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Big Data, Miniregistrys: A Rapid-turnaround Solution to Get Quality Improvement Data into the Hands of Medical Specialists.
Lisa J Herrinton, PhD; Donald F Dell, MD; Betsy Clevenger, MD; Amy J Carmack-Phillips, MD
The cost to build and to maintain traditional registries for many dire, complex, low-frequency conditions is prohibitive. The Community Ambassadors Program provided an opportunity to rapidly and effectively communicate clinical quality questions, knowledge of disease, clinical workflows, and improve opportunities. Each miniregistry required 1 to 2 hours of collaboration with a specialist. Turnaround was 1 to 14 days.

22 Expanding Access to Care and Improving Quality in the Mid-Atlantic States: Safety-Net Clinics, Kaiser Permanente’s Community Ambassador Program. Jared Lane K Maeda, PhD, MPH; Vesna J. Lastow, MD, MPH; Susan E Holden, MD, MPH; Michael A. Horning, MD, MSc, FACMT; ILSA; Bernadette C. Lofts, MD, MPH
The Community Ambassador Program (CAP), in the Mid-Atlantic States Region includes Kaiser Permanente’s employed nurse practitioners, physicians, ancillary and physician assistants to work in the safety-net clinics and share best practices through a long-term community collaboration. The authors conducted an evaluation of 18 safety-net clinics that participated in the CAP in 2012. The Community Ambassadors provided an estimated 32,249 encounters to 11,886 patients. Performance was at or near 90% for 2 adult quality measures (weight screening and tobacco use assessment). For breast cancer screenings, however, performance among the Community Ambassadors was much lower (48%). The program expanded access and improved quality of care.

Pirates, Scoundrels, and Kings
William Lynes, MD
ISBN-10: 1475665613
Philadelphia, PA: Saunders; 2012
Paperback. 450 pages $23.95

If you are a Permanente author and would like your book cited here, please send an e-mail to mac@r.cnlin.org.
41 Use of ERC-1671 Vaccine in a Patient with Recurrent Glioblastoma Multiforme after Progression during Bevacizumab Therapy: First Published Report.
Daniela A Bota, MD, PhD; Daniela Alexandru-Abrams, MD; Chrystel Pretto, PhD; Florence M Hoffman, PhD; Thomas C Chen, MD, PhD; Beverly Fu, NP; Jose A Carrillo, MD; Virgil EJC Schijns, PhD; Apostolos Stathopoulos, MD, PhD

Glioblastoma multiforme is a highly aggressive tumor that recurs despite resection, focal beam radiation, and temozolomide chemotherapy. ERC-1671 is an experimental treatment strategy that uses the patient’s own immune system to attack the tumor cells. The authors report preliminary data on the first human administration of ERC-1671 vaccination under a single-patient, compassionate-use protocol. The patient survived for ten months after the vaccine administration without any other adjuvant therapy and died of complications related to his previous chemotherapies.

Special Report
Balazs I Bodai, MD, FACS; Phillip Tuso, MD, FACP; FASN

As breast cancer becomes a chronic condition rather than a life-threatening illness, survivors not only have the challenge of dealing with multiple long-term side effects of treatment protocols, but may also be forced to address the preexisting comorbidities of their therapies, which often include multiple other issues. It is imperative that the information available regarding survivorship issues be accessible in an organized and useful format. This article is a modest attempt to provide a comprehensive review of the long-term medical issues.

Special Report
80 Nutrition Reconciliation and Nutrition Prophylaxis: Toward Total Health.
Phillip Tuso, MD, FACP; FASN; Sam Beattie, PhD

Malnutrition by definition may be an abnormality in either under- or overnutrition. Nutrition reconciliation means that all patients have their nutritional status reconciled on admission to and discharge from the hospital. Nutrition reconciliation is defined as the process of maximizing health by helping align an individual’s current diet to the diet prescribed for him or her by the health care team. Nutrition prophylaxis is a proactive intervention to prevent a medical complication.

COMMENTS

88 The First International Congress on Whole Person Care—A Report.
Gary Huffaker, MD, MA; David Petrie, MD, FACP; Joel Kreisberg, DC, CCH

This report on the First International Congress on Whole Person Care, sponsored by McGill University, is based on the experiences of two attending authors who developed a poster of Integral Theory that emphasized the importance of taking multiple perspectives in all areas of human inquiry to allow a “big picture” perspective on medicine. Interiors (thoughts, intentions, will) of both physician and patient are as important as the exteriors (measurable parameters, such as lab results) which are often emphasized.

92 Changing Medicine and Building Community: Maine’s Adverse Childhood Experiences Momentum.
Leslie Forstadt, PhD; Sally Cooper, MD; Sue Mackey Andrews

Physicians are instrumental in community education, prevention, and intervention for adverse childhood experiences. In Maine, a statewide effort is focusing on education about adverse childhood experiences and ways that communities and physicians can approach childhood adversity. This article describes how education about adversity and resilience can positively change the practice of medicine and related fields. It exemplifies the collective impact model by increasing community knowledge, affecting medical practice, and improving lives.
Atrial Fibrillation and Cor Triatriatum

**Case Reports**

Ruptured Intracranial Lipoma—
A Fatty Outburst in the Brain.
Vinod Chaubey, MD; Ganesh Kulkarni, MD; Lovely Chhabra, MD

Intracranial lipomas are rare congenital lesions that occur because of abnormal differentiation of embryogenic mениnges. These lipomas are usually seen incidentally on brain imaging, and are usually asymptomatic and do not require treatment. The authors present a case of ruptured intracranial lipoma, discovered in an elderly patient presenting with dizziness and episodes of falls.

Atrial Fibrillation and Cor Triatriatum Sinister: A Case Report.
Avilla, MD; Jeffrey J Cavendish, MD; Jonathan Kei, MD, MPH; Jennifer Kiss Krishnaswami, MD, MAS; Thomas Alloggiamento, MD, MS; Sukhvinder Kaur Nagi, MD, PhD; Ashok Krishnaswami, MD, MAS

A 29-year-old man presented to our hospital with palpitations, shortness of breath, and orthopnea. After being admitted, he progressed to cardiacogenic shock and respiratory failure, which required ventilator support and cardioversion. Subsequent evaluation revealed a fibromuscular membrane across the left atrium, requiring urgent corrective surgery.

**Clinical Medicine**

Image Diagnosis: Arachnoid Cyst.
Andrew C. Karnazes; Jonathan Kei, MD, MPH; Minh V Le, MD

A 14-year-old boy presented with 3 months of generalized headache that had increased in intensity and frequency with associated light-headedness. Primary arachnoid cysts result from developmental abnormalities; more rare secondary cysts develop as a result of head injury, meningitis, tumors, or as a complication of brain surgery.

**Nursing Research & Practice**

Workplace Violence in the Emergency Department: Giving Staff the Tools and Support to Report.
Julie Sterne, MHA, MSN, RN; Erin Larson, MSN, RN; Maria Levy, RN; Michon Dohlmans, MSN, RN

Workplace violence is increasing across the nation’s Emergency Departments, and nurses often perceive it as part of their job. Reporting processes were inconsistent, and nurses often did not know what actions constitute violence and underreported it. A staff nurse-led workgroup developed an initial survey and a reporting tool, and education was provided. A posteducation survey documented the reporting of violent acts has increased, and staff perceived the Emergency Department to be a safer environment.

**Book Review**

40 Years in Family Medicine.
Review by Robert W Hogan, MD

A 14-year-old boy presented with 3 months of generalized headache that had increased in intensity and frequency with associated light-headedness. Primary arachnoid cysts result from developmental abnormalities; more rare secondary cysts develop as a result of head injury, meningitis, tumors, or as a complication of brain surgery.

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The Panel Management Questionnaire: A Tool to Measure Panel Management Capability

Elizabeth Ann Rogers, MD, MAS; Danielle Hessler, PhD; Kate Dube; Rachel Willard-Grace, MPH; Reena Gupta, MD; Thomas Bodenheimer, MD, MPH; Kevin Grumbach, MD

ABSTRACT

Context: To meet demands for evidence-based chronic and preventive services and to improve performance, primary care practices are turning toward team-based strategies such as panel management, in which nonclinicians address routine preventive and chronic disease care tasks for a group of patients. No known validated instruments have been published for measuring panel management implementation.

Objective: To describe development and evaluation of the Panel Management Questionnaire (PMQ), a self-report tool measuring panel management capability in primary care.

Design: Cross-sectional study for questionnaire validation.

Main Outcome Measures: We developed the 12-item PMQ from a conceptual framework to measure 4 domains of panel management and tested the questionnaire for internal and external validity. Data were assembled from self-administered cross-sectional surveys that included the PMQ instrument sent from February 2012 through May 2012. We surveyed 136 staff and 204 clinicians in 9 county and 5 university adult primary care clinics. Additional data came from clinic quality measures routinely collected the quarter before the survey.

Results: The PMQ scale demonstrated good internal consistency (Cronbach α = 0.92 and 0.84 for staff and clinicians, respectively). Staff and clinician PMQ scores in each clinic were correlated (Kendall τ = 0.43, p < 0.05). The clinic-level median PMQ score was positively associated with a composite clinic quality measure (Kendall τ = 0.42 for staff, 0.28 for clinicians).

Conclusions: The PMQ measures self-reported panel management capability and may be a useful assessment and research tool for panel management implementation in primary care practice.

INTRODUCTION

Despite widely accepted evidence-based guidelines in the US for chronic and preventive services, patients receive only 55% of those recommended. To bridge this gap between demand and capacity, the concept of primary care has evolved to include population management, requiring a shift for clinicians to assume responsibility for the health of all patients assigned to their panel. However, estimates suggest that a primary care physician working in a traditional practice model would spend 21.7 hours per day providing recommended services for a panel of 2500 patients. A team-based care strategy with delegation of routine preventive and chronic care tasks to allied health personnel can increase capacity in primary care, and it has been proposed as a way to address the demands for evidence-based chronic and preventive services.

Panel management is the tools and processes for population care applied at the level of a primary care panel. It involves identifying patients who have unmet preventive and chronic care needs and reaching out to them during or outside a clinic visit. In the panel management model, a team made up of a primary care clinician and designated staff, often medical assistants, is collectively accountable for a defined panel of patients, and the nonclinician staff share increased responsibility for routine preventive and chronic care. Implementation of panel management has been linked to improvements across multiple quality measures, including rates of cancer screening, immunizations, diabetes care, cardiovascular disease care, blood pressure control, and smoking cessation counseling.

Panel management is emerging as a prominent component of transformed models of high-performing primary care and is a requirement for achieving recognition as a patient-centered medical home. In this environment, it is important to define and measure how clinics are achieving new care models.

The process of transitioning a practice to a team-based model can be challenging and time-intensive. The effectiveness of the team can vary, and complex interventions have variable success rates with multiple determinants. As clinics adopt panel management, they require validated instruments to measure practice capability, both as a tool for quality-improvement cycles and for research aimed at investigating how panel management affects clinical outcomes. We could find no validated instruments for measuring facets of panel management implementation. However, several approaches may be considered. One could examine clinic quality measures for preventive and chronic care services to evaluate whether panel management is effectively closing care gaps. However,
if quality measures are faltering, this approach does not provide information about which upstream panel management components are not functioning well, limiting targeted improvements. Moving upstream, one could measure actual panel management practices using direct observation, but this is time- and resource-intensive, limiting practical clinical application. A third approach is to assess the capability of the practice for panel management on the basis of a conceptual model of its key components, which could then facilitate improvement in effectiveness.

We developed and tested the Panel Management Questionnaire (PMQ), a self-report instrument for primary care staff and clinicians to assess capability in panel management. The objective of this study was to assess the psychometric properties and internal validity of the PMQ instrument as well as its external validity by investigating its association with clinic performance in closing care gaps.

METHODS

Participants and Setting

We conducted a cross-sectional survey of staff and clinicians in primary care practices using a self-administered questionnaire between February 2012 and May 2012. The study included nine of ten clinics providing comprehensive adult primary care services in a county health department-administered system (one clinic not providing staff respondents was excluded) and all five comprehensive adult primary care practices in a university-administered system. At the time, most clinics had been oriented to the principles of panel management and encouraged to implement this care model. All practices were located in San Francisco, CA. All staff and clinicians at the clinics were invited to participate in the survey.

Panel Management Questionnaire Instrument

Guided by the literature and our own experiences facilitating the adoption of panel management, we developed the PMQ on the basis of a conceptual model of 4 domains of panel management. The domains were as follows: 1) Nonclinician staff assigned to panel management must have the ability to use patient registries and protocols to properly identify care gaps—patients who are not up to date on evidence-based preventive and chronic care services; 2) Once the care gaps are identified, the staff must be able to educate and counsel patients about these care gaps; 3) A practice must have standing orders authorizing staff to deliver or to place pending orders for services without waiting for the clinician to initiate an individual order for each patient; and 4) There must be a sense of shared accountability among staff and clinicians for quality of care, requiring both empowerment of the staff to fulfill this role and the clinicians’ trust in the staff to take responsibility for these tasks. The 12-item PMQ includes 1 item to represent each of these 4 domains, with each item applied to 3 representative service areas: immunizations, cancer screening, and diabetes care (Figure 1). For the domains of identifying gaps and educating patients, the staff items asked about confidence in performing these tasks, and the clinician items asked about confidence in staff members’ competence.

For the other 2 domains, items inquired about staff members’ and clinicians’ endorsement of standing orders and shared responsibility. These 2 clinician questions used reverse wording to guard against acquiescent behaviors as well as to more clearly assess clinician trust in the staff and acceptance of the shift in staff role.

We developed survey questions through consultation with Medical Directors, clinical leaders, and practice facilitators from both systems. Four staff and 4 clinicians provided feedback on readability and face validity of the PMQ. A 10-point Likert scale was used for each item, with 10 indicating the highest level of agreement. We calculated a PMQ subscale score for each service type (eg, immunizations) by averaging the scores of the 4 domains for that service type, and a total PMQ score as the mean of all 12 items. Each question was weighted equally to calculate means. A score of 10 represented the greatest degree of panel management capability. Through review by staff and clinicians, and testing for face validity, the PMQ went through 9 iterations before reaching its final form. The final PMQ is available online at: www.thepermanentejournal.org/files/Spring2015/Questionnaire.pdf.

Respondent Measures

The survey included items on respondent characteristics, including hours or shifts worked per week and tenure. Clinicians were categorized as resident physicians, attending physicians, or nurse practitioners/physician assistants. Staff were grouped into two categories to differentiate those working in medical assistant roles from those working in other roles (eg, front desk staff) using the question, “Do you room patients, take vitals, or contact patients between visits about their routine chronic and preventive care tests?” Only staff answering affirmatively were instructed to complete the PMQ portion of the survey because these are the staff responsible in these systems for panel management tasks. The survey was offered in both Web-based and paper form. Respondents were entered into a raffle for $25 gift cards.
Clinic Quality Measures

Clinic quality measures for the three service areas included in the PMQ were collected from routinely reported clinic data. The measures were rates of patients with up-to-date pneumococcal and tetanus, diphtheria, and acellular pertussis vaccinations; breast cancer, colon cancer, and cervical cancer screening; and for patients with diabetes, testing of hemoglobin $A_\text{gc}$ and low-density-lipoprotein cholesterol. A composite measure of clinic quality was calculated as the mean of all the rates. These measures were available only for the nine county-operated clinics because of an interruption in routine collection of quality measures amid electronic health record transitions at the university-based clinics during the study period. All clinic quality measures were reported in December 2012, two months before initial survey responses.

Data Analysis

We examined internal validity of the PMQ using individual respondents as the unit of analysis. Descriptive statistics of median and interquartile range were used to document ranges and distributions. We conducted an exploratory factor analysis for the PMQ items stratified by employment group (staff or clinician) and PMQ service type (immunization, cancer screening, and diabetes). Internal consistency for each PMQ service area subscale and the total PMQ scale was examined with Cronbach $\alpha$. We considered an $\alpha$ of 0.60 as the minimum acceptable level of internal reliability.

We used Kendall $\tau$ to assess external validity, both to measure the degree of agreement between clinician and staff PMQ scores in each clinic and to measure the association between PMQ scores and related clinical quality measures for each clinic. Both used the clinic as the unit of analysis.

Data analysis was conducted using SPSS Version 20 (IBM, Armonk, NY) and Stata Version 12 (StataCorp, College Station, TX). The University of California, San Francisco Committee on Human Research approved the protocol. All individual-level responses were kept confidential. Clinic administrators received results aggregated at the level of their own clinic along with combined results for all clinics in their system for comparison.

RESULTS

Two hundred fifty of 398 staff (63%) and 204 of 359 clinicians (57%) responded to the survey. Of the 250 staff respondents, 136 reported working in direct patient care roles and were eligible for the PMQ. At the clinic level, the response rate ranged from 38% to 93% for staff and 43% to 100% for clinicians. The minimum number of respondents per clinic was 6 staff members and 2 clinicians, with smaller clinics having the highest response rates. Most of the staff worked 20 hours per week or more, whereas most of the clinicians worked 5 or fewer clinic sessions per week (Table 1). Table 2 shows clinic characteristics.

Descriptive data on PMQ items and factor-loading results for PMQ service-type subscales are shown in Table 3. Item scores tended to be higher among staff than clinicians, with the exception of the standing order items. In the exploratory factor analysis, eigenvalues consistently greater than 1.00 and scree plots suggested the presence of 1 factor in each service-type subscale. For staff, the PMQ subscale factor loadings were high, ranging from 0.76 to 0.92. For clinicians, factor loadings were all above 0.65 with the exception of scores for the standing order items, which ranged from 0.25 to 0.34.

The PMQ demonstrated good internal consistency. Cronbach $\alpha$ for the PMQ total scale was 0.92 and 0.84 for staff and
clinicians, respectively. Subscale score \( \alpha \) ranged from 0.86 to 0.91 for staff and from 0.63 to 0.68 for clinicians (Table 4). Because of the acceptable level of the Cronbach \( \alpha \) results and the theoretical importance of including all 4 domains of panel management in the staff and clinician PMQ scales, we retained the standing order items in the clinician PMQ scales despite their lower factor loading score.

The median score for the overall 12-item PMQ was 9.0 (interquartile range = 4.00) for staff and 6.0 (interquartile range = 3.88) for clinicians (Table 4). Median service-type PMQ subscale scores were highest for immunizations, followed by cancer screening and then diabetes care among both staff and clinicians. In analysis of results at the clinic level, the median of staff total PMQ scores ranged from 3.0 to 10.0, and the median clinician PMQ scores ranged from 4.3 to 8.5 (Figure 2). Staff and clinician total PMQ scores in each clinic were moderately correlated (Kendall \( \tau \) = 0.45, \( p < .05 \)). In the county clinics, we found support for external validity, with a trend for higher staff and clinician median PMQ scores at the clinic level to be associated with better clinic quality of preventive and chronic care (Kendall \( \tau \) = 0.42 and 0.28, respectively, for correlation of median staff and clinician PMQ scores with composite clinic quality measures).

**DISCUSSION**

Our study supports the internal and external validity of the PMQ as an instrument to measure self-reported degree of panel management capability in primary care practices. Factor analysis indicated that items generally loaded well on subscales, and the subscales and summary scale had very good internal reliability. The correlation between staff and clinician scores at the clinic level indicate a convergence between clinician and staff perspectives. This convergence from workers employed in different roles in a clinic supports the notion that the PMQ is measuring perceptions of a shared construct of panel management capability. The association with clinic quality measures previously shown to be improved by panel management supports the external validity of the PMQ.

The PMQ for clinicians appears to have less robust internal and external validity than the PMQ for staff. One reason may be that staff are better at assessing their own abilities of carrying out panel management, whereas clinicians, one step removed from the process, may less accurately assess staff or simply be unaware of what occurs when they are not in the room. In addition, the clinician PMQ included two negatively worded items to minimize the problems of inattention and acquiescence by respondents. Reverse coding can adversely affect reliability\(^26\) and may have contributed to the low score in the exploratory factor analysis for the clinician standing orders item. This low score may also reflect the complexity of the question in that a clinician is asked whether the staff should be using standing orders, which is less concrete than the other three questions, perhaps assessing the ideal of what panel management could be vs the reality of what it is. This

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**Table 3. Panel Management Questionnaire subscale descriptive statistics and factor loadings for staff and clinicians**

<table>
<thead>
<tr>
<th>Survey respondent category</th>
<th>Immunizations</th>
<th></th>
<th>Cancer</th>
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<th>Diabetes</th>
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<tr>
<td></td>
<td>Median (IQR)(^a)</td>
<td>Factor loading</td>
<td>Median (IQR)(^a)</td>
<td>Factor loading</td>
<td>Median (IQR)(^a)</td>
</tr>
<tr>
<td>Staff</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identification of care gaps</td>
<td>10.00 (2.00)</td>
<td>0.86</td>
<td>9.00 (5.00)</td>
<td>0.92</td>
<td>8.00 (5.75)</td>
</tr>
<tr>
<td>Counseling regarding gaps</td>
<td>9.00 (2.00)</td>
<td>0.87</td>
<td>8.50 (5.00)</td>
<td>0.90</td>
<td>8.00 (5.00)</td>
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<tr>
<td>Standing orders to close gaps(^b)</td>
<td>9.00 (6.00)</td>
<td>0.78</td>
<td>9.00 (5.00)</td>
<td>0.89</td>
<td>5.00 (8.00)</td>
</tr>
<tr>
<td>Shared accountability(^b)</td>
<td>10.00 (4.00)</td>
<td>0.86</td>
<td>9.00 (5.00)</td>
<td>0.86</td>
<td>7.00 (6.80)</td>
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<tr>
<td>Clinicians</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Identification of care gaps</td>
<td>7.00 (5.00)</td>
<td>0.86</td>
<td>7.00 (4.00)</td>
<td>0.86</td>
<td>6.00 (5.50)</td>
</tr>
<tr>
<td>Counseling regarding gaps</td>
<td>7.00 (4.00)</td>
<td>0.80</td>
<td>5.00 (4.00)</td>
<td>0.84</td>
<td>5.00 (4.00)</td>
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<tr>
<td>Standing orders to close gaps(^b)</td>
<td>10.00 (2.00)</td>
<td>0.25</td>
<td>9.00 (2.00)</td>
<td>0.29</td>
<td>9.00 (3.00)</td>
</tr>
<tr>
<td>Shared accountability(^b)</td>
<td>4.00 (7.00)</td>
<td>0.66</td>
<td>3.00 (5.00)</td>
<td>0.64</td>
<td>3.00 (5.00)</td>
</tr>
</tbody>
</table>

\(^a\) Items measured using a Likert scale of 1 to 10, with higher scores indicating greater agreement.

\(^b\) Questions used negative wording and were reverse coded.

IQR = interquartile range.
The Panel Management Questionnaire: A Tool to Measure Panel Management Capability

**Table 4. Panel Management Questionnaire descriptive statistics and internal consistency**

<table>
<thead>
<tr>
<th>Survey respondent category</th>
<th>Questionnaire scale or subscale</th>
<th>Median (IQR)*</th>
<th>Cronbach α</th>
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<td>Staff</td>
<td>Total scale</td>
<td>9.00 (4.00)</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>Immunization subscale</td>
<td>9.00 (3.00)</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>Cancer subscale</td>
<td>9.00 (4.50)</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>Diabetes subscale</td>
<td>7.00 (6.50)</td>
<td>0.88</td>
</tr>
<tr>
<td>Clinicians</td>
<td>Total scale</td>
<td>6.00 (3.88)</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>Immunization subscale</td>
<td>7.00 (3.88)</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>Cancer subscale</td>
<td>6.00 (3.50)</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Diabetes subscale</td>
<td>5.50 (4.50)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

* Items measured using a Likert scale of 1 to 10, with higher scores indicating greater agreement. IQR = interquartile range.

The hypothesis is supported by the consistently higher score on the clinician standing order question than on the other three questions (Table 3), probably reflecting clinician acceptance of panel management rather than the current status of standing order utilization. We elected to retain the “standing orders” question as part of the clinician PMQ both to maintain parallel questions between the staff and clinician surveys and because of the question’s usefulness as an assessment of clinician buy-in.

Practices and investigators could consider surveying only staff when assessing panel management capability. However, we believed it important to include the clinician PMQ even though less psychometrically robust because it may still be useful for practice coaching. Practice-wide acceptance of a new team structure is necessary for successful implementation, and both staff and clinician perspectives may give insight into areas amenable to focused training in the practice. For example, in one of the surveyed practices, the disparity between staff and clinician assessments sparked an important conversation among clinicians about how they can be assured that the staff are capable in their role as panel managers.

Subscale scores for immunizations were consistently higher than for cancer screening, which, in turn, had higher scores than for diabetes care. This pattern has face validity in that of the three, panel management of diabetes care is the most complex to master. In our experience, most clinics begin panel management work with immunizations, where care gap identification is dependent primarily on age and previous vaccination, and then proceed to cancer screening, which adds duration since last screening and knowledge of previous positive or negative test result to the algorithm. For diabetes care, in which care gap identification requires an understanding of target hemoglobin A1c and low-density-lipoprotein cholesterol levels, knowledge of past laboratory values, and duration since last laboratory testing, the algorithm is more complex. Because of this, as well as the need for additional monitoring of blood pressure, foot care, and ophthalmologic evaluation, clinics often reach this stage of panel management later.

The PMQ holds promise as a tool both for the pragmatic assessment and facilitation of panel management implementation and for research to better understand the process and outcomes of panel management. As a measure of practice capability, the PMQ may have particular application to efforts to redesign primary care practice. Practices could use the PMQ to measure baseline capability for panel management, identifying elements that are least developed and most likely to benefit from focused training and facilitation. The PMQ could also be used to track progress in developing capability for panel management in response to implementation efforts. For researchers, the PMQ could allow a time- and cost-efficient tool to further our understanding of predictors and outcomes of panel management capability. Finally, a majority of the PMQ is its association at the clinic level with quality measures, which are often reported for performance assessments. The positive trends for this association in our study suggest that practices with higher PMQ scores are very likely doing better at actual panel management, which would be one reason they achieve better quality scores. Although the correlation was not statistically significant, the analysis was limited by low statistical power (n = 9) at the clinic level.

**Limitations**

A limitation of our study is that we did not directly observe panel management practices to determine whether PMQ scores correlate at the individual, team, or clinic level with objective measures of staff practices. However, direct observation methods have their own limitations. There is no validated instrument for quantitatively scoring direct observation of panel management. We performed our study in a real-world context of facilitating adoption of panel management. Although we conducted direct observation in a limited manner to spot-check panel management implementation, the observations needed to create stable quantitative scores at the team or clinic level would require resources beyond the capabilities of most practice-based groups striving to evaluate primary care improvements. Moreover, some of the elements measured by the PMQ cannot be assessed through direct observation. In addition to correlating scores with clinic quality measures, one could consider a measure to assess patient experience of proactive care as a way to verify penetration of implementation.

Additional limitations of this study include respondents representing primary care clinics in only one city, which may limit generalizability. However, the sample was heterogeneous in that it included two different health systems and clinics of various sizes and in various stages of panel management adoption. Future directions can include verification of PMQ validity in additional patient populations and clinic types. The survey response rate was as low as 38% for staff and 43% for...
clinicians by clinic, which may have limited the precision of clinic-level estimates for testing external validity and introduced an element of nonresponse bias. However, overall response rates were comparable to or higher than response rates in other published surveys of clinicians. The strong agreement between staff and clinicians in each clinic was reassuring. A final limitation was the lack of routinely available quality measures for the university system at the time the study was conducted.

CONCLUSION

These results suggest that the PMQ is a valid tool to measure self-reported panel management capability, including the knowledge, system design, and philosophical acceptance of staff performing panel management. The PMQ may serve as a measure for research and evaluation that can be linked to downstream clinical quality measures. It can also be applied to efforts to redesign primary care practices through focusing on facilitation of and tracking progress in the adoption of panel management as one of the building blocks of high performing primary care.

Disclosure Statement

The author(s) have no conflicts of interest to disclose. The survey for this project was done in conjunction with a primary care transformation initiative supported by the Centers for Medicare and Medicaid Services Incentive Program under the Section 1115 California Medicaid Waiver. Dr Rogers was a primary care research fellow funded by NRSRA grant T32 HP19025.

