetoma does suggest the transformation of noninvasive to invasive fungal rhinosinusitis. Lee et al[10] found only 25% of their isolated invasive sphenoid fungal sinusitis to be acute, and only 4 cases over 12 years, highlighting the rarity of this distribution. Furthermore, all the patients in that situation presented with visual disturbances, which were absent in our patient.

In treatment of AIFRS, timely recognition of the underlying disease that caused the immunodeficiency and its correction, if possible, are essential to improve the survival rate in these patients. The goals of treatment in AIFRS are the reestablishment of the immune response in combination with systemic antifungal therapy and surgical débridement of necrotic sites. Surgical débridement of necrotic tissues is crucial to increase the delivery of antifungal drugs to affected tissues, reducing the fungal burden, and slowing the progression of disease. Additionally, débridement reduces stress on neutrophil development and helps bone marrow recovery.[3] In our patient, the source of his immunosuppression was known, and the patient was started on a regimen of filgrastim, but in the acute setting, the course of action left to us was surgical débridement and IV antifungal therapy.

Interestingly, there is no well-defined course for voriconazole therapy, given the rarity of AIFRS. Traditionally, amphotericin B has been used, but it also comes with substantial side effects. A 2002 randomized comparative study of voriconazole and amphotericin B in invasive aspergillosis found better outcomes and fewer side effects with voriconazole.[7] Additionally, the Global Comparative Aspergillosis Study found a similar result in a randomized controlled trial. This study had a median course of 7 days for IV voriconazole, followed by 76 days of oral voriconazole.[7,18] The Infectious Diseases Society of America guidelines for invasive aspergillosis now recommend voriconazole use.[19] As such, our decision was to use voriconazole as the primary antifungal therapy in our patient. He received IV voriconazole for 30 days, followed by oral voriconazole for 60 days after an infectious disease consult, with complete recovery and minimal side effects.

The outcome for our patient was good, with resolution of AIFRS. Success was attributed to early detection and treatment of a relatively limited extent of disease. In most cases of AIFRS, the morbidity and mortality are substantial. A meta-analysis by Turner et al[13] in 2013 examining survival in AIFRS found an overall survival rate of 49.7%, with intracranial involvement and advanced age being negative prognostic factors on multivariate analysis. In an analysis by Foshee et al[20] of 27 patients, patients with sphenoid involvement had a mortality rate of 56.3%. In a series of 29 cases reported by Monroe et al,[2] the median survival of this group was 3 months, with only 17% overall survival at 6 months. The study notes that a large proportion of patients in whom AIFRS develops will die of their disease or of other causes within 6 months of diagnosis. Extension beyond the sinuses portends worse prognosis. Recovery of immune function is believed to be vital to disease clearance. However, little other prognostic data are known regarding this rare patient population, specifically as it relates to long-term survival.[2] Treatment does relate to mortality. Before the advent of amphotericin B, mortality rates were as high as 90%. Mortality rates were reduced to 15% to 50% with combined use of surgery and newer antifungal medication.[2-4] The cause of immunosuppression may also have an effect on survival. Valera et al[3] found the mortality rate in patients with aplastic anemia and diabetes mellitus was high (near 100% when considering both groups together), whereas those with acquired immunodeficiency syndrome/human immunodeficiency virus (AIDS/

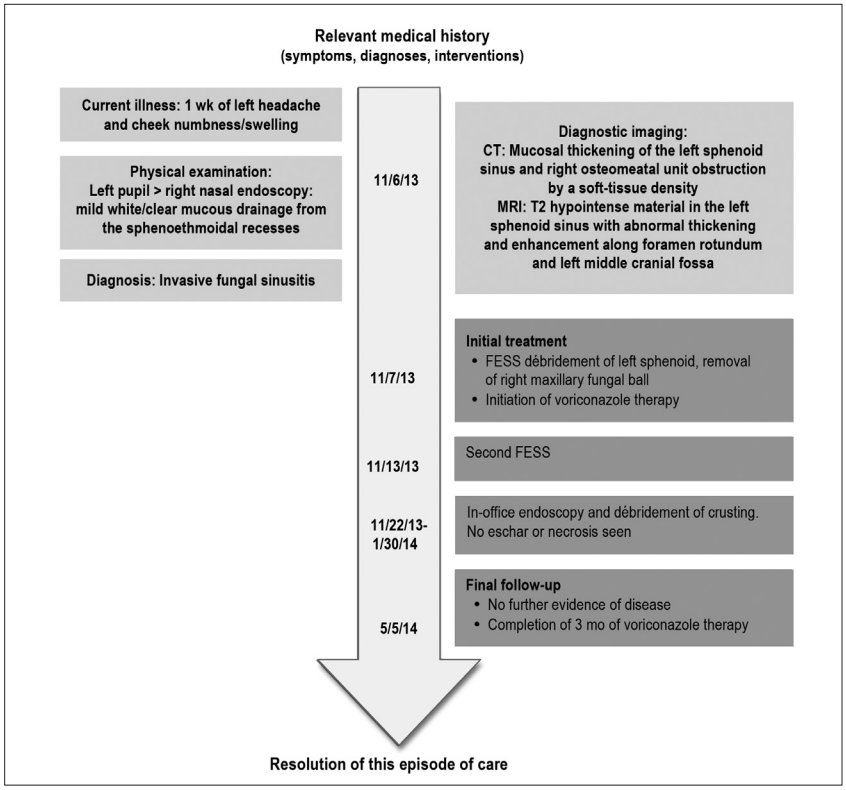

Figure 5. Timeline of the case. Dates are month/day/year.

CT = computed tomography; FESS = functional endoscopic sinus surgery; MRI = magnetic resonance imaging; > = larger than.

HIV) all had a good outcome. Patients with hematologic malignancies showed an intermediate prognosis; one-third of these patients died of AIFRS.[3]

CONCLUSION

AIFRS is a rare but deadly disease. Clinical suspicion must be high in the immunocompromised patient, because clinical signs and symptoms may be subtle. Prompt ancillary testing, including imaging and laboratory testing, can aid in diagnosis, but histopathologic evaluation is fundamental. The pattern of involvement is usually diffuse sinus disease, but it is often unilateral. Isolated sphenoid involvement is rare. Effective treatment relies on both addressing the underlying cause of immunosuppression and treating the fungal disease with surgical débridement and antifungal therapy. Morbidity and mortality are high, with orbital and intracranial extension signifying worse prognosis. Ultimately, timely diagnosis and treatment are critical to achieving satisfactory outcomes. ❖

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Fundamental Activity

The fundamental activity of medical science is to determine the ultimate causation of disease.

— Wilfred Batten Lewis Trotter, FRS, 1872-1939, English surgeon and pioneer in neurosurgery

The Art of Healing through Narrative Medicine in Clinical Practice: A Reflection

Aeman Muneeb; Hena Jawaid, MBBS, FCPS; Natasha Khalid, MBBS; Asad Mian, MD

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ABSTRACT

The art of medicine has roots that lie deep in developing the biopsychosocial connection. Understanding a human body (both its physiology and pathology) along with components of emotional and spiritual cores can lead to provision of excellent medical care and better outcomes. The harmonization of psychosocial consequences of a biological disease is helpful not just for health care professionals but also for patients. Where it keeps the empathy and compassion alive and results in greater patient satisfaction, it also helps boost the physician's morale.

Our objective is to reflect on the impact of narrative medicine on physician-patient dynamics for health care professionals in a clinical setting. This article was written after synthesizing the findings of evidence-based literature, retrieved from different sources, along with our own reflections on our encounters with patients.

One could infer from the evidence-based research that the practice of narrative medicine improves one's concern and understanding toward the patient. This requires more time from the clinician, but medical care without compassion and humaneness causes high rates of dissatisfaction among both patients and health care practitioners, along with the risk of recurrent ailments. Our own patient encounters provide a testimony to this inference. The biopsychosocial model carries the same holistic approach toward patients. The mainstay of treatment in any domain of medicine should contain thoughtfulness for the sufferer rather than sole consideration of the suffering.

INTRODUCTION

The art of medicine has roots that lie deep in developing the biopsychosocial connection. Understanding a human body (both its physiology and pathology) along with components of emotional and spiritual cores can lead to provision of excellent medical care and better outcomes. The harmonization of psychosocial consequences of a biological disease is helpful not just for health care professionals but also for patients. Where it keeps empathy and compassion alive and results in greater patient satisfaction, it also helps boost the physician's morale.

There is a new spectrum of interest among medical educators to help physicians-in-training develop core features of professionalism along with high ethical and moral standards by reflective exercises and writing patient experiences. A constellation of these reflective exercises is known as narrative medicine.

What is Narrative Medicine?

Narrative medicine has been defined by Charon[1] as "medicine practiced with narrative skills of recognizing, absorbing, interpreting and being moved by stories of illness." Narrative medicine uses a patient-centered approach to understand suffering, disability, ailment, and personhood in the practice of medicine.

Narrative medicine is an effective tool to strengthen the physician-patient kinship and care. This provides the physician a deeper understanding of the patient's disease from a broader aspect that includes his/her emotions, as well as the biological, cultural, familial, and existential situation. It aids the physician in establishing a therapeutic coalition to generate and to proceed to establish a differential diagnosis. It also helps to provide effective care to the patient, not only helping him/her heal, but also making the patient feel heard and understood by the health care professional.[1]

When sociologists studied medicine in the 1960s, they described lack of feelings and empathy toward patients as "detached concern."[2] This was meant to portray an encounter in which the physician focused on the disease but gave little thought to the patient's circumstances. Today with the development of the newly emerging knowledge from narrative disciplines, physicians are reinventing themselves by bringing the power of storytelling, appreciation, and analysis into routines of scientific clinical work.

Our objective in this article is to reflect on the impact of narrative medicine on physician-patient dynamics for health care professionals in a clinical setting.

Dry Leaves: Is Compassion Dying in the Clinic?

Physician-ethicist Edmund Pellegrino[3] suggests that writing one's experience with patients, colleagues, or difficult parts of a duty can expand a physician's awareness regarding meaning of illness and healing.

This article was written to consider the impact of narrative medicine on medical practice such as the reincarnation of the dying compassion in medical clinics.

A literature review was done and articles were collected on narrative medicine and humanism in medicine. The articles are reviewed here in light of our own experiences in the clinical setting. The benefits of narrative medicine for the physician were studied. A workshop was conducted at our university hospital regarding hands-on narrative medicine practice, and our work from the workshop is also a part of this piece.

Aeman Muneeb is a Medical Student at Aga Khan University in Karachi, Pakistan. E-mail: aemanmuneeb@live.com. **Hena Jawaid, MBBS, FCPS,** is a Senior Instructor in the Department of Psychiatry at Aga Khan University in Karachi, Pakistan. E-mail: hena.jawaid@aku.edu. **Natasha Khalid, MBBS,** is a Research Associate in the Department of Obstetrics and Gynecology at Aga Khan University in Karachi, Pakistan. E-mail: natasha.khalid@aku.edu. **Asad Mian, MD,** is an Associate Professor in the Department of Emergency Medicine at Aga Khan University in Karachi, Pakistan. E-mail: asad.mian@aku.edu.

LITERATURE REVIEW

Writer's Block: Why Write?

We believe that reflective writing may be one tool in a multimodal collection to protect and to promote physician mental and physical health. We have identified the following three characteristics of well-being as likely to be positively affected by writing: Emotional equilibrium, self-healing, and building community/reducing isolation.

In the process of writing, learners usually step back from the actual situation, fears, and pressure (of training, duty, or demand) to halt and to reflect on a bigger picture to consider dos and don'ts of professionalism in a given situation. Naomi Goldberg[4] calls the writing experience a "wild mind phenomenon" that is essential for students to cultivate reflective and meaningful imagination. This gives them the ability to express themselves metaphorically.

Dealing with Emotions: The Benefit to the Physician

Coulehan and Williams[5] wrote that physicians must cultivate a balance between emotional steadiness (the ability not to be overwhelmed by the patient's suffering) and emotional tenderness (the capacity always to be moved by that same suffering). A space to become familiar with physicians' emotions and those of others can reduce isolation. One of the authors of this paper reflects how she uses writing as a medium to destress herself after a long day at work.[6] According to her, this strategy is an ultimate mode of therapy that appears to work every time.

Downie[7] has categorized possible outcomes of humanities-based interventions as transferable skills, humanistic perspective, situational coping, self-awareness, and joint investigation. The writing-reading-listening model can make useful contributions to these hard-to-teach clinical dimensions.

Pellegrino[3] suggests that writing can be a hands-on, experiential method for increasing physician cognizance of the meaning of illness and of doctoring. Writing can be in the form of essays, short skits, plays, poetry, and critical incident essays.

The payback is not just for the writer of the story alone. Listening to the writing of colleagues offers learners a chance to sympathetically release their own helplessness and fears. Exposing learners to this position of reciprocity and equality offers them an alternative to the normally perceived role of physicians as unilateral and hierarchical.

The general hypothesis is made on this basis that it might be a "transfer effect"[8] in which skills practiced in these sessions generalize to other aspects of doctoring. Three dimensions that may be influenced by the writing process are narrative competence, empathy, and insights into the process of patient care itself.

Therapeutic Aura: The Benefit to the Patient

The writing itself holds a therapeutic effect for a sufferer.[1] Writing one's own story and being heard by peers can help learners clarify standards and rediscover their own ethical scope. It ignites the resolution pathway in the brain to take its action to resolve a matter or provide valid and rational explanation for a condition or emotion. The role of physicians is culturally considered as hierarchically superior and unilateral. The emotional reflection gives the patient a stable footing in the therapeutic alliance with the physician.[1] The writing can serve as a means of catharsis, and the emotions can be channeled into writing.

Not only does this benefit the sufferer, but others in the same situation may find relief in reading others' pieces. This can help form a strong tie between them, which can lead to mutual collaboration and support.

Psychological Theories and Narrative Medicine

Proto-Narrative Nucleuses

A study conducted in children in a hospital in Italy states how every autobiographical and fictional event told by a person is derived from "inner proto-narrative nucleuses."[9] This means that the pieces of prospective tales told by a person are gathered in a person's psychic archive. This is linked to his/her experiences and interpersonal relationships. These "inner proto-narrative nucleuses" are also derived from what the subject deciphers from all that s/he sees or hears around himself/herself.

In a person's psychic archive, then, are connections between the autobiographical and nonautobiographical stories. These result from the two intersecting dimensions that influence each other and affect how the person views his/her story in context of all that goes on around him/her. This has implications for a physician-patient relationship as the writer's (physician or patient) viewpoint may be influenced by what s/he has experienced before. An oncologist's approach toward a patient may, for example, harbor the influence of his/her experience with other patients. In a way, these "proto-narrative nucleuses" affect how we interact with the world around us and are thus of immense significance, not just in narrative medicine but also in the physician-patient relationship.

Theory of Uncanny

Freud's theory states that "uncanny is anything we experience in adulthood that reminds us of earlier psychic stages, of aspects of our unconscious life, or of the primitive experiences of human species."[10] The "uncanny" is when something in present life serves as a reminder of what has been long forgotten in our past. Storytelling can, hence, be one means to integrate our present with our past, our medical practice with our childhood experiences.[10] Or, if you integrate this with the "proto-narrative nucleuses," it serves as a means to place our present experience with those of the past and look at them in a holistic light.

Both these models/theories imply that whenever we tell a story, we put ourselves as one of the characters, either active or passive, and foretell the event from a personal situation that may have happened to us or someone else. We alter it and narrate it from our aspect of what could have occurred or should have been the cause or conclusion.

DISCUSSION: THE AUTHORS' TAKE ON NARRATIVE MEDICINE

Three pieces are presented here as examples of narrative medicine. The first one, a prose named "The Observer," was written by NK to document her experience dealing with a patient the same age as herself. Initially she was methodical in dealing with the patient but soon realized that her own problems were miniscule compared with what the patient faced with her chronic diagnosis.

The second example of narrative medicine is artwork (Figure 1) that was drawn by HJ to portray a patient with borderline personality disorder who feared relationships (R) penetrating her world/self (S) and had much difficulty separating the two. This caused problems in her life, which led to her seeking psychiatric help.

The third example is a poem, "Black and White," written by AM about a patient

The Observer
By Natasha Khalid, MBBS

The shift ends and I am writing the postdialysis weights of the patients as I ask them their names. My eyes are more focused on the weighing machine, rather than on the human being standing on it. "How much is my weight, again?" The question breaks my reverie about my envisioned optimal job, while writing down the weights of the patients in the log book. The girl standing on the weighing scale, the log book tells me, is the same age as me: 27. She's a pleasant-looking young woman wearing lovely eyeliner and a nicely styled Abaya (a veil usually worn by [a Muslim] woman as a symbol of religious/cultural beliefs). I wonder of all the other 27-year-olds, myself included, and their routine struggles, this one's issues take on a different dimension altogether given her almost daily dialysis routine. In a mere instant, I glance back at all my problems in life that presumably begin and end with the USMLEs [US Medical Licensing Examination]—problems I have chosen for myself. How every doctor I know in my age bracket is worried about the USMLE exam; how our day begins and ends with the thought of the number of hours we are able to study; how much we will score; how many publications and international electives we have under our belt; above all, whether we will match or not; how, if we don't match, our life is going to end. I realize every day we are stressed about the future—to the point that we fail to enjoy the present.[6]

who gets married, experiences "swaying" emotions, and feels that she can no longer accept her husband as her true love.

CONCLUSION: THE PHYSICIAN'S ART

Narrative medicine is an important and integral part of medical practice. The benefits are varied and reach out not just to the patient or the physician involved but also to listeners and readers of the narrative. This helps build empathy in the physician-patient relationship and can be of use as the patients feel themselves heard and understood while physicians get a chance to recognize their hopes and to confront their fears. It leads to the phenomenon of "transfer effect" whereby, through narrative medicine, a physician's practice can be modified. The benefits are available not only to a physician's practice but also to other health care professionals. Narrative medicine, then, is a powerful tool that we, as health care professionals, should hold onto to rejuvenate the components of care, integrity, empathy, and expertise within and without. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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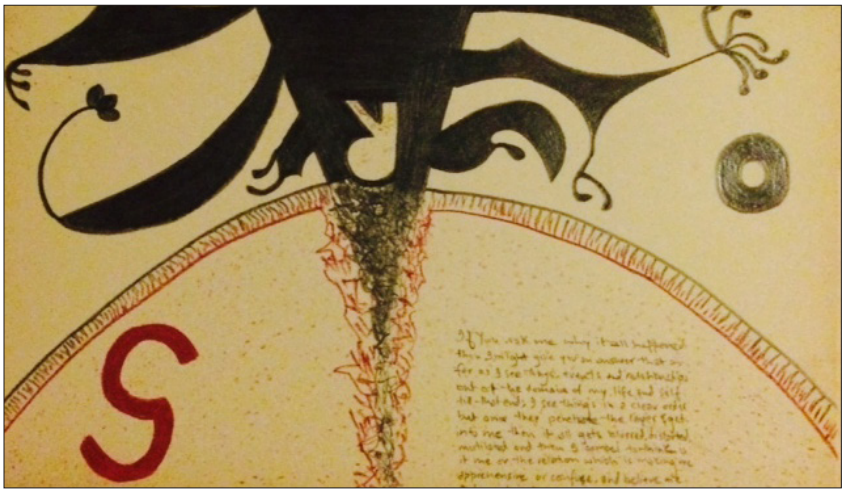

Figure 1. Artwork as example of narrative medicine by Hena Jawaid, MBBS, FCPS.
R = relationships; S = self.

Black and White
By Aeman Muneeb

When they stay around me,
It's all fun and games,
My existence, so beautiful.
My world perfect with these
Relationships.

A mere penetrance,
Into what is called self,
And all that ceases to hold
True.

When I saw you first,
Never for a moment,
Did doubt overshadow,
This emotion called love.

I feel on the edge,
Two days into our union,
I oscillate between,
Desperation and elation.

All appears ugly,
As I became your wife,
My meaning so distorted,
Darkness surrounds my life.

I want to run away,
Before my feelings again sway,
Truth be told, I no longer want thee,
"Borderline" is what they call me.

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Finding Purpose: Honing the Practice of Making Meaning in Medicine

Lois Leveen, PhD

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ABSTRACT

Despite decades of advances in diagnosing and treating a broad range of illnesses, many changes in our health care system impede true caregiving, leaving patients and practitioners dissatisfied and creating an emotional burden for practitioners that contributes to the staggering rates of physician burnout. Given this dissatisfaction and disconnection, practitioners and patients alike can benefit from structured opportunities to explore the expectations, assumptions, and emotions that shape our understanding of health and illness, and thus our experiences within the health care system. This article demonstrates how group discussions of poetry—something that might seem irrelevant to medical practice or physical wellness—can foster communication, connection, and collective reflection for physicians, interprofessional health care teams, and groups that include practitioners, patients, and families, allowing participants to once again find meaning in medicine.

INTRODUCTION

What is the purpose of a poem? The question might seem esoteric and, within the pages of this journal, irrelevant, especially given the daily demands made of health care practitioners and the emotional distress too many practitioners (and patients) feel in the current health care system. But as much of what physicians do becomes "mechanized work, often menial, squeezed of human emotion, meaningful moments, and personal conversation,"[1] it behooves us to understand how discussing a poem facilitates emotional openness and meaning-making through personal conversation. Ultimately, the purpose of a poem in the world of health care is to reconnect practitioners to their own sense of purpose.

WHY POETRY?

This process can be most clearly demonstrated not by explicating a particular poem, but by explicating how to guide discussions of poetry, drawing on examples from workshops I lead for physicians, interprofessional health care teams, and groups that include both practitioners and members of the public. Poetry is in part a practical choice; most poems are short enough that groups can read them together during the workshop, requiring no advanced preparation—a boon for busy practitioners. But the real power of poetry stems from the way a poem depicts experience. Poetry is typically indirect, even indeterminate. Poems demand careful deciphering. They can be daunting. Working together to understand a poem, to uncover and explore its possible meanings, provides an exceptional opportunity for the connection and reflection that is too often missing from health care today.

Unlike narrative medicine, which focuses on developing a clinical "narrative competence" in which diagnosis and treatment depend on understanding the stories actual patients tell,[2,3] poems provoke us to contemplate in ways that contrast with yet complement conventional clinical competence. Brief yet densely laden with content, a poem—as a physician in one of my workshops noted—can seem like a clinical encounter with a complicated patient. But a poem does not require us to arrive at an irrefutable diagnosis to determine the best treatment. Instead, an encounter with a poem treats *us*, by pushing our tolerance for ambiguity and uncertainty, deepening our comfort with collaboration, and enhancing our cognitive flexibility. These traits are increasingly identified as integral to true caregiving; they are also important for patients and their families to cultivate as they navigate the emotional and physical vagaries of illness.

DISCUSSING POETRY TO ADDRESS DIFFICULT EMOTIONS

My role in leading these discussions is not to reveal what the poem means; it is to pose questions, to coax participants into conjecturing, and to mediate the process through which we collectively deepen our understanding by probing multiple possibilities. Consider Denise Levertov's "Talking to Grief"[a,4]:

Ah, Grief, I should not treat you
like a homeless dog
who comes to the back door
for a crust, for a meatless bone.
I should trust you.

I should coax you
into the house and give you
your own corner,
a worn mat to lie on,
your own water dish.

You think I don't know you've been living
under my porch.
You long for your real place to be readied
before winter comes. You need
your name,
your collar and tag. You need
the right to warn off intruders,
to consider
my house your own
and me your person
and yourself
my own dog.

Lois Leveen, PhD, is a Kienle Scholar in Medical Humanities at Penn State College of Medicine in Hershey, PA. E-mail: lois@humanitiesforhealth.org.

The first question I might pose is why Levertov uses the extended metaphor of a dog to embody grief. What is the connotation of a dog? Of *a homeless dog*? Even in a small group the answers to these questions vary, and we take our time discussing each of them, our first indication of how subjective meaning can be. (I invite you, the reader, to pause to contemplate your own possible responses to such questions as you read this article, to gain a better sense of the process of reflection that participants experience in these workshops.)

Then I broaden our consideration from the analytical to include the physical, directing participants to repeat the word *dog* together three times, followed by *grief*, also three times. I invite them to describe the different corporeal sensations experienced when saying each word aloud. As participants detail the bodily effects of hard versus soft consonants and long versus short vowels, we connect these observations to their earlier postulations about what the metaphor, and the poem as a whole, might mean.

Even as I offer yet more prompts to spur discussion, I invite participants to pose their own questions, identifying what strikes them as interesting or odd and then allowing the group to riddle out possible interpretations. In each workshop, participants put forward new questions and original observations. Why is the word *Grief* capitalized? Why is *I should trust you* the only sentence set entirely in its own line? How do the stanza breaks divide different ideas in the poem? What's the effect of ending not one but two lines with *You need*? Who are the *intruders*, and how will Grief, the *you* addressed in the poem, *warn* them *off*? What's the effect of addressing the poem to that *you*? Would the final line express the same thing without the word *own*; what does that addition emphasize? As the facilitator, I draw attention to the steps involved in collective meaning-making by commenting on how each participant's contributions—whether s/he is posing questions or hypothesizing responses—expand our shared understanding of the poem. Although reading literary fiction on one's own may increase empathy, mentalizing, and other emotional competencies,[5] as the guide I emphasize how this collaborative process of deciphering, interpreting, and discussing a challenging poem improves the capacity for interpersonal connection as well as individual reflection.

Only after we have collectively honed our close reading of the poem do I ask what this literary work has to do with medicine. This is a big leap, and I never know where we will land; it depends on what connections the participants in a particular workshop make. Perhaps the most literal-minded respond that grief follows a death, and death is what happens when medicine fails. We can then unpack those assumptions by asking new questions: Is death the only thing that causes grief? Must we presume that death is a "failure" of medicine, rather than a certainty that we should help both the dying and those who care for them to navigate? Or participants might use the poem to reflect on the effects of metaphor in medicine, considering how the metaphors used to describe diseases and treatments shape the expectations of patients and practitioners, in ways that can be edifying, empowering, obfuscating, or even unintentionally harmful.[6-9] At a conference on alleviating burnout, physicians spoke candidly about personal and professional griefs they carry, griefs that they seldom have opportunities to speak about, let alone to ameliorate through the kinds of connections we forged while discussing the poem.

BROADENING THE MEDICAL MINDSET

Most physicians choose medicine because they seek a meaningful career, yet 21st-century medical training and practice offer few opportunities for meaning-making.[10] This, ultimately, is what a poem can provide. Premed and medical school courses, residency, and the continuous pressures of modern medical practice all emphasize getting swiftly to the right answer, to the detriment of practitioners and patients.[11,12] By contrast, poetry provides a way to hone a tolerance for ambiguity, what physician-poet Angela Andrews[13] terms "the capacity to not know," as a means to restore both the creative and the caring aspects of medicine. Cultivating this capacity collectively—whether in a group composed of physicians, of interprofessional teams, or of pracitioners, patients, and patients' family members—can have profound effects on our expectations and thus our experiences of illness and of health care.

Although reading for meaning is as important in medicine as it is in the humanities, the process is quite different. As we introduce poetry—or other humanities content—into medicine with the intention of enriching practitioners' (and patients') ways of thinking and interacting, we need to acknowledge that becoming adept at humanities approaches to analyzing and discussing this content can be challenging. My role as a humanities-trained educator and facilitator is to model a willingness to learn the language and practices of a new field (in my case, medical education and medical practice) as I guide participants through practices that may be quite new to them.

ANALYZING POETIC FORM TO UNDERSTAND THE PRACTITIONER-PATIENT RELATIONSHIP

Poems cannot be read the way patient histories are, even when they are by or about patients; poems yield such rich material for contemplation and discussion precisely because they are not intended as factual reports. This becomes especially apparent when we consider the formal aspects of poetry, which might include anything from alliteration, assonance, or imagery to rhythm and rhyme scheme. Although this sort of analysis may be unfamiliar to many health care practitioners, they often find it extremely edifying. Focusing on these tools poets use to convey theme and emotion along with information allows us to fathom some of the most challenging aspects of medicine, as in "Recurrence" by Judy Rowe Michaels[b,14]:

Won't meet my eyes, doesn't offer his hand,
jaw's locked down grim as a TV surgeon's.
My return has marked me *failure*.
Only two years ago that hand, gloved,
was probing me for tumor every month,
his mantra, gently, "I'm sorry, I'm sorry"
each time I flinched. Three years ago those hands
took out my ovaries, sampled tissue. Those eyes

broke the bad news to me when I woke up.
"Inoperable," he says now, heads for the door
muttering "Chemo." I block him: "Couldn't the scan
be wrong?" He pushes past. "Hell, why?
Thing lit up just like the Fourth of July."

This is a difficult poem. Not difficult because it is hard to determine what is going on; it's actually a straightforward account. What is difficult here is the emotional valence, for both patient and practitioner, which is why it is so powerful to discuss. Focusing first on formal aspects allows us to approach the difficult emotional content slowly, through deep reflection.

We might begin with simile, a poetic technique that initially appears in the second line. Why use simile to juxtapose one's own surgeon with *a TV surgeon*? What does the grimly locked jaw convey to the patient, and what should it convey to us? Here the ambiguity of poetry allows us to probe what is often hidden, even insidious, in such scenes: "He doesn't know how to show real emotion," lamented one workshop participant, a woman who had been treated for cancer. "They taught us that in medical school," replied another participant, one of the many physicians trained to mask her own feelings in front of patients. The poet's simile thus opens up a crucial conversation about what both patients and practitioners feel regarding *care*—a word that can refer to either deep compassion or coldly "clinical" treatment.

Participants may be even more distressed by the simile that closes the poem, finding *Thing* and *just like the Fourth of July* inappropriate and disturbing. How, they wonder, could a doctor speak this way? To answer that question, I guide the group through an examination of the lines between the two similes, considering how the poet deepens what we can learn about this surgeon and about the patient's relationship to him. As we discuss the way his jaw, his hand, his eyes are represented, I might share an example or two of blazon, a poetic form dating to the Renaissance, which catalogs each feature of the beloved's body. Is the idea of blazoning the surgeon apt or ironic? We might also consider how repetition and alliteration, two more techniques used in the poem, emphasize the shift from *I'm sorry, I'm sorry*—soft sounds conveying compassion—to the aggressive *p* of *pushes past*. The poet's unusual inclusion of italics leads us to postulate about whose *failure* the recurrence might be, and what surgeon and patient each might feel about this failure. The poem thus prompts us to discuss what support patients, families, and practitioners need when facing undesirable prognoses.

We might then reconsider the final lines: *"Hell, why?/Thing lit up just like the Fourth of July."* Although rhyme is a feature we often associate with poetry, this end-rhyme sets these two lines off from the rest of the unrhymed poem. What is the effect of the rhyme? How does it further or challenge themes we've already identified in the poem? What, ultimately, should we conclude about the similarities or the differences between reading a scan and reading a poem? If the purpose of poetry is to imbue us with a tolerance of ambiguity, does "Recurrence" require us to understand a medical scan as something that brings certainty or that evokes uncertainty, or both?

The answer to that question might depend on whether we are talking about the physical evidence of illness or the emotional effects that evidence will have, not only on patients and their families but on the practitioners who treat them. This returns us to the fundamental purpose of a poem in health care: its potential to allow us to come together to explore such challenging questions, in meaningful ways.

CONCLUSION

There are many ways to create opportunities for practitioners, patients, and patients' families to experience the reflection and connection that comes through discussions of poetry. The examples cited in this article draw on discussions I have led at medical conferences, during interprofessional brown-bag lunches in a primary care practice, and in public settings such as an art museum. Even in a single session in which participants have never met before, nearly everyone attending volunteers contributions to the conversation, sharing insights and emotional responses. Multiple sessions, which may be organized around a theme, can be even more effective, because they allow trust, camaraderie, and compassion to build among participants, while encouraging the habit of reflection and connection to be practiced over time. Varying the selection of poems enriches these discussions. Although some poems might directly address health, illness, or medical care, as "Recurrence" does, others can allow participants to contemplate complex topics such as race, family, language and cultural difference, or violence, or to probe powerful emotions such as fear, hope, love, or, as Levertov's poem so effectively shows, grief—all of which shape our experience of health and health care.

Even in a single session in which participants have never met before, nearly everyone attending volunteers contributions to the conversation, sharing insights and emotional responses. Multiple sessions, which may be organized around a theme, can be even more effective, because they allow trust, camaraderie, and compassion to build among participants, while encouraging the habit of reflection and connection to be practiced over time.