Acknowledgment

Without the close partnership of the leadership and staff of these 14 primary care clinics across San Francisco, this research would not be possible. The wisdom, expertise, and candid feedback of their clinic leadership, clinicians, and front-line staff were critical to the development of the Panel Management Questionnaire. The study team thanks the San Francisco Department of Public Health and the University of California San Francisco Medical Center for their support of this project.

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

References

Hand-Assisted versus Straight-Laparoscopic versus Open Proctosigmoidectomy for Treatment of Sigmoid and Rectal Cancer: A Case-Matched Study of 100 Patients

Fazli C Gezen, MD; Erman Aytac, MD; Meagan M Costedio, MD; Jon D Vogel, MD; Emre Gorgun, MD

ABSTRACT

Objective: The laparoscopic approach is increasingly used for surgical treatment of colorectal cancer. The aim of this study was to assess the efficacy of laparoscopic proctosigmoidectomy for cancer treatment by comparing postoperative outcomes among three groups: hand-assisted laparoscopic resection, conventional straight-laparoscopic resection, and open resection.

Methods: Patients who underwent hand-assisted proctosigmoidectomy because of rectal or sigmoid adenocarcinoma between September 2006 and July 2012 were case-matched to their straight-laparotomy and open-surgery counterparts. Tumor location, tumor stage, resection type, and year of surgery were the matching criteria. Patients who had an abdominoperineal resection were excluded from the study.

Results: Twenty-five patients underwent hand-assisted laparoscopic resection during the study period and were matched to 25 straight-laparoscopic and 50 open-surgery cases. The patients who underwent hand-assisted resection had higher rates of preoperative cardiac disease and hypertension than did the straight-laparotomy and open-surgery groups (76% vs 64% vs 26%; p < 0.0001 and 72% vs 68% vs 42%; p = 0.02, respectively). A history of previous abdominal operations was highest in the straight-laparotomy group (p = 0.01). The mean estimated blood loss was lowest in the straight-laparotomy group (p = 0.01). The straight-laparotomy group had the shortest median length of postoperative hospital stay (p = 0.04). Disease-free survival and overall survival was similar among the groups.

Conclusions: Although both hand-assisted and straight-laparoscopic proctosigmoidectomy appear to be as safe and effective as open surgery in short-term and midterm outcomes, straight-laparoscopic surgery seems to provide faster convalescence compared with open surgery and hand-assisted laparoscopic surgery.

INTRODUCTION

Since the first report of laparoscopic colectomy by Jacobs et al1 in 1991, laparoscopic surgery has been increasingly used for treatment of colorectal diseases.2-8 Compared with open surgery, the laparoscopic approach reduces postoperative pain, wound-related complications, and length of stay.2-5,7,8,10

Mastering laparoscopic techniques, however, requires commitment and can be challenging.11 Hand-assisted laparoscopic colectomy was first reported in 1996 as a technique facilitating use of the surgeon’s hand in the abdomen during laparoscopic procedures.12 This technique provides short-term benefits, including faster recovery and reduced wound-related complications compared with open surgery.2,13 Hand-assisted laparoscopic surgery (HALS) was introduced to facilitate the transition from conventional open surgery to advanced laparoscopic surgery.13 This type of surgery may ease mastery of laparoscopic techniques with the advantage of tactile sensation.14 Surgeons can use their hands for retraction and rapid hemostasis by using HALS. The role of HALS in the surgical treatment of colorectal cancer is still under discussion, partly because there is a discrepancy of data available.11 Therefore, we aimed to compare operative outcomes and oncologic results in patients who underwent open, hand-assisted laparoscopic, or straight-laparoscopic proctosigmoidectomy in this case-matched study.

METHODS

This study consisted of all patients who underwent hand-assisted laparoscopic proctosigmoidectomy with curative intent for rectal and sigmoid adenocarcinoma at our institution between September 2006 and July 2012. Those who had an abdominoperineal resection were excluded from the study. Patients who underwent HALS were case-matched with those who had straight-laparoscopic and open proctosigmoidectomy during the same period on the basis of the following criteria: tumor location (sigmoid colon or rectum), pathologic cancer stage (0, I, II, and III), type of resection (anterior or low-anterior), and year of surgery (± 3 years). Open and straight-laparoscopic counterparts were randomly matched to HALS cases in a 2:1:1 ratio, respectively, with the help of a computer-based program. Demographics, comorbid factors,
use of neoadjuvant chemoradiotherapy, perioperative outcomes, short-term outcomes (within 30 days after surgery), and oncologic results were compared between the 3 patient groups. The data were retrieved from institutional review board-approved, prospectively maintained cancer and laparoscopy databases.

Operative details of HALS and straight-laparoscopic techniques have been described previously. Total mesorectal excision was done for tumors located in the midrectum and low rectum, whereas partial mesorectal excision was performed for tumors in the upper third of the rectum. Use of any incision made after port insertion for anything other than specimen extraction was defined as conversion.

All operations were performed by specialized colorectal surgeons who were beyond their learning curve in laparoscopic techniques, using previously published institutional criteria. Anastomotic leak was defined as the occurrence of a break in the integrity of the anastomosis as documented by the combination of clinical, radiologic, and operative means. Local recurrence was defined as detectable local disease after surgery, developing with or without distant metastasis.

Categorical variables are reported here as frequency (percentage), and quantitative variables are reported as mean ± standard deviation except where otherwise noted. Associations with categorical variables were assessed by \( \chi^2 \) and Fisher exact tests. Associations with continuous variables were assessed by the Kruskal-Wallis and Wilcoxon rank sum tests. The comparison with respect to recurrence and survival was performed using a log-rank test with the Kaplan-Meier method. A level of \( \alpha < 0.05 \) was used to establish statistical significance of individual \( p \) values.

### RESULTS

A total of 25 patients who underwent hand-assisted laparoscopic proctosigmoidectomy for treatment of adenocarcinoma were identified. These patients were matched with 25 patients who underwent straight-laparoscopic resection and 50 patients who underwent open resection during the same period at our institution. The parameters of the case matching and clinical staging of cancer in the rectum are shown in Table 1.

There was no difference between the groups in sex, American Society of Anesthesiologists score, or body mass index (Table 2). Patients who underwent HALS were older than those in the straight-resection and

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**Table 1. Matching criteria and clinical staging of tumors**

<table>
<thead>
<tr>
<th>Criterion or stage</th>
<th>Hand-assisted laparoscopic surgery (n = 25), no. (%)</th>
<th>Straight-laparoscopic surgery (n = 25), no. (%)</th>
<th>Open surgery (n = 50), no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor localization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>8 (32)</td>
<td>8 (32)</td>
<td>16 (32)</td>
</tr>
<tr>
<td>Rectum</td>
<td>17 (68)</td>
<td>17 (68)</td>
<td>34 (68)</td>
</tr>
<tr>
<td>Preoperative clinical stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>11 (44)</td>
<td>11 (44)</td>
<td>24 (48)</td>
</tr>
<tr>
<td>II</td>
<td>7 (28)</td>
<td>7 (28)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>III</td>
<td>7 (28)</td>
<td>7 (28)</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Pathologic stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0, I</td>
<td>12 (48)</td>
<td>13 (52)</td>
<td>26 (52)</td>
</tr>
<tr>
<td>II</td>
<td>7 (28)</td>
<td>6 (24)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>III</td>
<td>6 (24)</td>
<td>6 (24)</td>
<td>12 (24)</td>
</tr>
<tr>
<td>Type of resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>7 (28)</td>
<td>7 (28)</td>
<td>14 (28)</td>
</tr>
<tr>
<td>Low-anterior</td>
<td>18 (72)</td>
<td>18 (72)</td>
<td>36 (72)</td>
</tr>
<tr>
<td>Year of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006-2008</td>
<td>2 (8)</td>
<td>2 (8)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>2009-2012</td>
<td>23 (92)</td>
<td>23 (92)</td>
<td>40 (80)</td>
</tr>
</tbody>
</table>

* \( p \) value was not significant.

---

**Table 2. Preoperative characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Hand-assisted laparoscopic surgery (n = 25)</th>
<th>Straight-laparoscopic surgery (n = 25)</th>
<th>Open surgery (n = 50)</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>67 ± 11</td>
<td>65 ± 13</td>
<td>59 ± 12</td>
<td>0.03</td>
</tr>
<tr>
<td>Sex (F/M)</td>
<td>11/14</td>
<td>15/10</td>
<td>18/32</td>
<td>NS</td>
</tr>
<tr>
<td>Median ASA score (range)</td>
<td>3 (1-4)</td>
<td>3 (1-4)</td>
<td>3 (1-4)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²), mean ± SD</td>
<td>28 ± 5</td>
<td>28 ± 5</td>
<td>30 ± 16</td>
<td>NS</td>
</tr>
<tr>
<td>Previous abdominal operation, no. (%)</td>
<td>4 (16)</td>
<td>14 (56)</td>
<td>18 (36)</td>
<td>0.01</td>
</tr>
<tr>
<td>Preoperative chemoradiation therapy, no. (%)</td>
<td>1 (4)</td>
<td>2 (8)</td>
<td>12 (24)</td>
<td>NS*</td>
</tr>
<tr>
<td>Tumor distance to anal verge (cm), mean ± SD</td>
<td>18 ± 10</td>
<td>14 ± 9</td>
<td>13 ± 11</td>
<td>NS</td>
</tr>
<tr>
<td>Comorbid factors, no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (28)</td>
<td>2 (8)</td>
<td>6 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18 (72)</td>
<td>17 (68)</td>
<td>21 (42)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>19 (76)</td>
<td>16 (64)</td>
<td>13 (26)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>2 (8)</td>
<td>2 (8)</td>
<td>5 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Liver disease</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (2)</td>
<td>NS</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1 (4)</td>
<td>0 (0)</td>
<td>5 (10)</td>
<td>NS</td>
</tr>
</tbody>
</table>

* \( p = 0.053 \).

ASA = American Society of Anesthesiologists; BMI = body mass index; F/M = female/male; NS = not significant; SD = standard deviation. 
open-resection groups (p = 0.03) and had higher rates of cardiac disease (p < 0.0001) and hypertension (p = 0.02). Distribution of patients with diabetes, pulmonary disease, or liver or renal disorders were comparable among the study groups. History of previous abdominal operations was highest in the straight-laparoscopy group (p = 0.01). The tumor distance to the anal verge was shorter (p = 0.09) and the rate of neoadjuvant chemotherapy was higher (p = 0.053) in the open-surgery group; however, these parameters were not significantly different among the groups.

Operative outcomes, conversion to open surgery in the laparoscopy groups, diverting stoma creation, and intraoperative complications were similar among the study groups (Table 3). Adhesions (n = 3) and unclear anatomy (n = 1) were the causes of conversion. The straight-laparoscopic resection group had the lowest estimated blood loss (p = 0.01). Mean specimen length was largest in the HALS group (29 cm [HALS] vs 23 cm [straight laparoscopy] vs 27 cm [open surgery]; p = 0.01). Although length of hospital stay was shortest in the straight-laparoscopic group (p = 0.04), the time to bowel movement, reoperation, readmission, and requirement of blood transfusion rates were comparable among the groups. Oncologic outcomes, including harvested lymph nodes; distance to resection margin; recurrence; and postoperative complications, such as deep venous thrombosis, urinary retention, urinary tract infection, anastomotic leak, ileus, wound infection, intraabdominal abscess, sepsis, and stomal complications, were similar regardless of operative technique (Table 4). No patients died within the 30-day postoperative period. All diverting stomas were reversed during follow-up. Disease-free and overall survival were similar in midterm follow-up among the groups (Figure 1). Follow-up times were comparable for the HALS, straight-laparoscopy, and open groups after surgery (23 ± 18 months vs 32 ± 16 months vs 29 ± 22 months, respectively; p = 0.08).

**DISCUSSION**

Our results showed that the two minimally invasive techniques for treatment of sigmoid and rectal cancer, HALS and straight-laparoscopic surgery, could provide similar outcomes compared with open surgery. Despite the fact that patients who underwent open surgery were younger, postoperative morbidity after straight-laparoscopic surgery and HALS was acceptable and comparable with open surgery. There was no evidence in our study to suggest that HALS was superior to straight-laparoscopic surgery. Whereas intraoperative blood loss and postoperative hospital stay were similar after HALS and straight-laparoscopic colorectal surgery in a systematic review, straight-laparoscopic surgery reduced estimated blood loss and shortened hospital

<table>
<thead>
<tr>
<th>Table 3. Intraoperative parameters and complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>Operative time (minutes), mean ± SD</td>
</tr>
<tr>
<td>Conversion, no. (%)</td>
</tr>
<tr>
<td>Estimated blood loss (mL), mean ± SD</td>
</tr>
<tr>
<td>Diverting stoma, no. (%)</td>
</tr>
<tr>
<td>Intraoperative complications, no. (%)</td>
</tr>
<tr>
<td>Intraoperative bleeding</td>
</tr>
<tr>
<td>Intraoperative vascular injury</td>
</tr>
</tbody>
</table>

NS = not significant; SD = standard deviation.

<table>
<thead>
<tr>
<th>Table 4. Postoperative and oncologic outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td>Median hospital stay (range, days)</td>
</tr>
<tr>
<td>Time to bowel movements (days), mean ± SD</td>
</tr>
<tr>
<td>Reoperation, no. (%)</td>
</tr>
<tr>
<td>Readmission, no. (%)</td>
</tr>
<tr>
<td>Transfusion, no. (%)</td>
</tr>
<tr>
<td>Postoperative complications, no. (%)</td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
<tr>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Anastomotic leak</td>
</tr>
<tr>
<td>Ileus</td>
</tr>
<tr>
<td>Wound infection</td>
</tr>
<tr>
<td>Intraabdominal abscess</td>
</tr>
<tr>
<td>Sepsis</td>
</tr>
<tr>
<td>Stoma complications</td>
</tr>
<tr>
<td>Oncologic outcomes</td>
</tr>
<tr>
<td>Harvested lymph nodes, mean ± SD</td>
</tr>
<tr>
<td>Distance to resection margin (cm), mean ± SD</td>
</tr>
<tr>
<td>Recurrence, no. (%)</td>
</tr>
</tbody>
</table>

*One patient in the hand-assisted laparoscopic surgery group and one patient in the open-surgery group had a local recurrence; the others had distant recurrences. NS = not significant; SD = standard deviation.
A recent study from our institution shows that hand-assisted laparoscopic surgery may be preferred as a minimally invasive treatment alternative for patients who are not appropriate for both types of laparoscopic proctosigmoidectomy techniques in our study. On the other hand, patients in the HALS group were younger and had higher rates of heart problems and hypertension. Laparoscopic surgery can be completed safely with hand assistance in patients with comorbid conditions and complex diseases. However, these comorbidities could be the factors prolonging hospital stay after hand-assisted proctosigmoidectomy in our patients. Because HALS improves postoperative recovery and reduces morbidity compared with open surgery, HALS may be preferred as a minimally invasive treatment alternative for patients who are not appropriate for straight-laparoscopic surgery. In recent studies, it has been shown that the laparoscopic colorectal cancer can be performed with similar costs compared with open surgery. Hospital costs for HALS and standard laparoscopic surgery were also comparable.

Benefits of HALS over straight-laparoscopic surgery on operating time have been shown in left-sided colectomy, total colectomy, and total proctocolectomy. On the basis of our results, hand assistance for laparoscopic rectal dissection may not be a factor in reducing the operating time. The type of prior surgery and surgeon factors may change operating time and the decision making for the operative approach in patients with a history of prior abdominal surgery. We did not have detailed information about the type of prior surgeries, and we did not evaluate surgeon factor in this study. We previously showed that having a prior abdominal operation worsens the postoperative outcomes after laparoscopic colorectal surgery. However, straight-laparoscopic colorectal operations can be performed safely in patients who had prior major laparotomy and may reduce rates of wound infection compared with open surgery.

Indeed, in our study, patients who underwent HALS had slightly higher rates of wound infections, although it was not statistically significant. Creation of a diverting stoma, which was similar among our study groups, was not performed depending on definitive criteria. The decision for creating a diverting stoma in our patients was given by the operating surgeons. Straight-laparoscopic, sphincter-saving rectal resection without diverting stoma can be performed selectively.

We noted a trend toward a higher rate of neoadjuvant chemoradiotherapy in the open-surgery group that was not statistically significant. The general approach of our group is to use neoadjuvant chemoradiotherapy in patients with extraperitoneal rectal tumors staged as cT3-T4 or any cN1. Because we evaluated pathologic staging for case-matching, neoadjuvant chemoradiotherapy may downstage disease. The tumor distance to anal verge and the number of harvested lymph nodes did not reveal statistical significance among the groups. In our experience, we do not believe laparoscopic approach is a limitation for lower pelvic dissection. In contrary, better laparoscopic vision allows for a very low rate of stapling. It has been previously reported that variances of pelvic anatomy or tumor size does not adversely affect postoperative outcomes of laparoscopic colorectal surgery. A recent study from our institution showed that laparoscopic surgery is associated with a lower risk of splenic injury during flexure mobilization.

As a retrospective study, our study has limitations because of its nonrandomized nature. Somewhat different follow-up periods between the groups may be considered a drawback of the study. Although the rate of the adjuvant treatment was not evaluated among the groups, all of our cases were discussed at our institutional tumor board, and the National Comprehensive Cancer Network guidelines were followed. We aimed to reduce potential biases by creating a case-matched study and including the patients who were treated in the same period. It is expected that the trial of the American College of Surgeons Oncology Group will provide more information related to oncologic outcomes after laparoscopic rectal resection.

**CONCLUSION**

Although both hand-assisted and straight-laparoscopic proctosigmoidectomy appear to be as safe and effective as open surgery in short-term and mid-term outcomes, straight-laparoscopic surgery seems to provide faster convalescence, possibly because of causing less surgical trauma compared with open surgery and with HALS.
ABSTRACT

Context: Disease registries enable priority setting and batching of clinical tasks, such as reaching out to patients who have missed a routine laboratory test. Building disease registries requires collaboration among professionals in medicine, population science, and information technology. Specialty care addresses many complex, uncommon conditions, and these conditions are diverse. The cost to build and maintain traditional registries for many diverse, complex, low-frequency conditions is prohibitive.

Objective: To develop and to test the Specialty Miniregistries platform, a collaborative interface designed to streamline the medical specialist’s contributions to the science and management of population health.

Design: We used accessible technology to develop a platform that would generate miniregistries (small, routinely updated datasets) for surveillance, to identify patients who were missing expected utilization, and to influence clinicians and others to change practices to improve care. The platform was composed of staff, technology, and structured collaborations, organized into a workflow. The platform was tested in five medical specialty departments.

Main Outcome Measure: Proof of concept.

Results: The platform enabled medical specialists to rapidly and effectively communicate clinical questions, knowledge of disease, clinical workflows, and improvement opportunities. Their knowledge was used to build and to deploy the miniregistries. Each miniregistry required 1 to 2 hours of collaboration by a medical specialist. Turnaround was 1 to 14 days.

Conclusions: The Specialty Miniregistries platform is useful for low-volume questions that often occur in specialty care, and it requires low levels of investment. The efficient organization of information workers to support accountable care is an emerging question.

INTRODUCTION

A disease registry is a tool for tracking clinical care and outcomes at the level of a population or patient panel.1 Registries can be used to focus attention on the most urgent patients, to tailor clinical decision support to the patient’s specific medical needs, to improve care coordination, to identify opportunities to improve care,5,6 or steward medical resources, to implement quality improvement,6 and to build reports needed for accreditation and public reporting,7 among other uses. However, many registries are disease specific, and because they are costly, they tend to be developed for high-volume conditions and settings. However, medical specialists want these tools to manage lower-volume conditions as well.

Nearly every health care worker who contributes to patient care also contributes to the patient’s electronic medical record (EMR), and these systems contain a wealth of information. Data in the EMR can be processed and displayed to provide a disease registry.

Big data is an emerging management concept6,7 that responds to data acquisition as an automated part of the business process. “Big data” brings together ideas about multiple varieties of data creators and demands for rapid access to data by decentralized data customers, together with exponential increase in data volume and relatively low-cost computing. These trends create a strong demand for analytics to apply new knowledge to the local context for the purpose of process improvement. Crowdsourcing, or co-creation, is the reorganization and decentralization of labor to increase efficiency, such that those who are immediately affected or have direct accountability are supported by platforms (or collaborative interfaces, combining technology, staff, and workflows) to contribute to problem solving. Crowdsourcing is particularly efficient for sharing specialized knowledge.8,9-10

This project was designed to deliver miniregistries, which are small datasets that can be routinely updated, to Chiefs of medical specialties by enabling them to collaborate rapidly with experts in population management and data analysis. Whether these miniregistries improved care was beyond the scope of the project because improvement requires separate, additional resources.11-13

This project was designed as an innovation, not as a traditional research project. Traditionally, research is organized into projects, with one project creating knowledge and a separate project implementing that knowledge through an intervention. The innovation framework is different; it uses iterative cycles to create knowledge and to test prototypes.14
Thus, from one cycle to the next, the results are used to refine implementation. Because implementation is a key endpoint, proof of concept (i.e., does it work?) is considered an important outcome. We worked with Kaiser Permanente’s (KP’s) Innovation and Advanced Technology Group\textsuperscript{15,16} to develop and to iteratively test and adapt the miniregistry platform, tinkering with staffing arrangements, technology, and workflow until the combination worked.

**METHODS**

The project was approved by the Kaiser Foundation Research Institute’s institutional review board.

KP is located in 7 regions, with each operating its own Epic-based EMR (Epic Systems Corp, Verona, WI). Although the present project engaged stakeholders across the national program, data processing was restricted to KP Northern California, which comprises 3.3 million members, 7000 physicians, and 21 Medical Centers. In Northern California, care is capitated, with members receiving all or nearly all their care from KP clinicians in owned facilities.

**Overview of Platform**

A conceptual model of the Specialty Miniregistry platform is shown in Figure 1. Clinical questions are generated at the level of the specialty department, and actionable metrics are returned to the specialty department. Collaboration among experts in medicine, population management, and information technology is structured and streamlined using the Specialty Miniregistry platform (circles in Figure 1). The Specialty Miniregistry platform is a combination of staff, technology, and workflows that make use of data in the EMR. The staff, technology, and workflows were specifically designed to meet the needs of the medical specialist whose experience with data and analytics may be limited. In addition, the platform was designed for efficiency, by structuring and minimizing the time required for collaboration and data processing. Maximizing the efficiency of the platform increases the number of clinical questions that can be addressed.

We tested the prototype and piloted the platform in two phases.

**Phase 1**

Phase 1 included creating an initial conception; engaging stakeholders and asking them to react to a description of the initial conception; clarifying how the platform was different from other tools and what kinds of problems the platform could best address; and finally, formalizing its purpose and general design in a set of business requirements.

**Initial Conception**

KP’s medical specialties departments have long aspired to build disease registries. However, the few that were built were too costly to generalize.\textsuperscript{17} Therefore, the initial concept was to

| Table 1. Key barriers and facilitators identified by stakeholders\textsuperscript{a} |
|------------------|------------------|------------------|
| **Perception**   | **Comment**      | **Resolution**   |
| **Barriers**     |                  |                  |
| The data will be discoverable | Legal clearance; administer through the Quality Department |
| A governance committee and governance structures are essential and will take substantial time and effort | Use governance structures that already exist in each of the specialty groups; place accountability on the Chief of specialty |
| Personal health information or proprietary data will be released | Train data handlers; place warnings into the reports as headings and watermarks |
| The data will not be valid | Develop workflows to enhance data validity and transparency; for each specialty, identify and consult with the clinician with the deepest knowledge of the specialty’s EMR tables |
| People don’t change | Elicit priorities from frontline clinicians to increase relevance and ownership; structure intake to drive accountability; provide reports that are designed to produce change |
| **Facilitators** |                  |                  |
| Use business terminology instead of research terminology | Rewrite the concept with help from a stakeholder who spans research and operations |
| We have experience with things like this | Partner with experienced individuals; further refine the scope; clarify differences with existing, related workflows |
| Performance-improvement committees are well organized to act on data | Engage with the performance-improvement committees |

\textsuperscript{a} Stakeholders included Medical Directors in clinical informatics and decision support, quality and risk management, technology, patient panel management, and care delivery, as well as Chiefs of medical specialties.

EMR = electronic medical record.
quickly get relevant, actionable data into the hands of Specialty Chiefs. Existing registries were expensive because nonphysician staff who supported the registries were trained to support a few high-volume clinical areas. This staffing model was not feasible for supporting a larger number of low-volume clinical areas. Therefore, we chose a crowdsourcing platform, one in which the medical specialist would be expected to contribute labor by specifying diagnostic codes, operational definitions of tests and therapies, and needed information about time frames. This information was used to write algorithms in SQL (structured query language) and statistical analysis software as needed to extract and process the data. We further expected the medical specialists to interpret the data.

**Stakeholder Engagement**

To understand operational barriers and facilitators, we interviewed Medical Directors in clinical informatics and decision support, quality and risk management, technology, patient panel management, and care delivery, as well as Chiefs of medical specialties. These stakeholders identified key barriers and facilitators, enabling us to align the work with existing accountabilities and priorities (Table 1).

**Needs Assessment and Differentiation**

We next interviewed Chiefs of medical specialties in Endocrinology, Pulmonology, Pediatrics, General Surgery, Vascular Surgery, Cardiology, Oncology, and Neurology. The interview elicited the specialty department's leadership and organization, specific clinical questions and needs for data, efforts taken in the past to address the clinical questions, trust in the validity of the EMR data, the existence of data-savvy physicians in the specialty department, readiness for acting on new information, and opinions about data governance.

Every Chief readily formulated and articulated questions for which they wanted data, but most thought these data could not be obtained. Regarding trusting the validity of the data in the EMR, the general sentiment was “it’s a starting point.” Queried about the ability to translate knowledge into action, the clinical leaders explained that without objective metrics, they could only make guesses about needed improvements and had little influence. The respondents were unanimous that Chiefs of medical specialties were best able to govern priorities and implementation. Each of the clinical leaders could name physicians in their department who “liked computers” or “liked research” and could help define algorithms and validate data.

**Templates**

The clinical questions were grouped into templates. A template is a category of tools and approaches that can be used to address a set of clinical questions that are common across diseases. The clinical questions posed by the clinical leaders fell into seven crosscutting templates: 1) Patient List, 2) Comparison with Benchmark, 3) Variation in Care, 4) Text Search, 5) Standardized Physician Assessments, 6) Patient-Reported Outcomes, and 7) Comparative Effectiveness Studies.

Given the pilot nature of this project, we decided to build capability for the first three templates as proof of concept. The Patient List template allowed identification of patients with suspected surgical site infections, elevated laboratory values, need for discontinuation of medications, approaching care transitions, and so forth. The Comparison with Benchmark template computed overall rates, proportions, and other statistics for comparison over time or against the benchmark. The Variation in Care template was similar but presented statistics by clinician and facility.

The fourth template, Text Search, will identify search terms in narrative reports, such as laboratory, pathology, imaging, and operative reports; for this, we opted to develop capability in natural language processing; this work is ongoing. The fifth and sixth templates, Standardized Physician Assessments and Patient-Reported Outcomes, require engagement of operational staff to enhance the EMR and patient portal; we deferred on these templates to gain experience before engaging EMR staff, who have other critical priorities. The seventh template, Comparative Effectiveness Studies, was judged to be out of scope because such studies require greater investment of expertise.

**Specification of Business Requirements**

At the completion of Phase 1, we specified the business requirements (Table 2).

**Phase 2**

Phase 2 included iteratively prototyping and piloting the platform, and then performing an evaluation.

**Creating the Prototype and Piloting**

During Phase 2, we created the prototype platform 1 clinical question at a time and iteratively adapted staff, technology, and workflows to optimize performance.