Whatever the format or specific literary content, the success of these discussions depends on assuring participants that they do not need particular expertise to contribute; they need only notice whatever strikes them in a poem and then work as a group to explicate the poem on the basis of those observations. Leading these discussions does require expertise, as any good teaching does, although in defining that expertise it is important to remember that what is being taught here is not mastery of content, it is a way of thinking and communicating. Understanding the formal structure of poetry allows me to help participants reflect on the effects of metaphor, assonance, rhythm, and similar elements, to deepen our exploration of the themes these elements convey. Nevertheless, it is important that I do not assume that I know what a poem means. Instead, what might be termed a "humanities-based proficiency" allows me to facilitate these discussions with genuine curiosity and a belief

that what participants contribute can and should shape my own interpretation along with theirs. In this way, I guide the group by modeling the practice of deepening my understanding through our collective contemplation. These are all skills that can be honed, in much the way leaders of Balint groups, Schwartz Rounds, or The Healer's Art courses learn the facilitation skills needed for those approaches.

One practical-minded reviewer of this article, noting that "the challenge of modern medicine is how to find the time," asked, "After attending your workshop, how many providers implement any aspect of what they learned … when they return to work?" This question is understandable, given the emphasis on performance measures and quantifiable outcomes that has come to dominate how we think about medical practice. But it grows out of the same pressures that produce the "mechanized" conditions described by Janisse.[1] Paradoxical though it may seem, only if we resist the demand that any intervention must have an immediate, measurable clinical impact, can we discover ways to bring back caring practices that will restore some of what has been lost in medicine. Indeed, the most important lesson learned in these poetry engagements is that although it may seem as if 21st-century medical training and our current health care system do not allow time for meaning-making, in truth we can create these opportunities with just an hour once a week or even once a month. As this article demonstrates, such opportunities for shared reflection allow participants to forge a sense of connection, enabling them to understand one another's perspective—and to appreciate something about themselves they may not otherwise have contemplated. That is the purpose of poetry. And through that purpose, we can find our own. ❖

[a] "Talking to Grief" copyright ©1978 by Denise Levertov is reprinted by permission of New Directions Publishing Corp.

[b] "Recurrence" copyright © 2010 by Judy Rowe Michaels is reprinted by permission of the poet.

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Relieving Tedium

Cuban cigar factories pay people to read stories aloud to their workers, to relieve tedium.

— Henry Alford, b 1962, American humorist and journalist

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Section A.

Article 1. (page 4) Ten-Year Trends in Preventive Service Use Before and After Prostate Cancer Diagnosis: A Comparison with Noncancer Controls

Which of the following are not recommended as routine follow-up care after prostate cancer treatment for early-stage disease?

☐ a. imaging for metastatic disease (eg, bone scan)
☐ b. screening for secondary primary cancers (eg, colorectal)
☐ c. prostate-specific antigen testing to monitor for recurrence
☐ d. general preventive care (eg, vaccinations)
☐ e. prevention and monitoring of comorbidities (eg, diabetes)

Which of the following follow-up care services after prostate cancer treatment was not assessed in this study?

☐ a. glucose and hemoglobin A_{1c} for diabetes screening and monitoring
☐ b. prostate-specific antigen levels for recurrence
☐ c. lipid panel testing for hypercholesterolemia
☐ d. influenza vaccinations

Article 2. (page 11) Patient Perspectives on Communication with Primary Care Physicians about Chronic Low Back Pain

Which of the following aspects of patient and practitioner communication are not supportive of patients:

☐ a. practitioners listening and showing empathy, sharing personal experiences of their own chronic pain
☐ b. practitioners reviewing previous treatments before beginning a conversation about treatment options
☐ c. practitioners assuring patients that they will be able to tell them how best to manage their back pain
☐ d. practitioners including follow-up instructions and letting patients know when it would be important to return for a visit

Providing care for patients with chronic low back pain is challenging because

☐ a. the best diagnostic tools are not widely available in primary care
☐ b. the structural cause of the pain is often not identifiable
☐ c. the treatment options are costly
☐ d. patients often have a difficult time articulating their pain experience and asking for help for this condition

Article 3. (page 16) Use of Epidural Analgesia as an Adjunct in Elective Abdominal Wall Reconstruction: A Review of 4983 Cases

With regard to the use of epidural analgesia in abdominal wall reconstruction and pulmonary complications, the use of epidural analgesia resulted in:

☐ a. increased incidence of pulmonary complications overall
☐ b. increased incidence of pulmonary complications in patients with an American Society of Anesthesiologists score of 3 or 4
☐ c. decreased incidence of pulmonary complications overall
☐ d. no difference in the incidence of pulmonary complications

In the present study, the use of epidural analgesia resulted in:

☐ a. significantly lower pain score on day 1 but not on day 2
☐ b. significantly lower pain score on day 1 and 2
☐ c. significantly lower pain score on day 2 but not on day 1
☐ d. no difference in pain score between the study groups

Article 4. (page 44) Urgent Need for Improved Mental Health Care and a More Collaborative Model of Care

Which one of the following statements is most correct?

☐ a. on average it takes five years to obtain treatment after symptoms of depressed mood begin, and more than two-thirds of depressed individuals never receive adequate care
☐ b. on average it takes almost ten years to obtain treatment after symptoms of depressed mood begin, and more than two-thirds of depressed individuals never receive adequate care
☐ c. on average it takes almost two years to obtain treatment after symptoms of depressed mood begin, and one-half of depressed individuals never receive adequate care
☐ d. on average it takes five years to obtain treatment after symptoms of depressed mood begin, and more than two-thirds of depressed individuals never receive adequate care

Which one of the following statements regarding collaborative care is false?

☐ a. collaborative care models reduce health care disparities in patients from different socioeconomic and ethnic backgrounds
☐ b. collaborative care is more effective than conventional care for treatment of depressed mood, anxiety disorders, bipolar disorder, and schizophrenia
☐ c. the larger number of providers from different subspecialties make collaborative care less cost-effective than usual care for the management of depressed patients with comorbid medical disorders, severe anxiety disorders, and serious chronic mental illness
☐ d. practitioners and patients report high levels of satisfaction with the management of depressed mood in collaborative care settings

Section B.

Referring to the CME articles, how likely is it that you will implement this learning to improve your practice within the next 3 months?

Key
5 = highly likely
4 = likely
3 = unsure
2 = unlikely
1 = highly unlikely
0 = I already did this

	Objective 1 Integrate learned knowledge and increase competence/ confidence to support improvement and change in specific practices, behaviors, and performance.	**Objective 2** Lead in further developing "Patient-Centered Care" activities by acquiring new skills and methods to overcome barriers, improve physician/patient relationships, better identify diagnosis and treatment of clinical conditions, as well as, efficiently stratify health needs of varying patient populations.	**Objective 3** Implement changes and apply updates in services and practice/policy guidelines, incorporate systems and quality improvements, and effectively utilize evidence-based medicine to produce better patient outcomes.
Article 1	5 4 3 2 1 0	5 4 3 2 1 0	5 4 3 2 1 0
Article 2	5 4 3 2 1 0	5 4 3 2 1 0	5 4 3 2 1 0
Article 3	5 4 3 2 1 0	5 4 3 2 1 0	5 4 3 2 1 0
Article 4	5 4 3 2 1 0	5 4 3 2 1 0	5 4 3 2 1 0

Section C.

What other changes, if any, do you plan to make in your practice as a result of reading these articles?

_____

_____

_____

Section D. (Please print)

Name _____

☐ Physician ☐ Non-Physician

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Cancer Screening Reminders: Addressing the Spectrum of Patient Preferences

Susan D Brandzel, MPH; Erin J Aiello Bowles, MPH; Arika Wieneke; Susan Carol Bradford, MS; Kilian Kimbel; Hongyuan Gao, MS; Diana SM Buist, PhD, MPH

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ABSTRACT

Context: Health care systems continue to seek evidence about how to optimize the efficiency and effectiveness of cancer screening reminders. Annual reminders to receive preventive services can be an efficient strategy.

Objective: To understand patient motivators and barriers to cancer screening and preferences about reminder strategies.

Design: We conducted 11 focus groups among adults recommended for cancer screening within Kaiser Permanente Washington. We held separate focus groups with women aged 21 to 49 years, women 50 to 75 years, and men 50 to 75 years. We used an inductive, validated coding scheme for analysis.

Main Outcome Measures: Motivators and barriers to obtaining recommended cancer screening and general cancer screening reminder content and modality preferences.

Results: Half of our participants were women aged 50 to 75 years, and 25% were men aged 50 to 75 years. Differences by age, sex, insurance status, financial status, and health beliefs all drove the participants' preferences for whether they seek these recommended services and how and when they wish to be reminded about recommended cancer screening. Most participants preferred personalized reminders, and many favored receiving reminders less than 3 months before the recommended procedure date rather than a consolidated annual reminder. Younger participants more commonly requested electronic reminders, such as texts and e-mails.

Conclusion: Optimizing cancer screening reminders within a health care system involves a multifaceted approach that enables members to request which form of reminder they prefer (eg, electronic, paper, telephone) and the timing with which they want to be reminded, while staying affordable and manageable to the health care system.

INTRODUCTION

Cancer screening remains the best method of detecting breast, cervical, lung, and colorectal cancers to reduce their associated mortality.[1-5] Motivating members to seek appropriate cancer screening requires a strong understanding of the motivators and barriers they face or perceive, which may differ by various factors such as sex, age, and race and ethnicity.[6,7]

Kaiser Permanente (KP) Washington (KPWA) is a mixed-model delivery system that provides health care and health insurance to approximately 650,000 members in Washington State. Before 2007, KPWA (then Group Health Cooperative) mailed separate reminders to members for breast and cervical cancer screenings, timed within a few months of when the screening test was due. Women overdue for the test would receive additional subsequent reminders for their mammogram or Papanicolaou test. After 2007, the preventive care outreach strategy was shifted to a consolidated, annual personalized letter sent around a member's birthday.[8,9] KPWA's annual birthday letter includes a list of all upcoming recommended preventive care services and their corresponding due dates. Each birthday letter includes up to 7 service recommendations tailored to individuals by age, sex, and comorbidities (eg, hemoglobin A_{1C} testing for diabetics). This approach was hypothesized to be more member centered and coordinated than sending individual, test-specific reminders, even if a recommended test was due far off into the future.[10] However, we previously reported important decreases in timely receipt of breast and cervical cancer screening after the transition from reminders with services tied to a due date vs the consolidated birthday reminder.[8,9]

Prior research about cancer screening reminders has predominately focused on how to improve single-service screening uptake,[11-14] with limited attention on the effectiveness of multiservice, consolidated reminders. To better understand the impact of our consolidated outreach strategy on cancer screening rates, we conducted a qualitative investigation to identify member-perceived barriers and motivators to cancer screening and their preferences about how to optimize cancer screening reminders. The goal of these discussions was to improve our understanding of how health system reminders might be leveraged to maximize participation in multiple recommended cancer screenings.

METHODS

Using electronic membership data, we randomly sampled KPWA members in western Washington State by sex and age to align with recommendations for breast, cervical, and colorectal cancer screening. (At the time of these focus groups, lung cancer screening was not yet recommended.) We excluded members enrolled in KPWA for less than one year, because they may not

Susan D Brandzel, MPH, is the Insights Director at Health Stories Project Insights in Seattle, WA. E-mail: susan.brandzel@hspinsights.com. **Erin J Aiello Bowles, MPH,** is a Research Associate for Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: bowles.e@ghc.org. **Arika Wieneke** is a Student in the School of Medicine at Western Michigan University in Kalamazoo. E-mail: aewieneke@gmail.com. **Susan Carol Bradford, MS,** is the Manager of Screening and Outreach for Kaiser Permanente Washington in Seattle. E-mail: bradford.s@ghc.org. **Kilian Kimbel** is a Research Specialist for Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: kimbel.k@ghc.org. **Hongyuan Gao, MS,** is a Programmer at Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: gao.h@ghc.org. **Diana SM Buist, PhD, MPH,** is a Scientific Investigator for Kaiser Permanente Washington Health Research Institute in Seattle. E-mail: buist.d@ghc.org.

have received a birthday letter yet, and members with a known history of cancer, because we felt this population would experience different motivations and barriers for seeking cancer screening. We obtained approval for all procedures from our Human Subjects Research Committee, and all procedures were in accordance with ethical standards.

Care is provided by KPWA Medical Group practitioners in its 25 primary and specialty care clinics. KPWA also serves as an insurer for individuals who receive most or all of their care by practitioners outside the KP system in our network. All our members, regardless of where they seek care, receive birthday letters from KPWA, and all members were eligible for our focus groups.

We mailed invitation letters to potentially eligible individuals in April 2013. For logistical reasons, we preset the dates of the focus groups. The letters included a toll-free number for members to call to volunteer or opt out. A project staff member screened respondents over the phone on a first-come/first-available basis until all groups were sufficiently populated. We scheduled focus groups to take place in the 3 largest regions of our member base: King, Pierce, and Snohomish counties. In each region, we conducted 1 focus group with women aged 21 to 49 years, 2 groups with women age 50 to 75 years, and 1 group with men age 50 to 75 years. Additional groups were conducted with older women (age 50-75 years) because of their eligibility for all 3 types of cancer screening of interest. Focus group times were intentionally varied throughout the day and evening to accommodate participants with different schedules. All 11 focus groups were held in June 2013.

We sampled individuals for our focus groups by age and sex because of the different screening recommendations. In each

Table 1. Description of study participants

Characteristic	Women aged 21 to 49 years, no. (%) (n = 21)	Women aged 50 to 75 years, no. (%) (n = 45)	Men aged 50 to 75 years, no. (%) (n = 24)
Group practice (primary care in KPWA)	12 (57)	33 (73)	17 (71)
High deductible (≥ $500/y)	14 (67)	26 (58)	12 (50)
Race[a]			
American Indian/Alaska Native	0 (0)	0 (0)	1 (4)
Asian	0 (0)	2 (4)	0 (0)
Black/African American	4 (19)	2 (4)	0 (0)
White	12 (57)	35 (78)	16 (67)
Mixed race	0 (0)	1 (2)	0 (0)
Unknown	5 (24)	5 (11)	7 (29)

[a] Race distribution of the participants was only partially known because Kaiser Permanente Washington (KPWA) obtains self-reported race information only from patients who receive all their care in the KPWA system.

Table 2. Participant quotes: Cancer screening motivators

Motivator	Quote
Family history	*"I think for the first mammography, it was [scheduled] because my mom died of cancer and we were all kind of panicky."* [Woman aged 50-75 years]
	"Because my family has a lot of cancer, and it's all different kinds. It would be nice to know which one I'll get. The joke in our family is it's not a matter of if, it's a matter of when and what kind." [Woman aged 50-75 years]
Friends	*"I have a friend who, every year when she goes and gets her mammogram, she posts it on Facebook."* [Woman aged 21-49 years]
	"My fabulous 5 girlfriends I had that I have known since second grade. We always get together, and they start talking about their health issues and 2 of them are nurses, they could not believe that I had never gone in for a full colonoscopy 'til I was 55 … . Peer pressure, yeah, they got to me." [Woman aged 50-75 years]
Stay healthy/believe in prevention	*"It's just an aspect of being healthy and that's probably the most important thing to me. To have a healthy mind, healthy body, and being functionally fit."* [Woman aged 50-75 years]
	"The primary reason [I get screened] is because I know it's in my best interest long term, and if I want to keep what I'm doing in my life, I need to stay healthy. [Man aged 50-75 years]
Practitioner recommendation	*"My doctor recommended it. I didn't really want to take the time to do the colonoscopy, but every year he said you just need to get in here and get it done, so I did, just this last year."* [Man aged 50-75 years]
	"I was trying to think about why I got my first one [Papanicolaou test]. I think just 'cause … the doctor told me to." [Woman aged 21-49 years]
Covered by insurance	*"If I can get anything free, I'm going to do it."* [Woman aged 21-49]
	"I knew you were supposed to have a colonoscopy by 50, I was 49.5. So, I had it because my deductible was paid for, but that was the only reason." [Man aged 50-75 years]
Media/celebrity diagnosis	*"I've been thinking a lot about Angelina Jolie's decision and the publicity it's receiving, and I think that those are really powerful reminders."* [Woman aged 50-75 years]
	"One thing that she [another participant] reminded me of was when Gilda Radner died. That really impacted me. Public figures that you relate to and feel connected to in some way wake you up [to the importance of cancer screening]." [Woman aged 50-75 years]

group, we included members with different insurance plans since costs borne by patients can vary greatly by the member and can play a role in decision making about seeking health care, even in an integrated delivery system. Therefore, some members had low- or no-deductible insurance plans, whereas others had higher annual deductible plans (≥ $500).

Our focus groups included 90 total participants. The same facilitator led all focus groups, each of which lasted approximately 90 minutes. Participants provided written informed consent before the beginning of the discussion. The facilitator used a semistructured guide to ensure consistency between groups but also allowed for relevant spontaneous discussion. The topic areas for the focus group discussions included the following: 1) motivators and barriers to obtaining recommended cancer screening, 2) impressions of the consolidated birthday letter (samples provided), and 3) discussion about general cancer screening reminder content and modality preferences. All focus groups were recorded and subsequently transcribed. Transcripts were coded using an inductive coding scheme developed and validated by the project team. Three team members participated in the coding calibration process by each coding 2 of the same transcripts. Robust agreement was established, which enabled the team to code the remainder of the transcripts individually.

RESULTS

Half of our participants were women aged 50 to 75 years, and 27% were men aged 50 to 75 years (Table 1). The younger women were less likely to receive their care in KP (57%), were more likely have a high-deductible plan (67%), and were less likely to be white (57%) than were the older women and men. Among the older men and women, most (nearly 75%) received their care within KP, and just over 50% had a high-deductible plan. Nearly all focus group participants indicated having had at least 1 prior cancer screening test. Many reported having most or all recommended testing.

Motivators

Participants cited a wide range of motivators for getting screened for cancer (Table 2). Common motivators were often personal, especially knowing someone who had been diagnosed with

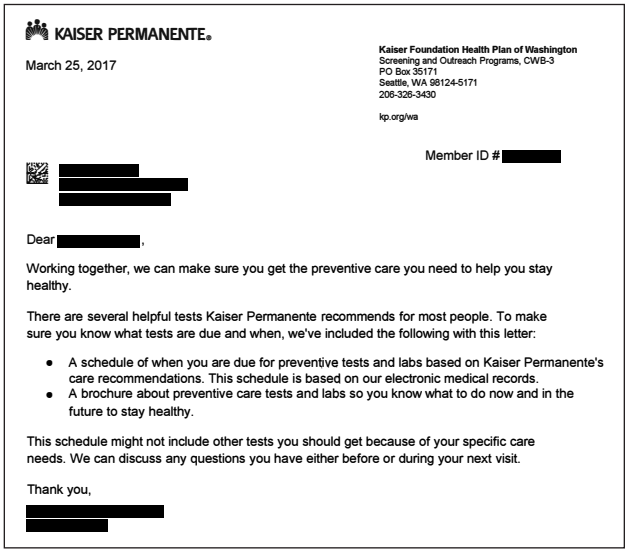
Table 3. Participant quotes: Cancer screening barriers

Barrier	Quote
Cost	*"In my particular plan, we have a high deductible, and so many of the tests require putting money on it. There are some preventive tests that we don't get charged for or that we get some reduced amount for, but it [has] definitely cost us money to have the test done."* [Woman aged 21-49 years] *"They said that if they found some abnormality, like a polyp, it would not be all covered … . Now it's going to cost you money."* [Man aged 50-75 years]
Not at risk	*"I've got no history in my family at all. I mean even my parents are still alive; I just lost my grandparents recently. Pretty long life. Until about 5 years ago, I've usually been in pretty good shape. I exercise every day, but I just haven't felt sick. I just don't get sick. I haven't felt the need [for screening]."* [Man aged 50-75 years] *"Especially someone like me who has no family history. I look at that [reminder] page and say, 'That's a waste of time.'"* [Woman aged 21-49 years]
Procrastination	*"Doctor says I need to do this … . I've got better things to do. I believe he is right. I have faith that he knows what he is doing. I don't know if I'm in avoidance or in denial, but I just kept putting it off, kept putting it off. No physical barrier, just mental attitude."* [Man aged 50-75 years] *"The only thing that I ever resisted was a colonoscopy. I was going to a doctor who had recommended one because of my family history when I was about 47 or 48. I said, 'I feel fine, everything is great, I'm under 50, I eat healthy, I eat pretty healthy,' and I didn't think it was necessary. I absolutely refused to do it. I don't know why I was so stubborn."* [Woman aged 50-75 years]
Fear	*"Nobody wants to be told they have cancer … . I think that's always there."* [Man aged 50-75 years] *"I think you're afraid of what you're going to find out."* [Woman aged 50-75 years]
Pain/discomfort	*"If you're getting screening for colon cancer, a lot of people are put off with the prep."* [Woman aged 50-75 years] *"A doctor recommended a colonoscopy, and I said, 'There's no way.' They were painful back then too, and I heard lots of stories that you really don't want to get that done."* [Woman aged 50-75 years]
Distrust	*"To heck with it, maybe it'll be a false-positive anyway. I just won't do it."* [Woman aged 21-49 years] *"Are you wasting a bunch of money having been poked and prodded for something that would never develop into anything bad?"* [Woman aged 21-49 years]
No time	*"Especially nowadays you can't just get in on the day you want. You have to really think out like 3 months in advance to be able to get in to see someone, and so same kind of idea, 'Well, I don't know what it's going to be like in 3 months, I'll wait.' … It just doesn't get done."* [Woman aged 21-49 years] *"It's hard enough to find time for yourself let alone a buddy to go with ya [for colonoscopy]."* [Woman aged 50-75 years]
Guideline confusion	*"I have heard different doctors say different [recommendations] … about how many years you go between, so I'm very confused about it at this point. First, because of that, I always [went] every 2 years, then every 5 years. I went in this last time and they said 'Oh, 10 years.' I don't know who to trust, basically."* [Woman aged 50-75 years] *"The frequency of when you need to do a mammogram has changed because of fashion or statistics or whatever, but anyway they have different years. Oh, you have to do it every 2 years; oh, you have to do it every year; you have to do it, … and it changes with your age too."* [Woman aged 50-75 years]

cancer or being committed to keeping themselves healthy. KPWA frequently promotes wellness and disease prevention programs, which were cited by some participants as having a positive impact on their motivation to stay well. Others, men in particular, were screened because their health care practitioner or spouse/partner told them to do so. Some participants reported that having the insurance coverage pay for screening was a motivator, or at least conveyed that it removed cost as a barrier. Media stories about celebrities getting screening or having cancer were also reported as impactful motivators.

Barriers

Although most of the participants reported getting some recommended cancer screening, they still expressed concrete or perceived barriers to obtaining it (Table 3). Cost was a concern raised by some participants, especially individuals with high-deductible plans. Some expressed concern about not knowing how much a screening test would cost them personally before undergoing the test. Others were aware their screening test could be free but were concerned about the possible expenses involved in any follow-up diagnostic procedures, for which they knew there were potential deductible charges and copays. Multiple participants reported they did not always get recommended cancer screening because they did not believe they were at risk. They considered themselves to be at low or no risk because they had no family history of cancer and/or were in overall good health. Some participants cited simple procrastination, either based in avoidance or distaste for the procedure. Some of the younger women expressed they could not find time to get cancer screening because of other conflicting responsibilities, such as family or work. Another commonly cited barrier was fear; either fear of the discomfort of the test or fear of the results. More specifically, women cited the pain associated with mammography, and both men and women aged 50 to 75 years reported strong dislike of the preparatory procedures required for having a colonoscopy.



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March 25, 2017

Kaiser Foundation Health Plan of Washington
Screening and Outreach Programs, CWB-3
PO Box 35171
Seattle, WA 98124-5171
206-326-3430

kp.org/wa

Member ID #

Dear ,

Working together, we can make sure you get the preventive care you need to help you stay healthy.

There are several helpful tests Kaiser Permanente recommends for most people. To make sure you know what tests are due and when, we've included the following with this letter:

- A schedule of when you are due for preventive tests and labs based on Kaiser Permanente's care recommendations. This schedule is based on our electronic medical records.
- A brochure about preventive care tests and labs so you know what to do now and in the future to stay healthy.

This schedule might not include other tests you should get because of your specific care needs. We can discuss any questions you have either before or during your next visit.

Thank you,

Figure 1. Birthday reminder letter.

Full-text version available at www.thepermanentejournal.org/files/2017/17-051-FullLetter.pdf.

A number of participants voiced distrust about the safety or accuracy of screening tests. At least 1 woman in each of the age 50-plus-years focus groups mentioned reticence to undergo mammography because of the associated radiation. Others harbored distrust having heard stories about poorly conducted colonoscopies that led to patient discomfort or injury. Finally, several individuals across age and sex expressed substantial confusion about screening guidelines, such as historical changes in cervical cancer screening guidelines from annual Papanicolaou test recommendations to longer intervals and changes to breast cancer screening guidelines, particularly for women in their 40s. Many were aware of guideline changes implemented around the time the focus groups were conducted but did not know if or how the changes affected them. Therefore, they cited confusion as a barrier to getting cancer screening, even when screening was explicitly recommended in their birthday letter.

Reminder Preferences

Most women gave positive feedback about the consolidated reminder letter. Some reported they would be motivated to make an appointment after receiving the letter. Many expressed appreciation for the letter because it gave the impression the health care system cares about them and their health. Many participants suggested simplifying and shortening the content to reduce reader fatigue. Participants also suggested including information on how far in advance cancer screening appointments need to be scheduled as well as instructions on how to make appointments online, and providing an online resource for more information on specific tests and procedures. (See Figure 1 for an example letter that incorporates their suggested changes; full-text version available at www.thepermanentejournal.org/files/2017/17-051-FullLetter.pdf.)

Modality Preferences

Each focus group discussed members' reactions to a paper reminder compared with other possible reminder types. Although the mailed reminder still appealed to some participants, many noted they would prefer getting an electronic version instead. Some cited environmental reasons for this preference; others simply wanted to prevent clutter. Still, others felt that eliminating paper could lead to a reduction in their health care costs because they assumed the paper letters were costly for KPWA to produce and mail. Finally, there was a small but vocal subset of mostly older participants (≥ 60 years) who wanted to receive their cancer screening reminders by phone so they could schedule the appointment and ask questions at the same time. They also indicated a phone call was more personal and therefore more appealing to them.

Timing of Reminders

Most participants thought that short-term reminders, which they defined as sent two to three months before a screening test was due, were more effective than annual consolidated reminders. They preferred this timing because it allowed them to make appointments at the time the reminder arrived (many facility and practitioner schedules are not available more than

two to three months in advance) and they were less likely to procrastinate getting the test because it was recommended soon. Participants also preferred test-specific reminders because different cancer screening tests are recommended at different intervals.

A smaller group of participants, who liked to plan further in advance, preferred getting consolidated reminders at a single time each year. Those who voiced this preference felt the lead time of this reminder strategy allowed them to plan long term, even if they were not able to make an appointment immediately for a time when the screening test was due. Some liked the idea of getting obligations (which they considered scheduling their cancer screening to be) planned and checked off their to-do list. Still others considered health care a priority in long-term planning or believed they could budget their finances better by knowing in advance what to expect. Finally, another subset of participants wanted both long-term and short-term reminders.

DISCUSSION

We undertook this qualitative evaluation to understand preferences about individual cancer screening reminders vs member-centered reminders that focus on the whole person instead of specific body parts or systems. Although there is substantial research demonstrating how to increase adherence to preventive services when one is considering a single needed service,[11-14] little research has been done on screening adherence when considering multiple indicated services.[8,9] This qualitative investigation revealed the complexity of making an effective cancer screening reminder system. Differences by age, sex, insurance, and financial status, as well as health beliefs all drove the participants' preferences for how and when they wish to be reminded to obtain recommended cancer screening services and whether they will seek these recommended services. Our findings emphasize the importance of having delivery systems implement multifaceted outreach strategies tailored to member preferences on outreach modality and timing.

Similar to previous studies, many focus group participants, particularly the younger women, wanted direct text or e-mail reminders sent to their mobile device.[15,16] At face value, electronically delivered reminders appear highly feasible. However, a combination of potential technologic challenges and the Privacy Rule, a part of the Health Insurance Portability and Accountability Act regulations that currently prohibits organizations from sending electronic messages directly to members that contain any identifiable health information,[17] would make such text reminders containing health information difficult, if not impossible, to develop and use. KP currently uses secure electronic mail messaging from its patient portal to communicate between patients and their clinical teams; this use may be expanded in the future to include more tailored reminders about preventive services. Importantly, even beyond the feasibility or regulatory environment, electronic reminders will not work for all members, primarily for reasons of it feeling impersonal, lack of Internet access, or low-technology literacy.

Although tailored outreach strategies sound simple, there are many operational challenges to tailoring timing, modality, and content of the reminders. For example, when it came to the content of the reminder itself, participants expressed a preference for being reminded in a relatively brief period before the test was due. However, those preferred time windows likely vary between individuals and require health systems to know detailed risk factors for each person to align the correct screening strategy and interval. There was also a strong desire for reminders to be more personalized with recommendations based on known risk factors, which requires collecting information from members when they enroll in a health care system and continuously keeping that up-to-date. Although such solutions may be technically feasible, there is a high cost associated with such customization.

In addition to preferences on how and when individuals are reminded, other factors played a role in activation and uptake, such as psychological, logistical, and financial barriers. Barriers such as distrust, fear, or not "feeling" at risk were identified as important reasons for avoiding recommended cancer screening. Logistical and financial barriers such as time and cost also played an important role in the participants' decisions whether to obtain recommended cancer screening. There may also be issues specific to certain member subpopulations that health systems should consider. We previously reported results from qualitative focus groups conducted with Latina and black/African American women about their experience and preferences for cancer screening reminders,[18] which highlighted the need to increase the level of knowledge regarding the benefits of preventive care, improve service access through expanded hours or additional clinic locations, and increase cultural competency among the health care professionals who recommend and provide the screening tests.

An important distinction in this work was our focus on understanding how annual preventive services reminders work to motivate individuals to receive recommended cancer screening tests. Most of the literature available regarding cancer screening reminders as well as barriers and motivators is most commonly focused on one test or disease.[19-21] Some of the barriers and motivators cited across age and sex were clearly test-specific, such as a dislike for breast compression during mammography or the arduous nature of the preparation for colonoscopy. But others spanned the horizon of cancer screening in general, such as family history or health beliefs about prevention.

Our focus groups yielded rich member opinions. We acknowledge the sample may have had an overrepresentation of highly motivated members and was also derived from one health care system and one geographic region. Because of logistical reasons, we had to prespecify our focus group dates, times, and locations, which may have also affected who was able to participate. Very few of the people who attended expressed that they had never received any recommended cancer screening. Therefore, these results have limitations to their generalizability. Although we included participants with a wide variety of insurance plans and deductible range, we did not have representation from uninsured populations. Had this population been involved in our discussions, we believe we would have heard that logistics such as transportation, hours of operation, and cost pose an even more prominent barrier

to receiving recommended cancer screening.[22] Finally, we were unable to include participants with limited English proficiency in these groups. Had we been able to do so, we may have also heard about important barriers pertaining to the content of health literature, such as a reminder letter, as well as culturally affected health care-seeking behavior.[23,24] Our study shows that even among an insured population there are important barriers for health care systems to overcome to improve cancer screening rates.

CONCLUSION

Optimization of cancer screening reminders involves a health care system being nimble enough to use a multifaceted approach: One that potentially enables the member to request which reminder modality or media format they prefer (eg, electronic, paper, and/or telephone), and the timing with which they want to be reminded, all while staying affordable and manageable to the health care system. There is likely no one-size-fits-all strategy for cancer screening reminders, and even sending members reminders in their preferred modality will not necessarily translate to increased adherence. But engaging the member preference when determining reminder modality and type warrants further exploration as to whether it might yield higher cancer screening rates and ultimately healthier populations. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Teens and Technology Transforming Acne Treatment

Donna Lee Ettel, PhD; Lora Rose LaManno, MSN/ED, RN, RD; Sarah Anne Neyra; Wallace John Ettel; George Leonard Ettel, III, MMS; Matthew Kevin Mitchell

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ABSTRACT

Introduction: Although the Internet contains many health Web sites with valid information, it also contains sites with false information.

Objective: To learn whether high school students searching health care information believe they are using evidence-based sites and to understand their topics of interest, frequently navigated sites, and trust/confidence in the credibility of information found.

Design: Cross-sectional.

Main Outcome Measures: Students at a private high school answered an anonymous survey inquiring about their belief that they were using evidence-based sites, topics of interest, search engines of choice, and their trust in information obtained. Descriptive statistics and multivariate analysis of variance were used to compare trends across grade levels.

Results: Of 705 students enrolled, 24.7% were absent or declined to participate. For the remaining students, 497 completed the surveys, representing a response rate of 70.5% (497/705) and a participation rate of 93.6% (497/531). Overall, 82% of students communicated that they believed they were using evidence-based sources when searching for health information ($p < 0.0006$). Findings showed that 42% searched general health information, and 43% investigated specific medical conditions; topics related to skin and acne were researched significantly more often ($p < 0.05$). Overall, most students (80%) reported using Google as their number 1 search engine ($p < 0.004$), 38% reported using WebMD Search ($p < 0.0002$), and 50% of students used Wikipedia (not significant).

Conclusion: Most students trust health information they learn from the Internet. We found it chilling that less than half of students obtained their information from a Web site with health care professionals' oversight.

INTRODUCTION

Although adolescents engage in online entertainment, it is their social and health information searches that shape their identity formation and autonomy.[1] The Internet's plethora of information has exponentially increased since its inception, and adolescents are relying on Internet sources to obtain information. However, such rapid growth has not been regulated, and concerns have been voiced about the quality of the available information. Many health care-related sites are not moderated by medical professionals and create the risk of incorrect information being disseminated.[1,2]

In this study, researchers focus on Internet searches related to the common skin condition acne. Evidence reveals that Internet searches related to acne serve as a major, if not primary, source of skin care information.[3] Previous research confirms that one of the most popular Internet searches among adolescents is related to acne. This may be because of the substantial psychological effects acne has on this age group.[4] High school students are a group of individuals who wish to maintain their social image while their bodies experience demands from varying levels of hormones.[5]

The interest displayed by adolescents related to acne inspired this research group to learn more about how teenagers use the knowledge gained from Internet searches. This study will investigate the types of asynchronous sites that students use to obtain health care information for treating acne and the degree of trust they have regarding the information found.[2,3]

Prior research assists us in understanding that adolescents seeking health information have multiple sources available to them, including physicians, families, schools, organized activities outside school, the Internet, and "the street."[3] In addition, many adolescents have access to mobile media, with almost 70% owning a smart phone in 2013.[6]

The availability of multiple sources of online information poses adolescents with the challenge of determining if a source is credible or faulty. If the information is influential, adolescents may be inclined to treat skin conditions via online sources, even though the effectiveness of advertised remedies may lead to poor outcomes. The choice to use advertised remedies rather than seeking the advice and direction of their primary care physician or even a dermatologist deprives the adolescent of a complete examination. Physicians and dermatologic specialists provide patients education about the facts; for example, why the skin overproduces oils and the consequences of fluctuating hormones, perspiration, stress, improper nutrition, and dehydration. Moreover, a consultation with their primary care physician fosters a physician-patient relationship in which a customized treatment plan can promote healthy skin, control acne, and prevent further skin irritation and risk of scarring.

When challenged with health-related issues, adolescents intentionally seek information. Although this inquisitive nature is

Donna Lee Ettel, PhD, is Adjunct Faculty at the University of South Florida Honors College in Tampa and Saint Petersburg College in FL. E-mail: ettel.donna@spcollege.edu. **Lora Rose LaManno, MSN/ED, RN, RD,** is the Education Coordinator for the Fresenius Medical Care Group in Tampa, FL. E-mail: lorarose01@aol.com. **Sarah Anne Neyra** is a Master's Student at University of South Florida in Tampa. E-mail: sarahneyra@mail.usf.edu. **Wallace John Ettel** is a Master's Student at the University of South Florida in Saint Petersburg. E-mail: wettel@mail.usf.edu. **George Leonard Ettel, III, MMS,** is a medical student at Nova University in Fort Lauderdale, FL. Email: georgeettel3@gmail.com. **Matthew Kevin Mitchell** is a Master's Student at the University of South Florida in Saint Petersburg. E-mail: mattm1492@gmail.com.

considered a normal aspect of the maturation process, approximately 80% to 90% of teenagers in the Western world experience behavioral/emotional and physical/psychological effects caused by acne.[4,7] Despite recent efforts to encourage physician-patient communication, it is thought that there were and are barriers deterring adolescents from communication with their physicians, and many adolescents have limited knowledge of how to identify the best sites to search for health information.[8]

Another reason may be the result of an inadequate Internet connection causing challenges in health-seeking activities. Adolescents in many rural areas have a dial-up Internet connection, which can downgrade connectivity and Internet access.[9] Communication with their physicians and other health care professionals may also lessen considering it was reported in the literature that only 39% of 500 Web sites found by the Google search engine (Google Inc, Mountain View, CA) provided reliable medical advice.[10] The remaining searches either offered incorrect information (11%) or failed to answer the health-related inquiry (49%).[10] These are important data considering that a recent systematic review article found that only 60% of adolescents and young adults had adequate health literacy skills.[11] Ideally, trust in a connected system of reliable and accurate electronic health care information would be valuable when addressing issues of health care quality, safety, education, and efficiency for adolescents.[12]

METHODS

Subjects

In a follow-up to the original study[3] of how adolescents obtain health information using electronic tools and again using a cross-sectional design, high school students in Grades 9 through 12 at a single private Catholic high school answered an anonymous survey. The survey of yes/no questions inquired about the following: 1) their belief that they were using evidence-based sites, 2) major topics of interest, 3) their use of WebMD Search (WebMD LLC, New York, NY), 4) their use of Wikipedia, the free-content encyclopedia (Wikimedia Foundation Inc, San Francisco, CA), 5) their use of Google, and 6) their confidence in the information obtained.

Homeroom teachers hand-delivered a letter describing the purpose of the study and a questionnaire tracked by a 6-digit identifying code to students in Grades 9 through 12 at a high school in the Southeastern US.

The school population consisted of 705 students (50.9% male) with a racial makeup that was 89.8% white and 4.1% African-American. Most students (88.1%) were Catholic, and 18.9% were from single-parent families. On the day the survey was distributed, 174 students (24.7%) were either absent or declined to participate. Of the remaining students, 497 of 531 (93.6%) completed the survey in about 30 minutes in the homeroom setting. Incomplete questionnaires were not included in the data analysis.

Statistical Analysis

Separate researchers double entered the survey data to ensure accuracy. Initially a multivariate analysis of variance was conducted to compare the four grade levels of students. For statistically significant findings, univariate analysis of variance was conducted for each of the survey items. The independent variable was the student's grade level. The dependent variables measured the students' response to the following questions: 1) their belief that they were using evidence-based sites, 2) their major topics of interest, 3) their use of WebMD Search, 4) their use of Wikipedia, 5) their use of Google, and 6) their trust level in the information obtained. All analyses were computed in SAS Version 8.0 software (SAS Institute Inc, Cary, NC), and significance was considered at the $p < 0.05$ level. The Educational Pastoral Team, which reports to the school board of the diocese, approved this study.

RESULTS

The response rate for this survey was 71%, with 497 of 705 returned surveys, and the participation rate was 93.6%. Of the completed surveys, freshmen returned 19.7% of them; sophomores, 45.7%; juniors, 16.1%; and seniors, 18.5%. On a 5-point scale from poor to excellent, 66% of students rated their health status as very good to excellent. The remainder rated their health as good to fair, and no student considered his/her health to be poor.

As shown in Figure 1, most students (82%) communicated that they believed they were using evidence-based sources while researching health care information ($p < 0.0006$). On average, a

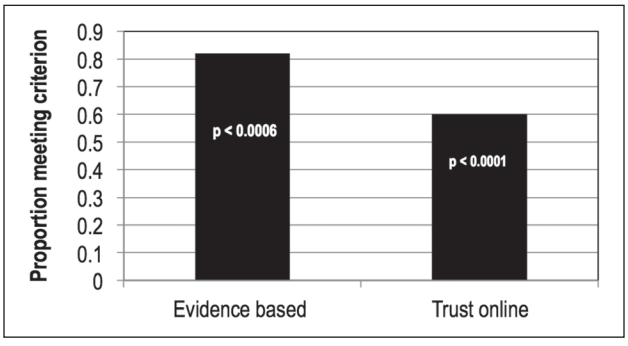

Figure 1. Proportion of students who believe they are using evidence-based sites and report having trust in the online information searched.

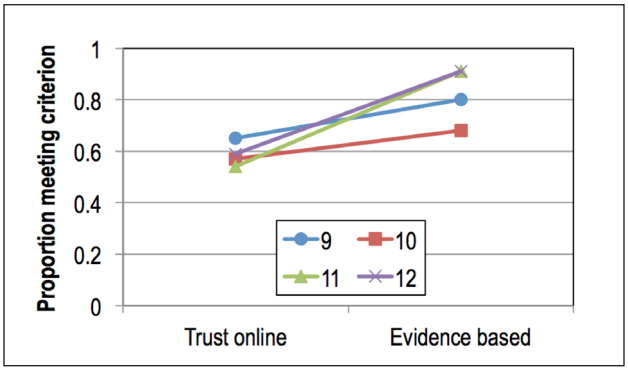

Figure 2. Students' responses, by grade level, regarding their trust in online health information obtained and their belief that they are using evidence-based sites when searching for health care information.

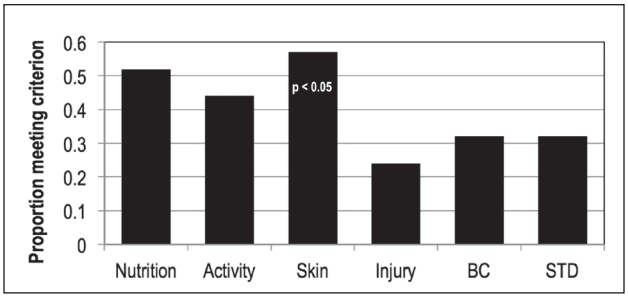

Figure 3. Overall means of common health topics that students search. The topic of skin was the most common topic researched with a statistically significant finding.

BC = birth control; STD = sexually transmitted disease.

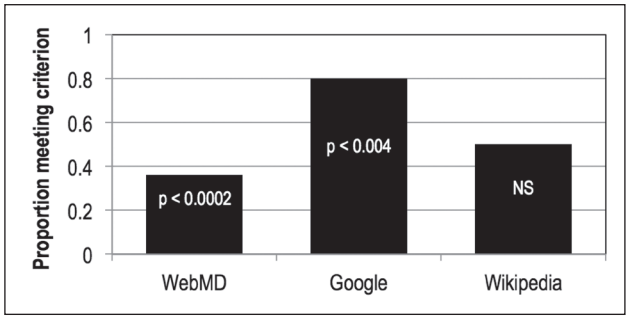

Figure 4. Overall means of high school students who use three search engines: WebMD Search, Google, and Wikipedia.

NS = not significant.

significant proportion of students (66%) acknowledged that they trust the online information ($p < 0.0001$) they accessed on the Internet. Figure 2 represents by grade level the students' response to both variables. Regarding "trust," it appears that freshmen (65%) and juniors (54%) were more likely to trust online information than were sophomores (57%) and seniors (59%). This contrasts with the second variable in which both seniors and juniors (92%) believed that the sites they used were more evidence based than the sites visited by underclassmen.

Although 42% of students reported using the Internet to search for general information related to health care, 43% reported searching for specific topics. Figure 3 summarizes the proportion of students who searched the Internet for specific health-related information and/or information about specific disease states. It was interesting to note that students searched topics related to skin (acne) significantly more frequently than other topics ($p < 0.05$).

As shown in Figure 4, most students (80%) identified Google as their primary search engine ($p < 0.004$), 36% of students reported using WebMD Search ($p < 0.0002$), and although not significant, 50% of the students reported using Wikipedia to search for health care information. Figure 5 summarizes by grade level the search engines of choice. By grade level, seniors' and juniors' use of Google was even higher than overall: 86% and 89%, respectively. Furthermore, seniors were more likely to use WebMD Search and Wikipedia than were other high school students.

DISCUSSION

The staggering growth of the Internet has provided its diverse audience with potentially the world's most powerful information source. However, this growth has been largely unregulated, and we are concerned about the quality of the information that the Internet provides and what sites teens access. Our results showed that most high school students in our study in Grades 9 through 12 believed that they were using evidence-based resources when conducting research on health care information. In addition, they reported being confident in and having trust in the information they obtained online.

Nearly 57% of the students reported they used the Internet to search for specific health care-related information and sought information related to skin care more frequently than the other health care-related topics. On average, a significant proportion of students (66%) reported that they trust online information ($p < 0.0001$), and 22% (not significant) acknowledged that they changed their behavior on the basis of information they found on the Internet.[3] Evidence-based research has found that acne treatment is vital for teenagers who are developing their identity and building self-confidence. Acne can have detrimental psychological effects on individuals, especially young adolescents, regardless of their personal or cultural background. Most behavioral modifications related to severe acne symptoms are psychological and may result in low self-esteem. These data may suggest that students are willing to correspond with professionals asynchronously if given the opportunity.

For those in hopes of having a "better" social life, without the physical hindrance of acne, adolescents choose to use remedies found online to modify behavior. These behavioral modifications may consist of changes in diet, home facial remedies, recommended medications, and changes in lifestyle. Consequently, even if the adolescent obtains accurate and valid information, further research is needed to determine whether a behavioral change has occurred and the length of time the change is maintained. More important, adolescents need to improve communication with their physicians.

There are several limitations to this study. Although many of our results are similar to those of other reports, the students in our study came from a single private Catholic high school and

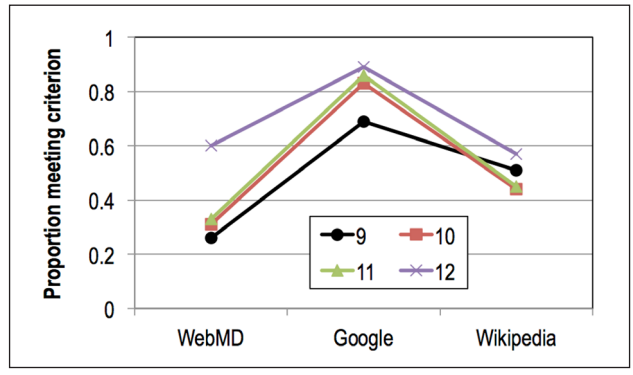

Figure 5. Most common search engines used by students, by grade level.

do not necessarily reflect the population at large. Thus, we feel these findings are not generalizable.

CONCLUSION

The large majority of students in our study have trust and confidence in the health information they receive from the Internet. Most students use Google as their primary source to find the answers to their health-related inquiries. These two findings combined reveal a potentially dangerous trend as well as a major need in our health care community for reliable sources. Although the Internet contains many Web sites with valid and accurate health information, it also contains Web sites with incomplete, contradictory, false, and sometimes harmful information. This finding raises questions about how to safeguard access to health care information for adolescents that is accurate, understandable, and culturally sensitive. Even though many of the students reported they trusted the information they found, it was chilling to note that less than half obtained their information from a Web site with oversight by health care professionals. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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User-Centered Design for Developing Interventions to Improve Clinician Recommendation of Human Papillomavirus Vaccination

Michelle L Henninger, PhD; Carmit K McMullen, PhD; Alison J Firemark, MA; Allison L Naleway, PhD; Nora B Henrikson, PhD, MPH; Joseph A Turcotte

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ABSTRACT

Introduction: Human papillomavirus (HPV) is the most common sexually transmitted infection in the US and is associated with multiple types of cancer. Although effective HPV vaccines have been available since 2006, coverage rates in the US remain much lower than with other adolescent vaccinations. Prior research has shown that a strong recommendation from a clinician is a critical determinant in HPV vaccine uptake and coverage. However, few published studies to date have specifically addressed the issue of helping clinicians communicate more effectively with their patients about the HPV vaccine.

Objective: To develop one or more novel interventions for helping clinicians make strong and effective recommendations for HPV vaccination.

Methods: Using principles of user-centered design, we conducted qualitative interviews, interviews with persons from analogous industries, and a data synthesis workshop with multiple stakeholders.

Results: Five potential intervention strategies targeted at health care clinicians, youth, and their parents were developed. The two most popular choices to pursue were a values-based communication strategy and a puberty education workbook.

Conclusion: User-centered design is a useful strategy for developing potential interventions to improve the rate and success of clinicians recommending the HPV vaccine. Further research is needed to test the effectiveness and acceptability of these interventions in clinical settings.

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection in the US.[1] This infection is associated with cervical, anal, and oropharyngeal cancers, as well as genital warts. The Advisory Committee on Immunization Practices recommends vaccination to prevent infection from the most common cancer-causing types of HPV.[2,3] The first HPV vaccine became available in 2006; however, the national coverage estimates for 2014 show that only 60% of US female teenagers aged 13 to 17 years begin the vaccine series (≥ 1 dose) and 40% complete the series (≥ 3 doses). For male adolescents, initiation and completion rates in 2014 were only 42% and 22%, respectively.[4] Although the HPV vaccination coverage rate for both female and male adolescents has improved during the past several years, it remains lower than with other adolescent vaccinations such as tetanus-diphtheria-acellular pertussis and quadrivalent meningococcal conjugate vaccines, which had national coverage rates at 88% and 79% in 2014, respectively.[4]

A clinician's recommendation for vaccination has been consistently demonstrated as one of the best predictors of vaccine acceptance.[5-11] However, a 2014 national survey of parents of adolescents found that 48% of parents reported no clinician recommendation for HPV vaccination and 16% reported receiving low-quality recommendations.[12] Only 36% reported receiving high-quality recommendations. In addition, the odds of vaccine initiation were 9 times higher when parents received high-quality recommendations vs no recommendation. Gilkey et al[12] defined high-quality recommendations as having 3 components: strength of endorsement (clinician described the HPV vaccine as "very" or "extremely" important), prevention message (clinician said the HPV vaccine prevents cancer), and urgency (clinician recommended same-day vaccination). Some research suggests that clinicians may procrastinate in recommending the vaccine to younger adolescents and do not consider their patients "off schedule" until they reach age 26 years, the upper limit of the recommended age range for vaccination.[13] Another study suggested that a clinician's recommendation might be even more critical in improving vaccination rates in male patients. When asked for a reason for not vaccinating, parents of sons were most likely to report that the clinician did not recommend the vaccine and that the parent did not know the vaccine was available for boys.[14]

Educational interventions can improve clinicians' knowledge and beliefs about the HPV vaccine.[15,16] Because clinicians are uniquely positioned to educate patients and parents, providing needed supports for clinician behavior change and empowering clinicians to recommend the vaccine could greatly increase HPV vaccine coverage. However, traditional intervention methods, such as clinician education and public awareness campaigns, are not having a large impact on HPV vaccination rates, which have plateaued at a level well below those of other adolescent vaccines that are required for school attendance.[17,18]

In this study, we employed user-centered design to develop interventions to help clinicians communicate more effectively about HPV vaccination. Although user-centered design is increasingly

Michelle L Henninger, PhD, is a Research Program Manager at the Center for Health Research in Portland, OR. E-mail: michelle.l.henninger@kpchr.org. **Carmit K McMullen, PhD,** is a Senior Investigator at the Center for Health Research in Portland, OR. E-mail: carmit.mcmullen@kpchr.org. **Alison J Firemark, MA,** is a Research Associate at the Center for Health Research in Portland, OR. E-mail: alison.j.firemark@kpchr.org. **Allison L Naleway, PhD,** is a Senior Investigator at the Center for Health Research in Portland, OR. E-mail: allison.naleway@kpchr.org. **Nora B Henrikson, PhD, MPH,** is a Research Associate at the Group Health Research Institute in Seattle, WA. E-mail: henrikson.n@ghc.org. **Joseph A Turcotte** is a Principal at the CGA Group in Seattle, WA. E-mail: joe@cgagroup.net

being used to drive innovation in health care and other industries,[19,20] it has not been used to design tools for improving vaccine uptake. User-centered design is a promising method to address low uptake of the HPV vaccine because the largest hurdle to improving uptake seems to be ineffective or insufficient communication among clinicians, parents, and teenagers about the vaccine.

METHODS

This project was conducted at the Kaiser Permanente Center for Health Research in Portland, OR, between September 2014 and August 2015. The Kaiser Permanente Northwest (KPNW) institutional review board determined this project to be exempt from institutional review board review.

User-Centered Design

User-centered (also known as "human-centered") design is increasingly being used to drive innovation in health care and other industries.[19] User-centered design employs "design thinking," system science, and ethnographic methods to obtain creative, implementation-ready solutions to complex problems. This approach focuses on the needs and preferences of the people who will ultimately be affected by clinical or policy changes. As a result, health care interventions designed according to these principles will suit the needs of time-constrained clinicians and staff and will operate within the complex structure and workflows of health care delivery organizations.[21,22]

The user-centered design cycle includes six steps: 1) understanding the environment, 2) framing opportunities, 3) imagining possibilities, 4) prototyping, 5) piloting, and 6) spreading innovation. We adopted the Kaiser Permanente user-centered design methods[23] and referred to design resources such as the Stanford Design Program's workshop modules[24] and previous experience holding workshops to engage stakeholders in priority setting to plan our approach for identifying intervention opportunities to improve postoperative recovery. For the current study, our goal was to complete the first three steps to generate one or more innovative intervention ideas that might be developed and tested in future work.

Interviews

Interview participants (N = 14) included 6 primary care clinicians, 5 subject matter experts (SMEs), and 3 representatives from analogous industries (described below). The primary care clinicians were current or former KPNW pediatric or family medicine physicians who volunteered to be interviewed for this project. The SMEs included 2 KPNW clinician performance consultants, a program coordinator from KPNW Clinical Quality Support Services, a social marketing and health communications consultant (JT), and a PhD-level researcher from a partner institution who specializes in vaccine compliance research (NH). Analogous industry representatives included a middle school guidance counselor, a marijuana legalization activist, and a retail curriculum expert from a large athletic retail company.

Two project team members (CM and AF) conducted semi-structured interviews[25] in person or by telephone. Interview guides were developed by the project team and included questions about knowledge, attitudes, and beliefs about HPV vaccination; typical workflow; potential barriers to recommending vaccination; and tools or processes that facilitate communication about or recommendation of the HPV vaccine. The interviews were audiorecorded and professionally transcribed to facilitate qualitative analysis.

Once the clinician and SME interviews were completed and findings synthesized by the project team, we consulted with the Kaiser Permanente Innovation Consultancy[26] to identify three analogous industries outside health care that had the potential to inform effective clinician endorsement of the HPV vaccine. We articulated the problems for which we were trying to design solutions before proceeding with analogous industry interviews. The problems we identified were as follows: 1) clinicians must communicate with both parents and teens, who may have different priorities and values; 2) clinicians must communicate about issues that may raise a taboo subject (ie, adolescent sexuality); and 3) clinicians need effective tools, training, or professional orientation to help them communicate more effectively with their patients. With these problems in mind, we selected a middle school guidance counselor because of that person's relevent experience advising parents and teens who may have different or even competing priorities. The marijuana legalization activist had the potential to offer unique insight into normalizing taboo or potentially stygmatizing topics, such as the link between HPV and sexually transmitted infections. Finally, the retail curriculum expert offered insight into training retail personnel to engage with customers and endorse products effectively.

Rapid Assessment Technique

We used rapid assessment techniques[27,28] to analyze qualitative interview data. Specifically, the interviewers (CM and AF) verbally debriefed the research team after each interview to summarize observations and key ideas. At least two team members reviewed each interview transcript; recurring themes and selected interviewee quotes were summarized in a spreadsheet (Microsoft Excel, Microsoft Corp, Redmond, WA) that was subsequently used in data analysis meetings.

Data Analysis Meetings

The research team held 3 internal data analysis sessions to synthesize findings from qualitative interviews by using methods from the Hasso Plattner Institute of Design at Stanford University, Stanford, CA.[29] The first 2 meetings focused on synthesizing data from the clinician, SME, and analogous industry interviews. The final meeting focused on developing and refining brainstorming prompts for use at the workshop. Each data analysis meeting lasted approximately 1.5 to 2 hours.

Workshop

We held a 4-hour data synthesis workshop at the Kaiser Permanente Center for Health Research, which was led by an investigator (CM) with assistance from the other members of our research team. Workshop participants (N = 17) included a KPNW pediatric physician, 2 KPNW clinician performance consultants, a KPNW Health Education program manager, 6 Kaiser Permanente Center for Health Research staff with experience in vaccine research or qualitive research methods, as well as all 6 authors of this article. Several of the stakeholders were also parents of preteens or teens, some of whom had recently discussed HPV vaccination with their

child's primary care clinician. Therefore, we were able to incorporate parent perspectives in the workshop as well.

The workshop agenda included a summary of the qualitative data analysis, presentation of brainstorming prompts in the form of "How might we?" statements (see Sidebar: "How Might We … ?" Questions Developed for a Data Synthesis Workshop), and an overview of the brainstorming process. Attendees then met in small groups to discuss the brainstorming prompts and develop at least one idea for a potential intervention. Each small group presented its favorite idea to the larger group, and all attendees voted on the best concepts. Each attendee voted for up to three intervention concepts. Approximately two weeks after the workshop, we conducted a one-hour follow-up Webinar to debrief and summarize the results of the workshop with the participants.

"How Might We … ?" Questions Developed for a Data Synthesis Workshop

How might we … ?

- Improve how clinicians communicate with parents and patients to enhance trust and rapport?
- Reframe discussions about human papillomavirus vaccination as opportunities for partnership and advocacy rather than as potentially difficult conversations?
- Help clinicians to elicit and understand each parent and patient's concerns about vaccination so that these can be accurately and effectively addressed?

RESULTS

Four primary themes emerged regarding how clinicians approach discussing the HPV vaccine with parents: 1) the importance of enhancing parents' trust in the clinician, developing rapport between the clinician and the parent, and effective communication skills on the part of the clinician; 2) clinician knowledge about common parental concerns about vaccination; 3) the ability to develop talking points and messaging to effectively address these common concerns; and 4) increasing clinicians' comfort with discussing difficult topics with their patients or parents (Table 1).

Table 1. Summary of clinician and subject matter expert interviews

Theme	Insights	Illustrative quotes
Enhancing trust, rapport, and communication skills	Agenda setting/managing the visit effectively Patience and persistence with patients and parents Using scripts and talking points to engage in positive conversations Establishing trust before making a recommendation Self-disclosure ("I'm a parent too"; "Here's what I did") Use of motivational interviewing techniques; eliciting and addressing specific concerns of patients and parents	"For the most part I wait until the very end of the visit so I've had a chance to talk with them, show I care about them as a person. We have talked about other things. Of course, it is like the number one thing I'm going to do in that visit, but they don't know that." "I have the most success getting vaccination rates when I build trust and allow people the time to make the decision. So, I have that in the back of my mind as well—that I have a little bit of time."
Enhancing clinician knowledge about parental concerns	Safety concerns (new vaccine, side effects, painful) Age-related concerns (11-13 too young) Sexuality concerns It's "extra" or "optional" so not important Sexual gender-related concerns ("just for girls")	"Because it's a newer vaccine, they feel like they … want to give it some more time and see how it works for other people first. Not their own kid." "If they refuse, it's usually because it's an assumption that this is a license to be sexually active." "They still want him to be a kid … parents are in denial. They just don't want to be talking about it yet."
Crafting talking points/ messaging	Increased focus on cancer prevention Decreased focus on sexually transmitted infections Tying vaccination recommendation into "coming of age" messaging Emphasizing benefits of early vaccination Importance of vaccination: "It changes lives" HPV for males: We recommend for everyone Protects gay men Prevention of regret later if child doesn't get vaccinated now (personal stories)	"It's a vaccine that works better if you start it before you become sexually active. That's why we're recommending it in the 11- to 13-year-old population." "The part to me that's just incredible is that we have a vaccine that can prevent [some cancers]. So, I'm really excited about it." "I was skeptical when it initially came out [but] the data [have] gotten better and better ... . I'm really seeing a difference in my adult patients now who've had the vaccine and those who haven't, in terms of their gynecologic health." "This is a vaccine that is changing people's lives."
Increasing clinicians' comfort with discussing difficult topics	Clinicians may be uncomfortable with the topic of teen sexuality and thus hesitate to bring up vaccination, especially with younger patients (aged 10-11 years). There is a disconnect between clinicians' perception and the reality of parents' attitudes (parents less "hung up" on sexual activity than clinicians think) Religious beliefs: Some clinicians might not mention the vaccine because of association with sexual activity Some clinicians struggle with the conversation; others do it well	"What we saw is that hesitancy of clinicians to engage parents around the need for HPV vaccination because of perceived hang-ups around the whole sex issue thing. That clinicians basically think that parents have a lot of hang-ups because of low likelihood for kids of that age to be sexually active, when in fact it seems like parents don't have a lot of hang-ups with that."

HPV = human papillomavirus.

Many themes that emerged from the analogous industry interviews (Table 2) were consistent with findings from the clinician and SME interviews: the importance of developing rapport, constructing effective messages that are salient to the receiver, and the willingness to keep trying when first attempts are unsuccessful. However, we also revealed some additional strategies, such as approaching the conversation as a "wellness advocate" (rather than as an expert), speaking in terms of "benefit language" (rather than technical language), and using compelling storytelling.

Stakeholders who participated in the data synthesis workshop generated 5 potential intervention concepts (Table 3), with 2 intervention concepts receiving greater than 50% of the attendees' votes. The most popular intervention concept, a "shared values approach," emphasizes determining the parent's values as they relate to vaccines and constructing messaging salient to these values. The second most popular intervention idea, *Ready, Set, Grow!* involved developing a puberty education workbook that would include information about adolescent vaccines and a tear-out worksheet to help prepare adolescent patients for discussing HPV vaccination at their next clinician visit.

DISCUSSION

Although coverage rates of other adolescent vaccines such as tetanus-diphtheria-acellular pertussis or quadrivalent meningococcal conjugate meet or exceed Healthy People 2020 targets,[30] the HPV vaccination coverage rate remains lower. Four leading medical associations, in collaboration with the Immunization Action Coalition and the Centers for Disease Control and Prevention, recently issued a call to action stressing the importance of clinicians educating their patients or parents about HPV and to strongly recommend vaccination against HPV.[31] The American Academy of Family Physicians describes a strong recommendation as one that emphasizes the safety, effectiveness, and importance of vaccination.[32] As well, the Centers for Disease Control and Prevention's "You Are the Key to HPV Cancer Prevention" campaign aims to improve the knowledge of clinicians about HPV-related cancers and vaccination, and it offers effective tools for discussing HPV vaccination with their patients or parents.[33]

Prior research has suggested that clinicians may communicate differently about HPV vaccine compared with the other adolescent vaccines.[12] For example, clinicians may frame the HPV vaccine as less important than the other vaccines or may even suggest deferring the vaccine to a later visit. A 2016 systematic review by Gilkey and McRee[34] found only 2 published studies of interventions designed to improve clinician recommendation of the HPV vaccination. The first study evaluated a social marketing campaign to increase initiation of HPV vaccination in

Table 2. Summary of analogous industry interviews

Industry	Insights	Illustrative quotes
Guidance counseling	Counselor often recommends interventions that parents and kids do not want Psychological counseling Educational testing If you see yourself as an advocate, you keep trying Raise the difficult issue repeatedly	"[S]ometimes parents don't want to hear what you have to say. And sometimes they are not going to take your advice or recommendation. That doesn't mean I'm not going to make it." "So, if they don't follow through the first time, connect again. Try to make that connection again with them."
Marijuana policy reform	Find ways to empower those who fear engaging with a topic Reframe as an opportunity to model the kind of [clinician/parent/person] you want to be Transform from expert know-it-all to a "wellness advocate" Use compelling stories Use potentially "taboo" topics as a "gateway" to discussing larger issues	"It really hasn't been that hard to explain because as we know, ending prohibition is far more logical than continuing down the road with our failed policies … . Trust me, I used to squirm too, but we have to get over it. It's time to evolve beyond pointing fingers and turn experiences with irresponsible use into teachable moments."
Athletic sales	Follow three steps to make the sale: Use engagement/rapport Discovery: Explore customer's needs Close the sale: Craft messaging that resonates Craft an effective message: Be authentic Choose words that affirm your recommendation Be prepared to respond to common objections Employ these training tools and strategies: Use a credible, strong facilitator (eg, famous athlete) Encourage role-playing Include storytelling Build intrinsic motivation Manage ego (adult learning) Speak in "benefit" language, not technical language Develop simple job aids	"In our stores we don't call [employees] salespeople. We call them athletes. And our job is to use our athletes to equip athletes." "You should use the words that feel right coming out of your mouth. And it should be authentic to you … but there are some specific word choices that you can craft that makes people want to say yes."

preteen girls in rural North Carolina.[35] The 3-month campaign included posters, brochures, a Web site, news releases, and physician recommendations. A follow-up survey indicated that 82% of respondent mothers had heard or seen campaign messages and 94% of respondent clinicians had used campaign materials with their patients or parents. Compared with nonintervention counties, vaccination rates in intervention counties increased by 2% within 6 months of the intervention launch.

The second study evaluated a multicomponent decision support intervention targeting both clinicians and families.[17] The clinician components of the intervention included immunization alerts in the electronic medical record, education, and feedback. Additionally, families received telephone reminders when vaccinations were due and a referral to an educational Web site. The study found that although parents from intervention clinics were more likely to discuss HPV vaccination with their child's clinician, they were no more likely to receive a strong vaccine recommendation from the clinician.