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Locate the platform in the Quality Department</td>
<td>Align with the Quality Department’s mission</td>
</tr>
<tr>
<td>Assign governance to the Chief of specialty</td>
<td>Articulate important, relevant, actionable priorities</td>
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<tr>
<td></td>
<td>Influence others to close gaps</td>
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<td></td>
<td>Protect personal health information and confidential business data</td>
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<td></td>
<td>Prevent use of the data for research without approval by the institutional review board</td>
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<tr>
<td>Ensure that care can be modified</td>
<td>Ensure the data and metrics can be used to influence others to make changes that improve care</td>
</tr>
<tr>
<td>Limit scope for tractability</td>
<td>Provide the right amount of information: not so little as to be unclear but not so much as to overwhelm</td>
</tr>
<tr>
<td>Reduce cost</td>
<td>Offer few but generalizable choices for report templates</td>
</tr>
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<td></td>
<td>Use EMR data only, no additional data collection</td>
</tr>
<tr>
<td>Ensure validity</td>
<td>Engage the specialist who has the deepest knowledge of the EMR data</td>
</tr>
<tr>
<td></td>
<td>Include a data validation step in the protocol</td>
</tr>
<tr>
<td>Maximize user-centeredness</td>
<td>Design the interface around the user’s preferences, capabilities, and limitations</td>
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<tr>
<td></td>
<td>Use technology that is transferrable across staff and role</td>
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<tr>
<td>Increase feasibility</td>
<td>Do not engage EMR operational staff</td>
</tr>
<tr>
<td></td>
<td>Minimize dependence on analytic expertise</td>
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</table>

EMR = electronic medical record.
Staffing for the platform included a Senior Epidemiologist, who performed the intake interview, drafted algorithms, and designed the final report, and a Senior Data Consultant, who extracted data from the EMR and used statistical analysis software to process the data. In addition, the work required effort by the Chief of the medical specialty, who sometimes engaged physicians in his/her department who had an understanding of codes, algorithms, epidemiology, or spreadsheets, or mere availability and interest with different Chiefs using somewhat different approaches. In addition, the Senior Data Consultant sought advice from an extract, transfer, and load programmer housed in the Data Warehousing Department. Although the extract, transfer, and load programmer did not extract data directly, his/her advice on the location of data was helpful. The EMR comprises thousands of data tables, and the extract, transfer, and load programmer possessed knowledge of the location of variables in the EMR. On average, this individual consulted for approximately four hours per specialty, with each specialty’s EMR tables being located together. Thus, the first report provided to a specialty was more costly than the second and subsequent reports to that specialty.

We simplified the technology over the course of the innovation, abandoning aspirations to use Web services and business intelligence software because of barriers related to staffing and collaboration. Ultimately, we realized that user-centered design was a key to success. User-centered design recognizes—as a first principle—the preferences, capabilities, and limitations of the end user (ie, the physician), those factors driving each stage of the design process. We therefore used highly accessible technology. SurveyMonkey (Palo Alto, CA) served as the user query to elicit, for each clinical question, the detailed clinical knowledge of diagnoses, procedures, tests, results, and therapies that would be operationalized into algorithms as written into computer programs. We used a spreadsheet to report the data and electronic mail to deliver the report.

The workflow comprised five steps: 1) intake interview and selection of the template; 2) completion of the user query; 3) initial programming, using SQL and statistical analysis software, to extract data from the EMR, build reports, and output results into a spreadsheet; 4) data validation; and 5) final coding and delivery.

During the intake interview, we explained the resource and used a script to define actionable questions: “Let’s imagine we generate the perfect report and the data show exactly what you suspect. To whom will you show the data? What do you expect them to do after they see the data? Have you talked to them? Should we instead focus on opportunities for which you have greater control?”

For each template (eg, Patient List), we developed a user query in SurveyMonkey to be completed by the Chief or a clinical delegate. The user query was written as a series of approximately 30 questions to elicit components of needed algorithms, such as diagnostic codes, tests, therapies, and timeframes. To validate the data, we provided simple crosstabulations. We then completed the programming and e-mailed the final spreadsheet. After the Chief’s approval of the report, we used cron, a job scheduler, to automate SQL and the statistical analysis software to extract, process, and output the data into a spreadsheet, and to send the spreadsheet to the physician through e-mail.

**Evaluation**

We assessed leadership engagement by the Medical Specialty Chiefs, logistical feasibility, hours of effort, overall turnaround time, and satisfaction using a brief satisfaction survey. We also noted translation toward improved clinical processes and outcomes, although this was not a primary goal of the project.

**RESULTS**

The Specialty Miniregistries platform was successful in engaging Chiefs of medical specialties and producing accessible and authoritative reports. The required meeting time was 1 to 2 hours; analytic effort, 8 to 32 hours; and overall turnaround time, no longer than 2 weeks. Data alone may be insufficient for population health management, and translation was not an immediate goal of the innovation; nonetheless, several reports were implemented into simple workflows.

Medical specialists expressed satisfaction that the platform was easy to use and effective. However, the evaluation revealed that additional work is needed to clarify data governance, particularly the need for institutional review board approval to use data for research that would be publicly disseminated at national specialty meetings.

Experiences with specialty groups are detailed here.

**Oncology**

The Oncology Department implemented a miniregistry to improve consultation among oncologists in the department for amyloidosis, a rare disease. The oncologists sought to improve quality and reduce variation in care by rapidly identifying patients with amyloidosis who had been newly diagnosed by a less specialized oncologist and reporting those cases to oncologists who specialized in amyloidosis. They therefore requested lists of cancer patients by cancer site. The Chief of Oncology first tested the Specialty Miniregistries platform through an initial request for a list of patients with amyloidosis. The amyloidosis list was automated and implemented into clinical care. A dedicated amyloidosis team of three oncologists proactively reached out to guide diagnosing physicians whose volumes of patients with amyloidosis is lower.

**Medical Genetics**

The Medical Genetics Department was concerned that genetic tests that are difficult to interpret were ordered by other departments without appropriate consultation. Focusing on ataxia, we performed a text search to identify who was ordering genetic tests. The search confirmed that physicians across a range of departments were ordering ataxia genetic tests without first consulting the Medical Genetics Department. Our work was one of several efforts organized by the Medical Genetics Department to address utilization of genetic testing, and together these efforts resulted in system-level changes.
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Rheumatology
Rheumatology was concerned that patients with gout were missing important laboratory tests needed to monitor their uric acid levels. They wanted to influence other departments, such as Pharmacy, to assume panel management of gout. We created a list of patients with uric acid levels in the top first percentile, showing that laboratory orders and procedures were missing and identifying preventable utilization. Discussions are under way about possible system-level changes.

Ophthalmology
The Ophthalmology Department Chief requested surveillance of surgical site infection after cataract surgery to enable a failure analysis. The tool was implemented, with each infection being investigated and discussed and “zero infection” reports being celebrated.

Pediatric Subspecialties
The pediatric oncologists wanted to improve the transition from pediatric to adult cancer care and therefore requested a list of teenaged patients scheduled for transition in the next year. The list was one of several tools used to understand and improve the care transition, with system-level changes now being discussed.

The pediatric hematologists wanted a better understanding of comanagement of sickle cell disease. They therefore requested a list of patients identifying their care providers together with the patient’s “last touch” with the Health Plan and with pediatric hematology.

Pediatric cardiology referred neonates needing surgery to an external provider facility, where there had been staff changes and seeming increases in the rate of late complications. Postdischarge utilization data were analyzed to assess complication rates before and after the staff changes. This latter experience provided an example of the use of data about outside providers to measure quality.

DISCUSSION
Numerous changes are needed to transform health care. Among these is the use of “precise and clinically relevant” data and metrics to identify care gaps, such as missing tests and medication dispensings, and inappropriate variations among providers, and to enable performance improvement activities in the clinical microenvironment. The Specialty Miniregistries platform was successful in using the EMR to provide these data and metrics. Keys to success included the design of the infrastructure and collaborative interfaces, and enabling the medical specialists to formulate the clinical questions.

Infrastructure and Interprofessional Interfaces
With respect to registries, primary care differs from specialty care in that physicians treat a larger number of high-volume conditions. Thus, it is efficient for population health scientists and technology workers who build and maintain primary care registries to specialize on clinical topics; the clinical training they receive on-the-job is well used.

Because specialty care encompasses a greater diversity of topics, knowledge transfer from clinicians to nonclinicians is more resource intensive; thus, collaboration and infrastructure development is more costly. To obtain the greatest return on investment, infrastructure for building registries in specialty care should be cross-cutting.

Crowdsourcing knowledge-intensive tasks to specialists, and building interfaces to support their collaboration, greatly reduced the time and complexity of knowledge transfer. Collaboration was narrowly focused on actionability, programming algorithms, data validity, and governance, with minimal discussion of clinical concepts. Use of medical specialists to develop algorithms, manipulate spreadsheets, and interpret the data was less costly than directing this work to analytic staff because of the specialists’ greater knowledge and more rapid cognitive processing of the clinical topic and clinical workflows. In addition, giving this task to the specialist enabled deeper insights from the data and gave the specialists an appreciation for needed improvements in medical documentation. It also increased their skill in using data.

We used a flexible, low-investment strategy to build the collaborative platform. This made it easier for the physician to use the platform, and it reduced the level of effort needed by scarce technology workers. Although physicians are well trained to formulate questions at the level of the individual patient, they generally are not trained to conceptualize questions at the level of a population. Nor do they have experience using EMR data or building algorithms. For this reason, the intake interview was an essential component of the platform. However, physicians know how to define clinical concepts, and they were successful in completing the user query to communicate operational definitions to the data consultant.

When we began our work, we aspired to discover a reduced set of quality metrics that might “roll up” from the clinical microenvironment to the Health Plan and beyond. The logical consequence is an infrastructure that is top-down, expensive, and difficult to adapt. We now believe that top-down approaches may not be adequately user-centered to the various stakeholders who need data, will be poor at addressing questions at the local clinical level, and may lose relevance as clinical processes evolve.

Asking the Right Clinical Questions
We anticipated that locating control of the clinical question with those at the frontline might be effective in improving care, because Medical Specialty Chiefs have direct accountability to their patients and physicians, knowledge of care delivery and data creation, and insight into improvement opportunities. Indeed, we observed that the process of formulating questions focused attention on modifiable units of change. In addition, data increased the Chief’s authority to set priorities, intervene with staff, and advocate
for system-level change. We further noted that the priorities expressed by the Medical Specialty Chiefs were at times exquisitely local. Chiefs sorted their priorities using intimate knowledge of past attempts to create change, the impact of information on key individuals and teams, and their ability to leverage influence over highly specific problems.

Many national specialty societies are developing metrics for general use across care delivery settings; some are intended for public reporting, others for local quality improvement. These metrics contain implicit clinical questions that may or may not correspond to local priorities and opportunities. Regardless of whether a metric is formulated at a national or local level, effort is needed to write algorithms, access data, compute metrics, and deliver reports. Even when specialty societies require participation in a centralized registry operated by the society, effort is needed to create and test data flows from the health care system to the national registry. The platform described here can be simplified and used for that purpose.

Alignment

Compared with primary care, specialty care is composed of smaller organizations of clinicians, and this smaller scale creates opportunities for collaboration, influence, and change that differ from those in primary care. Thus, discussion of the reports at Medical Specialty Chiefs meetings and use of the data to influence others may be the first step to translation. Nonetheless, even in specialty care, developing and testing new clinical workflows may require a burdensome initial investment that exceeds local capacities. When improvement activities require investments from other departments, such as laboratory or pharmacy, alignment becomes essential. Although data and metrics alone may not lead to change, well-designed metrics that are appropriately targeted, objective, and transparent can “start the conversation” and build alignment. However, engaging stakeholders in other departments to participate in formulating questions may result in greater clinical change.

Generalizability

The EMR data used by the Specialty Miniregistries platform is the same data used to create claims and for external reporting to meet accreditation and meaningful use criteria. We are confident that the platform could be implemented in health care delivery systems that are less integrated than KP, although the range of questions that can be answered may be narrower. For example, the data available in less integrated systems may not capture late clinical outcomes, but they would capture early outcomes. They would also provide detailed process information, including practice variation. Furthermore, as Health Information Exchanges are rolled out under the Affordable Care Act, possibilities for linking data across settings will increase. The innovation we present here is not the use of data; rather, it is the structuring of a collaborative interface to support the specialist’s contributions to the science and management of population health.

CONCLUSIONS AND FUTURE DIRECTIONS

The Specialty Miniregistries platform provides one solution for increasing access to valid, objective, and actionable knowledge about local care processes. The platform is useful where there are low-volume clinical questions that cut across knowledge domains, as is often the case in specialty care, although cross-cutting questions occur in primary care as well. As EMR vendors increase the usability and analytic capabilities of their products, the need for solutions such as the Specialty Miniregistries platform may diminish, although this is uncertain. Organization and management of information systems to support accountable care is a rapidly evolving topic.

In the meantime, the many and diverse professionals responsible for using and stewarding information to improve care delivery ask: What is a sensible set of investments? How do we train and support data creators to become data customers? How do scale and context drive the cost-effectiveness of infrastructure built for clinical measurement? What is the right family of platforms, and can we be discerning about the features of stakeholders and their needs that fit with any particular platform? As specialty societies and other national stakeholders become increasingly involved in creating public accountability through metrics, how will care delivery systems staff and organize their information workforce to support those expectations? These are the emerging questions that drive future research.

Disclosure Statement

Lisa Herrinton, PhD, has had unrelated research contracts with Medimmune (2013 to present), P & G (2006 to 2012), and Genentech (2008 to 2012). The author(s) have no conflicts of interest to disclose.

Acknowledgments

This research was funded by the Innovation Fund for Technology of Kaiser Permanente Information Technology. The fund’s staff provided advice about implementing an innovation project, but had no other role in the study. We wish to thank the many individuals across Kaiser Permanente’s regional and national program who provided perspective and advice on this project, including Scott Adelman, MD; David Baer, MD; Matthew Carnahan, MD; William J Chang, MD; Kavin Desai, MD; Robert Goldfien, MD; Bradley B Hill, MD; Stacy Month, MD; Charles Meltzer, MD; and Scott Peak, MD; from The Permanente Medical Group; John Broockey, MD; Robert W Chang, MD; Marc Klaau, MD; and Ronald K Loo MD; from the Southern California Permanente Medical Group; John Merench, MD, FACP; from the Colorado Permanente Medical Group; and Michael S Alberts PhD, MD; and Robert Unitan, MD; from Northwest Permanente, PC. The anonymous reviewers were instrumental in improving the clarity of the report. We also thank the US National Cancer Institute’s Training Institute for Dissemination and Implementation Research in Health, Bethesda, MD.

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

Author Contributions

Study design (Lisa J Herrinton, PhD; Liyan Liu, MD, MS; Richard Dell, MD; Amy L Compton-Phillips, MD); data collection (Liyan Liu, MD, MS; Andrea Altschuler, PhD); data analysis (Lisa J Herrinton, PhD; Liyan Liu, MD, MS; Andrea Altschuler, PhD); and manuscript preparation (Lisa J Herrinton, PhD; Liyan Liu, MD, MS; Andrea Altschuler, PhD; Richard Dell, MD; Violeta Rabrenovish, MHA; Amy L Compton-Phillips, MD).
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References

Data
Good data in a few patients are far better than mediocre or poor data in many patients.

— Guide to Clinical Trials, Bert Spilker, 1991
ORIGINAL RESEARCH & CONTRIBUTIONS

Expanding Access to Care and Improving Quality in the Mid-Atlantic States Safety-Net Clinics: Kaiser Permanente’s Community Ambassador Program

Jared Lane K Maeda, PhD, MPH; Jacqueline J Bradley, MSN, CRNP; Sarah R Eisler, MSN, CPNP; Maricia LoBrano, MD, MPH; Mindy R Rubin; Maritha Gay; Michael A Horberg, MD, MAS, FACP, FIDSA; Bernadette C Loftus, MD

ABSTRACT

Context: As part of its longstanding commitment to improve the health of the communities it serves, Kaiser Permanente (KP) established the Community Ambassador Program (CAP) in the Mid-Atlantic States Region. The CAP places KP-employed nurse practitioners, midwives, and physician assistants to work in the safety-net clinics and to share best practices through a long-term community collaboration.

Objective: To share the early experiences of the CAP and describe the initial results of the program’s impact on the safety-net clinics.

Methods: We conducted an evaluation of 18 safety-net clinics that participated in the CAP in 2012 to determine the program’s early impact in expanding access to care, increasing the capacity of safety-net providers, and improving the quality of care on evidence-based measures in the year following program implementation. The safety-net clinics are comprised of federally qualified health centers, free clinics, and other community-based organizations. The clinics were asked to respond to questions regarding their evidence-based practices promoted by KP and on primary care-related utilization.

Results: The Community Ambassadors provided an estimated 32,249 encounters to 11,988 patients. Performance by the Community Ambassadors was at or near 90% for 2 adult quality measures (weight screening and tobacco use assessment). For breast cancer screenings, however, performance among the Community Ambassadors was much lower (48%).

Conclusion: The CAP demonstrated some early success in expanding access and improving quality of care on several key measures for certain subpopulations. Despite these achievements, opportunities remain for quality improvement, expanded capacity, and enhanced data reporting infrastructure.

BACKGROUND

Safety-net clinics play a pivotal role in communities by providing access to preventive and primary health care services to the medically underserved, poor, and vulnerable populations. The safety-net clinics have been defined by the Institute of Medicine as providers who care for patients regardless of their ability to pay. Safety-net providers are a heterogeneous group and range from well-established federally qualified health centers (FQHCs) to smaller free clinics. Approximately 1100 FQHCs in the US provide care to more than 17 million patients each year, and this number is expected to grow to 30 million by 2015. Additionally, more than 1000 free clinics nationwide provide care to an estimated 1.8 million patients.

The changing US health care landscape has placed increasing demands on safety-net providers who must cope with a more clinically complex and shifting uninsured and newly insured population. Increasing the number of primary care providers in the safety-net setting has been proposed as one strategy to improve overall population health because primary care emphasizes prevention, detection, and early treatment.

Because of its longstanding commitment to improve the health of the communities it serves, Kaiser Permanente (KP) of the Mid-Atlantic States (KPMAS) established the Community Ambassador Program (CAP). KPMAS initially developed the CAP as a pilot project in 2008 to support the safety net in the communities served by KP in the Mid-Atlantic States Region. A diverse team of KPMAS staff shaped the CAP, which was modeled after a similar program in KP Southern California. The program places KP-employed nurse practitioners, midwives, and physician assistants to work in the safety-net clinics and improve the health of their (non-KP) patients, serve vulnerable populations, and share best practices. The goal of the CAP is to improve the health of the larger surrounding community within KP’s footprint by expanding access to care, increasing the capacity of selected safety-net providers, and improving quality of care on evidence-based measures through a long-term collaboration.
The specific objectives of the CAP were to match the expertise of select KPMAS staff with the identified needs of safety-net partners; to forge relationships between KPMAS and safety-net partners; to identify, to implement, and to evaluate outcomes in key areas of clinical focus; to support the clinical placement with the resources necessary to implement the program and to evaluate outcomes; to support and enrich the role of the Community Ambassadors in the field; to supplement the safety-net partnership with additional resources as needed such as training and education, grants, and expanded collaborations with KPMAS; to communicate regularly the goals, learnings, and outcomes of the program; and to identify unmet needs. Through this partnership, the Community Ambassadors were expected to export Permanente Medicine to the safety-net clinics by sharing evidence-based practices from the KP model of care as well as to contribute expertise in their area of clinical specialty. KPMAS also hoped to learn from the safety-net clinics how to better care for and to manage vulnerable populations with complex chronic conditions and challenging social needs.

The CAP initially began in 2008 with three clinicians (two nurse practitioners and one physician assistant) placed across one FQHC and two free clinics (one clinician based at each site). Although no formal data were collected from the initial pilot program in 2008, all three of the administrators of the safety-net clinics that were interviewed during the initial pilot perceived the program to be a success in improving continuity of care and in expanding access for patients with complex chronic conditions, bringing clinical expertise to the safety-net clinic partners, expanding Permanente evidence-based best medical practices, and building relationships between KP and the safety-net clinics.

Beginning in September 2011, KPMAS expanded the CAP to 18 safety-net clinics in Washington, DC, Northern Virginia, and suburban Maryland, which in total were served by 32 mid-level clinicians (25.16 full-time equivalents [FTEs]). The Mid-Atlantic safety-net clinics included a diverse mix of providers that comprised large FQHCs, free clinics, and other community-based clinics. The purpose of this article is to share the early experiences of the CAP and to describe the initial results of the program’s impact on the safety-net clinics.

**METHODS**

We conducted an assessment of the 18 safety-net clinics that participated in the CAP in 2012 to determine the program’s early impact in expanding health care access and improving quality of care in the year following program expansion. The types of clinics served by the Community Ambassadors included a mix of FQHCs (n = 6) that primarily served Medicaid patients, free clinics (n = 4) that served the uninsured, and other community-based clinics (n = 8). The community-based clinics comprised faith-based organizations (ie, Catholic charity), public-private partnerships (ie, county-sponsored community health care network, clinics dedicated to serving language minorities), specialty clinics (ie, teen and young adult reproductive health organization), and hospital-based outpatient clinics (ie, hospital-based pediatric program). Although the safety-net clinics that participated in the CAP were quite diverse in terms of the specific populations they served and types of services provided, all of the safety-net clinics had an overarching mission of caring for low-income, uninsured or underinsured, vulnerable, and underserved populations.

We asked the clinics to respond to questions regarding their improvements in care delivery and in adoption of evidence-based practices promoted by KPMAS. The clinics were also queried regarding their data collection infrastructure. We included a comments section in the assessments where the clinics could enter free text to provide any additional points that they wanted to elaborate on or to clarify. The assessments were completed by the safety-net clinic’s administrative officer, medical director, or designated staff.

We also asked the clinics to report on their utilization that included the number of unduplicated patients and encounters for primary care-related visits with a clinician (excluding behavioral health, dental, and other types of visits) at the clinic level in the year before and following implementation of the CAP. The clinics were requested to provide the counts on the basis of the subpopulation(s) (adult, pediatrics, and/or obstetrics/gynecology [Ob/Gyn]) served by their assigned Community Ambassador(s). In addition, we also requested that the clinics report on the utilization measures specifically for the Community Ambassador in 2012. Three of the non-FQHCs only collected utilization data based on their fiscal year (July through June), and four clinics were unable to disaggregate their data by subpopulation or to report for primary care visits only. Because of these aforementioned data issues, the reported counts of unduplicated patients and encounters in the following results section represent estimates. These estimates reflect data reported directly by the clinics of their closest approximation on their number of patients and utilization. In addition, one clinic that served the pediatric population was not able to report data for one of the years and was excluded from the analyses.

We also asked the safety-net clinics to report on standardized quality measures. Because the non-FQHCs and free clinics did not routinely collect standardized quality measures and had varying reporting capabilities, we asked only the FQHCs to report on the standardized quality-of-care measures. The 6 participating FQHCs were asked to submit their data on select Health Resources and Services Administration Uniform Data System quality-of-care measures and on select National Committee for Quality Assurance Healthcare Effectiveness Data and Information Set measures for hemoglobinA1c testing for adult and pediatric diabetics and breast cancer screening. The FQHCs were instructed to report on the quality measures at the clinic level for the subpopulation(s) (adults, pediatrics, and/or Ob/Gyn) served by their Community Ambassador in the 2011 (pre-CAP) and 2012
RESULTS

Improvements in Patient Care Delivery

All 18 of the clinics responded to the CAP assessment for a 100% completion rate. Seventeen of the clinics reported that the CAP helped them to improve the delivery of patient care. For example, 4 clinics reported in the open-ended section that the CAP allowed them to extend their service to weekend or evening hours. Another two clinics reported that the CAP enabled them to increase their capacity to provide pediatric care. Also, one clinic indicated that the CAP permitted them to increase their capacity for prenatal care.

Additionally, the CAP allowed clinics to provide new or enhanced clinical services, including the ability to provide on-site colposcopies (n = 2) and expand gynecology services (n = 5), such as breast exams and pap smears that were previously referred out. Furthermore, 14 of the clinics reported that the CAP allowed them to increase their capacity to offer same day appointments.

Adoption of Evidence-Based Practices

Several of the Community Ambassadors reported that they adopted evidence-based practices that were promoted at KPMAS. For example, the Community Ambassadors at three of the clinics reported that they implemented the A-L-L (aspirin, lisinopril, and lipid-lowering) medications program for patients with diabetic mellitus to reduce cardiovascular risk. The Community Ambassadors at two clinics reported that they implemented hypertension control protocols and immunization programs (i.e., pneumonia, hepatitis B). In addition, the Community Ambassador at one clinic developed a pilot project to integrate behavioral health with primary care through a partnership with the county primary care coalition.

Access to Care and Quality of Care

Among the participating safety-net clinics, the Community Ambassadors provided care to the adult population 18 years and older (n = 12 clinics), pediatric population birth to age 17 years (n = 4 clinics), and Ob/Gyn patients age 24 to 69 years (n = 5 clinics). The clinics could have served more than one subpopulation type.

At the clinic level, the overall change in the estimated number of unduplicated patients served by the safety-net clinics from pre- to post-CAP implementation increased by approximately 5% for adults and 11% for pediatric patients. However, the number of Ob/Gyn patients was relatively stable between years (-2%). On the basis of the number of patient encounters, the adult population was nearly unchanged (-1%), but there was a substantial increase in the number of pediatric (11%) and Ob/Gyn (6%) encounters (Table 1).

In 2012, the Community Ambassadors provided an estimated 14,571 encounters to 5287 adult patients, 5028 encounters to 1981 pediatric patients, and 12,650 encounters to 4720 Ob/Gyn patients (Table 2). This translates into an estimated 1191 encounters per FTE Community Ambassador for the adult population, 1047 encounters per FTE Community Ambassador for the pediatric population, and 1561 encounters per FTE Community Ambassador for the Ob/Gyn population. These counts represent an underestimation, however, because 5 of the clinics did not have the capability to report data at the provider level and were excluded from the provider-level analyses.

<table>
<thead>
<tr>
<th>Table 1. Estimated number of unduplicated patients and primary care encounters served by the safety-net clinics by subpopulation, 2011-2012*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subpopulation</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>No. of adult patients (≥ 18 years)a</td>
</tr>
<tr>
<td>No. of pediatric patients (0-17 years)b</td>
</tr>
<tr>
<td>No. of Ob/Gyn patients (24-69 years)c</td>
</tr>
</tbody>
</table>

a For three clinics, data are available for fiscal year only. Data are only included for clinics that provided results for both years.
b Data are available for overall clinic population only for four clinics (clinics are unable to stratify by age) and are included with the adult population.
c Data include nurse-only and behavioral health visits for one of the clinics in 2011.

| Ob/Gyn = obstetrics/gynecology. |

<table>
<thead>
<tr>
<th>Table 2. Estimated number of unduplicated patients and primary care encounters served by the community ambassador by subpopulation, 2012*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subpopulation</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>No. of adult patients (≥ 18 years)a</td>
</tr>
<tr>
<td>No. of pediatric patients (0-17 years)</td>
</tr>
<tr>
<td>No. of Ob/Gyn patients (24-69 years)c</td>
</tr>
</tbody>
</table>

a For three clinics, data are available for fiscal year only.
b Data are available for entire population only for four clinics (clinics are unable to stratify by age) and are included with the adult population.
c Ob/Gyn = obstetrics/gynecology.
From the quality-of-care process measures based on data from the FQHCs, the clinics performed close to or more than 90% for adult asthma therapy and adult weight screening in 2012. Additionally, the largest improvements in quality over time were made for adult weight screening (37% increase) and adult tobacco use assessment (24% increase). Smaller improvements in quality were made for cervical cancer screening (7%) and breast cancer screening among women (11% increase). However, the clinics' performance decreased between years for adult smoking cessation intervention (-11%) and modestly declined for adult hypertension control (-3%) (Table 3).

At the Community Ambassador level, performance was at or near 90% for two adult quality measures (weight screening and tobacco use assessment) in 2012. This compares with a 45% and 74% performance on the same Uniform Data System measures, respectively, by FQHCs in the state of Maryland overall. Performance for adult tobacco use screening, adult hypertension control, and cervical cancer screening were higher among the patients seen by the Community Ambassador than by the safety-net clinics in general. The Community Ambassador performance for adult hypertension control was higher than the clinics' performance (73% vs 64%) and performance by FQHCs in the state of Maryland (61%). For breast cancer screenings, performance among the Community Ambassadors was much lower (48%) (Tables 3 and 4).