Using a user-centered design approach, this project generated five potential interventions to help clinicians communicate more effectively with parents and youth about HPV vaccination. Two interventions, the "shared values approach" and *Ready, Set, Grow!,* received the most support from multiple stakeholders involved in this project. To our knowledge, neither of these approaches has been tested empirically to date.[17]

The "shared values approach" emphasizes the importance of the clinician's ability to assess and to respond to the parent's value system, as well as the social context in which parents are making health care decisions, as it relates to HPV vaccination. Researchers from the Canadian Immunization Research Network have suggested that there are actually several different types of vaccine-hesitant parents and that effective clinician

Table 3. Summary of intervention concepts and preference among 17 workshop attendees

Intervention	Key components of intervention	Attendee votes, no. (%)[a]
Shared values approach (inspiration from sales)	Target intervention at clinician Determine the patient's/parent's value system as it relates to the vaccine, and craft "benefit language" specific to those values Consider the social network/context in which patients and parents are making health care decisions Capitalize on trust in clinician and health organization Draw inspiration from sales approach to help build "demand" for vaccine	13 (76)
Ready, Set, Grow! (puberty education workbook)	Target intervention at patient Develop a set of workbooks for preteens, teens, and parents to celebrate milestone birthdays and/or transitions to middle school and high school Format could be print and/or online, preferably graphic in design and interactive in nature Content would cover a broad range of preventive health issues, including HPV and HPV vaccine and how to communicate effectively with clinician Workbook would encourage teens and parents to discuss key issues at home and complete a tear-out sheet or printout and prepare them to discuss vaccinations with the clinician.	11 (65)
The Pathway to "Yes"	Employ social marketing approach, which could evolve into clinician intervention Develop a messaging framework to effectively promote the benefits of HPV vaccination Conduct opinion surveys and focus groups of teens, parents, and clinicians Develop and test different messaging approaches for recommending the vaccine	8 (47)
Clinician training	Target intervention at clinician Conduct in-person clinician training that uses videos and role-modeling to demonstrate effective communication styles with a focus on building trust and rapport Give clinician toolkit of materials for future reference, including communication tools for use with teens and parents Mentoring approach: Clinicians will receive feedback/data about implementation and will adjust practice iteratively as needed Give continuing medical education credit for training	6 (35)
Workflow for addressing concerns	Target intervention at clinician and clinic-based workflows Before the visit, the staff will mail vaccine reminder letter and worksheet to bring to next visit At the visit, medical assistant will place patient in room and prepare for primary care clinician by reviewing worksheet (or providing again if needed), scaling questions to assess readiness/concerns, and providing educational information as appropriate while waiting for clinician In the examination room, primary care clinician will use appropriate communication tools (eg, motivational interviewing, empathy, conversation guides, or risk reduction graphs) After the visit, for hard or soft refusals, the clinician or staff will provide additional information for home review	4 (24)

[a] Each attendee was allowed to vote for up to three intervention concepts.
HPV = human papillomavirus.

response may differ according to hesitancy type.[36] For example, a parent who is misinformed about the safety of the vaccine should be provided with correct information and reassurance, whereas a parent who wants to delay vaccination until the child is older should be provided with reasons why vaccinating on schedule would be preferable. By accurately assessing the parent's values regarding vaccination, the clinician can more adequately respond with "benefit language" specific to those values. This intervention strategy also emphasizes capitalizing on trust in the clinician and the health care organization, for example, empowering the clinician as a resource to help filter through discordant information readily available through the Internet or social media. Specific to the Kaiser Permanente setting, stakeholders emphasized that the vaccination campaign could piggyback on the popular and effective Kaiser Permanente Thrive campaign.[37]

The second intervention concept, *Ready, Set, Grow!,* would involve a set of workbooks for teens and parents to celebrate milestone birthdays (transitions to middle school and high school). The stakeholders envisioned developing preteen (aged 10-12 years) and teen versions (aged 13-14 years) in print or preferably online formats. The stakeholders emphasized the importance of designing the workbooks to appeal to youth and suggested that a "graphic novel" format that was interactive in nature might be most effective. The workbooks would optimally cover a broad range of preventive health issues, including HPV and the HPV vaccine. However, the emphasis would be on helping youth learn how to critically evaluate health information available from multiple sources and communicate effectively with their clinician. The stakeholders envisioned tear-out (or printout) worksheets that youth could take to upcoming visits with clinicians, with one worksheet specifically devoted to HPV and other adolescent vaccines.

Although user-centered design is a novel and useful approach to addressing emergent health care issues, it also poses special challenges in research settings. Flexibility in incorporating health care clinicians in qualitative interviews and focus groups or workshops is essential because of scheduling constraints and, in some cases, union policies about "volunteering" work time for research efforts. Although we conducted interviews with several clinicians, we were able to arrange for only one clinician to attend the data synthesis workshop. Likewise, we had originally planned a full-day data synthesis workshop but later streamlined our agenda to a half-day workshop to better accommodate our clinician stakeholder.

Another challenge with this type of qualitative research includes ensuring that all the relevant stakeholders are involved and that they have adequate input into the development of the "How Might We?" questions (see Sidebar: "How Might We … ?" Questions Developed for a Data Synthesis Workshop) to be resolved at the data synthesis workshop. Other limitations of this project were that parents and youth were not included as interviewees (although several of the workshop participants were parents of preteens and teens), and the brainstorming questions for the workshop were developed by the project team without stakeholder input.

The scope of this project was purposefully limited to the first three steps of user-centered design: understanding the environment, framing opportunities, and imagining possibilities. The next three steps are prototyping ideas, piloting solutions, and operationalizing to spread innovation.[23] Prototyping involves quickly and inexpensively trying out ideas and rapid iteration until a final solution is determined. Importantly, end users are actively engaged in the prototype design process. Next, we would pilot the intervention in one or two of our pediatric clinics and assess changes in vaccination rates, as well as feasibility and acceptability to patients, parents, and clinicians. Assuming the intervention was successful, the final step would be to offer the intervention to pediatric clinics throughout the KPNW Region and nationally as appropriate.

CONCLUSION

User-centered design is an effective tool for developing interventions to improve HPV vaccination rates. We identified several potential interventions that could help clinicians communicate more effectively with parents and teens about the HPV vaccine. The next steps are to develop a prototype for an intervention with the input of key stakeholders, including teenagers, parents, and clinicians, and then conduct a pilot study in a clinical setting to assess effectiveness and feasibility. ❖

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"It Keeps Us from Putting Drugs in Pockets": How a Public-Private Partnership for Hospital Management May Help Curb Corruption

Taryn Vian, PhD; Nathalie McIntosh, PhD; Aria Grabowski, MPH

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ABSTRACT

Introduction: Health care sector corruption diverts resources that could otherwise be used to improve access to health services. Use of private-sector practices such as a public-private partnership (PPP) model for hospital governance and management may reduce corruption. In 2011, a government-run hospital in Lesotho was replaced by a PPP hospital, offering an opportunity to compare hospital systems and practices.

Objective: To assess whether a PPP model in a hospital can help curb corruption.

Methods: We conducted 36 semistructured interviews with key informants between February 2013 and April 2013. We asked about hospital operations and practices at the government-run and PPP hospitals. We performed content analysis of interview data using a priori codes derived from the Corruption in the Health Sector framework and compared themes related with corruption between the hospitals.

Results: Corrupt practices that were described at the government-run hospital (theft, absenteeism, and shirking) were absent in the PPP hospital. In the PPP hospital, anticorruption mechanisms (controls on discretion, transparency, accountability, and detection and enforcement) were described in four management subsystems: human resources, facility and equipment management, drug supply, and security.

Conclusion: The PPP hospital appeared to reduce corruption by controlling discretion and increasing accountability, transparency, and detection and enforcement. Changes imposed new norms that supported personal responsibility and minimized opportunities, incentives, and pressures to engage in corrupt practices. By implementing private-sector management practices, a PPP model for hospital governance and management may curb corruption. To assess the feasibility of a PPP, administrators should account for cost savings resulting from reduced corruption.

INTRODUCTION

Corruption is a serious challenge to achieving the goals of population health and sustainable development. In 42 of 109 countries surveyed by Transparency International, more than 50% of respondents said that the health care sector was corrupt or very corrupt.[1] The World Health Organization estimated that of the $5.7 trillion in worldwide health care expenditures in 2008, 7.3% or $415 billion was lost to health care fraud and abuse, including practices ranging from theft of medicines to organized crime rackets billing insurance funds for services that were never provided.[2] Beyond the financial costs are the social and human costs of corruption, especially in low-income settings. A study of 20 African countries showed that higher perceived national corruption was negatively associated with health outcomes, with more detrimental impact among lower social classes.[3] Other studies support these findings.[4-7] Researchers believe that the immediate and delayed effect of corruption on health outcomes, including mortality, is caused by disrupting access to and the quality of health care systems, and distorting the amount and allocation of national health care investments.[7]

Types of corruption that occur at point of service may include informal payments (a direct contribution, made in addition to any contribution determined by terms of entitlement, to health care practitioners for services to which patients are entitled),[8-11] embezzlement of medicines and supplies,[12,13] shirking (ie, avoiding or neglecting assigned work duties and responsibilities, or conducting private practice instead of the assigned task during public work hours),[14] and absenteeism (ie, habitual nonpresence of an employee at his/her job when the employee is capable of working).[15,16] Sometimes called "quiet corruption,"[17] these types of abuses siphon scarce resources away from health care facilities, increase costs, and undermine the functioning of the health sector.[18] Strategies for combating corruption include strengthening oversight of clinicians,[19-21] introducing fraud control measures or civil service reforms (eg, meritocratic recruitment, improved salaries, and decentralization), and changing health care financing systems.[22] However, these initiatives take time; are politically sensitive; require resources, expertise, and leadership; and have not always been successful.[23]

Public-private partnerships (PPPs) promote greater private-sector participation in the financing, delivery, and operation of government-initiated infrastructure projects and public services. In Europe, PPPs may provide a means to meet the challenge of how to pay for necessary health care infrastructure, especially in new member states.[24] Yet, although the European Commission's plan for investment encourages private financing of public infrastructure,[25] reliable evidence on PPP performance is scarce.[26] Value-for-money, transparency, and accountability are important factors to consider when contracting for facility management and clinical service delivery.

PPPs can involve different kinds of governance, financing, management, and risk-sharing arrangements,[27-29] and they provide an opportunity for public sector partners

Taryn Vian, PhD, is a Clinical Professor and an Associate Chair in the Department of Global Health at the Boston University School of Public Health in MA. E-mail: tvian@bu.edu. **Nathalie McIntosh, PhD,** is a Health Services Researcher at the Center for Healthcare, Organization and Implementation Research (CHOIR) at the Veterans Administration Boston Healthcare System in MA. E-mail: nathalie.mcintosh@va.gov. **Aria Grabowski, MPH,** is a Policy Advisor for Accountable Development Finance in Washington, DC. E-mail: aria.grabowski@gmail.com.

to benefit from private financing and management. In addition, there is some evidence that health sector PPPs improve the quality of care provided.[30-32] However, the context in which PPPs are implemented is critical in determining whether the investment is worthwhile.[28,29] Internal enablers (perceived need and intention to collaborate) and external enablers (the operating environment and market conditions) affect PPP success.[33] Governance of complex PPP relationships may use contractual or relational mechanisms that complement each other.[34] For example, contracts are often used to mitigate opportunistic behavior by the private partner through formal control systems, whereas relational mechanisms such as informal meetings can help build trust and enhance informal control and information sharing.[35] In health care settings where rampant corruption limits access to and decreases the quality of care, it is possible that the PPP model, through its private partner governance and management, might help curb corruption, creating a more favorable operating environment. Our overarching research question, therefore, is whether the use of health sector PPPs can reduce "quiet" forms of corruption during service delivery, such as employee shirking, absenteeism, and embezzlement.

In Maseru, Lesotho, a newly built PPP hospital replaced an aging, government-run hospital.[36,37] The private partner in this project, Ts'epong Ltd, a consortium made up of a private South African health care provider and several Lesotho-owned businesses, was responsible for designing, building, partially financing, equipping, and fully operating the new hospital.[37] The relationship between Ts'epong and the government was primarily contractual rather than relational.[38] The interests of the two entities were aligned by the agreement stipulating benchmarks related to the operation of the hospital (eg, types of services offered, numbers of patients seen, and standards of care quality), with fines being imposed if certain benchmarks were not met, and additional monies paid if some benchmarks were exceeded.[37] Ts'epong was then autonomous in how it managed hospital operations, with relationships in the Ts'epong consortium governed both contractually and relationally.

The PPP hospital, like its predecessor, provided publicly funded health care services in the capital district, the largest urban area in the country with approximately 20% of the population,[39] and referral services for the rest of the country. The PPP hospital opened in October 2011 just as the government-run hospital closed, and many staff from the old hospital were employed to work under the management of the private partner at the new hospital. The replacement of the government-run hospital with a PPP hospital provided an opportunity to assess changes stemming from the PPP via a quantitative study comparing measures of capacity, utilization, clinical quality, and patient outcomes[30] as well as a qualitative study assessing differences in roles and functions between the 2 hospitals.[40] Those studies showed that the PPP had better clinical outcomes and had changed many managerial practices compared with the government-run hospital. Differences between the 2 hospitals raised questions about whether changes put into place by the PPP might influence the scope of corrupt practices. To our knowledge, there have been no studies examining the association between PPP management systems and their effects on corruption. Therefore, the purpose of this article was to compare hospital systems and practices that related to corruption between the government-run hospital and the PPP hospital that replaced it using interview data that were previously collected. Our findings add to our understanding of value creation in hospital PPPs[41] and the role of autonomous governance in addressing corruption.

METHODS

Semistructured Interviews

We used a qualitative study design. In February 2013 to April 2013, about 1.5 years after the PPP hospital opened, an interview team consisting of 2 of the coauthors (NM and AG) conducted semistructured interviews with a purposeful sample of hospital leadership, subcontractors, consultants, and government officials, as well as a convenience sample of hospital technicians and support staff. These interviews were done as a part of a previous study to document perceptions and mechanisms by which the PPP may have altered innovation, technical knowledge and skills, and organizational culture, and how these changes may influence clinical outcomes.[40] Key informants were purposefully chosen to include members of the hospital executive team, service chiefs, and contractors who would have knowledge of how management systems operated under the PPP (eg, the hospital Director and Heads of the Nursing, Pharmacy, Finance, and Administration Services, clinical managers of each ambulatory clinic, and the subcontractors responsible for laboratory and maintenance services). We also selected government key informants who would have knowledge of the PPP and the hospital it replaced, including the Ministry of Health Head of Clinical Services, all staff of the PPP oversight unit, the financial controller, and the district statistician. To understand the perceptions of lower-level hospital employees, we interviewed a convenience sample of hospital physicians, nurses, technicians, and support staff.

Each interview lasted between 30 minutes and 60 minutes. Informants were first asked, "How do PPP hospital systems differ from the systems in place at the government-run hospital?" The functioning of each service (eg, pharmacy, laboratory) was then probed through questions such as "How does the hospital manage this function now? How does this affect performance? Is this different from how the function was managed previously?" We asked key informants to describe the most important factors driving performance, and what they thought were possible reasons for changes in performance between how the government hospital used to perform, and how the PPP hospital performs now. We did not directly ask participants about practices of occupational fraud or corruption. The interview team compared and consolidated notes after each interview to create a final written transcript.

Data Analysis

We used a modified Corruption in the Health Sector framework to guide the analysis of our interview data.[22] This framework is based on prior work by one of the authors[18] and has been used in corruption vulnerability assessments in

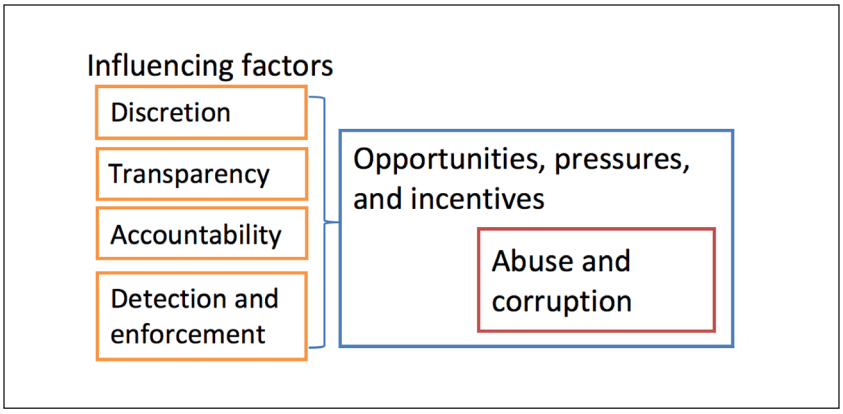

Figure 1. Corruption in the health sector framework

Albania,[42] Azerbaijan,[43] and Vietnam.[44] In this framework the five concepts of discretion, transparency, accountability, detection, and enforcement are associated with opportunities for abuse and/or pressures or incentives for abuse (Figure 1). We did content analysis of interview transcripts using these concepts as our a priori codes. We examined text describing management practices at the PPP or government-managed hospital and identified where these practices illustrated some aspect of the five concepts and/or where the informants mentioned abusive practices. Data were organized using spreadsheets (Microsoft Excel, Microsoft Corp, Redmond, WA).[45] The lead analyst (NM) performed initial coding, with review by a second member of the team (TV). We reached consensus on differences in coding through team discussions. We then grouped codes by management subsystems and made comparisons between the government-run hospital and the PPP hospital. The study was approved by the Boston University Medical Campus institutional review board and the Ethics Committee of the Lesotho Ministry of Health.

RESULTS

We interviewed 36 key informants, including 24 hospital executives, Chiefs of services, clinicians, technicians, and support staff; 8 government personnel from the Ministries of Health and Social Welfare; and 4 subcontractors/consultants. Fifteen informants were men (42%); 26 were citizens of Lesotho (72%; other nationalities included South Africa and 5 other countries). Twenty-three (64%) key informants had worked at both the government-run and the PPP hospitals.

The most common corrupt practices described at the government-run hospital were theft of medicines and equipment by clinical staff, absenteeism, and shirking. Participants stated that although the aforementioned problems had occurred in the government-run hospital, they were less frequent or had been eliminated in the PPP hospital. None described informal payments in either hospital.

Interviewees described anticorruption mechanisms that reduced opportunities for corruption or altered incentives, making corruption less likely. These were present in four management subsystems: human resources, facility and equipment management, drug supply, and security. The mechanisms are listed in Table 1 along with sample quotations showing how practices differed between the government-run and PPP hospitals.

Here we discuss the types of anticorruption mechanisms identified (ie, discretion, transparency, accountability, and detection and enforcement) and give evidence for each.

Discretion

Discretion is defined as the freedom or autonomy to use one's own authority and judgment to make decisions.[46] Through the PPP, discretion was limited by clear rules and consistent oversight. A major control on discretion was the implementation of a medication management system that tracked medicines by individual patient. At the government-run hospital, medications were stored and controlled at the ward level, and were dispensed without individual patient prescriptions. At the PPP hospital, when a physician ordered a medication, pharmacy staff entered the prescription into an electronic system. The staff member affixed a sticker with the patient's information to the back of the prescription and sent it to the appropriate ward, where a ward clerk received and accounted for it. This reduced the discretion of ward nurses regarding medications and limited opportunities for theft of medicines. One participant described the process: "Inpatient medication is [ordered] per person now, not for the entire ward. When it was for the entire ward [at the government-run hospital], that was why a lot of people were selling drugs on the outside. Now that is not easy to do. Everything that goes to the ward is recorded [in the electronic system]."

At the same time, discretion was increased at the PPP hospital by giving some staff greater authority to make decisions. For example, a pharmacy manager described how she could reorder medicines without having to get extra permissions. Her ability to make these decisions in a timely manner allowed her to keep lower amounts of stock on hand, thus reducing the opportunity for theft. The ability to get a fast decision was seen as driving performance in the PPP. "In government, it might take a long time to get a decision. There is so much red tape ... but here we know the decision will get made. You can trust that you'll get feedback, an answer." Participants also described how service heads were empowered to resolve issues: "If there is a problem you go to that department team leader. This results in more accountability because people are responsibly solely for their department."

Transparency

Transparency is defined as the active public disclosure of information on roles, policies, process, objectives, and results.[47] The PPP influenced transparency by disseminating written policies and procedures, improving electronic and paper data systems, and encouraging data-based decision making. Hiring and promotion procedures

Table 1. Public-private partnership (PPP) anticorruption practices by management systems

PPP practice	Anticorruption mechanism	Sample quotes comparing government-run hospital with PPP hospital
Human resources		
Written policies are disseminated	Transparency	*It is not that there were no policies and procedures [at the government-run hospital]. But [at the PPP hospital] we have access to them in how we do work … the policies are clear. I make sure staff have read them and understand them. Everything now, you write it down.*
Explicit work expectations	Accountability	*Back then [at the government-run hospital] we were civil servants, and we worked like civil servants. You only do something if someone is pushing.* *People had small businesses that they were running outside before [at the government-run hospital], because they didn't have to be here completely.* *Here [at the PPP hospital] you have a role. You know what to do. You can't just sit.*
Performance evaluations tied to rewards for good performance	Accountability, reducing pressure for corruption	*From when people join [the PPP hospital], they know that the 13th check [annual bonus] will be performance-based.* *Before [at the government-run hospital], some people … did good nursing, but they weren't appreciated. No one ever said "thank you." Now [at the PPP hospital] they are appreciated and rewarded. You might get the "best ward" award and all staff will get a voucher to buy things in shops.*
Explicit disciplinary processes	Transparency, discretion, accountability	*[At the government-run hospital] if there was a breakdown in discipline, and you wanted to do something about it, with civil service rules our hands were tied … [in the PPP hospital] you can immediately take care of problems with disciplinary action.* *A lot of discipline has taken place, disciplinary inquiry [at the PPP hospital]. [People are told] "If you do this, it is not tolerated here and we will follow disciplinary procedures." It is a tight knit community, so when that is done a few times, people hear about it and are deterred.*
Facility and equipment management		
Electronic tracking system for equipment (bar codes)	Accountability	*At [the government-run hospital] you heard about large equipment disappearing overnight, stolen … . It seems like there aren't so many security incidents at [the PPP hospital]. There are more controls [ie, an electronic tracking system].*
Inventory tracked by room of hospital where equipment is assigned	Discretion	*We are supposed to declare things [equipment] we move in and out of their assigned spaces [at the PPP hospital].*
Drug supply		
Weekly or monthly drug orders, rather than quarterly, via simplified direct order system, to reduce stock on hand	Accountability, reducing temptation or incentives to steal	*Here [at the PPP hospital], the pharmacy is not ordering large boxes but ordering very often, regularly.* *Purchasing [drugs] more often [at the PPP hospital] means less stock losses. The shelves are not stocked with a lot of drugs.*
Checking drugs received to ensure that the amount and quality of medicines received matches invoice	Accountability, detection (of possible collusion with supplier)	*[At the PPP hospital] when stock is delivered from a supplier, every box is opened and checked before it is put on the shelf. This way, the supplier can't short us.*
Integrated electronic pharmacy system allows query of stock levels in any location in real time, tracking individual medicines	Transparency, detection	*We had huge loss of medications at [at the government-run hospital]. Now [at the PPP hospital], you charge whatever [medicines] you are using for the patient. The pharmacy can see when stocks are low and reorder. That has really reduced theft.* *This [electronic pharmacy system] allows [us at the PPP hospital] to monitor systems so if one patient has a drug for too long there is an alarm [alert], so if one doctor prescribes and then another, it will be alerted. This is a big change [from the government-run hospital].*
Full inventory of stocks every 6 months, plus ad hoc inventories of in-house supplies	Detection, enforcement	*We do stock-take, a physical check compared to what is recorded in the system [at the PPP hospital]. If they don't add up, then we figure out who is accountable.*
Restrict supplies to wards; medicines are identified by patient name before being sent to the ward	Discretion	*At [the government-run hospital] when patients were admitted, we used to just get medicines in bulk, and the medication was used for multiple patients. Here [at the PPP hospital] prescriptions are ordered for patients directly, ordering per person, for 24 hours. [There was a] huge loss of medications at [the government-run hospital].*
Tracking and investigation of anomalous drug use	Transparency, detection	*There is a stock count [at the PPP hospital]: when they come in, the drugs are recorded. And then as they are distributed, it is recorded too. And if they don't match, we have to figure out [what happened].* *We can see if record-keeping is lacking [at the PPP hospital]. We might say to ward staff, "Seems like for bandages, you are using 12, but you recorded less." At first people would use medicines and not record the usage. They'd say "I have nothing," and I would say, "You are supposed to have 200!"*
Security		
24/7 security with trained guards, checkpoints, and security cameras	Detection	*We [at the PPP hospital] also have surveillance cameras in storerooms and in other areas. In [the government-run hospital there was] no surveillance. I see security here.* *Security is very disciplined here [at the PPP hospital], and you are sure they are patrolling around, maybe every 30 minutes. That helps them to be available most of the time. There is a sort of link between security and us now [compared with at the government-run hospital]. They [security] aren't just at the gate ... . [At the government-run hospital] they were just at the gate.*

were made more transparent, and communications were improved through frequent meetings and the creation of team structures and committees. One participant explained, "[In the PPP hospital] we have clear guidance on what you are supposed to do: standard operating procedures (SOPs). An SOP is like a recipe. It tells you, for example, this is how you admit a patient. These are the steps." Another participant described transparency in supply chain management: "Drugs used to be stocked out [out-of-stock in the government-run hospital], but now we use a control system. Every time I take the drug out, it says how many are left so we can order before you get to zero. This also helps because it keeps us from putting drugs in pockets." Transparent measures of performance were also available; several participants mentioned regular testing of competencies, and, at the unit level, balanced scorecards were used for performance management.

Accountability

Accountability refers to the obligation of those in authority to demonstrate effectiveness in carrying out goals and achieving results.[20] Participants described hierarchical accountability, that is, the answerability of individual agents to authorities above them.[19] To hold someone accountable requires that there are clear accountability relationships (ie, who is accountable to whom) and performance standards and procedures. It also requires tracking that standards are being upheld and mandates consequences for poor performance. Accountability is thus linked to transparency and enforcement.

The PPP influenced accountability by creating clear job descriptions and performance plans, tools to monitor individual compliance with standards, and methods to measure results. Information management systems were key to this process, but communication systems that conveyed expectations and facilitated discussions about performance were also important. This was especially noted in the human resources management systems in which participants described changes in performance expectations in the PPP hospital compared with the government-run hospital. One participant observed, "In government, people do whatever they want, whenever they want. … You can come 30 minutes late and be considered early." This was contrasted with the system under the PPP: "Time management has also changed [at the PPP hospital]. … There are clock machines. You put your hand in it, and key in your employment number. It reflects this. And when you clock out, it will show how many hours you worked." Participants described the use of regular team meetings to discuss progress toward performance goals as well as the presence of rewards for good performance (team and individual).

Not everyone, however, was able to adapt to the new expectations of accountability at the PPP hospital. Speaking of colleagues at the PPP hospital who had worked previously at the government-run hospital, one participant surmised, "People are not used to being disciplined; they are used to doing as they wish. There are some [who] have gone back to government, because they can open clinic at 7 [am] and close at 3 [pm], and nobody cares." The participant concluded that at the PPP hospital *"you either walk or run, no in-between,"* meaning either commit to working hard ("run") or get out ("walk"), but don't try to engage in occupational fraud or shirking ("no in-between").

Detection and Enforcement

Detection refers to the steps used to identify abuses of power, including investigation and audit, whereas *enforcement* refers to the process of defining and carrying out punishment of those who are caught abusing their authority or role for private gain.[48] The PPP has a biometric time attendance system that helps to detect unjustified absences from work, and it implemented bar codes on equipment and security checks at exit points to detect theft. Strong inventory control systems for medicines and equipment also included regular audits, both scheduled and unscheduled.

The PPP put into place disciplinary systems that allowed managers to impose consequences when employees were caught engaging in wrongdoing. If an employee committed a transgression, that worker was notified in writing of the reasons for the disciplinary notice, and the notice outlined a date and time of a disciplinary hearing, at which both parties had the opportunity to state their cases. The hearing resulted in decisions about disciplinary action or actions that were informed by guidelines regarding appropriate actions for different offenses. An interviewee described how at the PPP hospital there were about four cases per month that reached the level of having a disciplinary hearing, with one dismissal per month. Similarly, there was a process for employees to report grievances. Unit managers described how they appreciated the support from Human Resources that allowed them to discipline staff: "At [the government-run hospital] if you discussed with a person a problem, they would give you the 'eyes of fire.' Now [Human Resources] gives you support on what to do, and you don't have to fear that the [employee] will sue you." In addition, security systems put in place at the PPP hospital contributed to the sense that wrongdoing would be detected and punished. "It seems like there aren't so many security incidents at [the PPP hospital]. There are more controls. … They search the bags of staff when we leave. We want to promote a secure environment for the company, for patients, for staff. Everyone benefits."

DISCUSSION

Participants described how the PPP organizational structure and management systems reduced the incidence of theft of medicines and equipment, absenteeism, and shirking. Our findings suggest that this was done through changes in discretion and increased transparency, accountability, detection, and enforcement.

Anticorruption experts suggest that limiting discretion is an important control measure.[49,50] The PPP did this by creating clear guidelines and decision-making processes and by disseminating policies and procedures. Yet other research shows that giving individual managers more discretion—especially as it relates to disciplining employees—may also help control corruption.[51] We found evidence that the management of the PPP hospital used this mechanism as well, ensuring that individual unit leaders had discretion to impose sanctions on staff, while backing up unit leaders with guidance and support.

In an essay collection on transparency and accountability commissioned by the

Carnegie Endowment for International Peace, Lant Pritchett[52] argued that effective accountability requires a change in how agents perceive their role, and that problems such as absenteeism or poor performance cannot be solved by just providing additional funding for inputs and then monitoring indicators. According to Pritchett,[52] this "thin" approach to accountability ignores a core problem, that dysfunctional organizations do not enable accountable workers:

> *Once organizations have declined into dysfunction, a key problem is that formal mechanisms of accountability have ceased to have traction on the normal account of the frontline providers' behavior. Attacking that problem through "accounting" and "transparency" assumes one can beat a turtle into moving—that is, penetrate the hard defensive shell from external pressures that dysfunctional organizations have created.*[52]

Pritchett proposes replacing "accounting-based accountability" with a "thick" approach, a broader focus on high-performing systems and normative guidance.

The PPP hospital appeared to create accountability in this "thick" sense. The private partner in the PPP implemented processes and systems that enabled frontline workers—clinicians, support staff, and unit leaders—to do their work well, thereby reinforcing pride in their work and a commitment to the hospital's mission. As one PPP hospital staff said, "[Staff] are becoming interested in the business and [becoming] problem solvers. A culture of accountability in the staff has been created. [They take] pride in their job." Accountability was also facilitated and reinforced by these systems factors: standard operating procedures, trainings, and recognition awards that gave explicit guidance as to what was expected of staff, setting norms and standards. Without these external messages and rules, it is up to the individual alone to rely on his/her integrity when confronting temptations to abuse. In the government-run hospital, staff lacked support for doing good work. Although some staff persevered, many were unable to resist the pressures and opportunities to engage in corrupt practices. It is much easier to do good work when operating in a wholly accountable system.

The PPP hospital created several levels of accountability, combining more technical fixes associated with detection and enforcement (eg, regular audits, attendance monitoring) with an empowerment and incentives approach that helped workers to clearly understand their role and expectations for performance, and gave line managers the power to discipline wrongdoing while strengthening their ability to do their work well. This, in effect, created a change in organizational culture, from one in which opportunities, incentives, and pressures for abuse were common to one in which corrupt practices were not tolerated. This two-tiered approach to accountability mirrors deep "double-loop" organizational learning, in which organizations do not simply detect and correct individual issues but also attempt to change higher-order incentives, processes, and practices (ie, culture) that shift the way problems are framed and addressed.[53,54] For example, rather than simply instituting security checks at the exit of the hospital to catch equipment thieves, the PPP hospital worked to create a culture that nurtured employees' innate desire to do good work, so that it would be less likely for staff to even consider stealing hospital equipment. As a PPP hospital executive put it: "We took people out of [the government-run hospital], but the challenge is to take [the government run-hospital] out of the people. We have made strides, but there is more to do around work ethic and culture."