**DISCUSSION**

On the basis of this early evaluation, the leadership of the participating clinics considered the CAP to be a valuable support in the Mid-Atlantic States Region. The clinics were overwhelmingly satisfied with their participation in the CAP. In some cases, this program also helped the safety-net clinics to improve patient care delivery by extending their service hours, expanding programs, increasing capacity, and improving patient satisfaction. Additionally, the CAP allowed the clinics to increase access to care for specific subpopulations, as well as to improve the quality of care on certain key quality measures.

Although the Community Ambassadors provided nearly 1000 encounters per FTE for each of the subpopulations served, this was much lower than the target of approximately 4000 encounters per clinician. Several reasons for the lower-than-expected productivity include an underreporting of clinician encounters by the clinics, a high no-show rate of patients, electronic medical record (EMR) implementation that decreased the number of available appointment slots during this transition period, treating more complex patients who required longer visits, more procedure-based encounters by some Community Ambassadors, insufficient patient volume at a few clinics, and some initial learning by the clinics on how to best incorporate their Community Ambassadors into the clinic workflow.

On the basis of these findings, there is a potential for increased capacity by the Community Ambassadors.

In terms of improving quality of care, the largest improvements were made for adult weight screening, adult tobacco use assessment, and breast cancer screening among women. Despite these achievements, opportunities for quality improvement remain. For example, performance by the clinics and Community Ambassadors for breast cancer screening and adult hypertension control were much lower than the other quality measures. These represent areas of focus for targeted quality improvements.

**Table 3. Federally qualified health center clinic-level performance on select quality measures, 2011-2012**

<table>
<thead>
<tr>
<th>Quality measure</th>
<th>No. of clinics</th>
<th>2011</th>
<th>2012</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult weight screening and follow-up (≥ 18 years)</td>
<td>2</td>
<td>63</td>
<td>140</td>
<td>40</td>
</tr>
<tr>
<td>Adult tobacco use assessment (≥ 18 years)</td>
<td>3</td>
<td>51</td>
<td>4620</td>
<td>83</td>
</tr>
<tr>
<td>Adult tobacco cessation intervention (≥ 18 years)</td>
<td>2</td>
<td>74</td>
<td>140</td>
<td>54</td>
</tr>
<tr>
<td>Adult asthma therapy (18-40 years)</td>
<td>2</td>
<td>89</td>
<td>238</td>
<td>86</td>
</tr>
<tr>
<td>Adult hypertension control (18-85 years)</td>
<td>2</td>
<td>68</td>
<td>140</td>
<td>64</td>
</tr>
<tr>
<td>Cervical cancer screening among women (24-69 years)</td>
<td>5</td>
<td>56</td>
<td>8663</td>
<td>65</td>
</tr>
<tr>
<td>Breast cancer screening among women (40-69 years)</td>
<td>5</td>
<td>36</td>
<td>7569</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Per UDS guidelines, denominator of patients may be based on a sample of patients.
* Based on the UDS measure definitions.
* Based on the Healthcare Effectiveness and Data Information Set measure definitions.
* MD = Maryland; UDS = Uniform Data System.
Through the CAP, KP has experienced a bidirectional learning opportunity. KP has been able to nurture relationships with the safety-net clinics, learn more about the unique challenges of safety-net patients, and gain a better understanding of the safety-net clinic practices, challenges, and innovations. For instance, the Community Ambassadors indicated that they had to do more with less because they did not have access to KP’s resources. As a result, they needed to identify community resources for services such as specialty care for patients without the ability to pay. The Community Ambassadors also noted that they had to deal with treating a much more complicated patient population with challenging social needs. This experience allowed the Community Ambassadors to learn more about social services available in the community and how to treat a wider range of medical conditions that they had never previously dealt with at KP.

In return for their CAP participation, the safety-net clinics have been able to gain more clinicians in their clinic, leverage grant funding opportunities, receive technical assistance, obtain project resources, and acquire KP’s expertise. As an example, the Community Ambassadors helped two clinics to pursue grant resources for a school-based health clinic and a breast cancer initiative. The Community Ambassadors also helped to connect the clinics to local coalitions and best practices-related resources. Furthermore, the Community Ambassadors have helped to implement evidence-based practices such as the A-L-L (aspirin, lisinopril, and lipid-lowering) cardiovascular risk reduction program for patients with diabetes, hypertension control protocols, and routine immunizations at several clinics.

Although the CAP has been viewed largely as an initial success, it was not without some particular challenges. Some of the challenges to the early program implementation were malpractice coverage, contracts with the clinics, and limited space in the clinics to accommodate the Community Ambassadors. In addition, the initial pairing of clinics and Community Ambassadors did not always work and there was limited data collection capacity. Another important challenge was that of overcoming language barriers with the lack of resources in the clinic setting. For example, one clinic reported that its patient population spoke more than five different languages.

The CAP evaluation also encountered some data limitations. As previously mentioned, the safety-net clinics had varying reporting capabilities that made uniform data collection difficult. Several of the clinics, the free clinics in particular, did not have an EMR infrastructure. Because of this issue, the clinics without EMR capabilities were unable to report data at the clinic level or for the calendar year. In addition, these clinics were not able to stratify their data by subpopulation or disaggregate nurse-only and behavioral health visits from primary care visits. Furthermore, because the non-FQHCs are not required to routinely collect information on standardized quality measures, the sample of clinics that reported on these measures was restricted to the FQHCs. Among the FQHCs that reported on the quality measures, the data were unreliable or unavailable for some of the measures and there was a small sample size of clinics and patients. As part of future CAP participation, all clinics will be required to report on standardized utilization and quality measures so that comparisons across clinics can be made.

There were also a number of issues with regard to the clinics’ productivity during the evaluation period that affected utilization. For example, several clinics were in the process of implementing their EMR, which resulted in decreased productivity. Furthermore, three clinics reported that they lost several clinicians and grant funding during this timeframe that resulted in a net decrease in the number of patients and encounters. In several of the clinics, the Community Ambassador was the only consistent clinician because other clinicians were volunteer staff or left because of budget cuts. For example, one clinic stated that they experienced a budget cut from the county and lost a full-time physician as a result. The KP Community Ambassadors were able to fill this void, which had an impact in treating the uninsured and underserved in this particular community. The CAP allowed these clinics to sustain their operations and continue to serve their patient population during this challenging period. Although going into the program, KP did not intend to fill the gap of clinicians because of budget shortfalls, this was the case in a few circumstances.

**CONCLUSION**

KP’s CAP has demonstrated some early success in expanding access to care for certain subpopulations and improving quality on several key measures for diverse populations in the Mid-Atlantic States safety-net clinics. However, opportunities for expanded capacity and quality improvement remain. There are also data reporting challenges in clinics.

<table>
<thead>
<tr>
<th>Quality measure</th>
<th>No. of clinics</th>
<th>Performance (%)</th>
<th>Denominator of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult weight screening and follow-up (≥18 years)</td>
<td>2</td>
<td>90</td>
<td>3202</td>
</tr>
<tr>
<td>Adult tobacco use assessment (≥18 years)</td>
<td>3</td>
<td>88</td>
<td>2533</td>
</tr>
<tr>
<td>Adult hypertension control (18-85 years)</td>
<td>2</td>
<td>73</td>
<td>645</td>
</tr>
<tr>
<td>Cervical cancer screening among women (24-69 years)</td>
<td>5</td>
<td>80</td>
<td>3952</td>
</tr>
<tr>
<td>Breast cancer screening among women (40-69 years)</td>
<td>4</td>
<td>48</td>
<td>2246</td>
</tr>
</tbody>
</table>

*Based on Uniform Data System measure definitions. Denominator of patients may be based on a sample of patients.*
without EMR capabilities and information technology infrastructure that need to be addressed.

Some future directions of the CAP include a continued emphasis on tracking and measuring changes to patient health outcomes by focusing on additional quality measures that are most relevant and feasible given the capabilities of the data systems of the safety-net clinics. This emphasis will allow the CAP to continue to determine whether the program is having a measurable impact in improving long-term patient outcomes.

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

Acknowledgment
Mary Corrado, ELS, provided editorial assistance.

References

Public Health
Throughout human history, the major problems of health that men have faced have been concerned with community life, for instance, the control of transmissible disease, the control and improvement of the physical environment (sanitation), the provision of water and food of good quality and in sufficient supply, the provision of medical care, and the relief of disability and destitution. The relative emphasis placed on each of these problems has varied from time to time, but they are all closely related, and from them has come public health as we know it today.

— George Rosen, MD, 1910-1977, American physician, public health administrator, journal editor, and medical historian
ORIGINAL RESEARCH & CONTRIBUTIONS

Alcohol Intake, Beverage Choice, and Cancer: A Cohort Study in a Large Kaiser Permanente Population

Arthur L Klatsky, MD; Yan Li, MD, PhD; H Nicole Tran, MD, PhD; David Baer, MD, PhD; Natalia Udaltsova, PhD; Mary Anne Armstrong, MA; Gary D Friedman, MD, MS

ABSTRACT

Context: Heavy intake of alcoholic beverages is associated with an increased risk of developing several types of cancers at specific body sites. However, evidence is conflicting regarding alcohol-associated cancers in other sites of the body as well as the role played by choice of wine, liquor, or beer.

Objective: To study incident cancer risk from 1978 to 1985 and through follow-up in 2012 relative to light-to-moderate and heavy drinking and to the choice of alcoholic beverage in a cohort of 124,193 persons.

Design: Cohort.

Main Outcome Measures: 1) Cox proportional hazards models controlled for 7 covariates to analyze alcohol-associated risk of any cancer and multiple specific types. 2) Similar analyses in strata of drinkers with or without a preponderant choice of wine, liquor, or beer and with or without inferred likelihood of underreporting.

Results: With lifelong abstainers as referent, heavy drinking (≥ 3 drinks per day) was associated with increased risk of 5 cancer types: upper airway/digestive tract, lung, female breast, colorectal, and melanoma, with light-to-moderate drinking related to all but lung cancer. No significantly increased risk was seen for 12 other cancer sites: stomach, pancreas, liver, brain, thyroid, kidney, bladder, prostate, ovary, uterine body, cervix, and hematologic system. For all cancers combined there was a progressive relationship with all levels of alcohol drinking. These associations were largely independent of smoking, but among light-to-moderate drinkers there was evidence of confounding by inferred underreporting. Beverage choice played no major independent role.

Conclusion: Heavy alcohol drinking is related to increased risk of some cancer types but not others. Because of probable confounding, the role of light-to-moderate drinking remains unclear.

INTRODUCTION

In observational studies\(^1\)\(^-\)\(^6\) alcohol intake has been consistently associated with increased risk of cancers of the oral cavity, pharynx, larynx, esophagus, liver, large intestine, and female breast. Reports conflict about associations between alcohol consumption and risk of malignancies of the stomach, pancreas, lung, bladder, prostate, endometrium, ovary, cervix, and skin. Limited data suggest possible inverse (ie, protective) associations between alcohol consumption and the risk of renal cell carcinoma\(^7\)\(^-\)\(^8\) and several types of hematologic malignancy.\(^9\)\(^-\)\(^11\) It seems clear that a comprehensive study of the role of drinking in cancer risk should examine all cancer plus individual cancer types.

Although cancer risk is clearest for heavier intake of alcohol, some reports\(^1\)\(^-\)\(^5\) suggest that light-moderate (light-to-moderate) drinking is also linked to increased cancer risk. Among specific cancer types, increased risk of light-moderate drinkers has most consistently been found in studies of female breast cancer.\(^12\)\(^-\)\(^14\) The associations of lighter alcohol intake with cancer are relatively weak, and there are plausible confounders. Thus, the role of light-moderate drinking in cancer risk remains unresolved.

Because drinking and smoking are associated habits in many populations,\(^15\)\(^-\)\(^16\) tobacco use is a potential confounder of some alcohol-cancer associations. Incomplete control for smoking could produce spurious alcohol associations with tobacco-related cancer types.\(^17\) Underreporting of heavier intake is another possible source of spurious linkage of light-moderate drinking with increased risk of cancer.\(^18\)\(^-\)\(^19\) Other potential confounders include chronic infections, diet, adiposity, exercise, air pollution, radiation exposure, and various chemicals.\(^17\)\(^,\)\(^18\) However, most of these probably do not have sufficiently strong associations with drinking to explain the observed alcohol-cancer associations.

Independent roles for nonalcohol ingredients in alcoholic beverages have long been of interest. Early examples include reports of promotion of esophageal cancer by congeners in calvados (apple brandy)\(^20\) and a possible role for beer in the risk of rectal cancer.\(^21\) The latter was later considered confounded.\(^22\) In recent years, interest about this aspect has focused on hypothetical protective effects of phenolic compounds in red wine, especially resveratrol.\(^23\)\(^,\)\(^24\)

Hoping to cast light on several of these uncertainties, we have performed a cohort analysis in a large, multiethnic...
Northern California population. We report here data about risks for all cancer and specific cancer types associated with light-moderate and heavier drinking. The analysis is controlled for smoking and several other confounders. We also present data about risk of cancer among a strata of persons who drink preponderantly wine, liquor, or beer.

**MATERIALS AND METHODS**

**Study Population and Data**

The study protocols were approved by the Kaiser Permanente (KP) Northern California institutional review board. Baseline data were obtained from questionnaires given at health examinations from 1978 through 1985. The examinees were a multiethnic cohort of 124,193 men and women (mean baseline age = 41.0 years) who had no history of cancer and who were members of a comprehensive prepaid health plan in the San Francisco Bay Area. Usually taken as a voluntary routine health appraisal, the examination included health measurements, self-classified ethnicity, and queries about sociodemographic status, habits, medical history, and symptoms. Data about alcohol consumption were supplied during the examination on a special check-sheet questionnaire. The study cohort comprised 79.8% of all examinees; the remainder included persons who took the examination during absences of a special research clerk and persons who declined, largely because of lack of fluency in English.

Lifelong abstainers were defined as persons who reported drinking no alcohol during the past year and “never or almost never” before the past year. Ex-drinkers were nondrinkers during the past year who indicated prior alcohol drinking. Current drinkers described usual drinking as less than one drink per month ("special occasions only”), more than one drink per month but less than one drink per day, or as daily number of drinks, one to two, three to five, six to eight, and nine or more. Drinkers received separate questions about the number of days per week that they drank wine, liquor, or beer. Wine, liquor, or beer “preponderance” was defined among persons reporting more than one drink per month as exclusive intake of one beverage type or drinking the beverage type more days per week than either of the other two; preponderance was “none” for persons reporting more than one type with equal frequency.

**Subjects with Cancer**

Occurrence of cancer was ascertained from the KP Cancer Registry, which covers all subscribers and contributes to the local Surveillance, Epidemiology, and End Results (SEER) program. Codes were translated into International classify ethnicity, and queries about sociodemographic status, habits, medical history, and symptoms. Data about alcohol consumption were supplied during the examination on a special check-sheet questionnaire. The study cohort comprised 79.8% of all examinees; the remainder included persons who took the examination during absences of a special research clerk and persons who declined, largely because of lack of fluency in English.

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**Table 1. Selected traits of study cohort and cancer subjects**

<table>
<thead>
<tr>
<th>Trait</th>
<th>Cohort, number (%)</th>
<th>Cancer, number (%)</th>
<th>Crude rate/1000 person-years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>124,193 (100)</td>
<td>16,837 (100)</td>
<td>8.4</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>55,040 (44.3)</td>
<td>8853 (47.5)</td>
<td>9.2</td>
</tr>
<tr>
<td>Women</td>
<td>69,153 (55.7)</td>
<td>9784 (52.5)</td>
<td>7.8</td>
</tr>
<tr>
<td>Race and ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>33,625 (27.1)</td>
<td>5131 (27.5)</td>
<td>8.1</td>
</tr>
<tr>
<td>White</td>
<td>68,597 (55.2)</td>
<td>11,072 (59.4)</td>
<td>9.5</td>
</tr>
<tr>
<td>Asian</td>
<td>13,344 (10.7)</td>
<td>1522 (8.2)</td>
<td>5.9</td>
</tr>
<tr>
<td>Hispanic</td>
<td>5620 (4.5)</td>
<td>614 (3.3)</td>
<td>5.7</td>
</tr>
<tr>
<td>Other</td>
<td>2767 (2.2)</td>
<td>274 (1.5)</td>
<td>5.7</td>
</tr>
<tr>
<td>Usual alcohol intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>14,726 (11.9)</td>
<td>2065 (11.1)</td>
<td>7.6</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>3974 (3.2)</td>
<td>738 (4.0)</td>
<td>11.3</td>
</tr>
<tr>
<td>&lt; 1 drink/day</td>
<td>71,805 (57.8)</td>
<td>9974 (53.5)</td>
<td>7.7</td>
</tr>
<tr>
<td>1-2 drinks/day</td>
<td>22,304 (18.0)</td>
<td>3807 (24.0)</td>
<td>9.7</td>
</tr>
<tr>
<td>≥ 3 drinks/day</td>
<td>10,051 (8.1)</td>
<td>1811 (9.7)</td>
<td>10.8</td>
</tr>
<tr>
<td>Alcoholic beverage preponderance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wine</td>
<td>16,765 (13.5)</td>
<td>2672 (14.3)</td>
<td>8.9</td>
</tr>
<tr>
<td>Liquor</td>
<td>8696 (7.0)</td>
<td>1922 (10.3)</td>
<td>12.8</td>
</tr>
<tr>
<td>Beer</td>
<td>11,218 (9.0)</td>
<td>1361 (7.3)</td>
<td>7.2</td>
</tr>
<tr>
<td>None</td>
<td>41,267 (33.2)</td>
<td>5826 (31.2)</td>
<td>8.0</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>59,558 (48.0)</td>
<td>7656 (41.1)</td>
<td>6.98</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>27,501 (22.1)</td>
<td>5031 (27.0)</td>
<td>10.22</td>
</tr>
<tr>
<td>&lt; 1 pack/day</td>
<td>20,762 (16.7)</td>
<td>3008 (16.1)</td>
<td>8.32</td>
</tr>
<tr>
<td>≥ 1 pack/day</td>
<td>11,351 (9.1)</td>
<td>2166 (11.6)</td>
<td>11.73</td>
</tr>
<tr>
<td>Unknown</td>
<td>5021 (4.0)</td>
<td>776 (4.2)</td>
<td>9.54</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25 kg/m²</td>
<td>75,529 (60.8)</td>
<td>9699 (52.0)</td>
<td>7.30</td>
</tr>
<tr>
<td>25-29 kg/m²</td>
<td>34,597 (27.9)</td>
<td>6378 (34.2)</td>
<td>10.09</td>
</tr>
<tr>
<td>≥ 30 kg/m²</td>
<td>14,067 (11.3)</td>
<td>2560 (13.7)</td>
<td>10.01</td>
</tr>
<tr>
<td>Unknown</td>
<td>2319 (1.9)</td>
<td>302 (1.6)</td>
<td>7.84</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No college</td>
<td>34,069 (27.4)</td>
<td>5979 (32.1)</td>
<td>9.88</td>
</tr>
<tr>
<td>Some college</td>
<td>42,480 (34.2)</td>
<td>6118 (32.8)</td>
<td>7.88</td>
</tr>
<tr>
<td>College graduate</td>
<td>44,899 (36.2)</td>
<td>6196 (33.3)</td>
<td>7.82</td>
</tr>
<tr>
<td>Unknown</td>
<td>2745 (2.2)</td>
<td>346 (1.9)</td>
<td>8.04</td>
</tr>
</tbody>
</table>

*Not all respondents answered all questions.*

*There were also 1113 drinkers who did not state an amount of usual intake. These drinkers were included in a separate category in some models, but we present no data about these results.

*Among drinkers of > 1 per month (never drinkers, ex-drinkers, and drinkers of < 1 drink per month were excluded). Preponderant beverage drinkers reported more days per week consuming that beverage than either of the other 2 beverage types; if 2 or more types were reported with equal frequency, preponderance was “none.”
Classification of Diseases, Ninth Revision (ICD-9) codes and the composite incidence of codes 140 to 209 (N = 18,637) was studied as “all cancer.” Endpoints studied included any cancer and multiple specific cancer types. We report here data about the 15 types of cancer with 150 or more incident cases plus the following 3 composites: 1) Upper airway digestive (UAD) cancers included 552 subjects with 1 or more of codes 140 (lip), 141 (tongue), 143 (gum), 144 to 145 (mouth), 146 (oropharynx), 148 (hypopharynx), 149 (other oral cavity), 150 (esophagus), and 161 (larynx). 2) Hematologic malignancies included 1639 subjects with 1 or more of codes 201 (Hodgkin disease), 202 (non-Hodgkin lymphoma), 203 (multiple myeloma), 204 (lymphocytic leukemia), 205 (myelocytic leukemia), and 206 to 208 (other leukemia). 3) “Alcohol-related” malignancies included 9246 subjects with 1 or more of the following types: UAD, codes 153-154 (colorectal), 155 (liver), 162 (lung), 172 (melanoma), and 174 (breast).

Table 1 presents selected distributions in the study population and subjects with cancer.

Analytic Methods
Subjects were followed until December 31, 2012, or until a diagnosis of cancer, their death, or other termination of Health Plan membership. The mean follow-up was 17.8 years, yielding an estimated 2,216,631 person-years of follow-up. Multivariate models used the Cox proportional hazards model. Alcohol was studied categorically. In most models, lifelong abstainers were the referent with 4 other categories: ex-drinkers, less than 1 drink per day (2 categories combined), 1 to 2 drinks per day, and 3 or more drinks per day (3 categories combined). Models for all persons and for subgroup strata included as covariates age (continuous), race or ethnicity (white referent, black, Asian, Hispanic, other), education (no college referent, some college, college graduate), body mass index (< 25 kg/m² referent, 25-29 kg/m², ≥ 30 kg/m²), marital status (married referent, never married, formerly married), and cigarette smoking (never smoked referent, ex-smoker, current < 1 pack per day, current ≥ 1 pack per day).

Beverage choice was studied among persons reporting more than one drink per day. These drinkers were stratified into persons defined as reporting preponderance as wine, liquor, beer, or none. Models limited to each of these preponderance beverage groups ascertained the role of total alcohol in each stratum. These models used less than one drink per day in each preponderance as referent, plus one to two and three or more drinks per day as the other categories.

Among light-moderate drinkers, we studied strata of persons inferentially suspected or not suspected of underreporting alcohol intake. These strata were derived from subjects with at least two computer-aided examinations (index measurement and at least one other examination before or after). Suspected underreporters either reported heavier intake at another time or had an alcohol-related diagnosis (death certificate, hospitalization, or outpatient) at some time. A more detailed description of this method has been published.7 We report hazard ratios (HRs), 95% confidence intervals (CIs), and associated p values. The term significant is used in this article for p values < 0.05. We refer to persons reporting 3 or more drinks per day as “heavy” drinkers and to those reporting less than 1 or 1 to 2 drinks per day as “light-moderate” drinkers.

RESULTS
All Cancer
The risk of any cancer was increased by 10% to 20% in daily drinkers (Table 2). The progressive nature of this relationship was partially masked by rounding; for example, for all persons the HR was 1.10 at less than 1 drink per day, 1.15 at 1 to 2 drinks per day, and 1.23 at 3 or more drinks per day. The magnitude of the increased risk was generally similar for the sexes, race/ethnic groups, and smoking strata but did appear to weaken after 20 years. Ex-drinkers also had a higher risk than lifelong abstainers, but not for cancers diagnosed after 20 years.

<p>| Table 2. Adjusted hazard ratios for all cancers by alcohol intake versus never drinkers in all subjects and selected groups* |</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>No. of cancer subjects</th>
<th>Alcohol intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ex-drinker (95% CI)</td>
<td>&lt; 1 drink/day (95% CI)</td>
</tr>
<tr>
<td>All</td>
<td>18,637</td>
<td>1.2 (1.1-1.3)^a</td>
</tr>
<tr>
<td>Sex and race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>8853</td>
<td>1.2 (1.1-1.4)^b</td>
</tr>
<tr>
<td>Women</td>
<td>9784</td>
<td>1.2 (1.0-1.3)^c</td>
</tr>
<tr>
<td>White</td>
<td>11,072</td>
<td>1.4 (1.2-1.5)^d</td>
</tr>
<tr>
<td>Black</td>
<td>5131</td>
<td>1.1 (1.0-1.3)</td>
</tr>
<tr>
<td>Asian</td>
<td>1552</td>
<td>1.0 (0.7-1.4)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>614</td>
<td>1.2 (0.8-2.0)</td>
</tr>
<tr>
<td>Baseline smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>7656</td>
<td>1.2 (1.0-1.4)^e</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>5031</td>
<td>1.3 (1.1-1.6)^f</td>
</tr>
<tr>
<td>Smoke &lt; 1 pack/day</td>
<td>3008</td>
<td>1.1 (0.9-1.4)</td>
</tr>
<tr>
<td>Smoke ≥ 1 pack/day</td>
<td>2166</td>
<td>1.2 (0.9-1.6)</td>
</tr>
<tr>
<td>Interval between baseline examination and cancer diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer before 10 years</td>
<td>5185</td>
<td>1.4 (1.2-1.6)</td>
</tr>
<tr>
<td>Cancer in 10-20 years</td>
<td>6295</td>
<td>1.3 (1.2-1.5)^g</td>
</tr>
<tr>
<td>Cancer after 20 years</td>
<td>7157</td>
<td>1.0 (0.9-1.2)</td>
</tr>
</tbody>
</table>

* Separate Cox proportional hazards models controlled for age, sex, race or ethnicity, body mass index, education, marital status, and smoking.

1 p < 0.001.
2 p < 0.01.
3 p < 0.05.
CI = confidence interval.
Specific Cancers

Table 3 presents data for specific cancer types and several composites. Heavy drinkers had a significantly increased risk of the following cancer types: UAD, colorectal, lung, melanoma, and breast. Light-moderate drinkers had an increased risk of all of these except lung cancer. The following types of cancer were unrelated to baseline alcohol intake: stomach, pancreas, liver, kidney, brain, thyroid, prostate, bladder, cervix, ovary, uterine body, and hematologic system. Ex-drinkers were at increased risk of UAD, liver, breast, and brain cancers. Table 3 includes data about the relationships of total alcohol intake to the alcohol-related composite; as expected, the HRs were larger than those for all cancer and were progressive with increasing alcohol intake.

Among UAD subgroups, heavier drinkers had an increased risk of each type. For example, for esophageal cancer the HR was 2.2 (CI = 1.0 to 4.9, p < 0.05), for laryngeal cancer it was 1.9 (CI = 1.2 to 3.0, p < 0.01) and for the remaining UAD cancers it was 2.6 (CI = 1.4 to 4.5, p < 0.001). The lower risk of heavy drinkers for hematologic malignancies was of borderline significance (p = 0.06). Among hematologic subtypes, all had inverse alcohol relationships, but p was < 0.05 only for lymphatic leukemia (HR = 0.5; CI = 0.3 to 0.98).

Alcohol-Associated Risk in Never Smokers

The data in Table 2 show generally similar alcohol-associated cancer risk among smoking strata, including never smokers. For the alcohol-related composite, the HR among never smokers reporting 3 or more drinks per day was 1.3 (CI = 1.1 to 1.6, p < 0.001). Three types of cancer had significant relationships among never smokers reporting 3 or more drinks per day, with these HRs: UAD = 1.3 (CI = 1.1 to 1.6), liver = 4.2 (CI = 2.2 to 2.8), and melanoma = 1.8 (CI = 1.2 to 2.8), all with p < 0.001.

Covariate Associations

Table 4 presents selected covariate data for all cancer and for the alcohol-related composite. For all cancer, age, male sex, black race, obesity, and smoking were associated with increased risk. For the composite, women had higher risk, driven by the large number with breast cancer, and black persons had slightly lower risk than whites, driven by the virtually total absence of melanoma. Smoking was slightly more strongly related to the composite, driven by the large number of lung cancer cases.

Beverage Preponderance Strata

With drinkers of less than 1 per day as referent, there was a significantly increased risk among heavy drinkers in the groups with a beer preponderance and with no beverage preponderance (Table 5); these findings were similar for men and women (data not shown). Analyses in the alcohol-associated composite showed that heavy drinkers in all preponderence groups evinced significant associations, with a slightly larger HR for the beer preponderence group; these HRs were similar for men and women (data not shown) except for liquor preponderence (HR for men = 1.7, p < 0.001; for women, HR = 1.1, not significant). Relationships of heavy drinkers in preponderence groups differed for the individual cancers except that all groups showed significant associations with UAD; only beer was significantly associated with breast cancer; only wine was significantly related to melanoma. The no preponderence group had a significantly higher risk of liver cancer.