Creating a "thick" sense of accountability or engaging in double-loop organizational learning is difficult and generally takes time, but it may result in a deeper and more long-lasting accountability, with anticorruption practices embedded into the organization's institutional fabric. The PPP's contractual requirements to meet cost and quality standards create strong incentives for the private partner to implement management practices that expedite change in anticorruption culture. This may be further facilitated by the private partner in its ability to manage operations autonomously, without government involvement. The speed and level of change, without the impetus of the PPP contract or the expertise, resources, and leadership of the private partner, may be difficult to achieve otherwise.[55]

Despite evidence of gains in quality of services,[30-32] PPP hospitals have been criticized for being unaffordable.[56] The true cost of a PPP, however, may be lower than expected if benefits associated with reduced corruption are taken into account.[41] Organizations with high levels of abuse are unwittingly paying the cost of corruption as part of their operating expenses, like a "secret tax."[48] Although it is difficult to quantify benefits from corrupt practices averted, some studies have documented the potential savings from prevention efforts.[57-59] In estimating the economic viability of a PPP initiative, policy makers should likewise consider potential cost savings. It could be useful if future evaluations of PPP models measured perceived corruption and corruption risk factors to better understand how corruption manifests, how corruption is controlled, and the potential savings of implementing anticorruption practices. Researchers in Lesotho could build further evidence by comparing stockout rates, absenteeism, and other performance measures in the PPP hospital compared with government-managed hospitals over time.

European policy researchers have hypothesized that in the future, governments may try to separate facilities management contracts from PPP infrastructure contracts to allow more frequent repeated competition, thus encouraging redesign to reduce waste and improve efficiencies.[24] Our findings suggest that controlling corruption is another aspect of contract performance that should be considered in evaluating the productive efficiencies possible through PPP contracts.

CONCLUSION

Our findings show that corruption can be curbed in a hospital setting and that a PPP model for hospital governance is one positive mechanism in that it leverages the management expertise of the private sector. The PPP hospital implemented rules, policies, and practices across a number of management systems that changed levels of discretion; increased transparency, accountability, detection, and enforcement; and decreased opportunities, pressures, and incentives to engage in corrupt practices. The PPP approach of implementing, en masse, private-sector management

rules, systems, and structures may succeed in creating a culture that limits losses and waste in a facility with entrenched corrupt practices. ❖

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Awesome Citadels

Few institutions have undergone as radical a metamorphosis as have hospitals in their modern history. In developing from places of dreaded impurity and exiled human wreckage into awesome citadels of science and bureaucratic order, they acquired a new moral identity, as well as new purposes and patients of higher status.

— Paul Starr, PhD, Pulitzer Prize-winning professor of sociology and public affairs

Evaluation of a "Just-in-Time" Nurse Consultation on Bone Health: A Pilot Randomized Controlled Trial

Douglas W Roblin, PhD; David Zelman, MD; Sally Plummer, RN; Brandi E Robinson, MPH; Yiyue Lou, MS; Stephanie W Edmonds, PhD; Fredric D Wolinsky, PhD; Kenneth G Saag, MD, MS; Peter Cram, MD, MBA

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ABSTRACT

Context: Evidence is inconclusive whether a nurse consultation can improve osteoporosis-related patient outcomes.

Objective: To evaluate whether a nurse consultation immediately after dual-energy x-ray absorptiometry (DXA) produced better osteoporosis-related outcomes than a simple intervention to activate adults in good bone health practices or usual care.

Design: Pilot randomized controlled trial, conducted within the larger Patient Activation After DXA Result Notification (PAADRN) trial (NCT01507662). After DXA, consenting adults age 50 years or older were randomly assigned to 3 groups: nurse consultation, PAADRN intervention (mailed letter with individualized fracture risk and an educational brochure), or usual care (control). Nurse consultation included reviewing DXA results, counseling on bone health, and ordering needed follow-up tests or physician referrals.

Main Outcome Measures: Change from baseline to 52 weeks in participant-reported osteoporosis-related pharmacotherapy, lifestyle, activation and self-efficacy, and osteoporosis care satisfaction.

Results: Nurse consultation participants (n = 104) reported 52-week improvements in strengthening and weight-bearing exercise ($p = 0.09$), calcium intake ($p < 0.01$), osteoporosis knowledge ($p = 0.04$), activation ($p < 0.01$), dietary self-efficacy ($p = 0.06$), and osteoporosis care satisfaction ($p < 0.01$). Compared with PAADRN intervention participants (n = 39), nurse consultation participants had improved dietary self-efficacy ($p = 0.07$) and osteoporosis care satisfaction ($p = 0.05$). No significant improvements in osteoporosis-related outcomes were achieved vs PAADRN controls (n = 70).

Conclusion: "Just-in-time" nurse consultation yielded a few improvements over 52 weeks in osteoporosis-related outcomes; however, most changes were not different from those obtained through the lower-cost PAADRN intervention or usual care.

INTRODUCTION

There are a number of steps between a patient receiving a screening test for disease—such as a dual-energy x-ray absorptiometry (DXA) test for assessment of bone density and diagnosis of osteoporosis—and when the screened patient is informed of results and started on a treatment plan to address related health issues. Between each step, there is potential for a "care gap," which, singly or in the aggregate, may result in suboptimal changes to treatment and health outcomes that the screening test is intended to initiate.[1]

In the case of DXA tests, a radiology technologist or technician administers the test but does not interpret results or initiate a treatment plan. Results are forwarded to a physician (typically a radiologist or rheumatologist) for interpretation. That step might take several days. The interpretation is then frequently forwarded to the ordering physician, typically a patient's primary care physician (PCP), who is responsible for ensuring that the patient is notified of the results and, if needed, for developing a treatment plan. These additional steps may take days or weeks. Each delay dilutes the effectiveness of what might have been a "teachable moment"—completion of the DXA, especially in terms of immediacy of results and an opportunity to inform and guide the patient on next steps in osteoporosis prevention or treatment.

Integrated health care delivery systems are well positioned to implement cost-effective solutions to closing these care gaps by "[g]etting work done by the right person at the right time."[2pS459] Nonphysician clinicians, such as nurses (registered and advanced practice), dietitians, and clinical pharmacists, often have scopes of practice, training, and clinical experience that would allow them to assist physicians in diagnosis and treatment of patients for maintaining good bone health.[1,3]

Greater involvement of nurses in osteoporosis-related care has involved a range of intervention strategies focusing on the following: 1) extent of role integration (standalone vs part of a multidisciplinary team); 2) mode of delivery (one-on-one patient consultations by visit or by telephone, patient groups); 3) clinical outcomes which are the focus of protocol (antiresorptive therapy, patient dietary intake, or exercise frequency); and 4) targeted patient population (young women, postmenopausal

Douglas W Roblin, PhD, is a Professor of Health Management and Policy at Georgia State University School of Public Health and a Consulting Senior Research Scientist at the Center for Clinical and Outcomes Research in Atlanta. E-mail: droblin@gsu.edu. **David Zelman, MD,** at the time of this study was a Rheumatologist with The Southeast Permanente Medical Group, Inc, in Atlanta, GA. E-mail: rheumexpert@gmail.com. **Sally Plummer, RN,** at the time of this study was a Consulting Nurse Educator at the Center for Clinical and Outcomes Research in Atlanta, GA. E-mail: sallyplummer23@gmail.com. **Brandi E Robinson, MPH,** is a Senior Project Manager at the Center for Clinical and Outcomes Research in Atlanta, GA. E-mail: brandi.e.robinson@kp.org. **Yiyue Lou, MS,** is a Biostatistician in the College of Public Health at the University of Iowa in Iowa City. E-mail: yiyue-lou@uiowa.edu. **Stephanie W Edmonds, PhD,** is a Graduate Research Assistant in Internal Medicine and a Doctoral Candidate in the College of Nursing at the University of Iowa in Iowa City. E-mail: stephanie-edmonds@uiowa.edu. **Fredric D Wolinsky, PhD,** is the John W Colloton Chair in the College of Public Health at the University of Iowa in Iowa City. E-mail: fredric-wolinsky@uiowa.edu. **Kenneth G Saag, MD, MS,** is a Professor of Medicine in the Division of Clinical Immunology and Rheumatology at the University of Alabama at Birmingham. E-mail: ksaag@uabmc.edu. **Peter Cram, MD, MBA,** is a Professor of Internal Medicine in the Division of General Internal Medicine at the University of Toronto and the Director of General Internal Medicine at the University Health Network and Mount Sinai Hospital in Ontario, Canada. E-mail: peter.cram@uhn.ca.

women, patients with confirmed osteoporosis, men and women).[4-20] Evaluation designs for assessing impact of these nurse interventions include pre-/postintervention designs with or without controls, as well as randomized controlled trials (RCTs). Durations of health outcome assessments range from several months to a year or more. Evidence is inconclusive whether the nurse role can be adapted to close care gaps in osteoporosis-related care and to improve patient outcomes.

We conducted a pilot RCT to evaluate whether a registered nurse, working under the supervision of a rheumatologist, could improve patient adherence to behaviors that promote good bone health. The nurse was available immediately after DXA ("just in time") and had a scope of practice that allowed for reviewing DXA results, counseling patients on self-management strategies and lifestyle to address osteoporosis and maintain good bone health, and entering orders (if needed) for additional diagnostic tests as well as follow-up visits to the patient's PCP or other specialists. The intervention goal was to achieve improvements in guideline-concordant, osteoporosis-related pharmacotherapy, frequency of weight-bearing and strengthening exercise, calcium and Vitamin D intake, activation and osteoporosis self-efficacy related to diet and exercise, and satisfaction with osteoporosis care during a one-year period, compared with similar participants enrolled in either the Patient Activation After DXA Result Notification (PAADRN) trial (NCT01507662) intervention or usual care (control) group.

METHODS

Study Setting and Population

This nurse consultation pilot RCT was conducted at Kaiser Permanente Georgia (KPGA) within the context of the larger, multisite PAADRN study, a double-blinded, parallel, pragmatic RCT.[21] The PAADRN protocol was reviewed, approved, and monitored by the institutional review board of each of the three participating sites. In addition, the nurse consultation pilot RCT protocol was reviewed, approved, and monitored by the KPGA institutional review board.

Eligible patients were KPGA members age 50 years or older who were scheduled for DXA between March 2013 and May 2014 at KPGA's Crescent Center medical facility. Consistent with the PAADRN protocol, we excluded patients who were unable to read, speak, or understand English; prisoners; and those unable to provide informed consent because of perceived cognitive disabilities. Informed consent was obtained from all KPGA participants before we initiated the baseline interview.

Randomization and Allocation

Randomization and allocation procedures for the nurse consultation study were coordinated with PAADRN study procedures (Figure 1). Each day during the study period, the DXA schedule was queried to identify eligible members who had DXA scheduled in the subsequent 2-week window on a day the nurse consultant was also scheduled to be available. Those members were randomly assigned at KPGA to the nurse consultation study group or to the PAADRN study using the random number function of analytic software (SAS 9.4, SAS Institute Inc, Cary, NC). Randomization was designed to yield approximately a 2:1 (pilot RCT study:PAADRN study) ratio and a sample size of approximately 150 participants receiving nurse consultation. Among those allocated to PAADRN at Crescent Center, randomization to the PAADRN intervention or usual care group was done at the University of Iowa coordinating center following standard PAADRN procedures.

Randomization and allocation to the nurse consultation pilot RCT or to PAADRN occurred before mailing an invitation letter to eligible KPGA members. This was necessary because the composition of the invitation letter needed to describe the specific time requirements, risks, and benefits of the nurse consultation pilot RCT (eg, allowing time for a baseline interview plus a consultation session after DXA completion) compared with PAADRN (eg, allowing time only for a baseline interview). Thus, from invitation through baseline interview, study assignment to the nurse consultation pilot RCT or PAADRN was not concealed to patients or project staff. Among PAADRN participants, however, allocation to the intervention or usual care (control) group (described in the "PAADRN Protocol" section) occurred after the baseline interview and was concealed to patients and project staff.

At approximately 52 weeks after the baseline interview, a subsequent interview was conducted by telephone by trained

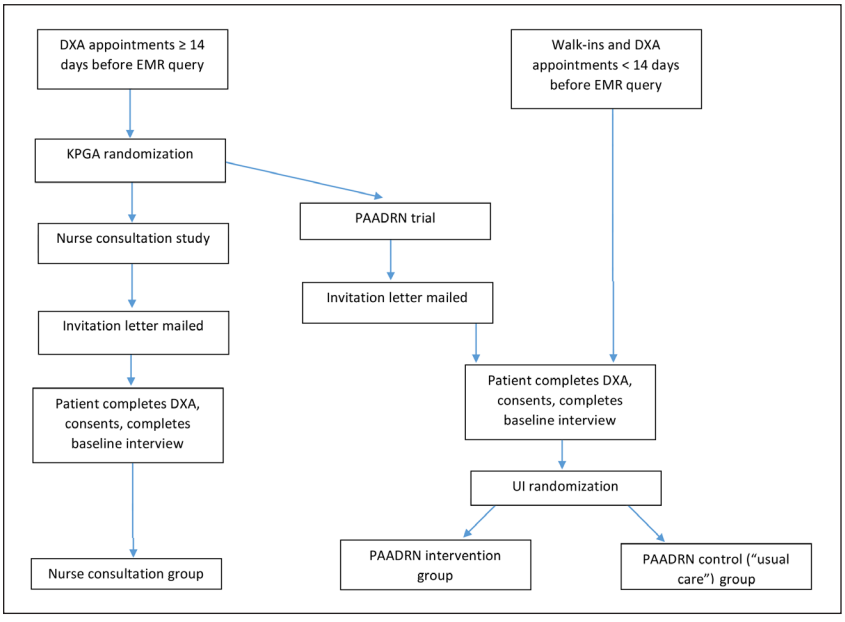

Figure 1. Participant contact, recruitment, and allocation process.

DXA = dual-energy x-ray absorptiometry; EMR = electronic medical record; KPGA = Kaiser Permanente Georgia; PAADRN = Patient Activation After DXA Result Notification; UI = University of Iowa.

staff at the University of Iowa coordinating center. These interviewers were blinded to patients' allocation to the 3 study groups (ie, nurse consultation, PAADRN intervention, PAADRN usual care).

Recruitment

After randomization, letters inviting participation in the nurse consultation pilot RCT or PAADRN study were mailed to patients' home addresses approximately 7 to 10 days before the DXA appointment. Both letters stated the voluntary nature of study participation. The PAADRN study letter indicated that consent and 15 to 20 minutes after the DXA would be required for an interview with a research assistant. The nurse consultation pilot RCT letter indicated that consent and 30 to 45 minutes after the DXA would be required for the research assistant interview plus the nurse consultation. This letter also briefly described the nurse consultation. Both letters indicated that a $20 gift card would be provided to compensate for a participant's time. The nurse consultation pilot RCT letter further indicated that the nurse consultation would not require a copayment, which is typically required of a nurse educator visit. Eligible participants who did not specifically decline participation were called by a research assistant approximately 2 days before the appointment either to ascertain interest or to remind them of the research appointment and procedures after their DXA.

Nurse Consultation Procedures

The nurse consultant for the pilot RCT was a senior licensed registered nurse who had practiced for many years with KPGA both in primary care and administration. Before conducting consultations for the pilot RCT, she shadowed the supervising physician (a senior KPGA rheumatologist) during his office visits with patients who presented for initial treatment of osteoporosis.

The nurse consultant was responsible for counseling pilot RCT participants for both prevention and primary treatment of osteoporosis after the DXA. She reviewed the patient's medical history with attention to indications of fracture risk (including DXA T-scores) and provided general education

GUIDELINES FOR PHYSICIAN OVERSIGHT AND NURSE EDUCATION CONSULTATION IN THE PATIENT ACTIVATION AFTER DXA RESULT NOTIFICATION (PAADRN) STUDY: OSTEOPOROSIS MANAGEMENT DELEGATED TO REGISTERED NURSE

A. OVERVIEW OF THE ENCOUNTER PROTOCOL

The purpose of the protocol is to provide guidelines for physician oversight of a registered nurse (RN) who will provide educational consultation to patients following a dual-energy x-ray absorptiometry (DXA). The RN, using standardized procedures and protocols, will be responsible to educate and to manage research study participants for both prevention and primary treatment of osteoporosis. Procedures and protocols for screening, diagnosis, and referrals for follow-up care will be consistent with the implementation of the Kaiser Permanente (KP) Georgia National Clinical Practice Guidelines: "Osteoporosis/Fracture Prevention Clinical Practice Guideline Summary."[1]

B. PURPOSE OF THE ENCOUNTER PROTOCOL

The RN is delegated to perform all the medical acts in the protocol without the direct or immediate observation, supervision, or approval of the delegating physician. Immediate consultation with the delegating physician or his/her designee is available at all times. Critical laboratory results will be communicated to the delegating physician or his/her designee the same day received by the RN. Supervision will be provided by the delegating physician. Each chart will be forwarded on the day of the encounter to the delegating/supervising physician and each order will be co-signed by the delegating physician.

C. DETAILS OF THE ENCOUNTER PROTOCOL

1. Assessing osteoporosis during the RN consultation

Diagnosis of normal bone mass, low bone mass/osteopenia, or osteoporosis is made by the RN after review of clinical history, physical findings, and results of the DXA scan. The RN will initiate therapy on the basis of the treatment plan listed below and recommendations of supervising the physician.

Clinical history/physical findings:

Review DXA scan results and risk factors using Fracture Risk Assessment Tool (FRAX) model. Information should be obtained regarding risk factors including, but not limited to:

- age
- height/decreased height/weight
- smoking/alcohol history
- diet/history of poor calcium/Vitamin D intake
- exercise level/tolerance/mobility
- personal/family history fracture
- personal/family history osteoporosis
- history of osteoporosis medication
- previous DXA results
- pre-/postmenopause
- low testosterone
- kyphosis/back pain
- fall assessment (history falling to ground past 6 months, review medication for balance risks)
- history of medications that increase fracture risk (ie, leuprolide [Lupron], chemotherapy)
- history of corticosteroid use (5 mg/d prednisone or equivalent for > 3 mos)
- history of anticonvulsants, blood thinners, proton pump inhibitors, selective serotonin reuptake inhibitors, antacids
- current medications/vitamins
- drug allergies
- pregnancy/nursing
- hypocalcemia
- dysphagia/reflux
- history of hypertension, diabetes mellitus, chronic kidney disease, asthma
- history of hyperthyroidism, anorexia, organ transplant, gastric bypass
- history of liver disease
- history of rheumatoid arthritis.

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2. Education on osteoporosis and fracture prevention

Define and review pathophysiology of osteoporosis.

- Review consequences of untreated osteoporosis and steps to mitigate osteoporosis
- Review DXA results and fracture risk
- Recommend calcium carbonate (OsCal-Calcium, Tums, Caltrate)
  - Premenopausal: 1000 mg (elemental calcium) daily with food
  - Postmenopausal: 1200 mg (elemental calcium) daily with food
  - Men over 50 years of age: 1200 mg (elemental calcium) daily with food
  - Do not exceed 1500 mg/d
  - Use calcium carbonate/citrate/phosphate. Bone meal/dolomite/oyster shell may contain lead
  - Take calcium carbonate with meals, but no more than 500 mg at one time
  - Take with 8 oz water or juice
  - Take with Vitamin D
  - Separate calcium from other medicines, iron, zinc, or folic acid by 2 hours (thyroid by 4 hours)
  - Avoid other antacids. Limit aspirin and nonsteroidal anti-inflammatory drugs
  - Wheat bran, whole grain cereals, and foods high in oxalates decrease absorption of calcium
  - Take calcium 1 hour before/2 hours after high-fiber meal
  - Increase exercise, fluids, fiber, and fruit to avoid constipation
- Recommend calcium citrate (Citracal, Calcitrate) for decreased gastric acidity (elevated pH), H_2 receptor antagonist/proton pump inhibitor use, or bariatric surgery. Take calcium citrate on an empty stomach with 8 oz water
- Recommend vitamin D3
  - Pre-/postmenopausal women and men over 50 years of age: 1000 IU/d
  - Do not take with cholestyramine, mineral oil, magnesium-containing antacids, orlistat, cimetidine (Tagamet), or vitamin A
- Diet
  - Food sources high in calcium include dairy, dark green vegetables, beans, and calcium-fortified orange juice
  - Decrease caffeine, soda, sodium, and alcohol
- Exercise
  - Advise regular weight-bearing and muscle-building exercise daily
  - Discuss exercise program with primary care physician (PCP)
- Tobacco
  - Advise tobacco cessation
  - Refer to PCP and/or smoking cessation class
- Regular eye examinations
  - Maintain visual acuity to assist in fall prevention
- Home safety proofing
  - Advise assessment/removal of rugs
  - Advise installation of grab bars as needed
  - Advise use of nightlights/adequate lighting
  - Advise securing electrical cords
- Patient handouts
  - Osteoporosis Treatment/Prevention Instructions (for patient after visit summary)
  - Osteoporosis handouts from KP Clinical Library (all Regions) optional
  - Osteoporosis handouts from National Osteoporosis Foundation and National Institute of Arthritis and Musculoskeletal and Skin Diseases optional
  - Lexi-Patient Education (Lexicomp) handouts optional.

3. Laboratory work

- Before recommending/initiating drug therapy, consider orders (if not done in past 12 months) for 25-hydroxyvitamin D, calcium, creatinine, Vitamin D, or as recommended by the supervising physician
- For suspected secondary osteoporosis (Z-score -2.0 or lower) recommended workup will be provided to the RN by the supervising physician on case-by-case basis
- Vitamin D assays for deficiency:
  - If 21-30 ng/mL, recommend ergocalciferol 50,000 IU orally 3 times/wk for 4 weeks, then 1000 IU/d
  - If < 20 ng/mL, postpone bisphosphonate until after prescription above.

4. Medications

- Recommend initiation of osteoporosis medication for:
  - Postmenopausal women with a history of fragility fracture
  - Women aged 65 or older with T-score -2.5 or less
  - Postmenopausal women with a FRAX 10-year risk of hip fracture 3% or greater or major osteoporotic fracture of 20% or higher. If T-score is below -1.0 but above -2.5, use FRAX score
  - Optional for postmenopausal women younger than age 65 years or men younger than age 70 years with T-score -2.5 or lower, but without FRAX hip 3%/major osteoporotic fracture 20% or greater
  - Men age 70 years or older with prior fragility fracture, T-score -2.5 or lower, or FRAX hip 3%/major osteoporotic fracture 20% or greater
  - Steroid use 3 months or more and FRAX hip 3%/major osteoporotic fracture 20% or greater
- Order PCP consultation for medication initiation and refills. All medications will be provided by member's PCP
- Present if requested and only after supervising physician consultation, with medication treatment options based on patient history and assessment of contraindications
- If patient is receiving medication or if medication orders are pending, stress compliance with long-term therapy to reduce fracture risk
- If patient is receiving medication or if medication orders are pending, instruct patient to report side effects/symptoms of medication; give handout. Instruct to stop medication and call PCP or 911 immediately for symptoms of anaphylaxis (itching/hives, swelling of face/hands/mouth/throat, tingling of mouth/throat, tightness in chest, trouble breathing), unusual/severe stomach pain, or jaw pain
- Assess for treatment contraindications and secondary osteoporosis. Consult with/refer to endocrinology/rheumatology: hypocalcemia, chronic kidney disease Stage 4 or 5/last glomerular filtration rate (GFR) < 30, severe gastroesophageal reflux disease, pregnancy/nursing, difficulty swallowing or cannot stay upright for at least 30 minutes, current use of cancer chemotherapeutic agent or anticonvulsants, history/consideration of organ transplant, bariatric surgery, inability to follow instructions, poor prognosis, suspected secondary cause (Z-score -2.0 or lower), fracture during osteoporosis treatment/atypical

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or low-impact subtrochanteric stress fracture, contraindications/intolerances to first- or second-line therapies, premature menopause, history of corticosteroid use, history of gonadotropin-releasing hormone/leuprolide (Lupron) therapy or medroxyprogesterone (Depo-Provera) use, or hyperthyroidism.

5. Medication options for women

- FIRST-LINE therapies
  - Alendronate (Fosamax)
    - Dose: 70 mg/wk; take with 8 oz water 30 min before activity/drink/medications; upright 30 minutes
    - Contraindications: Women of childbearing age without contraception, GFR < 30-35, Vitamin D level 30 ng/mL or less, hypocalcemia, teeth/gum problems
    - Precautions: Esophageal disease, gastritis, ulcers
  - Risedronate (Actonel)
    - Nonformulary alternative when alendronate is contraindicated or not tolerated
    - Dose: 5 mg/d or 35 mg/wk; take with 8 oz water 30 minutes before activity/drink/medications; upright 30 minutes
    - Contraindications: Women of childbearing age without contraception, GFR < 30-35, Vitamin D level 30 ng/mL or less, hypocalcemia, teeth/gum problems
- SECOND-LINE therapies are used when first-line agents are contraindicated or cannot be tolerated. The following second-line therapies have not been shown to significantly reduce nonvertebral fractures of the hip or wrist, however. Consider specialist referral.
  - Raloxifene (Evista)
    - Option for postmenopausal women with low risk for thrombotic complications
    - Option for women at high risk for breast cancer
    - Dose: 60 mg/d orally without regard to meal
    - Contraindications: Active/history thromboembolism, increased risk of stroke
    - Precautions: Discontinue 72 hours before prolonged bedrest; avoid one position for long period. Report swelling, warmth, pain in calves
  - Ibandronate (Boniva)
    - Nonformulary option for postmenopausal women older than age 65 years with prior vertebral fracture
    - Dose: 2.5 mg/d orally or 150 mg/mo; take 60 minutes before food/drink/medications; sit 60 minutes
    - Precautions: See bisphosphonates
  - Nasal calcitonin (Miacalcin)
    - Nonformulary option for postmenopausal women older than age 65 years with prior vertebral fracture
    - Dose: 200 IU/d (1 spray) alternating nostrils (activate pump before first dose)
    - Precautions: Osteogenic sarcoma, pernicious anemia, renal disease, hypersensitivity to salmon protein or gelatin diluent
- THIRD-LINE therapies for postmenopausal at high risk of fracture when first- and second-line therapies contraindicated or not tolerated. Refer to specialist.
  - Zoledronic acid (Zometa)
    - Nonformulary option for postmenopausal women older than age 65 years with high risk and prior vertebral fracture
    - Hypercalcemia associated with malignancy
    - Dose: 5 mg intravenously annually
    - Precautions: Renal dysfunction, asthma
  - Teriparatide (Forteo) (recombinant parathyroid hormone)
    - Nonformulary option for high-risk women not tolerant of or responsive to other agents
    - Dose: 20 µg/d subcutaneously in thigh/abdomen wall
    - Contraindications: Paget disease, elevated alkaline phosphatase, open epiphyses, prior external beam or implant radiation involving the skeleton
    - Precautions: Recent urolithiasis, digitalis; treatment should not exceed 18-24 months.

6. Medication options for men

- Alendronate, 10 mg/d or 70 mg/wk
  - For men age 70 years or older with prior fracture, osteoporosis/T-score -2.5 or less, or FRAX 3%/20% or greater
  - Optional for men under age 70 with osteoporosis/T-score -2.5 or less, without FRAX 3%/20%.

7. Medication management for women and men taking corticosteroids

- Men/women on prednisone 5 mg (or equivalent) for 3 months or greater and with FRAX 3%/20% or greater. Refer to specialist.
- First-line: Alendronate 10 mg/d or 70 mg/wk, risedronate 5 mg/d or 35 mg/wk.
- Second-line: Teriparatide for glucocorticoid-treated patients intolerant of or responsive to other agents.

8. Hormone Therapy

- Initiating/continuing hormone therapy solely for the prevention of osteoporosis is not recommended.

D. ELECTRONIC MEDICAL RECORD DOCUMENTATION OF THE ENCOUNTER

- Progress notes will be completed on all patient contacts and documented in the medical record. HealthConnect chart documentation will include *chief complaint* = "Clinical Research Study," *supervision type* = "Clinical Trial" (vs RN Supervision), and *primary diagnosis* = "V70.7A Clinical Trial Participant Examination"
- Diagnosis and KP codes will be coded in HealthConnect and documented in the progress note. (Medicare requires osteoporosis diagnosis must be in progress note and note must indicate some level of evaluation/treatment performed during encounter)
- PCP will be notified of assessment findings and treatment electronically via HealthConnect progress note
- Patients who cannot be managed under protocol will have a notation in the chart by both the RN and the supervising physician. Reasons for protocol deviation and off-protocol treatment plan will be documented.

Reference

1. Osteoporosis/fracture prevention clinical practice guideline summary [Internet]. Oakland, CA: Kaiser Permanente Medical Care Program: Care Management Institute; 2010 Nov [cited 2017 Jun 14]. Available from: https://providers.kaiserpermanente.org/info_assets/cpp_oh/oh_osteoporosisfracturepreventionguidelinesummary_dec2013.pdf. [Password protected.]

about lifestyle (ie, dietary calcium, supplemental Vitamin D, strengthening and weight-bearing exercise) to maintain good bone health and to reduce fracture risk. She was provided with a National Institutes of Health brochure on effective osteoporosis self-management practices to distribute to patients at the time of consultation.[22] After each visit, the visit was documented in the KPGA electronic medical record (EMR) as a "research visit" using an Epic SmartSet (Epic Systems Corp, Verona, WI) to help organize and standardize each visit's documentation. At the end of each day, the nurse consultant's EMR visit notes, including the DXA scan, and recommended orders were reviewed by the supervising physician. The nurse consultant also had discretion to phone the patient the following day and provide an additional limited phone consultation regarding the DXA results and treatment recommendations of the supervising physician.

The nurse consultant was delegated to perform specific medical acts in accordance with an approved, written clinical protocol without the direct or immediate observation, supervision, or approval of the delegating physician; however, immediate consultation with the supervising physician or his designee was available at all times. A clinical protocol for conducting the nurse consultation was developed by the research team and then reviewed and approved by physicians with the KPGA Preventive Medicine and Rheumatology Departments (see Sidebar: Guidelines for Physician Oversight and Nurse Education Consultation in the Patient Activation after DXA Result Notification [PAADRN] Study: Osteoporosis Management Delegated to Registered Nurse). Procedures and protocols for screening, diagnosis, and referrals for follow-up care were consistent with KPGA clinical practice guidelines: "Osteoporosis/Fracture Prevention Clinical Practice Guideline" (November 2008, November 2010) and its "Guideline Revision Summary" (2008-2010).

Tasks delegated to the nurse consultant included, but were not limited to, entering orders for appropriate laboratory and other diagnostic tests, and entering orders for other services, such as physician visits for further treatment and evaluation. Ordering prescription medications was specifically excluded from delegated medical acts.

The supervising physician provided oversight to the nurse consultant's training, order entries, and visit documentation. He ensured that the nurse consultant was aware of regulatory requirements and acceptable standards for osteoporosis screening, diagnosis, and treatment. He met with the nurse consultant on a regular basis to review any national or KPGA-specific changes to osteoporosis-related protocols or procedures. At the end of each day, he reviewed and signed orders made by the nurse consultant. If he considered some orders to be incorrect or unnecessary, he informed the nurse consultant, including reasons for not approving the order. He also entered into the KPGA EMR any additional orders for patients as needed.

The KPGA EMR facilitated implementation of the study protocol and coordination of care between the nurse consultant and the supervising physician. Components of the protocol were implemented as a template in the EMR to standardize documentation. The EMR allowed entry of orders for approved services and rapid review of orders and consultation notes by the supervising physician.

PAADRN Protocol

Participants of PAADRN who were randomly assigned to the PAADRN intervention group received directly from the University of Iowa a mailed letter with individualized fracture risk and a bone health education brochure within approximately four weeks of the DXA. The letter described results of their DXA (lowest T-score) and interpretation (osteoporosis, low bone mineral density [osteopenia], or normal) and presented a graphic portrayal of the ten-year probability of sustaining a major osteoporotic fracture, calculated by the FRAX Fracture Risk Assessment Tool (available at www.shef.ac.uk/FRAX/). These materials are described elsewhere.[23-25] The PAADRN intervention participants also received the usual KPGA mode of communicating DXA results and action steps, described in the next paragraph.

Participants who were randomly assigned to the control group received "usual care." Communication of DXA results to controls followed a more circuitous route than the direct-to-patient, tailored letter received by intervention participants. After DXA, a rheumatologist's clinical impression would be forwarded to the ordering practitioner, who might further review and possibly annotate the rheumatologist's impression before eventually forwarding the summary interpretation and recommendations (if any) to the patient.

Members of KPGA assigned to the nurse consultation pilot RCT were excluded from participation in the PAADRN study. Thus, participants in the nurse consultation pilot RCT did not receive the direct-to-patient, tailored letter on fracture risk with an accompanying educational brochure.