Suspected Underreporter Strata

Among light-moderate drinkers, increased alcohol-associated cancer risk was concentrated in the stratum suspected of underreporting. For example, among persons reporting 1 to 2 drinks per day on the index examination but

| Table 3. Adjusted hazard ratios of alcohol intake versus never drinkers to incidence of specific cancers and selected composites* |
|---|---|---|---|---|---|---|
| Cancer type (ICD-9 code) | No. of cases | Ex-drinker (95% CI) | < 1 drink/day (95% CI) | 1-2 drinks/day (95% CI) | ≥ 3 drinks/day (95% CI) |
| Upper airway digestive* | 552 | 2.9 (1.9-4.6)* | 1.1 (0.8-1.6) | 1.5 (1.1-2.3)* | 2.5 (1.7-2.8)* |
| Stomach (151) | 403 | 1.1 (0.7-1.8) | 0.9 (0.7-1.2) | 0.8 (0.6-1.4) | 0.8 (0.5-1.3) |
| Colorectal (153-154) | 2148 | 1.1 (0.9-1.4) | 1.1 (1.0-1.3) | 1.2 (1.0-1.4)* | 1.4 (1.1-1.7)* |
| Liver (155) | 213 | 1.9 (1.0-3.7)* | 1.0 (0.6-1.5) | 1.5 (0.9-2.5) | 1.5 (0.8-2.7) |
| Pancreas (157) | 535 | 1.3 (0.8-2.0) | 0.9 (0.7-1.2) | 1.1 (0.8-1.5) | 1.0 (0.7-1.5) |
| Lung (162) | 1989 | 1.2 (0.9-1.5) | 1.0 (0.9-1.2) | 1.0 (0.8-1.2) | 1.3 (1.1-1.6)* |
| Melanoma (172) | 1164 | 1.4 (0.9-2.2) | 1.6 (1.2-2.1)* | 1.9 (1.4-2.6)* | 2.2 (1.6-3.1)* |
| Breast (174) | 3639 | 1.3 (1.1-1.6)* | 1.1 (1.0-1.2)* | 1.2 (1.1-1.4)* | 1.3 (1.1-1.5)* |
| Cervix (180) | 727 | 1.2 (0.7-2.0) | 1.0 (0.8-1.3) | 1.0 (0.8-1.4) | 1.0 (0.7-1.6) |
| Uterus (182) | 689 | 0.7 (0.4-1.3) | 1.0 (0.8-1.2) | 1.0 (0.7-1.3) | 1.1 (0.7-1.7) |
| Ovary (183) | 341 | 1.2 (0.6-2.5) | 1.2 (0.9-1.6) | 1.2 (0.8-1.8) | 1.2 (0.7-2.2) |
| Prostate (185) | 3408 | 1.1 (0.9-1.3) | 1.1 (0.9-1.2) | 1.1 (1.0-1.3) | 1.1 (1.0-1.4) |
| Bladder (188) | 813 | 1.3 (0.9-2.0) | 1.2 (0.9-2.6) | 1.3 (0.9-1.7) | 1.1 (0.8-1.6) |
| Kidney (189) | 383 | 1.3 (0.8-2.0) | 1.0 (0.7-1.4) | 0.9 (0.6-1.4) | 1.0 (0.6-1.6) |
| Brain (191) | 186 | 2.7 (1.2-6.3)* | 1.5 (0.8-1.9) | 1.5 (0.7-2.5) | 1.4 (0.6-2.1) |
| Thyroid (193) | 172 | 0.8 (0.3-2.3) | 1.0 (0.6-1.6) | 0.8 (0.3-1.1) | 0.6 (0.3-1.4) |
| Hematologic (201-208) | 1639 | 0.8 (0.6-1.1) | 1.1 (0.9-1.2) | 1.0 (0.8-1.2) | 0.8 (0.6-1.0) |
| Alcohol-relatedd | 9246 | 1.4 (1.2-1.5)* | 1.1 (1.0-1.2)* | 1.2 (1.1-1.3)* | 1.5 (1.3-1.6)* |

* Separate Cox proportional hazards models controlled for age, sex, race or ethnicity, body mass index, education, marital status, and smoking.

* Includes ICD-9 codes 140 (lip), 143 (tongue), 143 (gum), 144-145 (mouth), 146 (oropharynx), 148 (hypopharynx), 149 (other oral cavity), 150 (esophagus), and 151 (larynx).

* p < 0.001.

* p < 0.05.

* p < 0.01.

* Includes codes 201 (Hodgkin disease), 202 (non-Hodgkin lymphoma, 203 (multiple myeloma), 204 (lymphocytic leukemia), 205 (myelocytic leukemia), and 206-208 (other leukemia).

* Includes upper airway digestive, liver, colorectal, lung, breast, and melanoma.

CI = confidence interval; ICD-9 = International Classification of Diseases, Ninth Revision.
considered likely underreporters, the HR for any cancer was 1.4 (CI = 1.3 to 1.7, \( p < 0.001 \)), whereas among those considered unlikely to be underreporters, it was 1.1 (CI = 0.9 to 1.2). More details have been published.\(^{19} \)

**DISCUSSION**

**Disparate Alcohol-Cancer Relationships**

Our analyses confirmed the presence of increased risk in drinkers for most of the cancer types consistently related to alcohol in prior reports. The exception was liver cancer, possibly because there were relatively small numbers of this type. Because never smokers, ex-drinkers, and heavy drinkers with a beer preponderance had an increased risk of liver cancer, we left this type of cancer in the alcohol-related composite. We also found that drinkers had an increased risk of lung cancer and of melanoma. We found no support for an alcohol association with stomach cancer, pancreatic cancer, or any type of genitourinary cancer in either sex. A slight inverse relationship with hematologic malignancies was of borderline significance. A weakening of this inverse association since our previous report\(^{20} \) may be caused by a reduction in alcohol intake with increasing age. These disparities in alcohol-cancer associations are masked in the models for all cancer because the positive associations dominate.

Except for lung cancer, the increased cancer risk of baseline drinkers was present in both light-moderate drinkers and heavy drinkers, with progressive associations for all. The strongest alcohol-cancer associations among light-moderate drinkers were those with melanoma and breast cancer.

**Hypothetical Mechanisms**

Although ethyl alcohol is not a mutagenic carcinogen, its first metabolite acetaldehyde probably is.\(^{26,27} \) Hypothetically plausible mechanisms for alcohol-cancer associations vary with the sites. Genetic factors influencing alcohol metabolism may modulate alcohol-associated risk.\(^{5,26,27} \) For UAD cancers it has been proposed that alcohol may operate as a promoter or facilitator of smoking-associated risk.\(^{5,28} \) For UAD cancers, liver cancer, and breast cancer, a role has been proposed for acetaldehyde, which might damage DNA and thus act as a carcinogen.\(^{26,27} \) Chronic liver disease, usually cirrhosis, is intermediary between heavy alcohol intake and hepatocellular cancer, analogous to the situation for chronic viral hepatitis and cancer.\(^{26,27} \) There is evidence that an alcohol-estrogen interaction is involved in the breast cancer association.\(^{12-14} \) Estrogenic hormones are an established risk factor for breast cancer, and several analyses, including ours,\(^{14} \) show the increased breast cancer risk concentrated in women with estrogen-sensitive tumors. It has been suggested that relative folate deficiency may be involved in the relationships between alcohol and colorectal cancer, breast cancer, and others.\(^{29} \) A more detailed discussion of these and other potential mechanisms is beyond the scope of this report.

### Table 4. Adjusted hazard ratios of selected covariates to risk of all and alcohol-related cancer\(^{a} \)

<table>
<thead>
<tr>
<th>Trait (referent)</th>
<th>All cancer, n = 18,837</th>
<th>Alcohol-related cancer, n = 9246</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (× 10), years</td>
<td>1.7 (1.7-1.7) (^{p} )</td>
<td>1.7 (1.6-1.7) (^{p} )</td>
</tr>
<tr>
<td>Men (women)</td>
<td>1.2 (1.1-1.3) (^{p} )</td>
<td>0.6 (0.6-0.6) (^{p} )</td>
</tr>
<tr>
<td>Black (white)</td>
<td>1.1 (1.0-1.1) (^{p} )</td>
<td>0.9 (0.9-1.0) (^{p} )</td>
</tr>
<tr>
<td>Asian (white)</td>
<td>0.8 (0.8-0.9) (^{p} )</td>
<td>0.9 (0.8-0.9) (^{p} )</td>
</tr>
<tr>
<td>Hispanic (white)</td>
<td>0.8 (0.7-0.9) (^{p} )</td>
<td>0.7 (0.6-0.8) (^{p} )</td>
</tr>
<tr>
<td>Body mass index &gt; 30 kg/m(^{2} ) (&lt; 25 kg/m(^{2} ))</td>
<td>1.1 (1.1-1.2) (^{p} )</td>
<td>1.1 (1.0-1.1) (^{p} )</td>
</tr>
<tr>
<td>Ex-smoker (never)</td>
<td>1.2 (1.1-1.3) (^{p} )</td>
<td>1.2 (1.1-1.3) (^{p} )</td>
</tr>
<tr>
<td>Smoke &lt; 1 pack/day (never)</td>
<td>1.3 (1.3-1.4) (^{p} )</td>
<td>1.5 (1.4-1.6) (^{p} )</td>
</tr>
<tr>
<td>Smoke ≥ 1 pack/day (never)</td>
<td>1.8 (1.7-1.9) (^{p} )</td>
<td>2.3 (2.1-2.4) (^{p} )</td>
</tr>
<tr>
<td>College graduate (no college)</td>
<td>1.0 (1.0-1.1)</td>
<td>1.0 (1.0-1.1)</td>
</tr>
<tr>
<td>Never married (married)</td>
<td>1.0 (1.0-1.1)</td>
<td>0.9 (0.9-1.0)</td>
</tr>
</tbody>
</table>

\(^{a} \) Cox proportional hazards models controlled for age, sex, race/ethnicity, body mass index, education, marital status, smoking, and alcohol intake. Please see text for definition of “alcohol-related cancer.”

\(^{p} \) CI = confidence interval.

### Table 5. Adjusted hazard ratios of cancer by preponderant beverage type\(^{a} \)

<table>
<thead>
<tr>
<th>Group</th>
<th>Hazard ratio for ≥ 3 drinks per day vs &lt; 1 per day (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wine, no. with cancer = 2671</td>
</tr>
<tr>
<td>All cancer</td>
<td>1.1 (1.0-1.3)</td>
</tr>
<tr>
<td>Hba(_{1c})-related composite</td>
<td>1.3 (1.1-1.5) (^{p} )</td>
</tr>
<tr>
<td>UAD</td>
<td>2.1 (1.1-4.2) (^{p} )</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1.7 (1.2-2.3) (^{p} )</td>
</tr>
<tr>
<td>Breast</td>
<td>1.1 (0.8-1.5)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>1.4 (0.9-2.0)</td>
</tr>
<tr>
<td>Liver</td>
<td>1.0 (0.3-3.6)</td>
</tr>
<tr>
<td>Lung</td>
<td>1.2 (0.8-1.7)</td>
</tr>
</tbody>
</table>

\(^{a} \) Cox proportional hazards models controlled for age, sex, race/ethnicity, body mass index, education, marital status, smoking, and alcohol intake among drinkers of more than 1 drink per month (never drinkers, ex-drinkers, and drinkers of < 1 drink per month excluded). Preponderant beverage reported more days per week consuming that beverage than either of the other 2 beverage types; if 2 or more types were reported with equal frequency, preponderance was “none.”

\(^{p} \) CI = confidence interval; UAD = upper airway digestive; Hba\(_{1c}\) = HemoglobinA\(_{1c}\).
Alcohol Intake, Beverage Choice, and Cancer: A Cohort Study in a Large Kaiser Permanente Population

Lung Cancer
The powerful relationship of smoking to lung cancer complicates the study of alcohol relations.15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35 Detailed analysis of a KP analysis27,28 show that the alcohol association primarily involved adenocarcinoma in heavy-drinking women. In that report the adenocarcinoma HR for 3 or more drinks per day among women was 2.1 (CI = 1.4 to 3.1, p = 0.0002), vs men with HR = 1.0 (CI = 0.7 to 1.5). The HR for squamous cell carcinoma among women reporting 3 or more drinks per day was 1.2 (CI = 0.7 to 2.0). The smoking-lung cancer association was stronger for squamous cell cancer than for adenocarcinoma, a fact lessening the likelihood that residual confounding by smoking was involved. We cannot explain the cell type specificity.

Melanoma
Although there are previous reports of a possible increased risk of melanoma in drinkers,36 the association of drinking with an increased risk of melanoma in this analysis is noteworthy for its strength in both heavy and light drinkers. We have presented data showing that the alcohol-associated risk is similar for men and women.37 In our data38 and several other reports,39 smoking is inversely related to melanoma, so residual confounding by smoking is not a plausible explanation for this finding. A noteworthy feature in our melanoma analyses is that the alcohol association is stronger for noninvasive than invasive disease,40 suggesting an earlier diagnosis in drinkers. Earlier diagnosis could, in turn, be related to higher socioeconomic status and more recreational sun exposure. Among light-moderate drinkers wine preponderance is related to increased melanoma risk, another possible indicator of higher socioeconomic status.41 We hope that further work by others will help to sort out the alcohol/smoking/melanoma puzzle.

Beverage Choice
Although the beverage type data suggest a slightly stronger association with beer than with wine or liquor, the differences were not large and the CIs overlapped. In this population, female heavy drinkers of beer have unfavorable lifestyle traits,36 which may account for the slightly increased breast cancer risk in these women. We interpret our data as suggesting little, if any, disparity related to specific beverage types.

Limitations
As with all reported analyses of alcohol intake and cancer, this study is observational, leaving uncontrolled confounders (eg, dietary habits, cigar and pipe smoking, environmental smoke exposure, occupational factors, or exercise) as potential factors in the findings. Despite known relative stability of drinking in this population,37 determination of alcohol habits only at baseline is another limitation. Changes in habits probably accounted for weakening alcohol associations with the passage of time.

The beverage choice data are limited by the fact that the primary queries about wine, liquor, and beer inquired about number of days per week rather than the usual number of drinks. Thus, we do not know the actual proportion of each person’s intake represented. We do know from more detailed data in a 1984 to 1985 subset of examinees that there was good correlation of these values to the total number of drinks per week of the beverage type, with an average of 80% to 90% of alcoholic beverages consumed as the preponderant type.36

Public Health Consideration
Should these findings influence medical advice from health care professionals to patients? Increased cancer risk is clearly one of multiple medical reasons to avoid heavy drinking. The more important issue is the possible cancer risk of light-moderate alcohol intake. This issue remains clouded by uncertainty about whether the findings are confounded by underreporting and other traits. However, at present, a possible increased cancer risk at moderate intake should enter into individual estimations of the overall risk-benefit equation for alcohol drinking, especially for young persons. For most persons older than age 50 years, the overall benefits of lighter drinking, especially the reduced risk of atherothrombotic disease,38,39 outweigh possible cancer risk. This is best evidenced by lower total mortality risk among middle-aged and older light-moderate drinkers.39 For younger persons, especially young women with no coronary disease risk factors, the breast cancer data suggest the wisdom of limiting alcohol intake to very modest amounts. As always in medical practice, advice needs to be individualized.40

Disclosure Statement
All authors have participated actively in the execution of the study and/or preparation of the manuscript. The authors(s) have no conflicts of interest to disclose.

Acknowledgments
The research was performed at the Kaiser Permanente Northern California Division of Research with support by grants from the Kaiser Foundation Community Budget Program to Dr Li as Principal Investigator. Data collection in 1978 to 1985 was supported by a grant to Dr Klatsky from the Alcoholic Beverage Medical Research Foundation of Baltimore, MD. We are grateful to Cynthia Landy for assistance with data collection in 1978 to 1985.

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

References
After a man has taken wine or other spirituous liquors he is at once revived and restored. The reason is that in the mouth, oesophagus and stomach there are certain vital and animal spirits constantly scattered, roaming and, as it were, keeping watch. [Because these spirits are] analogous and proportionate to (those) in wine ... they readily mix. Then, taking their new guests by the hand, as it were, convey them to the heart and brain.

— Thomas Willis, 1621-1675, English physician contributor to the disciplines of anatomy, neurology, and psychiatry; founding member of the Royal Society
Lake Bled lies at the eastern end of the Zaka Valley in the Alps of northern Slovenia. This photograph was taken from the courtyard of Bled Castle, which perches 130 meters above the lake and dates back to the 11th century. In the center of the glacial and tectonic lake, on Slovenia’s only island, stands the Church of the Assumption of Maria. The church was rebuilt in the 17th century and is famous for its 99-step Baroque stairway and 15th-century Gothic frescos.

Dr Glassner is an Emergency Physician at the Walnut Creek Medical Center in CA.
ORIGINAL RESEARCH & CONTRIBUTIONS

Maintenance of Certification Part IV Quality-Improvement Project for Hypertension Control: A Preliminary Retrospective Analysis

Vallerie A Kolasinski, MPH, CHES; David W Price, MD, FAAFP

ABSTRACT

Context: A Maintenance of Certification Part IV project was created on the basis of an existing, multifaceted hypertension improvement program.

Objective: To evaluate the impact of the Maintenance of Certification project, the effects of the improvement options on blood pressure control in hypertensive patients, and the participants’ perception of the workload related to participation in the project.

Design: Nonexperimental retrospective analysis.

Setting: Kaiser Permanente hospitals and medical office buildings in Northern California.

Intervention: Participants used one or more options from a defined menu of strategies to attempt to increase the percentage of hypertensive patients on their patient panels who had controlled blood pressure.

Main Outcome Measure: Proportion of hypertensive patients with blood pressure \( \leq 139/89 \) mm Hg.

Results: Fifty-two American Board of Family Medicine and 19 American Board of Internal Medicine certified physicians completed projects. Mean panel blood pressure control improved from 79.49\% (standard deviation [SD] = 11.32) to 84.64\% (SD = 7.80). The choice of improvement option was not associated with the level of improvement or with the participants’ perception of the workload related to completing the project.

Conclusion: Project participants improved the care of their patients without an increased perceived burden to their practice. We found no association between the choice of improvement option and either the level of improvement or the perception of workload.

INTRODUCTION

Approximately one-third of Americans have hypertension.\(^1,2\) If left unchecked, hypertension increases the risk of heart attack and stroke.\(^2\) Unfortunately, about half of those with hypertension have uncontrolled blood pressure.\(^2\) Because of the widespread public health impact of this condition, there have been many studies examining the effectiveness of quality-improvement (QI) programs focused on controlling blood pressure. A study conducted by Jaffe et al\(^3\) showed that a large-scale, multifaceted QI program focused on controlling hypertension can have a positive effect on blood pressure control.

QI aims to change aspects of the health care system to improve its efficiency and outcomes.\(^4\) Patient outcomes such as morbidity and mortality, recovery times, patient satisfaction, and costs are often used to evaluate QI programs.\(^4,5\)

Performance-improvement strategies help individuals and teams work within a system to improve their own work processes. In health care, performance improvement is often used to reduce variation among physicians in the same field of practice.\(^6\) The American Medical Association process for performance improvement includes assessment of current practice, implementing a change in practice to address shortcomings found during the assessment phase, and evaluation of the changes implemented. Many frameworks for performance improvement, including Plan-Do-Study-Act and Lean Six Sigma, have been implemented in health care settings.\(^7,9\)

Quality and performance improvement are incorporated into the continuous process of Maintenance of Certification (MOC) for American Board of Medical Specialties board-certified physicians. MOC is divided into four parts: professionalism, lifelong learning and self-assessment, cognitive expertise (passing a secure examination), and assessment of performance in practice.\(^10\) Quality and performance improvement are generally incorporated into this latter stage, MOC Part IV.\(^11\)

In 2011, The Permanente Medical Group (TPMG), under the auspices of The Permanente Federation, joined the American Board of Medical Specialties Multi-Specialty MOC Portfolio Approval Program to grant MOC Part IV credit to diplomates for QI projects completed in Kaiser Permanente Northern California (KPNC).\(^12\) The program is composed of member boards from the American Board of Medical Specialties that recognize that institutional QI projects can satisfy the requirements for MOC Part IV.\(^13\)

Under the program, participating organizations are allowed to designate QI projects for MOC Part IV credit. TPMG identified our ongoing...
hypothesis that the workload that the project required. We hypothesized: 1) there would be no statistically significant interaction between the physician’s panel improvement and the type of intervention chosen to complete the project, and 2) the type of intervention chosen would not affect the physician’s perception of workload.

The main outcome measure was the proportion of qualifying hypertensive patients with controlled blood pressure. A secondary outcome measure was the proportion of diabetic patients with controlled blood pressure. We also explored potential differences in the proportion of patients with controlled hypertension by the type of improvement option chosen; whether the number of improvement options completed had an effect on either the primary or secondary outcome measure; whether the type of intervention had an effect on the participant’s perception of the increased burden of completing the MOC project; and whether the participant engaged in discussions with other members of their health care team about improving care of their hypertensive patients.

Participants were TPMG physicians certified by the American Board of Internal Medicine and/or the American Board of Family Medicine. E-mail messages about the opportunity to participate in the MOC project were sent to physicians who were participating in MOC and whose certification would expire within ten years from the date of sending the e-mail. In addition, presentations were made to family medicine and internal medicine leaders who were encouraged to disseminate information about the new MOC project. Participants were self-selected and completed the project as individuals or as part of a group with their colleagues.

METHODS

This is a retrospective analysis of a QI program that was implemented through the Multi-Specialty MOC Portfolio Approval Program. This study was reviewed by the KPNC institutional review board and was designated as “not human subjects” research.

The QI project, described in the Introduction, took place across 22 KPNC Medical Centers and 48 medical offices.

To meet the qualifications of the Multi-Specialty MOC Portfolio Approval Program and to make the project more accessible to individual physicians, the improvement options from the original QI program were adapted so they could be implemented in a rapid-improvement cycle. The four improvement options were

1. employing tools, such as workflows, job aids, and patient education materials (Tools)
2. optimizing workflows with team members to take accurate blood pressure readings (Workflows)
3. reviewing evidence-based guidelines on appropriate care for hypertensive patients (Guidelines)
4. applying communication best practices to reinforce medication adherence or lifestyle changes (Communication).

Physicians commenced participation by visiting the project Web site, signing up for an account, and reading through the project description. The project description outlined the expected project length, eligible specialties, metrics, steps to participate in the project, group instructions, resources, how to fill out the attestation, and the project contact person for questions about the project.

Participants could choose to complete the project in a group with their colleagues or individually.

Participants were expected to work through the Plan-Do-Study-Act cycle, as outlined in the project description, to obtain a 1% to 2% increase in blood pressure control on their patient panel. In the Plan phase of the project, participants received monthly data that included the percentage of qualifying patients on their patient panel who had their blood pressure under control. Qualifying patients were determined on the basis of the Healthcare Effectiveness Data and Information Set (HEDIS) definition of patients between the ages of 18 and 85 years who had a diagnosis of hypertension (blood pressure ≥ 140/90 mm Hg) within the first 6 months of the year. Participants were expected to review their practices around that measurement and then select 1 or more improvement options to use to improve the rate of control among the qualifying patients on their panel.

In the Do phase of the project, participants implemented the improvement option or options for at least two months. Participants in the Study phase reviewed the results of their improvement option or options and planned their next steps. In the Act phase, participants were expected to implement these next steps. Participants were encouraged to complete as many Plan-Do-Study-Act cycles as necessary to achieve improvement, but two cycles were sufficient to obtain credit for the project.

After completing the requisite Plan-Do-Study-Act cycles, participants submitted an online attestation to receive both MOC and continuing medical education credit. The attestation included documentation of the starting and ending blood pressure control rates for their patient panel; improvements implemented; starting date, ending date, and number of QI cycles completed; how the participant reflected on the data; the perception of the impact the project had on the participant’s work; whether team changes were implemented; key
Physicians chose to implement between 1 and 4 improvement options, with those who reported 1 intervention showing the highest mean improvement ...

...attentions, or if their attestation was outside the date range that we were studying. Participants who incorrectly reported a rolling metric instead of a monthly metric were disqualified as outliers. Figure 1 shows the breakdown of included (n = 73) and excluded (n = 20) physicians.

Percentage improvement was calculated by subtracting the beginning metric from the ending metric. Reported free-text improvement options were categorized by an initial reviewer (VK) into one of four categories: Tools, Workflows, Guidelines, or Communication. A second reviewer (DP) checked categorizations for accuracy and agreement. Participants reported using multiple improvement options.

Descriptive statistics consisted of number of improvement options used, the types of improvement options used, and the impact the project had on the physician’s work. The χ² analysis of independence was used to analyze the interactions between team discussions and perception of workload.

RESULTS

Data were collected between September 2011 and November 2013. Project durations ranged between 2 and 15 months, with a mean length of 4.85 months (standard deviation [SD] = 2.85). Seventy-three physicians certified by the American Board of Family Medicine and American Board of Internal Medicine completed the project (Table 1). There was an increase in the overall metric from a mean of 79.49% (SD = 11.32) to 84.64% (SD = 7.80), as shown in Table 2. The difference between the 2 means is statistically significant at the 0.05 level (Z = -2.95). These data, along with data on project impact, are summarized in Table 2.

The two participants with no medical board selected were followed up with at the time of submission but were not updated in the database.

<table>
<thead>
<tr>
<th>Table 1. Baseline characteristics of participants (N = 73)</th>
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<tbody>
<tr>
<td>Specialty board</td>
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<tr>
<td>Family medicine</td>
</tr>
<tr>
<td>Internal medicine</td>
</tr>
<tr>
<td>No board selected*</td>
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</tbody>
</table>

*The two participants with no medical board selected were followed up with at the time of submission but were not updated in the database.
of the participants’ participation on their work was statistically significant. Participants who completed 1 or 2 improvement options were more likely to report that the project made their work somewhat easier ($\chi^2 = 20.84, \text{df} = 9$). However, the relationship between the specific intervention option and impact on workflow was not statistically significant ($\chi^2 = 4.41, \text{df} = 9$). A summary of these data appears in Table 4. Finally, the relationship between the team discussions and perception of impact was not statistically significant at the 0.05 level ($\chi^2 = 2.19, \text{df} = 3$). These data are summarized in Table 5.

**DISCUSSION**

As hypothesized, we found no statistically significant interaction between the type of intervention chosen and the resulting improvement; nor did the type of intervention affect the physician’s perception of workload to complete the project. Combined with an overall improvement in hypertension control, the results would indicate that participation in MOC within a QI setting does not have a negative effect on physician participants.\(^{14-16}\)

Although overall improvement was observed in this cohort, KPNC overall also showed improvement during that same timeframe, from 81% in mid-2011 to 86.7% at the end of 2013. It is probable that the observed increase in the MOC cohort may have been mirroring that of the entire area, especially since this project was based on previously implemented strategies.

At the same time, the hypertension project was designed to enable physicians to improve their practice and to meet their board certification requirements. Overall, participants showed improvement during the project, without increasing the perception of the burden of work, of which MOC is often accused. This project demonstrates that MOC Part IV projects based on a health system’s existing QI program is an effective way to document the part of MOC involving practice performance assessment.

A strength of this project is that it was based on an ongoing QI program that is familiar to our physicians. In addition, this project provided a framework for physicians to examine and explicitly reflect on their own strengths and weaknesses through the Plan-Do-Study-Act cycle and to implement improvement options that were tailored to their own experience.

Limitations of this project include the lack of a control group, participant self-selection, unaudited self-reporting of organizationally generated metrics, and a small sample size. The lack of a control group prevents the results of this study from being compared with those who did not participate in the project to determine whether the improvement observed was significantly different than in those who did not participate. Unfortunately, limited access to data outside the project database, paired with deidentified data from the project, prevented us from being able to obtain data for a control group.

Although this project was widely advertised to all TPG internal and

<table>
<thead>
<tr>
<th>Table 2. Mean improvement in blood pressure control(^{a})</th>
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<tr>
<td>Metric</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Overall metric</td>
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<tr>
<td>Diabetes subset</td>
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</table>

\(^{a}\) Data are mean percentages (and standard deviations) of patients with controlled blood pressure at the beginning and end of the Maintenance of Certification project. SD = standard deviation.

<table>
<thead>
<tr>
<th>Table 3. Effect of improvement option and project impact of the physicians work on patient improvement, N = 73</th>
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<tbody>
<tr>
<td>Statistic(^{a})</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Number of improvement options chosen</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
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<tr>
<td>3</td>
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<tr>
<td>4</td>
</tr>
<tr>
<td>Improvement options used</td>
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<tr>
<td>Tools</td>
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<tr>
<td>Workflows</td>
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<tr>
<td>Guidelines</td>
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<tr>
<td>Communication strategies</td>
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<tr>
<td>Perception of project impact on workload</td>
</tr>
<tr>
<td>Much easier</td>
</tr>
<tr>
<td>Somewhat easier</td>
</tr>
<tr>
<td>No impact</td>
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<td>Somewhat more difficult</td>
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</table>

\(^{a}\) Each statistic is calculated in relationship to the mean improvement. For improvement options used, participants could choose more than one improvement option to complete their projects. SD = standard deviation.

<table>
<thead>
<tr>
<th>Table 4. Number of participants completing an improvement option and their perception of impact on workload</th>
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<tbody>
<tr>
<td>Perception of impact</td>
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<td>----------------------</td>
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<tr>
<td>It has made my clinical and operational work</td>
</tr>
<tr>
<td>Much easier</td>
</tr>
<tr>
<td>Somewhat easier</td>
</tr>
<tr>
<td>No impact</td>
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<tr>
<td>Somewhat more difficult</td>
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</table>

\(^{a}\) $\chi^2$ analysis was used to determine whether a relationship existed between the type of improvement option completed and participants’ perception of project impact on their workload.
that participation in this MOC Part IV project did not have a negative effect on participants’ panels nor on participants’ perception of the work required to complete the project. Further studies should examine the effect of other organizational QI efforts for MOC Part IV on different conditions, in different practice settings, with larger samples of physicians from different specialties, and with control groups to help discern potential differences between participating and nonparticipating physicians.

Disclosure Statement

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

Acknowledgment

The authors would like to acknowledge Robert Knight, PhD, for his help with statistical analysis. Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

References


The Ischaemic Kidney

The ischaemic kidney secretes directly a vasoconstrictor substance which causes a permanent hypertension. This substance is active in the absence of the adrenals. The healthy kidney is capable of diminishing the action of this blood-pressure raising substance.

— Fasciolo JC, Houssay BA, Taquini AC. The blood-pressure raising secretion of the ischaemic kidney. J Physiol 1934:94:281-93
Use of ERC-1671 Vaccine in a Patient with Recurrent Glioblastoma Multiforme after Progression during Bevacizumab Therapy: First Published Report

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ABSTRACT

Objectives: Glioblastoma multiforme (GBM) is a highly aggressive tumor, which recurs despite resection, focal beam radiation, and temozolomide chemotherapy. At recurrence, the only second-line treatment approved by the US Food and Drug Administration is bevacizumab (Avastin). To date, no single agent has shown to extend the life of patients with progressive malignant gliomas after bevacizumab failure. Once the tumor recurs during bevacizumab therapy, it is universally fatal, with death occurring within a few weeks. ERC-1671 is an experimental treatment strategy, which uses the patient’s own immune system to attack the tumor cells. We report preliminary data on the first human administration of ERC-1671 vaccination, under a single-patient, compassionate-use protocol, to a patient with progressive, bevacizumab-resistant GBM.

Methods: Treatment involved sequential administration to the patient of GBM tumor cells and cell lysates combined from three different donors with GBM, followed by the patient’s own tumor cells and lysates.

Results: The patient survived for ten months after the vaccine administration without any other adjuvant therapy and died of complications related to his previous chemotherapies. The tissues collected after two vaccination cycles and at the time of death showed a robust immune response and no viable tumor.

Conclusion: These preliminary data strongly indicate that ERC-1671 could be effective in the treatment of progressive malignant gliomas. On the basis of these preliminary data, we are planning a larger study to assess the efficacy of ERC-1671 in the treatment of patients with recurrent GBM.

INTRODUCTION

Malignant gliomas are the most common type of primary brain tumor, with an incidence of approximately 10,000 new cases annually in the US. The standard treatment of these highly aggressive tumors is gross total resection followed by radiation therapy and temozolomide chemotherapy. Unfortunately, gross total resection is difficult because of the highly infiltrative nature of these tumors and their common involvement of essential areas of the brain. Invariably, malignant gliomas recur, and second-line therapy with bevacizumab (Avastin), an antiangiogenic agent, is administered in an attempt to stall the progression of tumor growth. With this treatment, the median survival has improved to only 18 months in the last decade. Once glioblastoma multiforme (GBM) recurs during bevacizumab treatment, it is universally fatal, with survival rates less than a few weeks despite aggressive treatments. Therefore, additional forms of therapy are sorely needed to treat patients with malignant gliomas.

Since 2000, immunotherapy has shown great promise for the treatment of cancer because the immune system can be induced to eradicate malignant cells. In addition, if successful in treating cancer in the initial phase, this method has the advantage of creating a memory response to prevent further tumor recurrences. In the past, research showed that proper activation of the immune response against cancer cells could prevent development of new cancer cells. For example, in colon cancer research, in situ analysis of tumor-infiltrating immune cells showed that tissues infiltrated with CD8+ T cells contributed to better patient survival. However, active vaccination for cancer therapy has shown modest results.

In addition, the literature reports that tumors have effective strategies to evade a fully functional immune system. For example, researchers showed that the presence of major histocompatibility complex Class 1 on tumor cells can play a role in cancer resistance, that the tumors may be unresponsive to interferons, and that tumor-induced immunosuppression can occur. Furthermore, recent data indicated that patients with an overactive immune response, such as an autoimmune disease, have a better prognosis compared with patients with normal conditions.
immune systems. The IgG species from these patients were identified to share important homology with both human and microbial peptides. Also, four patients with malignant brain tumors went into remission after intracranial infections, and multiple patients had better outcomes and increased survival after wound infections. These findings led to the hypothesis that tolerance to tumor-associated antigens can be reversed by cross-reactivity against foreign homologous antigens.

Previous publications from our group have extensively studied this hypothesis in rodent models and demonstrated that administration of allogeneic glioma cells and syngeneic tumor cell lysates to rats induced rejection of malignant gliomas and provided protection against future recurrences. If one strain of rats (Sprague-Dawley) is injected with glioma tumor cells derived from a different rat strain (Fischer 344), the foreign (allogeneic) tumor cells will be rejected and no tumor will grow. However, if the same rats were then injected with glioma tumor cells generated in their strain (syngeneic), the previously allogeneic vaccinated groups were able to significantly reduce tumor growth, and complete rejection of tumors was noted in some rats. Using this principle, we hypothesized that if two patients have a tumor of a similar type and histologic grade, transplantation of tumor tissue from one patient to another might induce a robust immune response and expose the immune system to peptides shared between the two tumors, thus allowing the immune system to recognize and attack tumor-specific antigens.

In the present report, we translate to the clinical arena this original idea of using allore cognition and coadministration of syngeneic tumor antigens to patients to overcome the ability of the malignant gliomas to evade the immune system. We use the patient’s immune system to recognize intact, same-species, nonself major histocompatibility complex molecules on the surface of donor cells and to directly eliminate the tumor cells by an immune-mediated response. This process is well documented and well described in acute allograft rejection. In this article, we present the first use of the ERC-1671 vaccine to treat a patient with advanced GBM whose cancer relapsed during bevacizumab treatment.

**METHODS**

**Vaccine Production**

ERC-1671 was manufactured under conditions of good manufacturing practices by Bio Elpida (Dardilly, France). Surgically removed GBM tissues provided the raw material. The tumor tissues were collected, under protocols approved by an institutional board review, in the operating room under aseptic conditions. The tumor specimens were transported in sterile culture medium and fully tested for viral infections, including human immunodeficiency virus, hepatitis B virus, hepatitis C virus, cytomegalovirus, syphilis, and human T-lymphotropic virus. The tumor samples were sent in temperature-controlled sealed packs to the good manufacturing practices site immediately after the surgery.

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**Figure 1.** Treatment scheme for intradermal administration of ERC-1671 vaccine for patients with recurrent glioblastoma multiforme after failure to respond to bevacizumab therapy. ERC-1671 doses A to C contained approximately $1 \times 10^6$ dinitrophenol-modified allogeneic tumor cells and $1 \times 10^6$ dinitrophenol-modified allogeneic tumor lysates from Donors 1 to 3, respectively. Dose D contained approximately $1 \times 10^6$ dinitrophenol-modified autologous tumor cells and approximately $1 \times 10^6$ dinitrophenol-modified autologous tumor lysates from the patient. Cy = cyclophosphamide (50 mg/m$^2$) orally; GM-CSF = granulocyte-macrophage colony-stimulating factor (sargramostim).
At the manufacturing site, the tumor was dissociated on a single-cell suspension, and the cells were haptenized using dinitrophenol. The haptenized cells were then separated into two different specimens, and one of the specimens was lysed to obtain the lysate component. Both the cellular component and the lysate component were then irradiated to make sure that none of the remaining tumor cells had the ability to replicate.

**Treatment Scheme**

The treatment process (Figure 1) involved 4 monthly cycles of vaccination with GBM tumor cells and lysates generated from 3 different donors with GBM (the allogeneic component) as well as from the patient’s own tumor (the autologous component). ERC-1671 treatment was administered together with a manmade form of granulocyte-macrophage colony-stimulating factor, sargramostim (Leukine), as adjuvant therapy, following the oral administration of a low dose (50 mg/m²) of cyclophosphamide (Endoxan). This treatment combination was developed during the preclinical studies, and it produced the maximal tumor response in rats.

Each monthly cycle consisted of 5 intradermally administered treatment doses. One dose was composed of a freshly mixed shot of both a cellular component and a lysate component, stored in separate vials. The cell vial contained a suspension of $10^6$ to $10^8$ irradiated dinitrophenol-modified tumor cells, and the lysate vial contained the equivalent of a lysate of $10^6$ to $10^8$ irradiated dinitrophenol-modified tumor cells. The ERC-1671 A, B, and C product doses were prepared from 3 different GBM-affected donors, whereas the ERC-1671 D dose was derived from the patient’s tumor. The monthly treatment was continued for as long as the tumor responded to treatment.

**CASE STUDY**

A 43-year-old man presented to the University of California, Irvine Medical Center in June 2008 with headaches, hiccups, fatigue, and hypersomnia. Magnetic resonance imaging (MRI) revealed a left frontal lobe tumor. He underwent craniotomy with gross total tumor resection (more than 95% of the contrast-enhancing area) on June 26, 2008. The histopathologic analysis showed the diagnosis of GBM (World Health Organization Grade IV astrocytoma). From July 2008 to September 2008, the patient was treated with fractionated radiation therapy with concomitant temozolomide chemotherapy. The patient was maintained on 12 cycles of adjuvant temozolomide chemotherapy from September 2008 until October 2009. Because the patient was stable and the tumor did not demonstrate recurrence on neuroimages, the decision was made to follow his disease progression with serial brain MRIs and observation. In February 2010, tumor growth was noted on the brain MRI. The patient immediately underwent craniotomy with subtotal tumor resection (about 70% of the tumor was removed). The pathologic findings were consistent with GBM, with moderately high Ki-67 labeling index (Figure 2).

In March 2010, the patient began a clinical trial with bevacizumab (Avastin) and bortezomib (Velcade). His bortezomib therapy was discontinued after nine cycles, as required by the study protocol, but he continued to receive bevacizumab therapy. In March 2012, the patient experienced further tumor progression, as shown on his brain MRI, with the tumor now crossing the corpus callosum and progressing toward the left temporal area (Figure 3A). The patient underwent immediate debulking of the contrast-enhancing area and some of the adjacent abnormal fluid-attenuated inversion recovery (FLAIR) areas of his tumor (Figure 3B), which again showed pathologic findings consistent with GBM (Figures 2 and 4).

As no other options for his treatment-resistant, recurrent glioblastoma were available, an application for compassionate use of ERC-1671 was made to the US Food and Drug Administration with the patient’s consent, and he was administered ERC-1671 vaccine under a single-patient protocol approved by that agency. The first cycle was administered immediately after resection, and the remaining 3 cycles were given at monthly intervals (Figure 1). After the second cycle of vaccination, a tumor biopsy was obtained to evaluate the treatment response. Because the biopsy specimen showed extensive inflammatory changes and very few proliferating tumor cells, the patient did not receive any adjuvant treatment in addition to the vaccine. Ten months after starting the ERC-1671 treatment and almost 11 months since...
The progression of his cancer during bevacizumab therapy, the patient remained stable, with no new neurologic findings and a Karnofsky Performance Scale score of 70.

However, in late December 2012 the patient suddenly died of congestive heart failure and pneumonia—common complications in patients who have had extensive chemotherapy (including one year of temozolomide, one year of bortezomib, and two years continuous bevacizumab treatment). An autopsy showed no active brain tumor (Figures 2 and 4). The cause of death on the autopsy findings was congestive heart failure, pulmonary congestion and edema, and congestive hepatosplenomegaly.

MRI of the brain with and without a contrast agent from March 2012 showed the resection cavity in the patient’s left lateral frontal convexity involving his middle frontal gyrus immediately anterior and superior to the pars triangularis (Figure 3). The pars triangularis appeared to be involved with the tumor extending back into the insula and arcuate fasciculus toward the Wernicke area. It also appeared that most of the tumor recurrence was medial and superior to the resection cavity extending toward the ependymal surface of the lateral ventricle and the corpus callosum. The postresection MRI from March 2012 showed partial resection of prior enhancing nodules (Figure 3), with residual FLAIR signal suggestive of residual nonenhancing tumor.

The MRIs obtained at the end of vaccination Cycles 1 through 4 show slowly progressive increase in the FLAIR signal and contrast enhancement around the resection bed (Figure 3). This finding raises the question of tumor progression vs pseudoprogression generated by the immune inflammation and justifying the need for a biopsy after two vaccination cycles.

The initial immunohistochemical findings of the tumor showed a left frontal GBM with O(6)-methylguanine DNA methyltransferase positivity of 30%, epidermal growth factor receptor (EGFR) positivity of 5%, EGFR variant 3 negative, and phosphatase and tensin homologue 60% of the cells were positive. The specimen collected from the resection before the vaccine administration in March 2012 showed immunohistochemical findings for O(6)-methylguanine DNA methyltransferase of 30%, EGFR of 30%, EGFR variant 3 negative, and phosphatase and tensin homologue of 60%. The tumor had a high Ki-67 index of 15% (Figure 2). The specimen collected after 2 cycles of the vaccine showed scattered lymphocytes, B cells, and macrophages infiltrating the specimen, with a Ki-67 index of 3% to 5% (Figure 4).

Analysis of the autopsy specimen revealed slight vascular endothelial hyperplasia and focally variable permeation by macrophages. Collagen deposition was observed in close relationship with the blood vessels, and there were no definitive Ki-67-positive glioma cells, consistent with a nonproliferating, nonviable tumor (Figures 2 and 4). There was perivascular infiltration of mononuclear inflammatory cells, both T and B lymphocytes (Figures 2 and 4).

**DISCUSSION**

Recurrence of malignant gliomas after surgery, radiation therapy, and adjuvant chemotherapy is universal.\(^4\)\(^6\)\(^9\) Gross total resection is ineffective in eradicating the entire tumor because of the infiltrative nature of malignant gliomas.\(^4\) The only approved treatment for glioblastoma at recurrence is bevacizumab, which was found to have an estimated 6-month progression-free survival rate of 42.6% and an overall survival of 9.2 months.\(^20\)\(^21\)
In the end, all GBMs recur during bevacizumab therapy, and the survival after recurrence is usually only a few weeks. ERC-1671 aims to provide a new and innovative approach to treating patients with GBM. The vaccine is composed of four cycles and includes administration of glioblastoma tumor cell lysates and tumor cells from the patient and three different donors with GBM. With the use of genetically different heterozygous individuals with brain tumors at the time of the vaccine administration, the patient’s immune system is exposed to numerous tumor antigens identical to those of the patient’s own tumor. It is as if this action creates a cascade immune response in which the homologous tumor antigens are sequentially recognized by the immune system and eliminated. In addition, this process also leads to sensitization of the immune system in recognizing cross-reactive allogeneic tumor antigens, enabling the attack of the patient’s own brain tumor.

Our patient with confirmed GBM on histopathologic examination received four cycles of the vaccine. He received no other adjuvant chemotherapy or radiotherapy. On the basis of previous experience with patients with GBM, the expected survival after recurrence while the patient is receiving bevacizumab therapy is only a few weeks. Our patient survived for ten months without adjuvant chemotherapy. Furthermore, we showed that the tumor displayed less aggressive features throughout the treatment and after completion of the treatment. Figure 2 shows evidence that the tumor’s Ki-67 decreased after the patient received the vaccine and completed the treatment. In addition, the blood vessel proliferation and hyperplasia, features of aggressive GBM, slowly receded throughout the treatment (Figure 5). The patient also mounted a strong immune response to the vaccination (Figure 6), as evidenced by T lymphocytes, B cells, and macrophage infiltration of the tumor specimens after completing only two cycles of vaccination, which was evident at the time of autopsy (Figure 5). Similar to our preliminary data in an additional four patients, no clinically significant adverse events were noted with this therapy, and the only side effects noted were mild headaches and local erythema at the injection site.

Despite these promising immunologic responses evidenced by histopathologic analysis, the MRI suggested that the patient’s tumor appeared to progress. As described by Figure 3, there was increased FLAIR signal as well as increased contrast enhancement around the resection cavity. A possible explanation for these imaging findings could be that our vaccine produced a very strong immune response in the patient, which produced a beneficial inflammation around the tumor bed because of the influx of inflammatory cells in the area. This idea is supported by the histopathologic finding of macrophage, B-cell, and T-cell infiltration found in various tumor specimens obtained from biopsy and autopsy. Hence, proposed criteria related to immune response might represent better measurement of our immune-based therapy. In the absence of clinical progression, similar imaging changes (pseudoprogression) were previously reported for patients receiving dendritic cell vaccination. The inflammatory cytokines could also produce dilation of the blood vessels and shunting of more blood to the involved areas of the brain, thus leading to the enhancement seen on the contrast images.

**CONCLUSION**

These preliminary observations suggest that ERC-1671 could be effective in the setting of a malignant glioma that has become resistant to the available treatments. However, the effectiveness of this immunotherapeutic approach cannot be established in a pilot study such as this, which had only one patient. Even though no definite conclusions can be made about the efficacy of this treatment, our results indicate that the vaccine was well tolerated, could be safely administered to our patient, and produced promising immunologic responses seen on histopathologic analysis. A larger study to assess how these histopathologic changes clinically benefit our patients with recurrent GBM is being planned. 

**Disclosure Statement**

Dr Bota is a consultant for Novocure; she has received research support from Epitopoietic Research Corporation. Dr Carillo is on the Speakers Bureau of Sigma Tau and Novocure. The author(s) have no other conflicts of interest to disclose.

*Figure 5. Immunohistochemical staining after 2 cycles of vaccination show CD3+ lymphocytes (A-C), CD20+ B cells (D-F), and abundant CD68+ macrophages (G-I) infiltrating the tumor specimen. Autopsy specimen shows abundant infiltration of tumor cells by CD68+ macrophages (J-L).*
Use of ERC-1671 Vaccine in a Patient with Recurrent Glioblastoma Multiforme after Progression During Bevacizumab Therapy: First Published Report

References


Myrtle Beach, SC, has been a seaside retreat since the early 20th century. The city has grown enormously, but historic buildings and the tranquil shoreline remain. Dr Davenport and his family have been visiting Myrtle Beach each summer for over 40 years.

Dr Davenport is the former Director of Primary Care Services for Kaiser Permanente Orange County and an Emeritus Physician with the Southern California Permanente Medical Group.

Summer Storm at Myrtle Beach
photograph

John Davenport, MD, JD
ABSTRACT

Long-term survival rates after a diagnosis of breast cancer are steadily rising. This is good news, but clinicians must also recognize that this brings new challenges to the medical community. As breast cancer becomes a chronic condition rather than a life-threatening illness owing to advances in early diagnosis and more effective treatments, health care practitioners must recognize and manage the long-term sequelae of the constellation of therapeutic modalities. Survivors of breast cancer represent a unique and extremely complex group of patients; not only do they have the challenge of dealing with multiple long-term side effects of treatment protocols, but many are also forced to address the preexisting comorbidities of their therapies, which often include multiple other issues. Therapies have additional and/or additive side effects that may interfere with treatments directed toward the new primary diagnosis of breast cancer. Our mandate is to establish a smooth transition from patient with breast cancer to survivor of breast cancer while providing ongoing and future guidance.

Certainly, the information and resources to accomplish this transition are readily available; however, they are scattered throughout the literature and therefore are not easily accessible or available to the primary care physician. It is imperative that the information available regarding survivorship issues be accessible in an organized and useful format. This article is a modest attempt to provide a comprehensive review of the long-term medical issues relevant to survivorship after the diagnosis and treatment of breast cancer. A predicted shortage of oncologists by 2020 is well-recognized. Therefore, the bulk of long-term care will become dependent on the primary care physician. This shift of care means that these physicians will need to be well educated in the long-term medical issues related to breast cancer treatment.

INTRODUCTION

It is estimated that there are approximately 2.5 million survivors of breast cancer in the US. This figure will expand to 3.4 million in 2015, representing an increase of 31%. The millions more worldwide are probably grossly underestimated because of the poor or inefficient reporting systems and the lack of reliable cancer registries in third-world countries.

In 2006, the Institute of Medicine (IOM) issued a milestone comprehensive report, From Cancer Patient to Cancer Survivor: Lost in Transition. Of the 10 recommendations regarding cancer survivorship by the IOM, the issues receiving the utmost attention to date have been the provision of a summary of diagnosis, treatment received (treatment summary), future follow-up care plans, and healthy lifestyle recommendations. A recent Special Series Overview eloquently described a number of major topics that have been addressed by world-renowned experts since the IOM recommendations were published. These include long-term cardiovascular issues secondary to treatment protocols, bone health, the increased risk of second primary malignancies (SPMs), the development of lymphedema, and other issues that, although extremely important, may not be life-threatening. Multiple other concerns have been inadequately addressed, including the increased risk of venous thromboembolism in the setting of malignancy, the failure of adherence and compliance to prescribed adjuvant hormonal therapies, and lifestyle changes with recommendations for effective modifications.

Although of major importance, issues regarding sexuality and fertility preservation are not addressed in this review. The reader is directed to excellent reviews of breast cancer and sexuality, as well as extensive guidelines regarding fertility preservation. In addition, nonspecific symptoms secondary to treatment protocols (eg, fatigue, insomnia, pain, cognition) are omitted because recent and thorough reviews of these issues are readily available. Furthermore, these are excluded because many are nonspecific symptoms and are not unique to a diagnosis of breast cancer.

Survivorship care programs provide an important component of the patient treatment pathway but fail in the elaboration and communication to the patient regarding many issues relevant to long-term survival. Most long-term care plans inadequately address the most important medical issues involving the long-term consequences of survivorship. Although the primary recommendations of the 2006 IOM report are sound, we would add the importance of patient education regarding some of the long-term sequelae of this disease and its treatment. These include the symptoms of the issues addressed in this article: cardiovascular diseases (CVDs) secondary to treatment modalities, bone health, SPMs, lymphedema, thromboembolic risks, long-term compliance with oral medications, and finally, lifestyle interventions.

Although most people with breast cancer will not die of breast cancer,
their comorbidities (eg, obesity, hypertension, hyperlipidemia, and diabetes mellitus [DM]) will most certainly affect disease-free survival (DFS) and, ultimately, overall survival (OS). In this review we address lifestyle changes, which are largely dependent on body mass index (BMI) and include diet and exercise, and review recommendations regarding these issues. Survivors of breast cancer represent a unique group who must be cognizant of the long-term side effects of their treatment protocols and be given information to encourage a proactive approach to their overall health. Finally, a robust reference resource list is included in this article for those who wish to delve into specific issues in greater depth.

CARDIAC ISSUES

Although breast cancer is the most feared disease by most women in the US, it is far from the leading cause of death in women.23,24 CVD is the number 1 killer of women, claiming well over 400,000 lives each year. Sadly, nearly 50% of women are unaware that heart disease is the leading cause of death among women.23 Survival of patients with breast cancer has dramatically increased in the last 2 decades, largely owing to earlier detection by advanced mammographic screening technologies, increased patient awareness, and of course more effective treatment modalities.24 This success, however, may lead to an unintended increase in the incidence of mortality due to CVD. Although each year many women succumb to CVD, the risk of death due to CVD may be greatly increased in survivors of breast cancer by the addition of adjuvant therapies, regardless of cancer stage, at the time of diagnosis.