Measures

Guideline-Concordant Pharmacotherapy

The primary PAADRN end point was guideline-concordant pharmacologic treatment at 52 weeks. The algorithm for determining guideline-concordant pharmacologic treatment was based on the 2010 National Osteoporosis Foundation guidelines in effect at the time of the PAADRN study[26] and is described in detail elsewhere.[27] Essentially, the algorithm is based on the 2-by-2 cross-classification of whether the patient was taking osteoporosis pharmacologic treatment (bisphosphonates, calcitonin, estrogen/hormone therapy, estrogen agonist/antagonist, parathyroid hormone, or denosumab) and whether this was guideline-concordant. In this pilot RCT, guideline-concordant pharmacotherapy was measured only at 52 weeks after enrollment.

Combined Exercise Frequency

Combined exercise frequency at baseline and at 52 weeks was assessed from 2 items: "In the past 30 days, how many times per week were you engaged in aerobic activity?" and "In the past 30 days, how many times per week were you engaged in strength training?" Examples of aerobic activity and strength training were provided with each item. Response categories were none, 1 to 2, 3 to 4, or 5 or more times per week. These categories were weighted 0, 1.5, 3.5, and 5, respectively. A combined exercise score was the sum of the weighted values and resulted in possible scores of: 0, 1.5, 3, 3.5, 5, 6.5, 7, 8.5, and 10. This score represents the relative number of sessions

per week during which the recommended activities occurred.

Total Calcium

Total calcium (mg/d), at baseline and 52 weeks, was estimated from responses to food sources (4 items), calcium supplements (1 item), and daily multiple vitamins (1 item).[28] Calcium from food sources was assessed by frequency (0-1, 2-3, 4-6, 7 or more units) per week for cups of milk, ounces of cheese, servings of yogurt, and cups of calcium-fortified beverages. Midpoints of response categories for fewer than 7 d/wk were used for intake estimation. The 7 d/wk category was scored as 7. Each amount was multiplied by the following quantities to obtain an estimated calcium intake: 300 mg per milk serving, 200 mg/oz (200 mg/28 g) cheese, 300 mg per yogurt serving, 80 mg/cup (80 mg/0.24 L) serving of calcium-fortified beverage. The sum of these quantities was divided by 7 to get an average estimate of milligrams per day. Two other survey items assessed calcium from supplements: "Do you take calcium supplements?" and "Do you take a daily multiple vitamin?" To the milligrams-per-day estimate from food sources, a "Yes" response to these items added 250 mg/d and 75 mg/d, respectively.

Supplemental Vitamin D

Vitamin D supplementation was assessed by the item assessing daily multiple vitamin use. The use of supplemental Vitamin D at baseline and 52 weeks was binary coded.

Osteoporosis Knowledge

We used the 10-item (true/false) scale of the "Osteoporosis and You" questionnaire to measure osteoporosis knowledge at baseline and at 52 weeks.[29,30] Each item was a 5-response Likert scale ("strongly agree" to "strongly disagree") that we recoded into correct (assigned a value of "1") or incorrect (including a neutral response; assigned a value of "0") knowledge of osteoporosis. Correct responses (for true statements, or strongly disagree or disagree for false statements) were coded "1" and incorrect responses were coded "0." We summed the recoded values to the 10 items to create a summary score ranging from 0 to 10 (PAADRN baseline $\alpha = 0.68$).

Activation

We used 6 of the 22 items from the Patient Activation Measure to measure general patient knowledge, confidence, and self-efficacy related to health at baseline and 52 weeks.[31,32] Each item has 4 response options ranging from "strongly agree" to "strongly disagree." Item responses were initially recoded from "1" (lowest activation) to "4" (highest activation), including reverse coding of responses where needed (PAADRN baseline $\alpha = 0.66$). Item scores were summed and then subsequently converted to a score ranging from 0 (least activated) to 100 (most activated) following the same approach used for the 13-item shortened version of the Patient Activation Measure.

Osteoporosis Self-Efficacy

Osteoporosis self-efficacy (OSE) at baseline and 52 weeks was measured with 2 subscales: exercise (OSE-Exercise, 10 items, PAADRN baseline $\alpha = 0.97$) and diet (OSE-Diet, 11 items, PAADRN baseline $\alpha = 0.96$).[33] These items represent attitudes toward initiation, maintenance, and persistence of osteoporosis-related behaviors. Each item was a 10-point Likert scale, ranging from 1 ("not at all confident") to 10 ("very confident"). The OSE-Exercise and OSE-Diet subscale scores were each computed as the mean of the component item response scores.

Osteoporosis Care Satisfaction

Osteoporosis care satisfaction was measured both at baseline and 52 weeks for participants with prior DXA scans.[34] This 5-item scale assessed patient satisfaction with DXA notification, understanding DXA results, understanding osteoporosis treatments, receiving adequate information to make an informed decision, and overall satisfaction with bone health care (PAADRN baseline $\alpha = 0.77$). Each item was a 5-point Likert scale, ranging from 1 ("strongly dissatisfied") to 5 ("strongly satisfied"). The scale score was the sum of the item scores, ranging from 5 to 25.

Participant Characteristics

At baseline, the following patient characteristics were collected: age, sex, race/ethnicity, educational attainment, literacy and numeracy, prior DXA, self-reported health status, DXA T-scores, height and weight, and comorbidities related to computing the FRAX score.

Statistical Analysis

To assess balance in the 3 study groups at baseline, we compared participant characteristics of pilot RCT participants at KPGA's Crescent Center medical office with 1) PAADRN intervention participants and 2) PAADRN usual care participants who were also recruited during the duration of the pilot RCT at KPGA's Crescent Center medical office (ie, between March 2013 and May 2014). Baseline characteristics were compared using a χ^2 or *t*-test as appropriate to the measure's distribution.

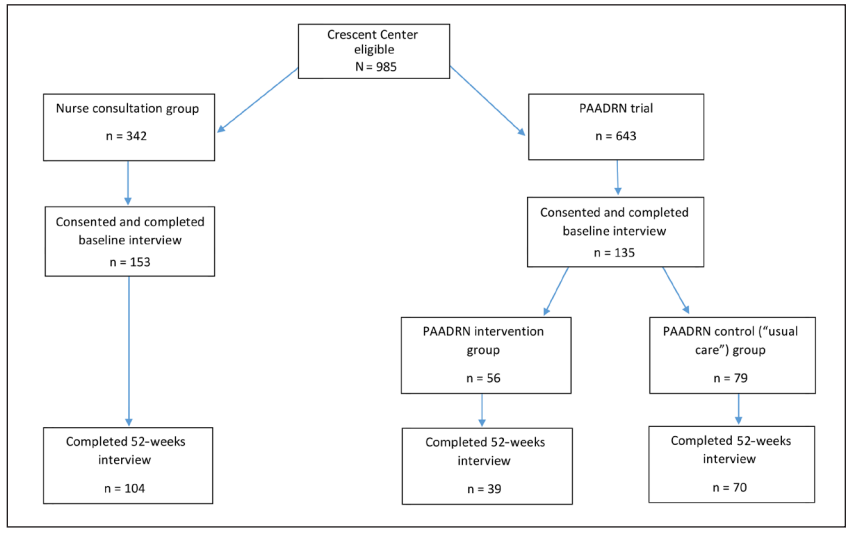

Figure 2. Nurse consultation pilot study: randomization, allocation, and retention.

PAADRN = Patient Activation After DXA Result Notification.

We assessed 52-week change for the 9 outcomes (ie, guideline-concordant pharmacotherapy, total calcium, supplemental Vitamin D, combined exercise, osteoporosis knowledge, activation, OSE-Diet, OSE-Exercise, osteoporosis care satisfaction) *within* each of the 3 study groups. We were primarily interested in change from baseline to 52 weeks in the outcome measures for pilot RCT participants. The null hypothesis was no significant difference between baseline and 52 weeks for participants in each group, and the alternative hypothesis was a significant improvement within each group.

We then assessed pairwise differences in 52-week change on each outcome *between* pilot RCT participants and either 1) PAADRN intervention participants or 2) PAADRN usual care participants. The null hypothesis was no significant difference in change between pilot RCT participants and either of the PAADRN study groups; the alternative hypothesis was a significant improvement in the nurse consultation group compared with either one of the PAADRN study groups.

This was a pilot RCT and not fully powered statistically at the level of the much larger PAADRN study; therefore, we initially considered any *within*- or *between*-group difference with $p \leq 0.10$ to be statistically significant. We chose 2-tailed vs 1-tailed statistical tests to allow for bidirectional change in study outcomes because of recent concerns about 1) overuse of bisphosphonates among adults with low risk of fragility fracture[35] and 2) excessive calcium intake particularly through use of supplements.[36] Because we were making many pairwise comparisons within the nurse consultation group (ie, 52 weeks vs baseline) and between treatment groups (ie, pilot RCT vs PAADRN intervention or pilot RCT vs usual care) on 9 outcomes, we subsequently used a Bonferroni adjustment[37] for each of these sets of comparisons to lower the critical p value from ≤ 0.10 to ≤ 0.01 (ie, 0.10/9). All tests of differences in outcomes were conducted on observations unadjusted for participant covariates.

Finally, we also examined effects as being potentially clinically significant at the level of an individual participant. A clinically significant effect was defined as a difference in outcome of one-half of a standard deviation (SD) of the baseline distribution.[38-40]

All data management and statistical analyses were performed using SAS 9.4 (SAS Institute Inc, Cary, NC).

RESULTS

At baseline, the study sample initially included 153 participants in the nurse consultation group, 56 in the PAADRN intervention group, and 79 in the PAADRN usual care group (Figure 2). Of these, 68% (104 of 153) of nurse consultation participants, 70% (39 of 56) of PAADRN intervention participants, and 89% (70 of 79) of PAADRN control participants completed both baseline and 52-week interviews (Figure 2).

Baseline characteristics of participants who completed both baseline and 52-week interview—and who comprise the final analytic sample—are displayed in Table 1 (Table 2 for characteristics of the initial study sample). Participants in each group, on average, were relatively well matched on baseline characteristics. Participants in the nurse consultation group, however, were several years older than

Table 1. Baseline characteristics of participants randomly assigned to a "just-in-time" nurse consultation and to PAADRN intervention and control groups who completed a 52-week follow-up interview

Characteristic	Nurse consultation (n = 104)	PAADRN intervention (n = 39)	PAADRN control (n = 70)	p value (consultation vs intervention)	p value (consultation vs control)
Age, years, mean (SD)	70.7 (6.1)	66.2 (8.7)	68.7 (7.7)	0.001	0.059
Sex, no. (%)					
Men	19 (18.3)	6 (15.4)	17 (24.3)	0.686	0.337
Women	85 (81.7)	33 (84.6)	53 (75.7)		
Race, no. (%)					
White	69 (66.3)	25 (64.1)	43 (61.4)	0.631	0.749
Black	33 (31.7)	14 (35.9)	26 (37.1)		
Other/unknown	2 (1.9)	0 (0.0)	1 (1.4)		
Education, no. (%)					
High school or less	18 (17.3)	7 (17.9)	10 (14.3)	0.775	0.878
Some college	39 (37.5)	14 (35.9)	30 (42.9)		
College graduate	25 (24.0)	7 (17.9)	17 (24.3)		
Postgraduate	22 (21.2)	11 (28.2)	13 (18.6)		
Literacy, mean (SD)	4.4 (0.72)	4.7 (0.52)	4.5 (0.9)	0.050	0.730
Numeracy, mean (SD)	4.6 (0.98)	4.9 (0.65)	4.7 (0.9)	0.040	0.434
Prior DXA, no. (%)					
No	37 (35.6)	19 (48.7)	30 (42.9)	0.152	0.333
Yes	67 (64.4)	20 (51.3)	40 (57.1)		
Self-reported health, no. (%)					
Excellent/very good	50 (48.1)	18 (46.2)	40 (57.1)	0.227	0.499
Good	39 (37.5)	19 (48.7)	22 (31.4)		
Fair/poor	15 (14.4)	2 (5.1)	8 (11.4)		
Baseline DXA, no. (%)					
Normal	32 (30.8)	15 (38.5)	21 (30.0)	0.233	0.871
Low BMD	56 (53.8)	22 (56.4)	40 (57.1)		
Osteoporosis	16 (15.4)	2 (5.1)	9 (12.9)		
Fracture risk, no. (%)					
Low	60 (57.7)	30 (76.9)	40 (57.1)	0.083	0.848
Moderate	28 (26.9)	7 (17.9)	21 (30.0)		
High	16 (15.4)	2 (5.1)	9 (12.9)		

BMD = bone mineral density; DXA = dual-energy x-ray absorptiometry; PAADRN = Patient Activation After DXA Result Notification; SD = standard deviation.

those in the PAADRN intervention and usual care groups ($p < 0.01$ and $p = 0.02$, respectively) and had a higher proportion with "high" fracture risk than those in the PAADRN intervention group ($p = 0.03$).

During 52 weeks, participants in the nurse consultation group reported, on average, significant improvements in 6 of the 9 outcomes: total calcium (113 mg/d or 33% of baseline SD, uncorrected $p < 0.01$; Table 3); osteoporosis knowledge (0.35 points or 19% of baseline SD, $p = 0.04$); activation (16.12 points or 126% of baseline SD, $p < 0.01$); osteoporosis care satisfaction (2.41 points or 70% of baseline SD, $p < 0.01$); combined exercise frequency (0.46 points or 17% of baseline SD, $p = 0.09$); and OSE-Diet (0.29 points or 17% of baseline SD, $p = 0.06$). After Bonferroni corrections, 52-week improvements in total calcium, activation, and osteoporosis care satisfaction remained significant (adjusted p values ≤ 0.01). Of these, improvements in 2 outcomes were likely clinically significant (ie, change ≥ 50% of the baseline SD): activation and osteoporosis care satisfaction.

In contrast, participants in the PAADRN intervention or usual care group reported, on average, significant improvements over 52 weeks in 3 of the 9 outcomes. Both the PAADRN intervention and usual care participants reported improvements in activation and osteoporosis care satisfaction (both uncorrected $p < 0.01$). Additionally, PAADRN intervention participants reported improvements in calcium intake ($p = 0.07$); and, PAADRN usual care participants reported improvements in combined exercise frequency ($p = 0.07$). After Bonferroni corrections, 52-week improvements in activation and osteoporosis care satisfaction remained significant (adjusted p values < 0.01). As with nurse consultation group participants, PAADRN intervention participants and usual care participants had clinically significant improvements in activation (138% and 109% 52-week change as a percent of baseline SD, respectively) and osteoporosis care satisfaction (109% and 67% 52-week change as a percent of baseline SD, respectively).

Comparisons between study groups, however, yielded few statistically significant differences. The 52-week improvement in OSE-Diet was greater, on average, among nurse consultation participants than among PAADRN intervention participants (net change of 0.52, $p = 0.07$). However, the 52-week change in osteoporosis care satisfaction was lower among nurse consultation participants than among PAADRN intervention participants (net change of -2.15, $p = 0.05$). With Bonferroni corrections, neither of these effects was statistically significant.

Table 2. Baseline characteristics of all consenting participants randomized to a "just-in-time" nurse consultation and to PAADRN intervention and control groups

Characteristic	Nurse consultation (n = 153)	PAADRN intervention (n = 56)	PAADRN control (n = 79)	p value (consultation vs intervention)	p value (consultation vs control)
Age, years, mean (SD)	70.4 (6.3)	66.6 (8)	68.2 (7.9)	< 0.001	0.018
Sex, no. (%)					
Men	30 (19.6)	9 (15.0)	21 (23.6)	0.434	0.463
Women	123 (80.4)	51 (85.0)	68 (76.4)		
Race, no. (%)					
White	97 (63.4)	32 (53.3)	50 (56.2)	0.171	0.54
Black	53 (34.6)	28 (46.7)	37 (41.6)		
Other/unknown	3 (2.0)	0 (0.0)	2 (2.2)		
Education, no. (%)					
High school or less	30 (19.6)	14 (23.3)	18 (20.2)	0.651	0.624
Some college	47 (30.7)	21 (35.0)	34 (38.2)		
College graduate	40 (26.1)	11 (18.3)	19 (21.3)		
Postgraduate	30 (19.6)	14 (23.3)	18 (20.2)		
Literacy, mean (SD)	4.5 (0.8)	4.6 (0.8)	4.5 (0.9)	0.362	0.636
Numeracy, mean (SD)	4.7 (0.9)	4.7 (0.9)	4.7 (1.0)	0.761	0.931
Prior DXA, no. (%)					
No	59 (38.6)	30 (50.0)	39 (43.8)	0.128	0.422
Yes	94 (61.4)	30 (50.0)	50 (56.2)		
Self-reported health, no. (%)					
Excellent/very good	79 (51.6)	30 (50.0)	51 (57.3)	0.735	0.648
Good	54 (35.3)	24 (40.0)	29 (32.6)		
Fair/poor	20 (13.1)	6 (10.0)	9 (10.1)		
Baseline DXA, no. (%)					
Normal	50 (32.9)	21 (35)	27 (30.3)	0.205	0.623
Low BMD	78 (51.3)	35 (58.3)	51 (57.3)		
Osteoporosis	24 (15.8)	4 (6.7)	11 (12.4)		
Fracture risk, no. (%)					
Low	91 (59.5)	47 (78.3)	53 (59.6)	0.028	0.945
Moderate	41 (26.8)	10 (16.7)	25 (28.1)		
High	21 (13.7)	3 (5.0)	11 (12.4)		

BMD = bone mineral density; DXA = dual-energy x-ray absorptiometry; PAADRN = Patient Activation After DXA Result Notification; SD = standard deviation.

DISCUSSION

In this pilot RCT of a nurse consultation immediately after completion of a patient's DXA, we found that 52 weeks later participants reported significant improvements on 6 of 9 outcomes before adjustment for multiple comparisons (total calcium, exercise frequency, osteoporosis knowledge, dietary self-efficacy, activation, and osteoporosis care satisfaction), but significant improvements in only 2 outcomes after Bonferroni adjustments (activation and osteoporosis care satisfaction). The magnitude of improvement in activation and osteoporosis care satisfaction suggests that for many participants these improvements were clinically meaningful.

Among PAADRN intervention and usual care participants with similar baseline demographic and clinical characteristics, significant improvements in outcomes were achieved on only 3 of 9 outcomes before adjustment for multiple comparisons. After Bonferroni adjustments, only 2 of these outcomes remained significant; the magnitude of change in these 2 outcomes (activation and osteoporosis care satisfaction) suggested that for many participants these improvements were also clinically meaningful.

Although these *within*-group findings are encouraging of the potential benefits

Table 3. Effects of a "just-in-time" nurse consultation on osteoporosis pharmacotherapy and osteoporosis-related behaviors, knowledge, and self-efficacy compared with matched PAADRN intervention and control participants[a]

Outcome measure	Nurse consultation (n = 104)	PAADRN intervention (n = 39)	PAADRN control (n = 70)	p value (consultation vs intervention)	p value (consultation vs control)
Proportion with guideline-concordant pharmacotherapy					
52 weeks	0.70 (0.46)	0.72 (0.46)	0.67 (0.47)	0.853	0.672
Combined exercise (sessions of exercise per week)					
Baseline	3.69 (2.77)	4.63 (3.18)	4.44 (2.09)	0.085	0.056
52 weeks	4.15 (3.18)	4.33 (2.93)	4.91 (2.66)	0.753	0.101
Δ52-BL	0.46 (2.79)	-0.29 (2.85)	0.47 (2.16)	0.153	0.980
p value (Δ52-BL)	0.094	0.522	0.073	—	—
Total calcium (average daily calcium in diet, mg/d)					
Baseline	917.86 (341.81)	920.97 (339.93)	990.1 (325.15)	0.961	0.165
52 weeks	1030.94 (332.25)	1012.45 (294.91)	1026.53 (358.52)	0.761	0.934
Δ52-BL	113.08 (314.48)	91.48 (309.57)	36.43 (293.91)	0.714	0.107
p value (Δ52-BL)	< 0.001	0.073	0.303	—	—
Proportion with vitamin D supplementation					
Baseline	0.58 (0.50)	0.54 (0.51)	0.63 (0.49)	0.682	0.499
52 weeks	0.59 (0.49)	0.51 (0.51)	0.60 (0.49)	0.432	0.860
Δ52-BL	0.01 (0.43)	-0.03 (0.49)	-0.03 (0.42)	0.674	0.561
p value (Δ52-BL)	0.820	0.744	0.567	—	—
Osteoporosis knowledge					
Baseline	7.61 (1.81)	7.26 (2.00)	7.66 (1.54)	0.320	0.846
52 weeks	7.95 (1.63)	7.58 (1.57)	7.78 (1.88)	0.240	0.523
Δ52-BL	0.35 (1.65)	0.39 (1.74)	0.09 (1.70)	0.895	0.324
p value (Δ52-BL)	0.035	0.19	0.67	—	—
Activation (scale points)					
Baseline	58.95 (12.81)	62.58 (12.92)	63.63 (14.64)	0.135	0.027
52 weeks	75.07 (16.38)	80.36 (17.52)	79.66 (17.37)	0.094	0.079
Δ52-BL	16.12 (19.37)	17.78 (20.49)	16.03 (16.72)	0.654	0.974
p value (Δ52-BL)	< 0.001	< 0.001	< 0.001	—	—
OSE-Exercise (scale points)					
Baseline	8.11 (1.82)	8.01 (1.61)	8.3 (1.90)	0.773	0.514
52 weeks	8.11 (2.07)	7.62 (2.15)	8.43 (1.60)	0.223	0.278
Δ52-BL	0 (1.63)	-0.39 (2.00)	0.02 (1.47)	0.235	0.934
p value (Δ52-BL)	0.985	0.232	0.895	—	—
OSE-Diet (scale points)					
Baseline	8.51 (1.73)	8.41 (1.34)	8.77 (1.43)	0.752	0.286
52 weeks	8.81 (1.54)	8.18 (1.84)	8.94 (1.23)	0.043	0.551
Δ52-BL	0.29 (1.51)	-0.23 (1.42)	0.18 (1.33)	0.068	0.645
p value (Δ52-BL)	0.059	0.32	0.257	—	—
Osteoporosis care satisfaction (scale points)[b]					
Baseline	19.22 (3.45)	18.78 (3.96)	19.37 (3.04)	0.645	0.834
52 weeks	21.58 (2.67)	23.45 (1.57)	21.41 (3.12)	0.004	0.769
Δ52-BL	2.41 (3.75)	4.56 (4.26)	2.11 (3.01)	0.045	0.694
p value (Δ52-BL)	< 0.001	< 0.001	< 0.001	—	—

[a] Restricted to participants who completed baseline and 52-week interviews. Guideline-concordant pharmacotherapy was assessed only at 52 weeks.

[b] Among participants with prior dual-energy x-ray absorptiometry (DXA): 56 in the nurse consultation group, 18 in the PAADRN intervention group, and 35 in the PAADRN control group.

OSE = osteoporosis self-efficacy; PAADRN = Patient Activation After DXA Result Notification; Δ52-BL = change between baseline and 52-week follow-up.

of a "just-in-time" nurse consultation after DXA, between-group comparisons were less encouraging. Compared with PAADRN intervention participants, nurse consultation participants experienced greater improvement in diet self-efficacy (p = 0.07). Yet, Bonferroni adjustments nullified the statistical significance of this finding, and the magnitude of the improvement in diet self-efficacy (17%) was not likely clinically meaningful for many nurse consultation participants. Furthermore, we found relatively less improvement in osteoporosis care satisfaction among nurse consultation participants compared with PAADRN intervention participants (and about the same relative improvement compared with usual care participants).

This latter finding is intriguing and generally consistent with the larger PAADRN study findings. The PAADRN intervention—a timely, tailored, direct-to-patient letter with personal fracture risk information and an educational brochure—appears to be particularly potent in improving osteoporosis care satisfaction compared with usual care.[41] On other outcomes (eg, guideline-concordant pharmacotherapy, total calcium Vitamin D supplementation, frequency of weight-bearing and strengthening exercise), the PAADRN intervention was typically marginally better than usual care over a 52-week period.[27,42]

Two other integrated delivery systems that conducted RCTs of similar nurse consultations found somewhat more encouraging results. In a Geisinger Health System study, a brief nurse consultation with periodic phone follow-up found no improvements in osteoporosis pharmacologic treatment at 12 months compared with a control group, although, patients who received nurse consultation reported significant increases in calcium intake and exercise frequency compared with the control group.[16] In a HealthPartners study, a 2-hour nurse educational consultation (with or without DXA), increased calcium and Vitamin D intake, but not exercise frequency at 12 weeks compared with a matched control group of postmenopausal women without consultation.[15]

This pilot RCT of a nurse consultation after DXA has limitations. It was conducted at only one of several DXA sites in a single health maintenance organization. One nurse conducted the consultations. Thus, it is not possible to disentangle the effects of a "just-in-time" nurse consultation after DXA that can be generally attributed to this model of care from effects specific to the study setting or practice style of the nurse consultant. Outcomes were self-reported by participants and may be subject to bias. We attempted to minimize participant bias by selecting either measures for validated scales or methods that generated averages consistent with those used for estimating similar outcomes, such as calcium intake and Vitamin D supplementation in the US national population.[43-47] Patient satisfaction is an outcome contingent on patient expectations, which we did not measure. Patients may have expected something more from a nurse consultation (eg, medication prescribing, which was outside the nurse's scope of practice) than what they expected from mailed materials (eg, the PAADRN intervention). If so, then patient satisfaction with the nurse consultation might have been attenuated compared with the PAADRN intervention or usual care.

CONCLUSION

This pilot RCT of a nurse consultation provided to older adults immediately after DXA yielded modest benefits to osteoporosis-related treatment, knowledge, self-efficacy, or lifestyle (diet and exercise) compared with either a lower-cost, tailored, direct-to-patient letter conveying personal fracture risk (through text and a figure) or the usual care (ie, a generic letter on DXA results without standardized annotation or display of fracture risk). ❖

Disclosure Statement

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Comparing Hospital Processes and Outcomes in California Medicare Beneficiaries: Simulation Prompts Reconsideration

Gabriel J Escobar, MD; Jennifer M Baker, MPH, CHES; Benjamin J Turk, MAS; David Draper, PhD; Vincent Liu, MD, MS; Patricia Kipnis, PhD

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ABSTRACT

Introduction: This article is not a traditional research report. It describes how conducting a specific set of benchmarking analyses led us to broader reflections on hospital benchmarking. We reexamined an issue that has received far less attention from researchers than in the past: How variations in the hospital admission threshold might affect hospital rankings. Considering this threshold made us reconsider what benchmarking is and what future benchmarking studies might be like. Although we recognize that some of our assertions are speculative, they are based on our reading of the literature and previous and ongoing data analyses being conducted in our research unit. We describe the benchmarking analyses that led to these reflections.

Objectives: The Centers for Medicare and Medicaid Services' Hospital Compare Web site includes data on fee-for-service Medicare beneficiaries but does not control for severity of illness, which requires physiologic data now available in most electronic medical records.

To address this limitation, we compared hospital processes and outcomes among Kaiser Permanente Northern California's (KPNC) Medicare Advantage beneficiaries and non-KPNC California Medicare beneficiaries between 2009 and 2010.

Methods: We assigned a simulated severity of illness measure to each record and explored the effect of having the additional information on outcomes.

Results: We found that if the admission severity of illness in non-KPNC hospitals increased, KPNC hospitals' mortality performance would appear worse; conversely, if admission severity at non-KPNC hospitals' decreased, KPNC hospitals' performance would appear better.

Conclusion: Future hospital benchmarking should consider the impact of variation in admission thresholds.

INTRODUCTION

When people book a commercial airline flight, they expect more than a safe ride. They can compare prices and find information on flight delays or lost luggage. Further, they can expect that, in general, the service they receive from a given airline will be similar whether they buy their ticket in Denver, CO, or Lexington, KY. Contrast this with the current situation in health care, where information on what actually happens to patients—whether in terms of safety, quality, cost, or service—that would permit a consumer to make an informed choice is much more scarce, and where processes and outcomes for a given procedure or illness vary dramatically from site to site, even within a single system. This lack of transparency even affects clinicians but is particularly true for consumers without formal medical training.

One major difference between these two industries, of course, is that the end products are different. Generally speaking, once a customer has paid for an airline ticket, it is unlikely that his or her past travel history will have a huge impact on the flight time between Denver, CO, and Chicago, IL, or on the airline's revenue. On the other hand, this is clearly not the case with respect to a patient's medical history when someone boards an ambulance or walks into a clinic. In the assessment of health care quality, risk adjustment—accounting for baseline risk—is critical.

During the last few decades, a slow but continued transformation has been occurring in medicine, one that seeks to move institutions to save lives and decrease suffering through the improved use of information. This transformation has led to the development and publication of risk-adjusted outcome reports that compare and benchmark the institutions' performance. Risk-adjusted benchmarking is primarily a branch of health services research, itself a descendant of epidemiology. It has a much lower public profile than do other branches of medicine. Although risk-adjusted benchmarking is largely driven by statistics and informatics, its practitioners must also consider organizational psychology and political science to carry out their work.

Risk-adjusting techniques are becoming increasingly important as more medical care in the US takes place in integrated systems. Quality-assurance departments can examine and compare what processes are in place at high-ranking centers that differ from processes at lower-ranking centers. When these comparisons are conducted properly and are supported by political will, discoveries and improvements follow. This approach to process improvement has a strong track record in multiple areas of medicine, ranging from the care of newborns[1] to that of adults.[2-4] Using rigorous risk adjustment methods for ranking institutions is crucial to ensure that interinstitutional differences are attributed to differences in processes and not differences in the characteristics of the

Gabriel J Escobar, MD, is the Regional Director for Hospital Operations Research for The Permanente Medical Group, Inc, at the Division of Research in Oakland, CA. E-mail: gabriel.escobar@kp.org. **Jennifer M Baker, MPH, CHES,** is a Public Health Program Specialist for Contra Costa Public Health Clinic Services in Martinez, CA. E-mail: calhounjennifer1@gmail.com. **Benjamin J Turk, MAS,** is a Data Analyst for the Division of Research in Oakland, CA. E-mail: benjamin.j.turk@kp.org. **David Draper, PhD,** is a Professor of Applied Mathematics and Statistics at the University of California, Santa Cruz. E-mail: draper@soe.ucsc.edu. **Vincent Liu, MD, MS,** is the Regional Director for Hospital Advanced Analytics for The Permanente Medical Group, Inc, at the Division of Research in Oakland, CA. E-mail: vincent.x.liu@kp.org. **Patricia Kipnis, PhD,** is the Principal Statistician for Decision Support at Kaiser Foundation Health Plan. E-mail: patricia.kipnis@kp.org.

underlying population. Thus, in the best scenario, benchmarking can save lives and decrease morbidity, which is a major reason health services researchers devote so much effort to improving risk adjustment methods. However, this does not mean that benchmarking processes are uniformly useful (or similar), and substantial concerns exist regarding both the proliferation and the quality of individual benchmarking systems.[5,6] Those working in this field recognize that one *should* entertain doubts about what we do, particularly given both practical and theoretical concerns about the limitations of the methods we employ.[7,8]

One notable example of this expansion is a recent set of hospital rankings (*US News Best Hospitals*) issued by *US News & World Report.*[9,10] The new rankings are remarkable for two reasons: One that would be easily comprehensible to most of its readers, and one that is less obvious. The "easy" reason is that, unlike most rankings in the popular press (and unlike its previous incarnations in the magazine), the more recent set of rankings use objective, publicly available data rather than "expert" opinion. (Rankings based on this approach have poor correlation with patient outcomes.[11]) The less obvious reason is that, unlike benchmarking done by (to give one important example) the federal government's Centers for Medicare and Medicaid Services' (CMS) Hospital Compare Web site,[12] this particular report included not just data on fee-for-service Medicare beneficiaries. Remarkably, they now also include data from some large managed care providers, which are not available from the Medicare data warehouse. Non-fee-for-service patients constitute approximately 31% of all beneficiaries[13] and are referred to as Medicare Advantage patients.

In this article, we reflect on a benchmarking study described in the Sidebar: Benchmarking Study on Effects of Including Physiologic Severity Adjustment. The findings of this study led us in a different direction than originally anticipated. We started with one question: Compared with the outcomes of other patients in California, once a patient enters one of Kaiser Permanente Northern California's (KPNC's) hospitals, how does s/he fare? We ended up asking two other, more speculative, questions. What factors affect the decision to admit a patient to the hospital in the first place? How would one study these factors?

STUDY SETTING: HOW WE GOT TO OUR INITIAL QUESTION

The setting for our work is KPNC, a capitated integrated health care delivery system. Under a mutual exclusivity agreement, 9500 salaried physicians of The Permanente Medical Group, Inc, provide care for 4.1 million members of Kaiser Foundation Health Plan, Inc, at more than 200 clinical care locations, which include 21 hospitals operated by Kaiser Foundation Hospitals, Inc. Its comprehensive information systems—built around a common medical record number—permit KPNC to track information throughout the continuum of care, including care covered by the Health Plan but delivered elsewhere.[14] The Epic (Epic Systems Corp, Intergalactic, Verona, WI, www.epic.com) electronic medical record (EMR), known internally as KP HealthConnect, was fully implemented during a 5-year period ending in 2010.

In our department, the KPNC Division of Research, our team focuses on the outcomes of hospitalized adults. It is known that KPNC gets high marks for quality in multiple areas.[15,16] However, outside Kaiser Permanente, much less is known about the intense degree of self-examination conducted by internal KPNC departments. In our specific area of expertise, which includes risk adjustment of hospital outcomes,[17-22] our work has focused on addressing variation in mortality across hospitals.

For a layperson, the term *practice variation,* when not defined in research terms, might refer to something inevitable and innocuous. It makes intuitive sense that a patient who was in a major motor vehicle crash who is treated at a small hospital might do worse than one treated at a major trauma center; similarly, common sense would suggest that a patient with pneumonia in both lungs and a bloodstream infection (sepsis) will do worse than a patient with "walking" (mild) pneumonia. It also makes intuitive sense that individual physicians' practicing "styles" differ; such variation may in fact be desirable. However, when health services researchers talk about practice variation, they are talking about a far more problematic and insidious issue—the fact that processes, costs, and outcomes for *very similar* patients vary across similar institutions. Moreover, this variation, sometimes referred to as *residual* variation, persists after statistical adjustment for many patient characteristics. Consequently, a major proportion of the efforts of both health services researchers and health care quality assurance teams focuses on identification of best practice and, optimally, eliminating variation from best practice.

RECONSIDERATION OF BENCHMARKING

There are limitations to the analyses described in the Sidebar: Benchmarking Study on Effects of Including Physiologic Severity Adjustment. Our restriction to the ten conditions accounting for most of the deaths means that our analyses may not apply to conditions that have relatively low mortality but which may have high morbidity and/or cost. Admissions data used to estimate the likely severity of illness are based only on KPNC data. Given lack of such data from non-KPNC hospitals, this was a reasonable step, but one can question the approach and the degree of generalizability.

Going into this study, we knew that measurement of physiologic severity of illness would have an effect because it is known that adding clinical data to hospital risk adjustment has a huge impact.[23,24] Multiple studies, including our own, suggest that at least one-half of the predictive ability of models that predict hospital mortality comes from physiologic measures,[17,25] which is a major reason severity scores have face validity among clinicians. Presumably, if hospitals functioned as isolated entities, the distribution of their patients' severity of illness at admission would be a direct reflection of the general health of their local area. However, and this is particularly true in California, where many hospitals now function as parts of systems with varying degrees of integration, the severity of illness distribution is now likely to be shaped by two factors. The first is the degree to which systems are in place to prevent hospitalization. An increasing proportion of processes that formerly required hospitalization can now be handled on an outpatient basis, as can be seen, for example, with congestive heart failure.[26] In general, the more effective a health care organization is in deploying such systems, the more likely it

BENCHMARKING STUDY ON EFFECTS OF INCLUDING PHYSIOLOGIC SEVERITY ADJUSTMENT

INTRODUCTION

The Centers for Medicare and Medicaid Services (CMS) Hospital Compare Web site (www.medicare.gov/hospitalcompare/) provides risk-adjusted comparisons of processes and outcomes of hospitalized Medicare patients using a transparent and reproducible method developed by the team of Harlan Krumholz, MD, at Yale University in New Haven, CT.[1,2] Analyses based on the basic method have yielded insights on implementation of quality improvement projects.[3,4]

Existing CMS data transfer protocols are such that a substantial proportion of Medicare members, Medicare Advantage patients, are not included in the analyses; only fee-for-service Medicare members are included. Almost all (99.8%) Kaiser Permanente Northern California (KPNC) Medicare members are in the Medicare Advantage program. Consequently, the sample for KPNC hospitals in the Hospital Compare Web site is extremely small and nonrepresentative, and the risk adjustment method sets all KPNC hospitals' performance as "Number of cases too small" or "Not available," effectively eliminating the utility of the Web site for benchmarking KPNC hospital performance. Also, CMS data are limited in that they capture only a patient's acute diagnoses (eg, "this patient is being admitted for acute appendicitis") and comorbid conditions (eg, "this patient also happens to have diabetes and arthritis"). One of the most important dimensions of a patient's illness—admission severity of illness—is not captured. Currently, Hospital Compare is unable to account for this type of severity difference between patients because CMS does not mandate capture of these data. Furthermore, the lag time for CMS data availability (years) exceeds that of KPNC data (1 to 2 months), although 7 of our hospitals are now assigning severity of illness scores in real time.

Comparing our outcomes with those of an external benchmark is highly desirable. Because multiple studies have shown that physiologic data have a large impact on risk adjustment,[5-9] KPNC now routinely employs severity of illness scores using detailed physiologic data (laboratory test results and vital signs). Thus, there is value to estimating what the magnitude of the effect of adjusting physiologic severity might be if these data were included in Hospital Compare.

Table 1. Description of study cohort

Primary condition[a]	CMS[b]		KFH Medicare[c]	
	Hospitalizations,[d] no.	Mortality, %	Hospitalizations, no.	Mortality, %
Hospital Compare AMI	20,076	14.8	2922	12.5
Hospital Compare heart failure	43,424	10.9	5721	12.5
Hospital Compare pneumonia	44,522	12.3	5559	12.8
Sepsis	63,295	28.9	8566	25.2
Acute CVD	28,834	19.7	3877	21.6
Aspiration pneumonia	12,311	27.9	796	37.8
Catastrophic conditions	14,145	27.9	1553	27.0
Other cardiac conditions	34,177	6.7	4226	7.4
Highly malignant cancer	21,501	24.8	2890	24.8
Trauma	54,443	5.4	5539	5.6
Conditions combined	361,728	16.7	42,432	16.6

[a] See Appendix: Part 2 (www.thepermanentejournal.org/files/2017/16-084-Appendix.pdf) for the approach we employed to group individual International Classification of Diseases diagnosis codes into primary conditions.
[b] Refers to California fee-for-service Medicare beneficiaries with claims for the 2009 and 2010 calendar years, excluding all Kaiser Permanente Northern California (KPNC) and Southern California hospitals. Hospitalizations from hospitals with small numbers are included.
[c] Refers to Northern California Kaiser Foundation Health Plan's members with Medicare Advantage coverage for the 2009 and 2010 calendar years. A small number of KPNC fee-for-service members (592 of the combined 35,523 patients) were included in the analyses, as were hospitalizations from hospitals with small numbers.
[d] Refers to the number of *hospitalizations* included in a given analysis; Appendix: Part 1, Table 1.1 (www.thepermanentejournal.org/files/2017/16-084-Appendix.pdf) provides a table in which an individual patient is the unit of analysis.
AMI = acute myocardial infarction; CMS = Centers for Medicare & Medicaid Services; CVD = cardiovascular disease; KFH = Kaiser Foundation Hospitals.

METHODS

We obtained CMS hospitalization data for all non-KPNC California fee-for-service Medicare beneficiaries for the 2009 and 2010 calendar years. Then, with the generous help of Dr Krumholz's team, we formatted KPNC hospitalization data so that the structure was the same, permitting us to merge KPNC data with CMS data. We limited our analyses to the top 10 diagnoses that accounted for 75% of inpatient deaths in 2009 and 2010: Acute myocardial infarction, congestive heart failure, pneumonia, sepsis, stroke, aspiration pneumonia, catastrophic conditions (eg, ruptured aortic aneurysm), other cardiac conditions, malignant cancer, and trauma. Table 1 summarizes the study population serving as the base for our analyses. We replicated the Hospital Compare risk adjustment method (adjusting for patients' age, sex, admission diagnosis, whether hospitalization began in the Emergency Department, and the burden of comorbid illnesses). We then compared processes (use of the Intensive Care Unit, use of assisted ventilation, and length of stay) and outcomes (30-day mortality and 30-day readmission from hospital discharge) across the 323 hospitals in our cohort.

Taking advantage of KPNC's rich information systems, which have permitted us to develop a variety of automated severity measures,[5-8] we assigned hospital records *simulated* severity of illness scores. These scores were imputed on the basis of the reasonable inference that illness severity at admission would tend to be similar in patients with similar characteristics. Using the 2009 and 2010 KPNC hospital cohort, in which each hospitalization record had an admission severity of illness score, called the Laboratory-based Acute Physiology Score (LAPS),[6,10] we developed a predictive model for severity of illness (a continuous variable—the higher the LAPS, the sicker the patient). This model can be conceived as follows:

$$\text{LAPS} = f\ (\text{age, sex, diagnosis, comorbidities, Emergency Department admission or not})$$

This model provided us with coefficients that could be used to assign each non-KPNC hospitalization a simulated severity score,

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which we called SIMLAPS. We took additional precaution and assigned the SIMLAPS to all KPNC hospitalizations using the same process. Thus, in our simulation, we explored the effect on the outcomes rates of having the additional information to more accurately measure severity of illness in the non-KPNC hospitals.

RESULTS

Our findings are detailed in the online Appendix for interested readers (available at www.thepermanentejournal.org/files/2017/16-084-Appendix.pdf). They are summarized as follows. Appendix: Part 4 shows that KPNC hospitals are larger and serve larger numbers of Medicare beneficiaries than do most other California hospitals. Most KPNC hospitals performed better than the remaining California hospitals did with respect to both process and outcomes measures. Furthermore, this relationship held when hospitals were assessed globally (ie, all ten conditions pooled together) as well as with respect to individual primary conditions. However, despite being part of an integrated system, residual variation in both process and outcomes measures persists in the system, as is described here and in Appendix: Part 4.

Examination of hospital rankings using the simulated scores did not yield any surprises. Figure 1, which reports data for 3 of the abovementioned 10 conditions, provides an illustrative example. (Additional data are provided in the online Appendix: Part 5.) The overall distribution of rankings showed a similar picture to that obtained without the SIMLAPS for all 3 conditions. However, the range of hospital rankings increased because of the additional error incurred in the SIMLAPS estimates. The KPNC hospitals had better performance, and significant residual variation persisted after incorporation of severity of illness, consistent with what we had observed in our internal severity-adjusted analyses for almost 10 years. Intriguingly, Figure 1 shows that KPNC's performance was best among patients with sepsis, as is evident by the distribution of adjusted mortality rates. Patients with sepsis account for the largest proportion of hospital deaths in both the KPNC (27%) and CMS (30%) cohorts. At KPNC, sepsis care has been the focus of intense analytic and targeted quality improvement efforts since 2008.[11,12]

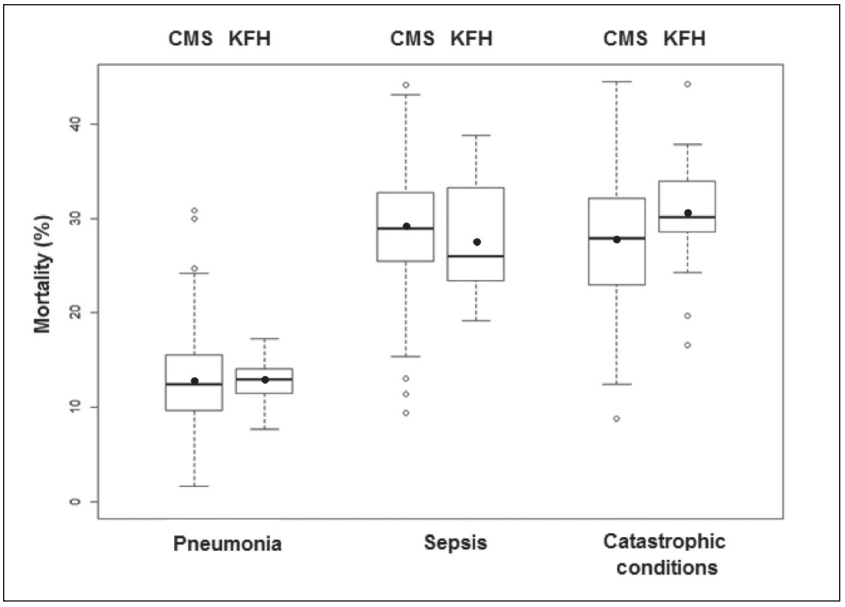

Figure 1. Risk-adjusted 30-day mortality rates for 3 primary conditions with high mortality rates (community-acquired pneumonia, sepsis, and catastrophic conditions) in California hospitals caring for fee-for-service (left, CMS [Centers for Medicare and Medicaid Services]) and Kaiser Foundation Hospitals, Inc (right, KFH) Medicare Advantage beneficiaries.[a]

[a] Analyses control for age, sex, admission venue, principal diagnosis, present-on-admission comorbidities, and a simulated severity of illness score (see text for details). The unit of analysis is a hospital with at least 50 cases. Central dot is the mean mortality rate for all hospitals; boxplot shows the median, interquartile range, and 2.5th and 97.5th percentiles of the mortality distribution across all hospitals; and hollow dots show individual observations outside the 2.5th and 97.5th percentiles.

Figure 2 shows how having SIMLAPS also allowed us to assess the impact of randomly varying LAPS, thus simulating both natural variation (eg, one influenza season might be worse than another) and systemic trends outside KPNC. We did this by randomly shifting the overall severity of illness distribution in the non-KPNC hospitals by 0.15 standard deviation to the left (ie, making non-KPNC patients healthier at the time of admission) or to the right (making them sicker). This is shown graphically in Figure 2, which compares global performance regarding mortality in 3 scenarios: when severity is not included, when it is included but the severity distribution is unaltered, and when the CMS severity distribution is decreased or increased.

Figure 3 shows 2 KPNC quarterly trend lines for the period from March 2010 through May 2015. The dashed line shows the discharge rate from our acute care hospitals, which fell from approximately 72/1000 to approximately 61/1000 members (a 15% decline) during this period. During this time, KPNC made major increases in its hospitalization prevention and case management programs. The solid line shows the average severity of illness of patients admitted to the hospital, using our more sophisticated LAPS Version 2, or LAPS2, which also includes vital signs and patients' neurologic status.[8] During this period, the mean LAPS2 for all admissions increased by 33% (from 54 to 72), whereas other internal analyses have found that the proportion of extremely ill patients (LAPS2 $\geq$ 110 as well as a high comorbidity burden) almost doubled, from 5% of all emergency admissions to 9%. Thus—some would consider it ironic—success in one area (achieved by enhancing outpatient care and case management efforts) may be leading to problems in another (emergency admissions are sicker, making hospital care for nonelective admissions harder and more complicated). Moreover, it is also clear that KPNC has not eliminated physician-level variation; for example, using very recent internal data, we found that the mean (76 to 100) and median (68 to 99) LAPS2 for patients hospitalized with community-acquired pneumonia both vary considerably across our 21 hospitals. ❖

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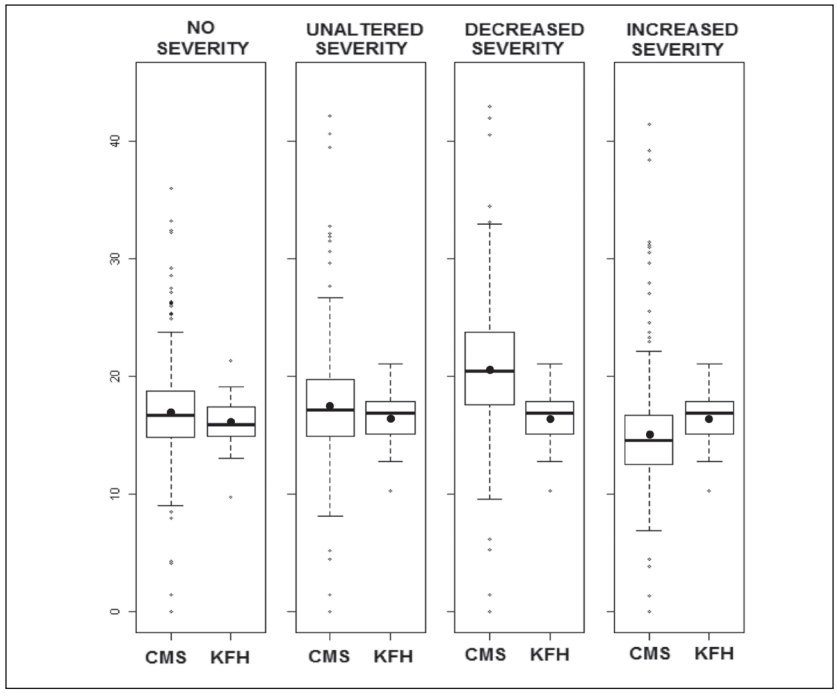

Figure 2. Risk-adjusted 30-day mortality rates (%, y axis) among California hospitals caring for fee-for-service Medicare (left, CMS [Centers for Medicare and Medicaid Services]) and Kaiser Foundation Hospitals (right, KFH) Medicare Advantage beneficiaries.[a]

[a] The unit of analysis is a hospital with at least 50 cases. Central dot is the mean mortality rate for all hospitals; boxplot shows the median, interquartile range, and 2.5th and 97.5th percentiles of the mortality distribution across all hospitals; and dots show individual observations outside the 2.5th and 97.5th percentiles. All analyses control for age, sex, admission venue, principal diagnosis, and present on admission comorbidities. In the first pair of rankings (far left, labeled *NO SEVERITY*) no other variables are included in the risk adjustment, whereas in the second pair (*UNALTERED SEVERITY*), a simulated severity of illness score is added to all hospitalizations. The third pair (*DECREASED SEVERITY*) shows the effect of *decreasing* severity of illness among CMS hospitalizations, whereas the fourth panel (*INCREASED SEVERITY*) shows the effect of *increasing* severity of illness among CMS hospitalizations. See text for description of how severity distributions were varied.

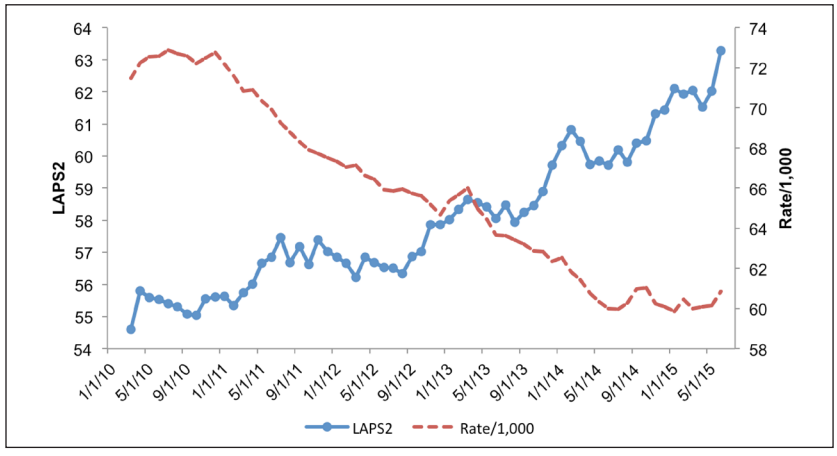

Figure 3. Change in discharge rate and severity of illness.[a]

[a] The figure shows a progressive decrease in the discharge rate of Kaiser Permanente Northern California's 21 acute care hospitals. Concurrently, the average severity of illness score among patients admitted to these hospitals, as measured by the Laboratory-based Acute Physiology Score, version 2 (LAPS2, described in citation 8) has shown a progressive increase over this 5-year time period.

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is that the severity of illness distribution for admissions coming through its Emergency Department will be shifted (ie, patients will be sicker). Put differently, as outpatient illness prevention improves, the patients coming into the Emergency Department will be more likely to consist of sicker patients in whom preventive efforts failed. The second factor is the admission threshold for individual physicians. It is known that this threshold varies considerably across individuals, as can be seen, for example, with the decision to admit a patient with pneumonia.[27] It is also suspected, although a more mechanistic description still eludes us, that clinicians who practice together tend to practice similarly (ie, admission thresholds will vary *across* hospitals more than *within* hospitals). Thus, aggregate practice variation can affect estimates of the quality of hospital care.[28]

Considering all these factors together, a major limitation of hospital benchmarking became apparent to us; given the potentially powerful effects of admission thresholds, hospital quality of care (as currently measured using only data from *hospitalized* patients) may play a smaller role in explaining variation in hospital outcomes than is assumed. It is entirely possible that hospitals with low thresholds for admission might "benchmark better" than those that do not. This phenomenon would be enhanced if patient case mix measures (particularly those with limited or no severity component) were biased in such a way that less sick patients look sicker than they really are.

The notion that it might not be possible to adjust for case mix underlies a different approach to measuring hospital quality, the concept of "failure to rescue" developed by Silber et al,[29,30] who argue that a hospital's ability to "rescue" a patient after a complication is a better reflection of its quality than its risk-adjusted mortality rate. However, to our knowledge, so far no one has examined the relationship between admission thresholds and "failure to rescue." Furthermore, although the "failure to rescue" construct has an attractive theoretical basis as well as strong face validity among clinicians, it is not being used for routine benchmarking.

Consideration of the importance of the admission threshold has led us to reflect on another factor that can affect hospital rankings: The impact of patients near the end of life. Intuitively, it would seem that, if a hospital were more or less likely to admit patients near the end of life (as opposed to, say, diverting them to hospice), it might have a higher or lower death rate. Thus, the apparent performance of hospitals that admitted more patients near the end of life might appear worse.

Until recently, concerns about this issue have been somewhat theoretical because obtaining information about advance health care directives (eg, a patient's preferences in the event s/he were to experience cardiac arrest in the hospital) on a large scale from paper charts has been difficult.[31] However, in an era in which a large proportion of US hospitals have deployed or are deploying comprehensive EMRs, ignoring this issue will become less tenable.

In previously published work, using data from the Epic inpatient EMR (in which specifying a patient's resuscitation preference is a "hard stop," without which it is not possible to admit a patient), we have found that, despite the limitations of our data systems, one can strongly infer that consideration of patients near the end of life must become an important benchmarking component.[21,32] We reported that approximately 11% of all KPNC hospitalized adults have a "do not resuscitate" order on admission, with another approximately 2% with a "partial code" or "comfort care only" order. Among patients admitted through the Emergency Department, approximately 18% have a "do not resuscitate," "partial code," or "comfort care only" order at admission. Moreover, our published analyses found that the impact of including care directives on hospital rankings is profound. Although our sample included only 21 hospitals, 3 (14%) of the 21 had a statistically significant change in their observed-to-expected mortality ratio when care directives were included (ie, their rankings changed dramatically). This proportion is sobering, given the importance accorded to hospital rankings for public reporting. Furthermore, in 2009, in internal, unpublished analyses in which we employed a 6-month mortality risk measure, we found an almost 3-fold variation across our hospitals in the proportion of patients with a predicted mortality risk of 30% or greater. The problem of face validity cannot be ignored, either, because clinicians may be skeptical of risk adjustment models that do not consider patient physiology or end-of-life care preferences.

WHAT MIGHT FUTURE HOSPITAL BENCHMARKING LOOK LIKE?

One aspect of this is very clear; future risk adjustment methods should incorporate laboratory data, vital signs, nurse-captured indicators (eg, mental status, functional status, care order status, and indicators of frailty), care directives, and oxygenation status. Including these data elements, in addition to improving the quality of the risk adjustment, would enhance benchmarking's face validity among clinicians and health care organizations. In addition, the *range* of outcomes and process measures needs to be expanded; at a bare minimum, benchmarking should include the use of intensive care and assisted ventilation.

However, further research also must be conducted on the admission threshold, including what quantifiable factors determine it and what its impact is when one varies it systematically. This may need to include simulation studies. Some of these studies may need to incorporate more "upstream" data and consider the relationship between inferences made when one varies the unit of analysis. One approach to the analysis of health care processes is to change the unit of analysis from an individual hospital encounter to an episode.[33] Thus, if one wants to assess pneumonia care, the analytic record would not be a pneumonia admission from July 12, 2012, to July 18, 2012, but, rather, one that began on July 9, 2012 (outpatient visit for cough and mild fever), spanned the hospitalization, and included the postdischarge follow-up visit on July 27, 2012. We have employed this episode-based approach to analyze the characteristics of respiratory syncytial virus infections in infants,[34] and KPNC uses a software package that subdivides our population into *episode treatment groups*[35,36] for internal quality assurance and quality improvement. However, if the goal is to assess *hospitals*, this basic approach would need modifications.

We conclude this report with some informed speculation on what kind of research one might conduct that incorporates consideration of the admission threshold (which is driven by events in the *outpatient* setting) in the assessment of *hospital* performance. One important component of this kind of work is the need to

go "upstream" and incorporate data on patient status preceding hospitalization. This could take the form of including trending terms for patients' illness severity (eg, incorporate a severity score for the week preceding admission), which are known to increase statistical models' predictive performance.[37] Such work could also incorporate measures identifying whether some sort of screening was taking place for the most common conditions that tend to drive a hospital's overall performance. For example, although we and others have documented that patients with sepsis have high mortality and morbidity *after* their hospitalization, very little work has been done on what happened to such patients *before* hospitalization. Intuitively, patient trajectories as measured by data elements other than severity scores would seem to have high information value. For example, patients with infection who go on to experience sepsis without antibiotic treatment may have very different outcomes from patients with similar illnesses seen in the outpatient clinic and treated with oral antibiotics (ie, such patients, in whom sepsis develops *despite* treatment, may have "hidden" illness severity).

Future studies should also include incorporation of hierarchical variables. These are variables that do not vary by patient, but by hospital. One could test variables that capture hospitals' historical tendency to admit low-risk as well as high-risk patients (including patients near the end of life), for example, the percentage of patients with mortality risk less than 2% or more than 30%, respectively, averaged during a 3-year period. It would also be possible to incorporate variables that measure integration (eg, proportion of patients belonging to health plans with hospitalization prevention systems in place). A variety of methods, including simulation, would need to be employed, and it would make sense to make systematic comparisons of rankings when models do and do not include such hierarchical variables. These kinds of analyses would also require a larger sample of hospitals.

Finally, it is imperative that we expand the domain of measures that address how hospitals respect patient choices regarding care near the end of life. Although incorporation of care directive data in risk adjustment models is important, it can only be considered a first step, particularly given the fact that, with respect to hospital care of such patients, the critical component is the decision to admit at all.

CONCLUSION

Practice variation undermines medicine's moral authority and the notion that medicine is a science rather than an art. In the face of analyses that control for patient characteristics but still show variation in processes, costs, and outcomes, the presence of residual variation raises not just questions of fairness and competence[38-40] but even of the very basis for valuing health care. This thought is summarized by two scholars, Stuart H Altman and Uwe E Reinhardt, as follows[41]: "[S]ignificant variations in the per capita use of health care, unrelated to differences in outcomes, undermined the traditional argument that reductions in health care spending would inevitably entail commensurate reductions in the quality of health care."

Benchmarking is a critical tool in the struggle against unnecessary practice variation. Properly conducted—and when situated in receptive health systems—it can motivate substantial quality improvement and thus save lives, improve quality, and decrease suffering. In addition to conducting research on improving actual hospital benchmarking, our profession must also do a better job of explaining it to the public, which should include informed "blue-sky" speculation and use of simulation. After all, other scientists share their speculations all the time. Isn't it time that health services researchers did so as well? ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Convalescence

The sooner patients can be removed from the depressing influence of general hospital life the more rapid their convalescence.

— Charles H Mayo, 1865-1939, American medical practitioner and one of the founders of the Mayo Clinic

Atypical Presentation of Acute Angle-Closure Glaucoma in Maroteaux-Lamy Mucopolysaccharidosis with Patent Prophylactic Laser Peripheral Iridotomy: A Case Report

Malini Veerappan, MD; Garrick Chak, MD; Christine Shieh, MD; Pratap Challa, MD

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ABSTRACT

Introduction: Maroteaux-Lamy syndrome (MLS) is a rare progressive condition characterized by inflammation and scarring of multiple organs. Ocular complications caused by anterior segment abnormalities commonly cause visual impairment in MLS. Angle-closure glaucoma is one such complication, but there are limited data on presentation, workup, and management of this condition.

Case Presentation: This case report describes an atypical presentation of acute angle-closure glaucoma in a patient with MLS despite a prior prophylactic laser peripheral iridotomy—which would typically prevent an acute angle-closure attack—that was patent and intact at the time of angle closure.

Discussion: Because of severe congenital anterior segment crowding, high axial hyperopia, and constant accommodative demand in patients with MLS, we recommend performing two prophylactic laser peripheral iridotomies simultaneously in the same eye instead of one. The mechanism for this indication differs from that in patients at risk of acute angle-closure glaucoma because of lens zonulopathy alone. We hope that this case report may help prevent vision loss and optimize quality of life in patients with MLS who may be wheelchair-bound but are typically high functioning with normal intelligence.

INTRODUCTION

Maroteaux-Lamy syndrome (MLS), known as mucopolysaccharidosis type VI, is a rare autosomal recessive disease caused by a mutation in the *ARSB* gene. This gene encodes an enzyme called arylsulfatase B, which is involved in the breakdown of glycosaminoglycans (GAGs), specifically the GAGs dermatan sulfate and chondroitin sulfate. Mutations in this gene cause absent or reduced arylsulfatase B activity, which leads to an accumulation of GAGs in cell lysosomes and manifests phenotypically as progressive inflammation and scarring of multiple organ systems.[1-4] External features of MLS include macrocephaly, coarse facial features, macroglossia, short stature, and limited joint mobility. Other systemic findings include atlanto-axial instability, meningeal thickening, cervical stenosis, hearing loss, cardiac valve abnormalities, and restrictive/obstructive lung disease, but normal intelligence.[2]

Ocular complications causing severe vision loss are common in patients with MLS. These complications include corneal clouding (GAG deposition in the cornea), retinopathy (GAG accumulation in the retinal pigment epithelium, causing photoreceptor loss), and ocular hypertension/glaucoma caused by either the open-angle (GAG deposition in the trabecular meshwork) or angle-closure type (narrow anterior chamber with thickened cornea and iris).[1] Optic nerve changes, such as optic nerve atrophy, optic nerve swelling, and optic nerve sheath thickening, are also common.[5]

Typically, a single laser peripheral iridotomy is indicated for the pupillary block mechanism of angle-closure glaucoma (ACG). Currently, performing two laser peripheral iridotomies simultaneously is indicated for patients at risk of acute ACG because of lens subluxation causing pupillary block ACG.[6] Although these patients' anatomic risk factors predispose them to a mixed mechanism of ACG, if a patient with mucopolysaccharidosis presents acutely with the pupillary block variety of ACG in the involved eye, we recommend performing two simultaneous laser peripheral iridotomies (LPIs) prophylactically, particularly in patients with MLS, who possess normal intelligence and functional potential.

CASE PRESENTATION

Presenting Concerns

A 37-year-old, wheelchair-bound, 10-diopter (D) hyperopic white woman with MLS documented by arylsulfatase B enzyme assay presented with acute, painful visual decline in her left eye with light perception visual acuity. On presentation, the patient had a history of a patent LPI in each eye and was not receiving any ophthalmic medications. The affected left eye had trace nuclear sclerosis and was notable for acute ACG with an intraocular pressure (IOP) of 60 mmHg.

Records obtained from the patient's local ophthalmologist showed that her IOP in the preceding 8 years ranged from only 10 mmHg to 16 mmHg in both eyes. At 2 months before presentation, best-corrected visual acuity in the affected eye was 20/40 with a manifest refraction of +9.50 + 1.00 × 35. In the other eye, best-corrected visual acuity was 20/25 with a +10.25 lens. The patient reported 6 months of chronically intermittent headaches.

Therapeutic Intervention and Treatment

The patient was treated with maximally tolerated medical therapy using aqueous suppressants as well as oral acetazolamide. Despite the creation of a second LPI in the affected left eye, the patient remained in pupillary block with an IOP of 38 mmHg.

Malini Veerappan, MD, is a recent graduate from the Duke University School of Medicine in Durham, NC. E-mail: malini.veerappan@dm.duke.edu. **Garrick Chak, MD,** is a Clinical Associate in Ophthalmology at the Duke Eye Center at Duke University Medical Center in Durham, NC, and at the Kaiser Permanente West Los Angeles Medical Center in CA. E-mail: gchak@stanfordalumni.org. **Christine Shieh, MD,** is a Clinical Associate in Ophthalmology at the Duke Eye Center at Duke University Medical Center in Durham, NC. E-mail: cshieh2@gmail.com. **Pratap Challa, MD,** is an Associate Professor of Ophthalmology at the Duke University School of Medicine in Durham, NC. E-mail: pratap.challa@dm.duke.edu.