A further concern, demanding urgent attention, is that the rate of younger women (aged 35 to 44 years) who develop CVD is on the rise.25,26 Overlapping with this age group are the younger and young women receiving a diagnosis of breast cancer. Therefore, the diagnosis, treatment, and long-term sequelae of treatment may be converging on patients who are currently facing a breast cancer diagnosis and are thus subjected to “modern” protocols. As with the treatment of other malignancies occurring at young ages (eg, Hodgkin disease), the long-term sequelae of breast cancer treatment are just now, decades later, becoming fully realized. In fact, a subset of cardiologists in the US and internationally is focusing on a new subspecialty—cardio-oncology—a specialty in managing the long-term cardiovascular side effects of the treatment of malignancies.23 Many survivors of breast cancer are at significantly increased risk of death caused by CVD, far exceeding their risk of death resulting from the initial cancer itself or from a recurrent cancer.21,22,26,28,29

Chemotherapy

The development of multiple antineoplastic agents—many novel but also many older (decades old)—has dramatically increased breast cancer OS. Unfortunately, many of the chemotherapeutic agents used have the potential to cause cardiovascular complications, some acute but most chronic.30,31 The spectrum of CVD in the setting of breast cancer therapy includes congestive heart failure (CHF), myocardial ischemia, hypertension, arrhythmias, QT prolongation, bradycardia, pericarditis, acute coronary syndrome, and thromboembolic events (TEs).31-34

Anthracyclines: Doxorubicin and Epirubicin. Anthracyclines bind to the DNA of malignant cells, interfering with the replication process and resulting in cellular death. Anthracycline therapy has been shown to increase the development of CHF and cardiomyopathy by 2%,30-34 doubling to 4% if used in conjunction or sequence with trastuzumab.33,34-35

Of particular importance to the primary care physician, extensive data are available in the literature about the potential long-term sequelae of the cardiotoxicity of anthracycline-based therapy for survivors of breast cancer.31-34 Furthermore, it should be noted that anthracycline therapy may not result in cardiotoxicity, particularly CHF, which is clinically evident for 10 to 20 years after treatment.35,36-43

Alkylating Agents: Cyclophosphamide. Alkylating agents act by reacting with the proteins of the DNA of cancer cells by adding an alkyl group to them. This disrupts effective DNA replication, resulting in the apoptosis of cancerous cells. Cyclophosphamide therapy can lead to cardiac damage, resulting in heart failure in nearly 30% of patients receiving the drug.44-46

As with most chemotherapeutic agents, the risk of cardiotoxicity appears to be dose related.44-47 In addition to dose, prior anthracycline therapy, a history of mediastinal radiation, and elderly age are further risk factors for cardiotoxicity.44,45,47,49,50

Cytoskeletal Disruptors (Taxanes): Paclitaxel and Docetaxel. Cytoskeletal disruptors inhibit the process of cell division through the interruption of

Abbreviations

<table>
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<tr>
<th>Abbreviation</th>
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<tr>
<td>AET</td>
<td>antiestrogen therapy</td>
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<td>AI</td>
<td>aromatase inhibitor</td>
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<td>acute myeloid leukemia</td>
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<td>ATLAS</td>
<td>Adjuvant Tamoxifen Longer Against Shorter</td>
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<td>aTTom</td>
<td>Adjuvant Tamoxifen Treatment Offers More</td>
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<td>BCRL</td>
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<td>BCT</td>
<td>breast-conserving therapy</td>
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<td>BMD</td>
<td>bone mineral density</td>
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<td>BMI</td>
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<td>CHF</td>
<td>congestive heart failure</td>
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<td>estrogen receptor-positive</td>
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<td>FRAX</td>
<td>Fracture Risk Assessment tool</td>
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<td>HEALER</td>
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<td>HER2 +</td>
<td>human epidermal growth factor receptor 2-positive</td>
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<td>IOM</td>
<td>Institute of Medicine</td>
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<td>MDS</td>
<td>myelodysplastic syndrome</td>
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<td>OS</td>
<td>overall survival</td>
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<td>PE</td>
<td>pulmonary embolism</td>
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<td>RT</td>
<td>radiation therapy</td>
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<td>SEER</td>
<td>Surveillance, Epidemiology, and End Results</td>
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<td>SERM</td>
<td>selective estrogen receptor modulator</td>
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<td>SPM</td>
<td>second primary malignancy</td>
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<td>SSRI</td>
<td>selective serotonin reuptake inhibitor</td>
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<tr>
<td>TE</td>
<td>thromboembolic event</td>
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<td>WFPBD</td>
<td>whole-food, plant-based diet</td>
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<td>WI</td>
<td>Wellness Index</td>
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microtubular functions, which are essential for cell division. Taxanes have been incorporated in the treatment of breast cancer only since the 1990s and, as such, their long-term cardiotoxic side effects may not yet have been adequately identified and reported. Furthermore, the multiple-combination chemotherapies used, which have included the addition of a taxane-based agent, make it difficult to decipher the true incidence of cardiotoxicity attributable to these drugs, particularly when administered alone.29,45,51-54

Although the most common side effects of taxane therapies are related to arrhythmias, particularly bradyarrhythmia, myocardial ischemia has also been reported. The incidence with paclitaxel use is 0.5% to 5% and with docetaxel appears to approach 2%.33 CHF resulting from docetaxel has ranged from 2.3% to 8%.51,55 It should be noted that most data for the development of cardiotoxicity has accumulated from the use of paclitaxel.56

As noted previously, the cardiotoxicity of systemic therapies may become one of the most devastating consequences of the treatment itself, particularly when an additional comorbidity such as a history of coronary artery disease, hypertension, or smoking is added to the patient’s active problem list (Table 1).45,56-58

Radiation Therapy
The current standard of care for the treatment of early-stage breast cancer involves giving a patient an informed choice regarding surgical options.59-61 The effectiveness of breast-conserving therapy (BCT), beginning in the 1970s with quadrantectomy vs mastectomy, has been fully verified with numerous studies, some reporting more than 2 decades of follow-up data.62-67 These findings have resulted in BCT as the primary surgical option for most patients during the past 2 decades. An integral part of BCT is the mandatory addition of adjuvant radiation therapy (RT).63,64,68 This surge in BCT has resulted in a large number of patients who receive adjuvant RT for early-stage breast cancer; rates of recurrence and death are markedly reduced.69-75

Cardiac injury resulting from RT to the thorax has long been recognized. Because of the increasing number of patients who have become long-term survivors of breast cancer thanks to BCT and RT, attention has now been directed to the late side effects of RT. These include direct damage to the myocardium and the coronary arteries, resulting in an increase in CHF and myocardial infarction compared with patients who do not receive RT.29,33,76

Since the mid-1980s, the mean centigray cardiac exposure has decreased because of improved technologies, such as computed tomography for simulation for RT; nonetheless, even small amounts of radiation reaching the heart may be damaging.77,78 It is estimated that each centigray exposure the heart receives increases the risk of death due to heart disease by 3%.83,84 The incidence and severity of cardiac morbidity and mortality risk are far greater for left-sided disease by virtue of human anatomy.81,85-88

As with chemotherapy, the risk of death due to RT starts to rise 10 years after treatment and may not be fully manifest until the second decade after therapy.83,88 RT has a long-term effect; therefore, it is important to be cognizant of the lengthy delay in cardiac symptoms, particularly as the patient ages and becomes more vulnerable to the development of CVD.89 Because RT has evolved over the years, incorporating new technologies, administration schedules, and delivery of centigray doses, the side effects for contemporary patients may be somewhat lessened, although long-term follow-up is not yet available.79,80,94

Hormonal Blockade
Tamoxifen: Tamoxifen is a selective estrogen receptor modulator (SERM) and inhibits the growth of breast cancer cells by its antiestrogenic activity through its competitive inhibition of estrogen binding to estrogen receptors.75,90 Since its introduction in the 1970s, tamoxifen has been shown to reduce the risk of breast cancer recurrence and mortality by more than 30%.97,98 Tamoxifen has been heralded as one of the most important advances in the treatment of breast cancer because approximately 70% of these patients have estrogen receptor-positive (ER+) cancer.99-103

The side effects of tamoxifen therapy are typically those that accompany the onset of menopause. These include hot flashes, mood swings, depression, loss of libido, and vaginal dryness.101 In addition, tamoxifen increases the risk of thromboembolic complications, including deep venous thrombosis, pulmonary embolism (PE), and cerebral vascular events.104-107 Tamoxifen has also been associated with an increase in the development of endometrial cancer97,109; therefore, women receiving this form of hormonal blockade who experience spotting require urgent gynecologic referral for uterine biopsy to rule out cancer. Because tamoxifen is a SERM, a beneficial effect is an apparent decrease in the incidence of myocardial infarction and CVD-related death as well as offering protection from osteoporosis and fracture risk in postmenopausal patients.106-108

A final but important consideration for patients receiving tamoxifen therapy centers on the recognized interactions with this drug in two common comorbid conditions: coagulation and depression. An aging population results in an increasing incidence of cardiac arrhythmias and other conditions resulting in the need for long-term anticoagulative therapy. Tamoxifen potentiates the
action of warfarin by competing with its metabolizing enzyme, cytochrome P4503A4, which may result in major hemorrhagic consequences.\textsuperscript{101,109}

Antidepressants are one of the most commonly prescribed medications in the US.\textsuperscript{110,112} Commonly prescribed antidepressants classified as selective serotonin reuptake inhibitors (SSRIs) inhibit the enzyme CYP2D6 and thus may slow the metabolism of tamoxifen, resulting in a decrease of its potency and thereby increasing the risk of recurrence.\textsuperscript{113-116}

Aromatase Inhibitors: Letrozole, Anastrozole, and Exemestane: Aromatase inhibitors (AIs) work by blocking the enzyme aromatase, which converts adrenal androgens into estrogens. Whereas tamoxifen is employed in premenopausal women who have ER+ tumors, AIs are the estrogen blocker of choice in postmenopausal women whose cancer is ER+. AIs have been established as an effective adjuvant treatment in the postmenopausal group.\textsuperscript{101,117-119} In women, AIs have similar side effects to tamoxifen regarding menopausal symptoms (eg, hot flashes, mood swings, vaginal dryness, and loss of libido).\textsuperscript{97,101-120} The risk of CVD, including myocardial infarction, CHF, hypertension, and hyperlipidemia, remains controversial because published studies have failed to adequately resolve these issues.\textsuperscript{106-108,121-120} Until more definitive data are available, it would be prudent to err on the side of caution and consider those patients who are also receiving long-term AI therapy to be at an increased risk for the development of CVD.

Although arthralgias are an important side effect of AI therapy,\textsuperscript{101,122,123} a potentially more clinically important side effect is the development of bone loss. Osteopenia (a decrease in bone calcium content) and osteoporosis (a decrease in the actual bony matrix) are well-recognized side effects of AI therapy.\textsuperscript{127} Further discussion of bone loss are addressed in the section, Bone Health.

Targeted Biologic Therapies: Trastuzumab and Lapatinib

Targeted biologic agents are directed at protein kinases and the receptors that activate them. Approximately 15% to 30% of all breast cancers are human epidermal growth factor receptor 2-positive (HER2+) and, as such, the HER2 receptor tyrosine kinase pathway has become an important therapeutic target.\textsuperscript{128-134} The main function of the HER2/neu oncogene (now also called ERBB2) is to promote the differentiation, growth, and survival of cells, thereby enhancing the aggressiveness of these breast cancers, resulting in an overall outcome that is inferior to those patients not overexpressing this oncogene.\textsuperscript{135-139} Multiple studies have demonstrated a reduction in mortality and an increase in OS in HER2+ patients when trastuzumab has been incorporated into their treatment regimens.\textsuperscript{140-142} When used as a single treatment agent, trastuzumab increases the duration of survival, which is augmented by the administration of additional chemotherapeutic agents.\textsuperscript{128,138,142} The most severe complication of trastuzumab therapy has been its potential to adversely affect cardiac function; however, the exact mechanism of its cardiotoxicity remains unclear.\textsuperscript{131,144} The risk of trastuzumab-related cardiovascular events, as with other cardiotoxic agents, increases when additional CVD risk factors are noted, especially a history of coronary artery disease or impaired left ventricular dysfunction.\textsuperscript{56,145}

On a positive note, it appears that the cardiotoxic effects of trastuzumab are reversible as long as they are identified early through rigorous monitoring during administration.\textsuperscript{79,145-149} Lapatinib, an orally administered medication, appears to be associated with a lower incidence of cardiotoxicity compared with trastuzumab.\textsuperscript{150} It appears that the cardiotoxicity associated with lapatinib is not as severe and is also reversible.\textsuperscript{151} Lapatinib is a new targeted modality, and further clinical investigation is needed before definitive conclusions about its cardiac safety are made, especially in light of the fact that many treatment options employed in breast cancer therapy have been demonstrated to have delayed long-term toxicities. In addition, further follow-up studies need to be conducted to determine whether outcomes are comparable to those of trastuzumab therapy.\textsuperscript{140,152,155}

The cardiovascular complications of breast cancer treatment are an extremely complex subject, involving numerous variables that may be difficult to isolate. The multifocal approach to treatment includes many chemotherapeutic agents, alone and/or in combination, as well as RT modalities, options for hormonal blockade depending on menopausal status, and targeted therapies. Dosages, sequence of administration, and concordant or tangential approaches further complicate a thorough understanding of both the short-term and long-term toxicity of the administered therapies. The cluster of therapies such as anthracycline-based chemotherapy, right- or left-sided RT, trastuzumab administration, and hormonal blockade with AIs may contribute to an increased incidence of CVD.\textsuperscript{39,48,62,67,153-156} In particular, there have been recent concerns calling for further investigation of targeted therapies used in combination with RT and the potential for long-term cardiovascular side effects.\textsuperscript{92,147,154,157}

Table 1 summarizes the potential long-term cardiovascular side effects of chemotherapy.

Further complicating the multiple cardiotoxicities of breast cancer therapy are the long, well-recognized, preexisting conditions that predispose to CVD (obesity, hypertension, dyslipidemias, and DM). Patients with breast cancer, most of whom now are becoming long-term survivors, may harbor one or more of these comorbidities, all of which increase as the population ages. Because of the complexity of the long-term side effects of treatment modalities for breast cancer, those addressing survivorship care must be aware of the need to incorporate a multidisciplinary approach to issues surrounding assessment and management of CVD, which remains the leading cause of mortality in women.\textsuperscript{158} Lifestyle changes that address these concerns are discussed in greater detail in the section, Lifestyle Management and Breast Cancer.

BONE HEALTH

Women with breast cancer are at an increased risk for the development of bone loss and osteoporosis because of adjuvant therapies; these changes may be extremely rapid in onset. Osteoporosis is a “silent disease” that is often not
recognized until a fracture event. Osteoporosis results in the deterioration of the bony microstructure, particularly in the vertebral ribs, and hips, culminating in fragility fractures and an increase in overall mortality. Maintenance of bone integrity is an important issue in breast cancer care because weakening of the bony matrix represents a major factor in OS. Current therapies profoundly influence the metabolic effectiveness of the skeletal structure.

Risk factors for osteoporosis, excluding the diagnosis of breast cancer, are well recognized and include both non-modifiable and modifiable variables, particularly in the elderly population. Nonmodifiable risk factors include a family history of osteoporosis (genetically based), having a small, thin frame, increasing age, a prior fracture, and the early onset of menopause. These all contribute to the increased risk of osteopenia and osteoporosis (Table 2). In addition, indications for the treatment of other medical conditions necessitate certain pharmacologic interventions not specifically related to treatment of the breast cancer itself (Table 2). These include drugs commonly prescribed for gastrointestinal symptoms or diseases, psychotropic agents, glucocorticoids, hormonal therapies for thyroidal malfunction, anticonvulsants, and anticoagulants for treatment of cardiac disease such as atrial fibrillation.

Gastrointestinal complaints, including those related to gastroesophageal reflux and peptic ulcer disease, result in one of the most commonly prescribed medications: proton pump inhibitors, which approach 150 million prescriptions annually. These often-prescribed drugs decrease the intestinal absorption of calcium and therefore result in a decrease in bone mineral density (BMD), an effect that is reversible after discontinuation of therapy, usually within 12 months.

Nearly 10% of Americans are prescribed antidepressants annually. Second-generation antidepressants, SSRIs, are commonly dispensed and rank third in all drug classes prescribed in the US. Serotonin receptors are present in all major bone cells and, as such, the neuroendocrine system of bony structures may be subjected to interference by the administration of SSRIs.

Many survivors of breast cancer are prescribed medications for depression diagnosed either before or after their initial diagnosis of breast cancer. Patients with comorbidities such as depression are therefore at additional risk of BMD depletion. Add to this the compounding issues affecting depressed individuals, such as decrease in exercise, poor eating habits, lack of sun exposure, tobacco use, and an increase in alcohol intake, and the increased risk of fracture events rises even higher. Those caring for survivors of breast cancer must be aware of patients who are receiving antidepressants, particularly those receiving SSRIs, who may be at an increased risk of osteoporosis and subsequent fractures.

Long-term corticosteroid therapy, often employed in the treatment of multiple inflammatory and autoimmune diseases, is also a well-recognized risk factor for osteoporosis. Steroid therapy leads to osteoporosis by decreasing bone formation through multiple and complex mechanisms, which are beyond the scope of this review. As with the proton pump inhibitors, the osteoclastic effect of corticosteroid therapy appears to decrease fracture risk after discontinuation of therapy.

Multiple other drugs prescribed for patients with breast cancer for concurrent diseases, including anticonvulsant and anticoagulation medications, may affect BMD, further contributing to osteoporotic fractures, particularly in the aging population. The literature is conflicting, but one should be aware that these classes of medications might increase the risk of fracture events.

As, be they steroidal (exemestane) or nonsteroidal (anastrozole and letrozole), are associated with a substantial and often rapid decrease in BMD and an increased fracture risk. These medications appear to be significantly more effective than tamoxifen adjuvant therapy in ER+ tumors in postmenopausal patients, with longer overall DFS and without the additional risk of endometrial carcinoma. Tamoxifen, classified as a SERM, acts like an antiestrogen in some tissues (breast) and an estrogen agonist in others (bone) and therefore is considered as a bone strengthener in women who are postmenopausal, an effect not seen in the premenopausal population. As opposed to tamoxifen, AIs block the aromatization of androgens and thereby block their conversion to estrogens, resulting in bone loss. Recovery of BMD after completion of aromatase inhibiting therapy may be only partial, especially if exemestane (steroidal-based therapy) has been used as the initial choice of antiestrogen therapy (AET). Such reversible effects on bone density deterioration are similar to those reported with the discontinuation of other medications previously addressed.

Recent attention has been directed to patients who have been placed on a regimen of hormonal blockade therapy with tamoxifen, which is then discontinued after the appropriate duration. Postmenopausal women upon discontinuation of tamoxifen may suddenly experience an estrogen deprivation syndrome with respect to bone health; this results in the loss of the protective effects against the development of osteoporosis, with a subsequent increase in the risk of fracture. Thus, those providing long-term care for survivors of breast cancer must be aware that the abrupt discontinuation of tamoxifen requires

Table 2. Risk factors for osteoporosis

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<td>Age older than 50</td>
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<td>Family history</td>
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<td>Small, thin frame</td>
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<td></td>
<td>History of previous fracture</td>
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<td>Early-onset menopause</td>
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<td>Modifiable</td>
<td>Sedentary lifestyle</td>
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<td>Poor nutrition</td>
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<td>Excess protein, sodium, sugar intake</td>
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<td>Inadequate calcium and vitamin D, intake</td>
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<td>Tobacco use</td>
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Breast Cancer Survivorship: A Comprehensive Review of Long-Term Medical Issues and Lifestyle Recommendations
particular attention to bone fragility and its assessment.\textsuperscript{195-199} A further issue, yet to be adequately addressed, involves those patients in whom discontinuation of tamoxifen is followed by the administration of AIs, putting bone health and density at greater risk.

To further complicate the issue, recent studies suggest a beneficial effect in the extension of hormonal blockade, specifically tamoxifen, to ten years, exceeding the previously recommended years of therapy.\textsuperscript{178,199} Although these recommendations should be cautiously interpreted, the long-term suppression of bone density must be addressed. It is hoped that by the time patients who are just beginning hormonal blockade therapies reach their five-year mark, they will have a definitive answer and/or evidence-based medicine to strongly recommend continuing those therapies for an additional five years. Additional confounding variables, especially for long-term therapies, are adherence and compliance, which are discussed in the section, Adherence and Compliance.

Finally, an extensive variety of other medical conditions, diagnoses, and pharmacologic interventions have been implicated in contributing to the development or progression of decreasing BMD from osteopenia to osteoporosis.\textsuperscript{164,168,185,188} Many of these issues are addressed only by observational studies. Therefore, although these risk factors are important, their relevance to absolute risk increase awaits further results from ongoing trials.

Myriad medical conditions have been associated with the development of osteoporosis, but two particularly common diseases must be mentioned: thyroidal conditions and DM.

Hyperthyroidism is a common disorder affecting approximately 1 in 100 individuals, and it is often accompanied by the progression of osteoporosis, especially in postmenopausal women.\textsuperscript{200} Thyroidal disorders are often a comorbidity of patients with breast cancer, and thyroid hormone replacement therapy must be recognized because hyperthyroidism and the treatment of hypothyroidism may both result in bone resorption, resulting in an increased risk of osteoporosis.\textsuperscript{185,201,202} Conflicting results have been reported regarding thyrotoxic conditions and the effect of thyroxine replacement therapy, suggesting that many patients are overmedicated for hyperthyroidism and thus may be exposed to increasing their risk of osteoporosis.\textsuperscript{203,204} The relationship between thyroidal disease and osteoporosis remains controversial, and therefore, a diagnosis of thyroidal disease should be noted in addressing issues of survivorship in patients with breast cancer.\textsuperscript{185,205-208} Thyroidal dysfunction may be a risk factor for osteoporosis.\textsuperscript{209,210}

DM has emerged as a pandemic disease affecting more than 10% of the world population.\textsuperscript{211-213} Many patients diagnosed with breast cancer enter the cancer “arena” with a preexisting diagnosis of DM. Both type 1 and type 2 DM have been associated with the exacerbation of osteoporosis\textsuperscript{214}; however, the mechanism of bone weakening appears to differ between the 2 diseases. Type 1 DM (insulin-dependent) is caused by insulin deficiency resulting in hyperglycemia in young patients, and it may lead to a decrease in BMD, particularly in the spine and hips, resulting in an increased risk of fracture.\textsuperscript{215-222} Conversely, the evidence for type 2 DM (non-insulin-dependent) for the increased risk of fracture appears somewhat conflicting for reasons unknown.\textsuperscript{215,223-225} It has been suggested that the comorbidities of type 2 DM (visual impairment, gait-related neuropathy, advanced age, and obesity) may offer clues to the increase in fracture risk.\textsuperscript{215,224} Multiple studies have reported contrary results when analyzing data regarding the association of type 2 DM and osteoporosis. Some studies suggest no differences in BMD and type 2 DM; some, a lower risk of osteoporosis with type 2 diabetes; and still others, a higher risk.\textsuperscript{214,226-228}

Many medical diagnoses have been identified as potential risk factors for osteoporosis. These include gastrointestinal diseases (celiac disease, malabsorption syndromes, and irritable bowel disease), autoimmune disorders (rheumatoid arthritis and lupus), and other diseases or syndromes.\textsuperscript{200,229} Because an abundance of information exists regarding the development of osteoporosis caused by coexistent morbidities, patients with breast cancer must be thoroughly evaluated for potential comorbidities, particularly in the setting of hormonal blockade with AIs when used as long-term adjuvant therapy. Chronic conditions require the long-term use of medications that may further increase the risk of osteoporotic development. Extensive confusion surrounds the issue of osteoporotic comorbidities (both disease and drug related). Until further evidence is available, it would be prudent to consider these issues as potential risk factors for osteoporosis much the same as hypertension, dyslipidemias, and DM are regarded as risk factors for CVD and cerebral vascular diseases.

There are multiple modifiable risk factors for osteoporosis in the setting of breast cancer therapy. Most of these modifiable risk factors are related to lifestyle and include alcohol and/or tobacco use, nutritional concerns (including eating disorders), maintenance of a near normal BMI, and adequate physical activity.

The excessive consumption of alcohol, defined as greater than 2 U/day to 3 U/day (1 U equals a half-pint of beer [300 mL], a glass of wine [100 mL], 1 shot of distilled spirits [25 mL]), increases the risk of an osteoporotic fracture by up to 40% compared with those with moderate to no alcohol intake.\textsuperscript{230-232} Excessive alcohol intake results in suppression of bone-forming cells and calcium metabolism. Alcoholism is also associated with multiple nutritional deficiencies, including vitamin D deficiency, which results in the increased production of parathyroid hormone, thereby increasing bone resorption, thus further weakening BMD.\textsuperscript{232,233} Falls, resulting from chronic heavy drinking, further increase a patient’s risk of fracture events.

Tobacco use, both historic and current consumption, affects bone density and increases fracture risk, although the mechanism of action is not well understood.\textsuperscript{230,234,235} Inhibition of osteoblastic activity, excessive estrogen breakdown, and earlier onset of menopause have...
been suggested as possible causes of increased bone fragility in smokers.\textsuperscript{230,236}

Adequate nutrition plays a critical and complex role in bone health. Appropriate intake of calcium, phosphorus, and multiple other nutrients are essential in the maintenance of therapeutic levels of vitamin D\textsubscript{3}.\textsuperscript{237-238} It was once thought that obesity was protective against osteoporosis,\textsuperscript{239} but recent evidence fails to support this belief.\textsuperscript{240,241} Assessment and monitoring of BMD has been established as an effective and appropriate predictor of fracture risk. Osteoporosis is currently defined on the basis of BMD as established by the World Health Organization in 1994 using T-scores.\textsuperscript{199,242}

Multiple technologies are available for assessing BMD; however, dual-energy x-ray absorptiometry is the most commonly employed. For each BMD value calculated, a T-score representing the average peak BMD in a young, normal reference population and a Z-score representing the standard deviation of the patient’s calculated BMD from the patient’s expected age-matched cohort are calculated. Osteopenia (decreased levels of calcium in the bones) is defined as a T-score between -1.0 and -2.5. Osteoporosis (decreased level of the bony matrix itself) is defined as a T-score equal to or less than -2.5.\textsuperscript{243,244}

To further delineate the risk of fracture incidence, the World Health Organization has developed the Fracture Risk Assessment tool (FRAX), which is a risk-assessment software program that attempts to further delineate the absolute risk by combining BMD measurements and clinical and historical factors.\textsuperscript{199,242} Table 2 summarizes risk factors for osteoporosis.

**SECOND PRIMARY MALIGNANCIES**

SPMs, those cancers that occur after the diagnosis of a primary cancer, now constitute one-sixth of all malignancies reported to the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program.\textsuperscript{245}

Because patients with breast cancer constitute nearly one-fourth of all long-term cancer survivors,\textsuperscript{246,247} the issue of SPMs is particularly germane. Commonly, SPMs occur in survivors because of a genetic predisposition and increased susceptibility, caustic exposures to environmental toxins yet to be fully identified, and the carcinogenic proaccelerators of treatment modalities currently in use.\textsuperscript{1,248-249} Because survival rates for women with a breast cancer diagnosis continue to increase,\textsuperscript{250,251} the risk for development of SPMs also rises. Longer survival also increases the opportunity for SPMs to develop because increasing age is a well-recognized risk factor for all cancers.

The most important risk factor for SPMs appears to be age at the time of diagnosis. The younger one’s age at diagnosis, the more likely the potential for the development of an SPM. Although the development of a new breast cancer may not qualify specifically as an SPM, it is the most common second malignancy in patients with a primary breast cancer; it accounts for nearly 40% of all new malignancies.\textsuperscript{252} It may present in the ipsilateral or contralateral breast, but most often, such malignancies are found in the opposite breast, especially if the primary treatment of the initially diagnosed cancer included a mastectomy. The increased risk has been reported to approach 70% more than that of the general population during a 10-year follow-up period.\textsuperscript{252} Again, younger age at diagnosis has been identified as a predictor of increased risk.\textsuperscript{253,254}

Recurrence can be local, developing in or near the original site, resulting from a failure of primary treatment (even after mastectomy); regional, presenting as nodal involvement in the axillary, supraclavicular, or cervical anatomic locations; or distant, appearing in the bones, lung, liver, or brain. Most often, recurrence is predicated on the initial stage at the time of diagnosis; the higher the stage, the more likely a recurrence.\textsuperscript{255}

An issue of major concern and debate centers on the differentiation of an ipsilateral tumor recurrence after BCT vs the development of a true new primary malignancy. The question is simple; the answer is complex. Approximately one in five patients with breast cancer who have completed a five-year course of adjuvant therapy will experience a recurrence vs an SPM. Technologies exist to distinguish between the two and result in the opportunity to offer better-advantage therapeutic approaches depending on the differentiation.\textsuperscript{253,254,256} In addition, time to occurrence has been demonstrated to be significantly shorter in patients with an ipsilateral recurrence compared with those diagnosed with a new SPM.\textsuperscript{257}

**Signs and Symptoms of Breast Cancer**

**Primary or recurrent/local-regional:**
- Lump in the breast/chest wall/axilla
- Dimpling of the skin
- Nipple retraction
- Clear or bloody nipple discharge (spontaneous)
- Redness, scaling, thickening of nipple-areolar complex
- Rash on breast, unresponsive to antibiotics

**Distant recurrence:**
- New-onset localized bone pain lasting longer than 2 weeks (long bones, ribs, spine)
- Persistent chest pain, with or without cough
- Persistent abdominal pain
- Unintended weight loss
- Persistent headache
- Personality changes
- New-onset seizures
- Loss of consciousness

Follow-up of recommendations for patients who have completed therapy...
with a curative intent have been published by the American Society of Clinical Oncology. Regular physical examinations, varying from three to six months during the first three years and annually thereafter, are recommended. Mammograms are performed annually (with the exception of a six-month follow-up mammogram after completion of RT). Magnetic resonance imaging is indicated as an annual adjunctive screening tool in those patients who are BRCA gene positive and/or have a diagnosis of invasive lobular breast cancer. Follow-up in an asymptomatic patient does not call for regular bloodwork, advanced radiographic imaging, or surveillance with specific biomarkers.

In addition to the risk of the development of contralateral disease, survivors of breast cancer are at an increased risk for the development of additional SPMs. It is estimated that an SPM will develop in 5% of patients within 10 years of diagnosis because chemotherapy has been linked, specifically, to the development of secondary acute myeloid leukemia (AML) and, more rarely, myelodysplastic syndromes (MDS). The risk of AML or MDS appears to depend on the cumulative doses of anthracyclines and alkylating agents administered.

Recent controversies have questioned whether use of granulocyte colony-stimulating factors contributes to an increased risk of AML or MDS. The leukemogenic effect of granulocyte colony-stimulating factors is unknown at this time, but those involved in the long-term care of survivors of breast cancer should note that the addition of granulocyte colony-stimulating factors as part of the chemotherapy regimen may, in fact, increase the patient’s potential for the development of AML or MDS.

Although the absolute risk of the development of leukemia is likely to be low in survivors of breast cancer, it should be discussed with the patient, to educate about the potential signs and symptoms of these diseases.

Recent studies have reported the increased risk of SPMs, with the authors hypothesizing that such malignancies are dependent on multiple other factors in addition to treatment effects. The risk of developing an SPM, aside from a contralateral breast cancer, appears to be in the range of 5% to 7%. The most common sites for SPMs to develop are the pulmonary, gynecologic (endometrial and/or ovarian), colo-rectal, and integumentary (melanoma) systems. The fact that malignancies of the lung and the colon and rectum appear high on the list is not surprising because both are in the top 3 malignancies in women by incidence and mortality.