Table 1. Timeline of events

Date	Event	Relevant ophthalmic examination data[a]	Intervention[b]
Unknown	Bilateral LPI	Unknown	Uncomplicated postoperative course
7/2014	Headaches noticed	IOP OS 10 mmHg	None; good IOP control
1/9/2015	Headaches worsened, visited local ophthalmologist	IOP OS 16 mmHg	No drops
1/20/2015	Painful acute vision loss in left eye	IOP OS unknown	Referred to Ophthalmology
1/21/2015	Patient presented with severe headache	IOP OS 60 mmHg, VA OS LP	Laser PI OS; drops: pilocarpine, acetazolamide, brinzolamide-brimonidine, dorzolamide-timolol
1/22/2015	Persistent headache	IOP OS 38 mmHg, VA OS LP	Surgical PI OS
1/23/2015	Postoperative day 1 after surgical PI, no headaches	IOP OS 21 mmHg, VA OS CF	Continue therapy with acetazolamide, brinzolamide-brimonidine, and dorzolamide-timolol

[a] At the time of the event, before intervention.
[b] "Drops" indicate aqueous suppressant medical therapy.
CF = counting fingers; IOP = intraocular pressure; LP = light perception; LPI = laser peripheral iridectomy; NA = not available; OS = left eye; VA = visual acuity.

A surgical peripheral iridectomy was subsequently performed. The IOP decreased to 21 mmHg, and visual acuity improved to counting fingers. The anterior chamber (AC) deepened, but the view to the optic nerve remained hazy because of corneal edema and chronic corneal clouding. Medical therapy was continued, although pilocarpine treatment was held to avoid miotic-induced AC shallowing.

The patient's postoperative regimen included fluorometholone and 5% sodium chloride drops to facilitate corneal clearing. The timeline of events is summarized in Table 1.

Follow-up and Outcomes

Ancillary testing was performed at the postoperative visit 1 week after completion of iridectomy in the left eye (Table 2). Ultrasound biomicroscopy of the left eye revealed a shallow AC and a thickened cornea with central AC depth of only 0.38 mm, measured as the distance from corneal endothelium to the anterior iris border (Figure 1). B-scan ultrasonography demonstrated a thickened, congested sclera (Figure 2) and axial length of less than 20 mm in both eyes (19.53 mm in the right eye and 19.32 mm in the left eye). The retinal-choroidal-scleral thickness was very high,[7] and there was no evidence of vitreous debris, retinal detachment, or mass or tumor.

As of this writing, the patient uses her right eye to see, has stable IOP control, and is being followed closely for signs of angle closure in the right eye.

DISCUSSION

There are limited data on the presentation, workup, cause, and management of ACG in MLS, but the association has been reported in two studies.[8,9] In 1981, two cases of glaucoma associated with MLS were described by Lloyd-Jones and Hitchings.[8] In 1989, Cantor et al[9] described four patients with MLS who had increased IOP and features of glaucoma. Two of these patients had documented ACG that required surgical treatment. One patient had narrow AC depth peripherally but relatively normal depth centrally. This patient's cornea was too opaque to visualize the angle structures. The last patient had angle closure on gonioscopy.[9]

Possible mechanisms for glaucoma vary. Open-angle glaucoma in mucopolysaccharidosis has been attributed to GAG deposition in the trabecular meshwork.[10] With ACG, intracellular and extracellular GAG accumulation has been linked to thickening of the cornea and other anterior segment structures.[11] Specifically, GAGs are deposited in the intracytoplasmic vacuoles of macrophages in the Bowman layer, corneal stromal keratocytes, ciliary body stroma cells, and intracanalicular connective tissue cells of the trabecular meshwork, as well as extracellularly around the stromal keratocytes.[12] In addition, the constant accommodative demand from high hyperopia shifts the lens-zonule plane anteriorly and increases the risk of ACG. Across different types of glaucoma, optic neuropathy may occur secondary to GAG accumulation in ganglion cells and optic nerve compression caused by thickening of the optic nerve sheath and sclera.[1]

In our patient, after surgical iridectomy to treat the pupillary block component of acute ACG, the plan was to proceed with cataract extraction and lens insertion, primary posterior capsulotomy with anterior vitrectomy, and a glaucoma drainage device to treat the remaining components of ACG. A prophylactic second LPI was also performed in the contralateral eye because of the risk of acute ACG in the setting of shallow AC depth and high hyperopia. Potential challenges to additional surgery involved the patient's medical comorbidities (tracheostomy and multiple cardiac valve abnormities) as well as surgical positioning of the patient: a posterior cervical fusion had been performed for spinal cord decompression. Furthermore, the patient's extreme axial hyperopia increased her risk of aqueous misdirection or choroidal effusion and necessitated trimming of the posterior plate of the glaucoma drainage device because short axial length increased the risk of optic nerve touch.

Table 2. Patient parameters at 1-week postoperative visit

Parameter	Measurement
Anterior chamber depth, mm	OD: 1.19, OS: 0.38
Axial length, mm	OD: 19.53, OS: 19.32
Average keratometry, diopters[a]	OU: 43.50
Central corneal thickness, µm[b]	OD: 565, OS: undetectable because of corneal edema
Retinal-choroidal-scleral thickness, mm[c]	OS: 2.3

[a] Average keratometry measurement obtained using a manual keratometer.
[b] Central corneal thickness from a handheld pachymeter (Pachmate DGH 55, DGH Technology Inc, Exton, PA).
[c] Normal retinal-choroidal-scleral thickness is 1.3 mm.
OD = right eye; OS = left eye; OU = both eyes.

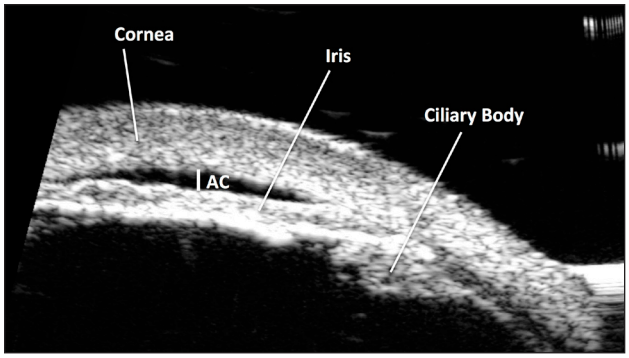

Figure 1. Ultrasound biomicroscopic image of the left eye. The cornea, iris, and ciliary body can be seen. The anterior segment is notable for angle closure with a shallow anterior chamber (AC) measuring 0.38 mm centrally.

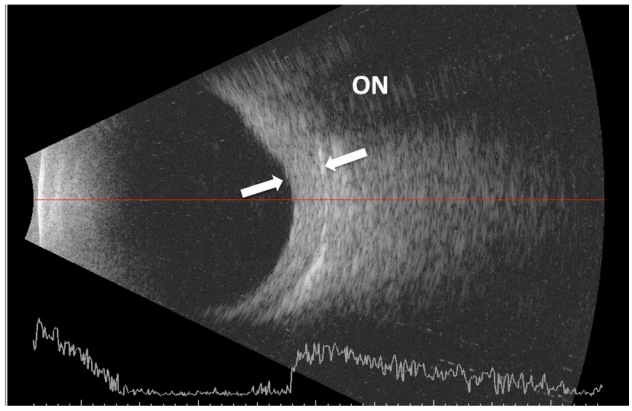

Figure 2. B-scan ultrasound image of the left eye. The white arrows indicate the thickened and congested choroid and sclera. The axial length is short, measuring 19.32 mm.

ON = optic nerve.

After being told the surgical risks, benefits, and alternatives, the patient elected not to proceed with the surgical plan. She cited the risks of anesthesia and surgery with her medical comorbidities, the fact that she was already 37 years old and her sister had died of MLS at age 33 years, and the fact that the affected eye had poor visual potential. At the time of this writing, our patient is functioning visually, using her right eye, with stable IOP control and no signs of angle closure.

CONCLUSION

This article presents a case report of an atypical presentation of acute ACG. Typically, angle closure despite a patent LPI is suggestive of plateau iris syndrome, iris bombé from encircling posterior synechiae, or lens subluxation. With an underlying diagnosis of MLS, this patient was predisposed to extreme pupillary block ACG because of congenital anterior segment crowding. Classically, performing two LPIs simultaneously in the same eye—at the 9-o'clock and 3-o'clock locations—has been considered for patients at risk of acute angle closure caused by lens subluxation. We present an example of a patient with MLS who would benefit from the same procedure with a different mechanism instead of lens subluxation: Pupillary block resulting from extreme axial hyperopia. Although an iridotomy is theoretically limited to treating only the pupillary block mechanism of angle closure and may not be effective in a patient with multiple angle-closure mechanisms, the fact that an acute surgical iridectomy was effective for this patient suggests that pupillary block was the overriding pathophysiology for angle closure. Therefore, performing 2 LPIs in the same eye as prophylaxis might be helpful for patients with similar ocular anatomy.

Despite having multiple medical comorbidities and limited mobility, patients with MLS are high functioning with normal intelligence and depend highly on their vision. We recommend consideration of this preventive modality for all patients with mucopolysaccharidosis to optimize the preservation of their quality of life. ❖

Disclosure Statement

This study was presented at the Women in Ophthalmology (WIO) Summer Symposium on August 8, 2015, in Scottsdale, AZ. Garrick Chak, MD, is supported by the Heed Ophthalmic Foundation, San Francisco, CA. The author(s) have no conflicts of interest to disclose.

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Deadly Sphenoid Fungus—Isolated Sphenoid Invasive Fungal Rhinosinusitis: A Case Report

Jason E Gilde, MD; Christopher C Xiao, MD; Victoria A Epstein, MD; Jonathan Liang, MD

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ABSTRACT

Introduction: Acute invasive fungal rhinosinusitis (AIFRS) is a potentially fatal infection, usually affecting immunocompromised patients. Isolated sphenoid sinus involvement is rare and has been reported in only a few cases. We discuss the clinical characteristics, histopathologic features, and differential diagnosis of AIFRS of the sphenoid sinus.

Case Presentation: A 57-year-old man with a history of refractory non-Hodgkin lymphoma and neutropenia presented with a 1-week duration of left-sided headache and ipsilateral cheek paresthesia. Nasal endoscopy showed mucoid drainage from the sphenoethmoidal recess. Magnetic resonance imaging demonstrated left sphenoid mucosal thickening and enhancement along the adjacent skull base. The patient underwent endoscopic sinus surgery with extended sphenoidotomy and débridement. The lateral wall and recess of the left sphenoid sinus demonstrated pale mucosa and fungal debris. Pathologic analysis demonstrated necrotic tissue and fungal hyphae with angioinvasion. Microbiology studies isolated *Aspergillus fumigatus*. The right maxillary sinus contained a synchronous fungal ball, which was removed during surgery; there was no evidence of tissue necrosis or invasive fungus in the maxillary sinus. He was treated with long-term voriconazole therapy, and 6-month follow-up showed disease resolution.

Discussion: AIFRS should be considered in the differential diagnosis of immunocompromised patients with nonspecific sinonasal symptoms. Usually, AIFRS is diffuse with multiple sinus involvement; however, isolated sphenoid AIFRS can occur. This is one of the few cases of AIFRS demonstrating isolated sphenoid involvement and is thought to be the first case showing a synchronous noninvasive fungal ball of another sinus cavity. Prompt recognition and surgical treatment may be curative and lifesaving.

INTRODUCTION

Acute invasive fungal rhinosinusitis (AIFRS) is a rare and often deadly infection that occurs primarily in immunocompromised patients. The incidence of AIFRS reported in the literature in immunocompromised patients is about 2%, with the most susceptible group being patients with hematologic diseases.[1] Other frequently affected patient groups are those with immunosuppression related to hematologic malignancy, bone marrow transplantation, poorly controlled diabetes, acquired immunodeficiency syndrome, immunosuppressive medications, and chemotherapy.[2]

AIFRS is most frequently caused by the *Aspergillus* and *Mucor* species. Studies have found a higher predisposition to aspergilli among patients with hematologic malignancies and to Mucoraceae among patients with diabetes mellitus.[2-5] Patients typically present with acute onset of signs and symptoms of sinusitis, with the most frequent symptoms reported being fever, nasal obstruction, headache, and purulent rhinorrhea with nasal crusting.[3] Pathophysiologically, the disease is characterized by fungal invasion into sinus tissue with frequent extension into adjacent structures. Treatment involves timely medical and surgical therapy. Surgical débridement of necrotic tissues is important in patients with AIFRS to reduce the fungal burden and to potentiate antifungal therapy. Short-term mortality ranges from approximately 20% to 80% across studies, largely dependent on extent of disease and recovery of immunologic function.[2,4,6,7]

CASE PRESENTATION

Presenting Concerns

A 57-year-old man presented initially to the Emergency Department with a medical history of chemotherapy-refractory diffuse large B-cell lymphoma, neutropenia, prior myocardial infarction after coronary artery bypass grafting in 2007, congestive heart failure, cardiomyopathy, and coronary artery disease with approximately a 1-week duration of left-sided headache centered along the left cheek and extending to the temple. The patient was then referred for a computed tomography (CT) scan that was initially read as sphenoid opacification without bony erosion. At the Head and Neck Surgery Clinic visit 2 days later, he affirmed he had numbness and swelling of his left cheek. He denied having nasal congestion, rhinorrhea, vision changes, fevers, chills, weight loss, and fatigue. His surgical history included laser trabeculoplasty in 2009 but no prior sinonasal procedures.

Examination revealed asymmetric pupils, larger on the left eye, with the rest of the ocular examination findings within normal limits. Nasal endoscopy in the clinic revealed bilateral inferior turbinate bogginess without lesions or erythema, no nasal polyps, and mild translucent white mucous drainage from the sphenoethmoidal recesses bilaterally.

Prompt CT and magnetic resonance imaging (MRI) were completed. Notable CT findings included mucosal thickening of the left sphenoid sinus and right osteomeatal unit obstruction by a soft-tissue density (Figure 1). Notable MRI findings included T2-weighted hypointense

Jason E Gilde, MD, is an Otolaryngology and Head and Neck Surgery Resident at the Oakland Medical Center in CA. E-mail: jason.gilde@gmail.com. **Christopher C Xiao, MD,** is an Otolaryngology and Head and Neck Surgery Resident at the Oakland Medical Center in CA. E-mail: chrisxiao@gmail.com. **Victoria A Epstein, MD,** is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: vepstein@gmail.com. **Jonathan Liang, MD,** is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: jonathan.liang@kp.org.

material in the left sphenoid sinus with abnormal thickening and enhancement along the foramen rotundum and the medial aspect of the left middle cranial fossa, eliciting concern for invasive fungal sinusitis with mild perineural/intracranial extension. Apparent T2 prolongation and enhancement of the left inferior rectus muscle and surrounding fat was favored to be artifactual (Figure 2). Chronic mucoperiosteal thickening of the right maxillary sinus with T2 hypointense and T1 hyperintense material, which was unchanged from a prior image in 2011, was thought to be compatible with proteinaceous/inspissated secretions.

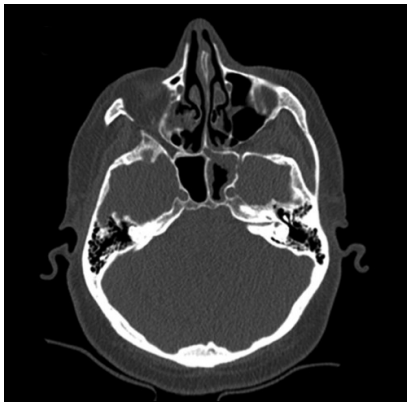

Figure 1. Computed tomography scan, axial view, without contrast enhancement. Mucosal thickening of the left sphenoid sinus is apparent. Possible dehiscence is demonstrated along the lateral wall of left sphenoid sinus.

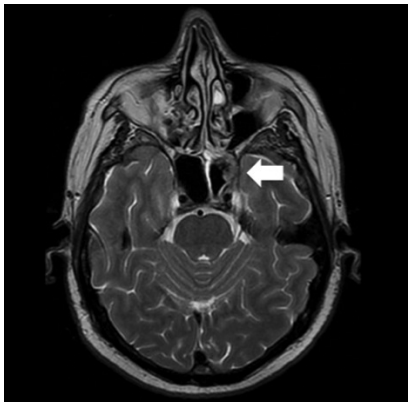

Figure 2. Magnetic resonance image, T2 weighted, axial view, with intravenous contrast enhancement. Hypointense signal is seen in the left sphenoid sinus with abnormal enhancement and thickening along the foramen rotundum and medial left middle cranial fossa (arrow).

Therapeutic Intervention and Treatment

The patient was admitted to the hospital that evening for intravenous (IV) antifungal therapy. Initial laboratory study results were remarkable only for neutropenia.

Endoscopic sinus surgery was performed the next morning. Procedures included left extended endoscopic sphenoidotomy, right endoscopic maxillary antrostomy, and right endoscopic anterior ethmoidectomy. Notable operative findings included left sphenoid with evidence of yellow-white necrotic tissue and fungal debris in the lateral wall and lateral recess of the sphenoid sinus (Figure 3). Intraoperative frozen section revealed fungal debris and necrotic tissue with submucosal presence of hyphae, consistent with invasive fungal sinusitis. On the right side, there was no evidence of invasive fungal sinusitis; well-perfused tissue was seen around a fungal ball in the right maxillary sinus, which was completely removed.

Final histopathologic analysis revealed sphenoid sinus contents consistent with acute invasive fungal sinusitis and numerous hyphae in the mucosal tissue, confirmed by positive Gomori methenamine silver nitrate stain, as well as necrosis (Figures 4A and 4B). Later, final microbiology culture isolated *Aspergillus fumigatus*. On postoperative day 1, filgrastim (Neupogen, Amgen, Thousand Oaks, CA) was started to address neutropenia after clearance by an oncologist.

Follow-up and Outcomes

On postoperative day 6, the patient was taken back to the operating room for a second look after follow-up MRI revealed possible residual left sphenoid sinus opacification. During the operative procedure, the left sphenoid lateral wall showed improved appearance of the mucosa and lacked eschar. The right maxillary sinus demonstrated a widened opening, with a thick granular appearance of the mucosa on the posterior wall. The maxillary sinus tested negative for fungal invasion on frozen sections.

The patient was discharged on hospital day 10. As an outpatient, he received IV voriconazole, 200 mg every 8 hours for 30 days, and then voriconazole orally, 200 mg every 12 hours for an additional 2 months. During the course of the next 3 months, he returned to clinic for repeated examinations and débridements.

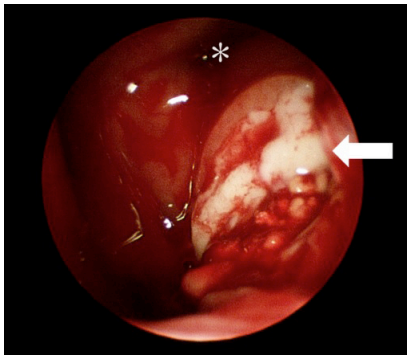

Figure 3. Intraoperative view of left sphenoid sinus, showing lateral wall (arrow) and opticocarotid recess (asterisk) with mucopurulence and tissue necrosis.

Follow-up MRI 1 month after discharge revealed substantial interval improvement with resolution of T2 hypointense fungal material in the left sphenoid sinus and in the region of foramen rotundum and bilateral maxillary and resolution of T1 hyperintensity in the right maxillary sinus.

At his six-month outpatient follow-up examination, nasal endoscopy revealed a healthy sphenoid sinus with a patent os and no evidence of recurrent sinus disease. The case timeline appears in Figure 5.

DISCUSSION

AIFRS is a rare disease, occurring in only about 2% of immunocompromised patients. The most susceptible group reported in the literature has been patients with hematologic malignancies. Valera et al[3] reported neutropenia, either caused by aplastic anemia or secondary to chemotherapy for hematologic malignancy, as the main cause of AIFRS (62%), a finding in agreement with other studies.[8,9] Regarding isolated sphenoid disease, as demonstrated in our patient, the rarity is increased. Of all sinus infections, the estimated incidence of sphenoid sinusitis is 2.7%. Isolated sphenoid sinusitis can be bacterial or fungal. Fungal sinusitis represents approximately 15% to 20% in all cases and is classified as noninvasive, invasive indolent, and fulminant. Only a few cases of sphenoid sinus aspergillosis have been reported in the published literature. Lee et al,[10] in 2009, reported that

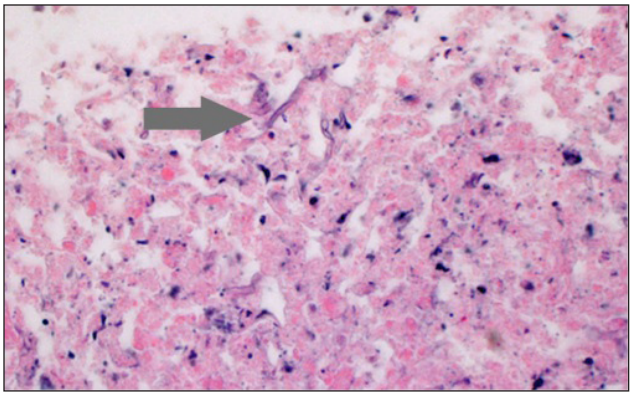

Figure 4A. Histopathologic specimen, hematoxylin-eosin stain, showing fungal hyphae (arrow) and necrotic tissue with submucosal presence.

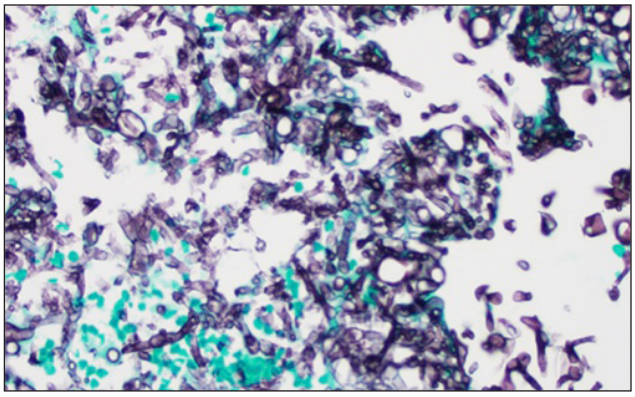

Figure 4B. Histopathologic specimen, Gomori methenamine silver nitrate stain, showing fungal elements stained black with sharp margins and a cleared center, against a light-green tissue background.

50 cases of noninvasive sphenoid aspergilloma were published since 1950. However, only a few cases of AIFRS of the sphenoid have been reported.[6,10]

The causative organism in our patient was *Aspergillus,* which, along with Mucoraceae, are the cause in most cases of AIFRS. *Aspergillus* has a predisposition for patients with hematologic malignancies, whereas Mucoraceae species tend to occur more often in patients with uncontrolled diabetes.[2,3,5] Both fungi are saprophytes, found worldwide in dust, decomposed substances, soil, and fruits, as well as in the throats, nasal cavities, and feces of healthy individuals. In immunocompromised patients, these fungi can be angioinvasive, resulting in thrombosis and ischemia of the nasal mucosa. The fungi can rapidly spread and invade paranasal structures, including the orbit and brain. Mucormycosis-causing species primarily invade the nose, lungs, and gastrointestinal tract, whereas *Aspergillus* species primarily invade the lungs and later spread to other organs.[4] *Rhizopus* has also been identified as a common causative organism in some cases, although its prevalence ranges greatly, between 0% and 26% in the series in the literature,[3,11,12] and was not reported in a 2013 meta-analysis of 398 patients by Turner et al.[13] Recently, dematiaceous fungi have now been recognized as causal organisms of AIFRS. Dematiaceous fungi are environmental pathogens, characterized by melanin in their cell wall. In 2010, Derber et al[14] reported that since 1987, there have been 14 published cases of invasive sinonasal infection caused by dematiaceous fungi in immunocompromised individuals.

For identification of patients with AIFRS, the history and physical examination findings are of paramount importance. Demographically, AIFRS tends to occur in the fifth decade of life and in female patients.[2,6,10,15] Patients traditionally present with signs and symptoms of sinusitis but may also display orbital and central nervous system signs and symptoms. For example, in the series of 32 patients described by Valera et al,[3] the most frequent symptoms reported were fever, nasal obstruction, headache, and purulent rhinorrhea with nasal crusting. Of these symptoms, headache has been cited as the most common presenting factor.[6,10,16,17] Clinical signs may include nasal discharge, epistaxis, orbital disorders (including oculomotor restriction and decreased visual acuity), and dysesthesia of the maxillary division of the trigeminal nerve. Posterior nasal discharge, although nonspecific, is frequently described. Be wary, however, of blood-streaked nasal discharge because this is considered a more specific indicator of AIFRS. Bleeding is related to either irritation of the sinus mucosa by the fungal infection or, at a more advanced stage, bone destruction of the sinus wall.[6] On nasal endoscopy, the most common signs seen are characteristic necrotic avascular and black crusts, granular serosanguinous rhinorrhea, septal perforation, and occasionally, visible hyphae.[4]

Additionally, the medical history will nearly always include an immunocompromised state, because it is the greatest risk factor for AIFRS. Monroe et al[2] reported that approximately one-fourth of the patients with AIFRS had more than one cause of immunosuppression.[2] AIFRS of a nonimmunocompromised patient is exceedingly rare. Lee et al[10] examined four cases of acute invasive sphenoid sinusitis and found one patient without a history of immunosuppression, and the others having either diabetes or multiple myeloma. In addition, any factor inducing decreased aeration of the sphenoid sinus has been classically described to constitute a risk factor for the development of fungal disease. For example, the presence of polyps on nasal endoscopy may contribute to obstruction of the ostium of the sphenoid sinus.

Our patient presented with headache but, interestingly, did not report other sinus complaints. Salient clinical findings included ipsilateral cheek paresthesia and pupil dilation, suggesting dysfunction of the maxillary division of the trigeminal nerve and oculomotor nerve, respectively. Nasal endoscopy revealed only mild, partially clear, white drainage from the sphenoethmoidal recess but no characteristic necrosis. The history of refractory diffuse large B-cell lymphoma aroused our suspicion for AIFRS, particularly when we considered the cranial nerve deficits and the risk of intracranial extension with AIFRS. It is critical, therefore, to keep AIFRS on the differential in immunosuppressed patients with both specific and nonspecific findings.

The distribution of disease in our patient was relatively unique. Valera et al[3] found a predominance of unilateral disease with bone erosion, with diffuse sinus involvement less common, orbital involvement being uncommon, and only a single case of intracranial extension. Sphenoid sinus involvement is less common than maxillary or ethmoid involvement, and isolated sphenoid disease is even rarer.[3] Moreover, simultaneous mycetoma has not been reported in the prior literature. The presence of the mycetoma does suggest the transformation of noninvasive to invasive fungal rhinosinusitis. Lee et al[10] found only 25% of their isolated invasive sphenoid fungal sinusitis to be acute, and only 4 cases over 12 years, highlighting the rarity of this distribution. Furthermore, all the patients in that situation presented with visual disturbances, which were absent in our patient.

In treatment of AIFRS, timely recognition of the underlying disease that caused the immunodeficiency and its correction, if possible, are essential to improve the survival rate in these patients. The goals of treatment in AIFRS are the reestablishment of the immune response in combination with systemic antifungal therapy and surgical débridement of necrotic sites. Surgical débridement of necrotic tissues is crucial to increase the delivery of antifungal drugs to affected tissues, reducing the fungal burden, and slowing the progression of disease. Additionally, débridement reduces stress on neutrophil development and helps bone marrow recovery.[3] In our patient, the source of his immunosuppression was known, and the patient was started on a regimen of filgrastim, but in the acute setting, the course of action left to us was surgical débridement and IV antifungal therapy.

Interestingly, there is no well-defined course for voriconazole therapy, given the rarity of AIFRS. Traditionally, amphotericin B has been used, but it also comes with substantial side effects. A 2002 randomized comparative study of voriconazole and amphotericin B in invasive aspergillosis found better outcomes and fewer side effects with voriconazole.[7] Additionally, the Global Comparative Aspergillosis Study found a similar result in a randomized controlled trial. This study had a median course of 7 days for IV voriconazole, followed by 76 days of oral voriconazole.[7,18] The Infectious Diseases Society of America guidelines for invasive aspergillosis now recommend voriconazole use.[19] As such, our decision was to use voriconazole as the primary antifungal therapy in our patient. He received IV voriconazole for 30 days, followed by oral voriconazole for 60 days after an infectious disease consult, with complete recovery and minimal side effects.

The outcome for our patient was good, with resolution of AIFRS. Success was attributed to early detection and treatment of a relatively limited extent of disease. In most cases of AIFRS, the morbidity and mortality are substantial. A meta-analysis by Turner et al[13] in 2013 examining survival in AIFRS found an overall survival rate of 49.7%, with intracranial involvement and advanced age being negative prognostic factors on multivariate analysis. In an analysis by Foshee et al[20] of 27 patients, patients with sphenoid involvement had a mortality rate of 56.3%. In a series of 29 cases reported by Monroe et al,[2] the median survival of this group was 3 months, with only 17% overall survival at 6 months. The study notes that a large proportion of patients in whom AIFRS develops will die of their disease or of other causes within 6 months of diagnosis. Extension beyond the sinuses portends worse prognosis. Recovery of immune function is believed to be vital to disease clearance. However, little other prognostic data are known regarding this rare patient population, specifically as it relates to long-term survival.[2] Treatment does relate to mortality. Before the advent of amphotericin B, mortality rates were as high as 90%. Mortality rates were reduced to 15% to 50% with combined use of surgery and newer antifungal medication.[2-4] The cause of immunosuppression may also have an effect on survival. Valera et al[3] found the mortality rate in patients with aplastic anemia and diabetes mellitus was high (near 100% when considering both groups together), whereas those with acquired immunodeficiency syndrome/human immunodeficiency virus (AIDS/

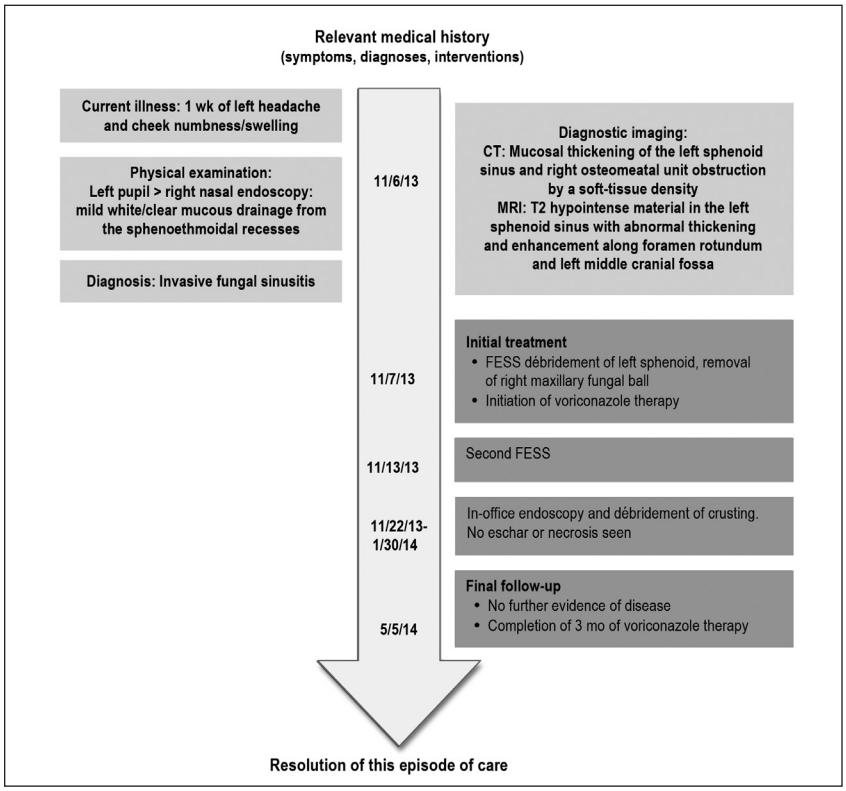

Figure 5. Timeline of the case. Dates are month/day/year.

CT = computed tomography; FESS = functional endoscopic sinus surgery; MRI = magnetic resonance imaging; > = larger than.

HIV) all had a good outcome. Patients with hematologic malignancies showed an intermediate prognosis; one-third of these patients died of AIFRS.[3]

CONCLUSION

AIFRS is a rare but deadly disease. Clinical suspicion must be high in the immunocompromised patient, because clinical signs and symptoms may be subtle. Prompt ancillary testing, including imaging and laboratory testing, can aid in diagnosis, but histopathologic evaluation is fundamental. The pattern of involvement is usually diffuse sinus disease, but it is often unilateral. Isolated sphenoid involvement is rare. Effective treatment relies on both addressing the underlying cause of immunosuppression and treating the fungal disease with surgical débridement and antifungal therapy. Morbidity and mortality are high, with orbital and intracranial extension signifying worse prognosis. Ultimately, timely diagnosis and treatment are critical to achieving satisfactory outcomes. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Fundamental Activity

The fundamental activity of medical science is to determine the ultimate causation of disease.

— Wilfred Batten Lewis Trotter, FRS, 1872-1939, English surgeon and pioneer in neurosurgery

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