Gynecologic malignancies are related to breast cancer through genetic predispositions (BRCA1 and BRCA2 genetic mutations) as well as conjoined risk factors, including obesity, nulliparity, delayed parity, and a history of hormone replacement therapy. Numerous epidemiologic studies have established the role of family history as an important risk factor for breast, ovarian, and other associated malignancies and have referred to this as “inherited cancer susceptibility syndromes.” In the early 1990s, a genetic link was discovered between breast and ovarian cancers through the identification of the mutated forms of the BRCA1 and BRCA2 genes. These genes, when healthy, produce tumor suppressor proteins that help repair damaged DNA, but when mutated, the ability to repair DNA is rendered ineffective.

The harmful mutations in BRCA1 or BRCA2 can be inherited from a mother or father, further amplifying the importance of a thorough acquisition of the patient’s family history. Although in the general population breast cancer will develop in about 1 in 8 women (12%) sometime in their lives, it will develop in 55% to 65% of women with a BRCA1 mutation and 45% of women with a BRCA2 mutation assuming they reach age 70 years. The general female population has slightly more than a 1% chance of ovarian cancer developing, in contrast to a 39% chance in those with a mutated BRCA1 gene penetrance and an 11% to 17% chance if affected by the BRCA2 mutation. Previous reports may have overstated the increased risk of breast and ovarian cancers associated with BRCA1 and BRCA2. Carriers of BRCA1 were reported to have a risk as high as 87%, and BRCA2 carriers, a risk as high as 84%. The incidence of ovarian cancers has also been previously overestimated in families with a history of breast cancer. In addition, BRCA1 and BRCA2 mutations have been associated with an increased risk of fallopian tube and peritoneal cancers.

Multiple other genes and their subsequent predisposition to the development of syndromes associated with the increased risk of breast cancer have been identified. Additional cancer susceptibility syndromes that have been noted are also an issue of concern deserving attention when providing care to long-term survivors of breast cancer. Nearly a dozen syndromes have been associated with hereditary breast (and ovarian) cancer mutations, and several excellent reviews of these issues are available.

Other inherited susceptibility syndromes and/or genes that may predispose to the development of breast cancer include the Li-Fraumeni syndrome (soft tissue carcinoma, osteosarcoma, neurologic tumors, adrenocortical tumors, and leukemia), Cowden syndrome (multiple hematomas, tumors of the thyroid gland and uterus), and the Lynch syndrome (colon, uterus, pancreas, brain, gastrointestinal tract, and the integumentary system). Numerous other syndromes have been described in association with the increased incidence of breast cancer, but their penetrance and incidence appear minimal.

The most common gynecologic malignancy seen in survivors of breast cancer is uterine cancer, which is probably because of the common use of tamoxifen as an adjuvant therapy for ER+ tumors. Most studies have demonstrated that the increased relative risk of endometrial cancer in patients receiving tamoxifen is 2 to 3 times higher than that of an age-adjusted, cohort population. Furthermore, the association of uterine cancer and tamoxifen use appears to be dose dependent and also increases with duration of use.
of endometrial cancer in patients who receive tamoxifen therapy, the 5-year DFS rate for breast cancer approaches a 40% higher rate than patients not receiving the drug; therefore the risk-benefit ratio for significant increases in survival appears to far outweigh the risk of uterine cancer, which, in most cases, is cured by hysterectomy.300,305

The development of colorectal malignancies has long been known to be increased in patients after the diagnosis of breast cancer.252 However, the reported incidence rates of colorectal cancer in association with breast cancer vary widely.306,307 When investigation of the association of the BRCA1 and BRCA2 gene mutations is undertaken regarding a potential increased risk of colon cancer, current results are inconsistent and conflicting. Some studies have shown an elevated risk of colon cancers in BRCA1 and BRCA2 carriers, but these findings have not been confirmed by others.308,309 Further investigation must be undertaken to verify or to refute an association of BRCA1 and BRCA2 mutations with colorectal cancers.

There appears to be a reciprocally elevated risk of skin cancer occurring after the development of breast cancer, and vice versa.310 The increase in the development of breast cancer and melanoma range from a onefold to threefold increased incidence of developing the other malignancy.275,310-313 As with the increased incidence of SPMs, the incidence of cutaneous melanoma is also age dependent; the younger a woman is at time of diagnosis with one or the other malignancy, the higher her risk of the other malignancy.310 These malignancies may share genetic predispositions such as BRCA2 mutations275,310 and mutations in the CDKN2A gene, which have been identified as definitive risk factors for melanoma and thus may inversely increase the risk of breast cancer.300-314 Despite the conflicting results reported to date, one should note that the development of an SPM is associated with a significant decrease in OS, which is particularly concerning.276

Treatment of early-stage breast cancer saw a major paradigm shift in the 1990s from modified radical mastectomy with or without adjuvant therapy to the increased use of BCT followed by radiation for control of local and/or local-regional recurrence.252 With this change came the increased use of RT as the preferred adjunctive approach in procedures that aim to conserve the breast.315-317 Survival has increased with BCT and RT, and therefore the use of RT has grown exponentially. Long-term side effects of RT assume an increasingly important role in the development of SPMs.

Thoracic malignancies after RT for BCT have become an area of great concern as the role of RT in the treatment of breast cancer continues to rise. Lung cancer accounts for 5% of SPMs after breast cancer treatment; considering the high survival rate of breast cancer, lung malignancies, as a new SPM in these patients, are of concern because the survival rate of lung cancer is quite low.315-317 Lung SPMs appear to be significantly increased among women who are younger than age 50 years at their diagnosis. Strikingly, the incidence in lung cancer appears as early as 1 year after treatment and the risk persists for an extended period of time. This phenomenon is perhaps not explained in the setting of RT and BCT because the long-term effects of RT have been well documented and follow a latent period of 5 to 10 years or longer.71,83,88,201,318-322 There may be an association in younger patients who have a higher increase in estrogen receptor negative tumors and an increased propensity for SPMs occurring as new lung malignancies.318,319,323

Initially, RT was used as an adjuvant therapy for patients undergoing BCT. However, even in the setting of mastectomy, RT has been used as adjuvant therapy in patients with 4 or more axillary lymph nodes involved with metastases.324-325 There is clear and consistent, prospective, randomized data showing an absolute OS benefit approaching 10% in addition to fairly dramatic benefits in local and local-regional control in these patients. On the other hand, the ability to make solid recommendations for adjuvant RT in women with lesser node involvement has been more elusive. Some recent evidence points to the benefits of RT even in patients who undergo mastectomy but have minimal lymph node involvement (1 to 3 positive lymph nodes) reported in the final pathologic synopsis.326

Thus, concerns about SPMs and RT in patients with breast cancer undergoing mastectomy with minimal nodal involvement will require future awareness and education for caregivers of survivors of breast cancer. As breast cancer survival continues to improve, and this improvement is largely attributable to adjuvant RT, understanding the long-term side effects of RT is assuming an increasingly important role. In addition to the commonly recognized SPMs, as described earlier, reports are beginning to emerge of less well-recognized SPMs secondary to RT, including the development of esophageal malignancies.315,327

The development of such malignancies has not been discussed in recent reports addressing SPMs, probably owing to their obscurity.78 Nonetheless, survivors of breast cancer and those providing follow-up care must be aware of these potential long-term complications, which have only recently been recognized. (See Sidebar: Risk Factors for Second Primary Malignancies.)

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**BREAST CANCER-RELATED LYMPHEDEMA**

Breast cancer-related lymphedema (BCRL) is a serious, chronic, debilitating, and common consequence of breast cancer treatment and has been addressed as incurable, or at least refractory, to conventional treatment modalities. Multiple lifelong morbidities include deformity, pain, a reduction in limb use, and extreme emotional distress often resulting in isolation.326-330 Many patients fear the development of lymphedema even more so than the diagnosis of the cancer itself or the loss of a
Breast cancer,\textsuperscript{328,329,331-333} Upwards of one in five patients may face the consequences of this irreversible, lifelong condition.\textsuperscript{339} In BCRL, there is an ongoing, progressive accumulation of protein-rich fluids and subsequent fibrosis in the affected limb because of the disruption of lymphatic anatomy.\textsuperscript{30,334-337} This condition remains poorly understood despite extensive research directed in attempts to identify its exact etiology.\textsuperscript{30,335,338}

BCRL is a well-recognized sequela of the treatment of breast cancer, including surgery and adjuvant therapies employed.\textsuperscript{10,339} The risk of the development of BCRL is a lifetime risk. Fibrosis may be slow to develop, which may account for the delay in the development of BCRL.\textsuperscript{334,337} BCRL may develop at any time after treatment; however, the condition develops in most patients within the first two to three years after treatment.\textsuperscript{332,340-342}

The incidence of BCRL, as reported, is incredibly misleading and quite confusing because it varies from 6% to 62%.\textsuperscript{25} This range represents an enormous variation and underscores our poor understanding of the condition.\textsuperscript{331,338,343-345} Some estimates of the incidence of BCRL even exceed 80%.\textsuperscript{332} Discrepancy of the reported incidence of BCRL appears to result from multifactorial variations of the definition of the condition, the absence of any standardized uniform measurements, the lack of patient symptom reporting, inadequate follow-up of complaints related to BCRL symptoms, varying follow-up periods, weak study designs, and, finally, poor documentation by health care professionals involved in the treatment of patients with BCRL.\textsuperscript{10,338,346-348} In addition, BCRL may develop in other regions, including the chest wall and/or the remaining breast tissue, an issue that has received little attention in the medical community.\textsuperscript{349,352}

Numerous predisposing risk factors for BCRL have been identified. These risks can be stratified into two major categories: disease specific (factors beyond the patient’s control) and lifestyle risks (factors that may be influenced or controlled by the patient’s proactive involvement). Although some of these risk factors may overlap, many nonmedical factors remain beyond the patient’s control. Factors beyond the patient’s control include the age at diagnosis, stage of disease, extent of surgical manipulation, need for adjuvant therapies, development of postoperative infections, and formation of seromas.\textsuperscript{10,333,354} Age has been addressed in several studies, and the evidence for this as being a definitive risk factor for the development of BCRL remains conflicting.\textsuperscript{346,353,354} An urgent and more recent concern is that breast cancer is being diagnosed in younger women. Because development of BCRL is a lifelong risk, the long-term survival of younger patients may result in an increased risk of BCRL over time, as with the risk of CVId.\textsuperscript{25,26}

The surgical treatment of breast cancer appears to be the primary predisposing factor for the development of BCRL. Therefore, the risk of BCRL may differ depending on the initial surgical option chosen by the patient. Mastectomy, as opposed to lumpectomy, may result in a significantly higher risk (a twofold to sixfold increase) of BCRL.\textsuperscript{341,353,356} The extent of axillary dissection and the ratio of positive to negative lymph nodes have also been identified as factors that may increase the potential for BCRL development.\textsuperscript{330,334,357-359}

Intuitively, it appears to make sense that the number of lymph nodes removed and, furthermore, those that are found to be involved with metastatic disease would increase the chance of BCRL developing owing to the disruption of the anatomic flow of lymph. Several studies do not support this concept and, in fact, offer little evidence for the mechanism of this pathologic event.\textsuperscript{339,354,360} A potential explanation offered is the fact that lymph node involvement early in the disease process allows the development of collateral channels for lymphatic drainage.\textsuperscript{360} On the other hand, multiple additional studies lend support to the hypothesis that the extent of nodal dissection or involvement with the disease are, indeed, factors that increase the propensity for the BCRL.\textsuperscript{330,334,340,357-359,361} Replacing the radical axillary dissections of decades ago, sentinel lymph node sampling is now the currently accepted, minimally invasive approach to breast cancer treatment in early-stage disease.\textsuperscript{328,362} Compared with traditional axillary dissection, multiple studies have well documented that sentinel lymph node biopsy for assessing and staging breast cancer results in a significant reduction in the development of BCRL.\textsuperscript{328,355,363-366} Nonetheless, despite the rapid adoption of sentinel lymph node biopsy, BCRL remains a concern; according to recent data, there is still more than a 7% or 8% chance of BCRL developing within the first 6 months after the biopsy procedure.\textsuperscript{328,353,367}

Chemotherapy has been well documented as an extremely effective adjuvant therapy to decrease recurrence and increase the OS of patients with breast cancer.\textsuperscript{368,369} Interestingly, the percentage of patients receiving such adjuvant therapies as related to the development of BCRL is poorly documented because of incomplete information gathering and secondarily, in large part, because of the outpatient administration of chemotherapy.\textsuperscript{370} The addition of chemotherapy to the breast cancer treatment regimen and its relationship to the incidence of BCRL remains largely unresolved. As the multidisciplinary approach to breast cancer increases, it is becoming increasingly difficult to separate various therapies and their long-term consequences. This is particularly true in the setting of BCRL. Polyagent therapies have been implicated with an increase in the incidence of BCRL.\textsuperscript{371-373} Particular attention has focused on the anthracycline-based therapies.\textsuperscript{374} It remains unclear why the addition of chemotherapy to the treatment of breast cancer may increase the incidence of BCRL. The issue of more advanced disease requiring adjuvant chemotherapy may skew the population that is more likely to experience BCRL. No studies, to our knowledge, have addressed or isolated a primary association. Therefore, it seems wise to be aware of the fact that chemotherapy, particularly anthracycline-based regimens, should be considered as a potential contributing risk factor for BCRL.

As previously mentioned, RT has become a mainstay in the adjuvant treatment of breast cancer.\textsuperscript{59-75} Although the ultimate role of adjuvant
RT in the development of BCRL is currently under review, substantial evidence has been reported supporting the idea that axillary RT increases the risk of BCRL.\textsuperscript{335-338,375,376} Presumably, RT-induced fibrosis results in scarring of the lymphatic system, resulting in further lymphatic flow disruption and the subsequent development of BCRL. Other studies have reported no increase in the incidence of BCRL after adjuvant axillary RT.\textsuperscript{372-374} Contemporary therapy involves sophisticated computed tomographic planning for appropriate simulation and allows for a more exact “targeted” zone for RT. As such, the potential for BCRL secondary to RT will, one hopes, be minimized in the near future.

Additional risk factors for BCRL include the postoperative complications of infection and seroma formation.\textsuperscript{336,352,355} Trauma, such as a shearing chest wall injury or dermal intrusion secondary to activities such as gardening and hiking, may also predispose a patient to the development of late-onset BCRL. Furthermore, surgery on the dominant side may also increase the incidence of BCRL.\textsuperscript{377}

Lifestyle issues that are modifiable by a patient’s behavior may also play an important role in BCRL risk. The most important modifiable risk factor is related to obesity as determined by BMI,\textsuperscript{330,338,354,355} A sedentary lifestyle contributes to obesity, and therefore increasing physical activity may help decrease a patient’s BMI. In fact, multiple studies have demonstrated the benefits of exercise to not only decrease BMI but also to decrease the risk of BCRL.\textsuperscript{10,354,378-380} In addition, exercise has been shown to have significant beneficial effects in cancer rehabilitation and, when coupled with an effective diet, including high vegetable and fruit consumption, has been shown to increase OS after breast cancer.\textsuperscript{381-383}

Finally, DM and hypertension, both associated with an increased BMI, have been identified as potential risk factors for BCRL, and these conditions may be altered by an effective diet and exercise program.\textsuperscript{10,338-354,355,381,385} Obesity, DM, and hypertensive states also increase the risk of CVD as previously discussed. (See Sidebar: Risk Factors for Breast Cancer-Related Lymphedema.)

### THROMBOEMBOLIC EVENTS

TEs, such as deep venous thrombosis and PE, are uncommon but serious potential consequences related to all malignancies, breast cancer being no exception.\textsuperscript{384} Cancers are prothrombotic states, and the association of malignancies and the development of hypercoagulability have been well recognized for more than 150 years. Initially described by Rudolf Virchow,\textsuperscript{385} this association has come to be known as the triad of Virchow or Virchow’s triad: damage to endothelial cells, hypercoagulability (elaboration of procoagulants), and stasis (alteration in blood flow).\textsuperscript{12,386,387} (Figure 1).

The risk of TE in cancer-affected patients is estimated to range from 15% to 20% and is the second-leading cause of death in those with cancer, although it is often seen in conjunction with multiple additional comorbidities.\textsuperscript{384,388}

The incidence of TE appears to be on the rise because of improved diagnostic imaging technologies, advanced and more effective therapeutic interventions, and, most importantly, increased long-term survival (DFS rates, measured in years after diagnosis and treatment).\textsuperscript{389} Multiple risk factors for TE in patients with cancer have been identified as significantly affecting morbidity and mortality. It has been estimated that patients in whom a malignancy was diagnosed have a 4- to 7-fold higher risk of TE compared with individuals without a cancer diagnosis.\textsuperscript{390,391}

In addition to the diagnosis of cancer, which itself is a thrombogenic and prothrombotic state,\textsuperscript{392-394} other risk factors for TE have been identified. As with all diseases, age older than 40 years remains
a primary risk factor for TE.\textsuperscript{395} Stage of disease at the time of diagnosis has also been associated with an increased risk of TE. The more aggressive the disease, the higher the chance of experiencing an episode of TE.\textsuperscript{396,399,400} Stage of disease dictates, in large part, further and more aggressive therapeutic interventions, including the more frequent use of invasive technologies and advanced chemotherapeutic regimens, which further increase the risk of TE.\textsuperscript{390,398-400} Chemotherapy increases TE risk through multiple pathways and mechanisms involving multifactorial issues, which are beyond the scope of this article. Several excellent reviews on the complex interactions of the association between chemotherapy and the increased risk of TE are available in the references provided.\textsuperscript{13,292,392} Again, it is important to mention that advanced and/or metastatic disease places patients at an increased risk of TE.\textsuperscript{400}

Most patients with breast cancer (upwards of 70%) have ER+ status, meaning their tumors are being fueled by endogenous estrogen.\textsuperscript{29-103,401,402} Having an ER+ tumor is important for 2 reasons. First, ER+ tumors tend to be less aggressive, and second, such tumors can be treated with an array of AETs. Tamoxifen has long been considered the primary antiestrogenic drug of choice for ER+ breast cancer. A major side effect, recognized early after its implementation, has been the increased incidence of TE.\textsuperscript{104-107} The risk of TE in patients receiving tamoxifen as adjuvant therapy is 1% to 2%\textsuperscript{395,403} and appears to be highest in the initial 2 years of treatment, although the risk remains throughout all years of therapy.\textsuperscript{390,404}

The recognition of the extremely effective role of AET in the treatment of most breast cancers has resulted in the so-called “third generation” of AETs, the AIs (letrozole, anastrazole, and exemestane).\textsuperscript{388-390,408} As previously stated, the effects of AIs on the circulatory system remain controversial.\textsuperscript{106-108,121-126} What seems to have been resolved is the incidence of AIs and TE.\textsuperscript{387} Multiple studies have now documented the decreased incidence of TE with the use of AIs in direct comparison to tamoxifen.\textsuperscript{327,346,407} Thus, it now appears that AIs do not increase the risk of TE in patients with breast cancer. What remains controversial are the long-term effects of AIs on lipid levels, which may affect cardiovascular profiles, and subsequent risk factors, which may contribute to CVD.\textsuperscript{106,110,121,126} Clearly, for those women with a history of TE, AIs are the drug of choice for adjuvant AET in the postmenopausal patient with an ER+ breast cancer.

Additional risk factors for TE exist in patients with breast cancer. Many contemporary patients receive long-term intravenous therapies, which extend beyond the short-term chemotherapy regimen. These include a one-year cycle of trastuzumab and/or pertuzumab as well as bisphosphonates for bone metastasis and protection against fractures. For the comfort of the patients, indwelling catheters are often placed for administration of such medications as well as to provide easy vascular access to monitor whole blood cell counts. Indwelling catheters may lead to thrombotic complications, the incidence of which is poorly documented in the literature.\textsuperscript{384,400,408,409} Additional risk factors for TE are not unique to patients with breast cancer but are often identified along with their comorbidities. These include any history of cardiac disease (myocardial infarction, CHF) and a history of TE.\textsuperscript{395,410} Obesity and its impact on breast cancer is described in the section, Lifestyle Management and Breast Cancer. Relating to the development of TE, obesity is a well-recognized risk factor.\textsuperscript{395,411,412} Overweight and obesity are often associated with a sedentary lifestyle and general immobility (lack of exercise). It is a modifiable lifestyle risk factor in most patients. Exceptions include increased immobilization caused by hemiplegia after nonfatal cerebral vascular events and fractures of the lower extremities and hips.\textsuperscript{104,384,392,413}

The mechanism by which malignant tumors cause a hypercoagulative state is incompletely understood and is likely multifactorial in nature. Numerous abnormalities in blood composition have been identified, including increased levels of clotting factors, excessive tumor production of inflammatory proteins (cytokines, tumor necrosis factor-α, interleukin-1β), C-reactive protein, and tissue factor from vascular endothelial cells, which all interfere with the normal hemostatic mechanism.\textsuperscript{405-407,393,414,415}

Angiogenesis (the formation of new blood vessels) has been identified recently as a process that may also interfere with the coagulation cascade because both tissue factor and vascular endothelial growth factor are produced by tumorous cells that acquire their own vascular supply.\textsuperscript{13,388,416,417} In fact, detection of tissue factor in breast cancer vascular endothelium has been shown to be proportionally related to the initiation of new blood vessel formation.\textsuperscript{418} Further linking angiogenesis and TE are the well-described role of platelet aggregation and the production of platelet dermal growth factor. As such, these also contribute to the risk of TE development.\textsuperscript{56,392,418} Angiogenesis may also result in the formation of blood vessel structures that are abnormal in their basic anatomic scaffolds and appearance and that display aberrant blood flow patterns.\textsuperscript{384} Such flow discrepancies may have a role in the development of TE.

A TE significantly decreases long-term survival rates in patients with cancer.\textsuperscript{384,400} Patients with a malignancy who experience a TE have a fourfold to eightfold higher risk of dying of TE than those who do not have a concurrent malignancy.\textsuperscript{119,422} Without doubt, patients with malignancies and an episode of TE have a poor prognosis. Furthermore, the risk of a recurrence of TE after an initial episode of TE is higher in patients who have a diagnosis of malignancy. The development of TE is well documented to lead to significantly decreased long-term survival in patients with breast cancer,\textsuperscript{405,423} and malignancies resulting in death often involve a thrombotic component.
Surprisingly, as high as the incidence of TE is, nearly three-fourths of Americans surveyed were unaware of the condition and its long-term sequelae.\textsuperscript{413,424} Because TE is a lifetime risk factor after breast cancer,\textsuperscript{401} it is incumbent on the survivorship care team to educate patients with breast cancer on the signs and symptoms of TE. Usually DVT is heralded by the sudden onset of pain, swelling, tenderness, and occasionally redness and/or warmth in an extremity. A PE, sometimes the sequela of untreated DVT, is heralded by the sudden onset of shortness of breath, chest pain exaggerated by deep breathing, a rapid or irregular pulse, lightheadedness, and occasionally hemoptysis. Education of patients regarding these symptoms can be lifesaving.\textsuperscript{425,426} (See Sidebar: Risk Factors for Thromboembolic Events.)

**ADHERENCE AND COMPLIANCE**

Many patients who are given prescriptions for medications fail to take them as directed or for the length of time recommended. Adherence and compliance are a concern in the management of malignancies because oral chemotherapeutic agents are increasingly being developed and used in long-term management.\textsuperscript{407} Of the nearly 400 antineoplastic agents in various stages of development, nearly one-fourth are planned as oral agents.\textsuperscript{428} Clearly, the increasing percentage of cancer patients who are prescribed or will be prescribed oral therapies will affect current oncologic treatment patterns. Breast cancer survivorship is on a steady rise,\textsuperscript{427,428} and this cancer is no longer thought of as an acute illness but rather a chronic condition. Therefore, long-term therapies are being increasingly used. Foremost of these interventions is the oral administration of drugs in the outpatient setting, allowing patients to mediate themselves with appropriate dosages and scheduling.

This major advance in cancer treatment comes with new concerns: adherence and compliance. Although adherence and compliance are ultimately related, they are distinct parameters. *Adherence* defines the taking of medication as prescribed, whereas *compliance* more specifically addresses taking the medication for the full term recommended. Compliance is also often referred to as "persistence."\textsuperscript{429,430} Some have called for the dismissal of the term *compliance* because it connotes an onus and dependence on the patients for their ultimate outcomes.\textsuperscript{431}

Regardless of definitions and disparities, the ultimate measure of outcome is *OS*.\textsuperscript{432} Although developments in oncology have resulted in major advances in survivorship, many are dependent on long-term administration protocols. As such, the issue of adherence and/or compliance to therapies recommended has become the latest oncologic challenge. This also provides increased impetus for survivorship programs to assume a major role in the care of these patients, that is, follow-up with adherence and compliance.

Adherence and compliance are important for women who are prescribed AET. AET has been definitively demonstrated for more than 30 years to decrease both recurrence and mortality in ER+ patients.\textsuperscript{75,97,98} Five years of AET, with either tamoxifen or AIs, results in a greater than 30% reduction in breast cancer recurrence and increased OS.\textsuperscript{97,98,433} Despite the strong documentation of the effectiveness of AET, it is both surprising and disappointing to note the incredibly high rates of noncompliance to a 5-year regimen, which range from 30% to 70%.\textsuperscript{434} Less than 80% compliance at 2.5 years has been associated with increased mortality.\textsuperscript{14} Nearly 25% of patients discontinue AET within the first year, and 50% become noncompliant by Year 4.\textsuperscript{433,435} Despite multiple trials that have shown higher recurrence rates and decreased survival,\textsuperscript{14,436,437}

Another point of major concern is that women younger than age 45 years have a greater risk of recurrence owing to more aggressive, higher grade tumors, and yet this group is most likely to discontinue therapy.\textsuperscript{433} Multiple studies have noted this,\textsuperscript{435,438,439} yet the issue of age has not been adequately addressed. Patients who are premenopausal when their breast cancer is diagnosed have a higher recurrence rate and increased mortality than those diagnosed in the postmenopausal state.

The poor adherence and compliance to 5 years of AET presents a major challenge. Although this is a large enough issue, we now face new reports strongly supporting a 10-year regimen. Results from the Adjuvant Tamoxifen Longer Against Shorter (ATLAS) trial and the Adjuvant Tamoxifen Treatment Offers More (aTTom) trial have clearly demonstrated improved outcomes by doubling the 5-year recommendation for AET.\textsuperscript{430,431} The ATLAS trial concluded that recurrence and mortality were lowered in patients given an additional 5 years of tamoxifen. Ten-year recurrence rates decreased by 29% in 6846 patients. Similar findings were reported in aTTom, which followed 6934 women with early-stage breast cancer. Although AIs have been clearly demonstrated to decrease recurrence rates in postmenopausal women with breast cancer, their indications for extended length of therapy are less clear and are currently undergoing further investigation. These reports demonstrate the increasing need for adherence and compliance for AET maintenance. Extensions of AET must also take into consideration the long-term side effects of these therapies. Risks of PE were noted in the ATLAS trial as well as the development of endometrial cancer; however, the risk of mortality was lower than the mortality due to breast cancer itself.\textsuperscript{441,442} Long-term side effects of the AIs have yet to be determined. Particular attention must focus on bone health and osteoporosis as well as the CVD risk associated with AIs.\textsuperscript{130,443} Clearly, poor adherence and compliance result in less effective disease outcomes and increased mortality.\textsuperscript{441}

AET is one of the most important recent advances in cancer treatment. As
A CALL TO ACTION

We, as caregivers, are letting our patients die by not taking a strong, proactive role in promoting healthy eating and an active lifestyle, and encouraging emotional resilience. These principles are the cornerstone of the rapidly emerging subspecialty known as lifestyle medicine. Current medical practice is reactive: surgery or a prescription for every illness. This needs to change. A paradigm shift to lifestyle medicine must be implemented immediately.

Dramatic effects using lifestyle interventions have been demonstrated in patients with chronic conditions, which now include breast cancer. Several large studies have conclusively shown that diet and exercise modifications can significantly improve total health.5,6,14 One prospective study of 23,000 participants evaluated adherence to 4 recommendations: no tobacco use, 30 minutes of exercise 5 times per week, maintaining a body mass index less than 30 kg/m², and eating a healthy diet (high consumption of fruits, vegetables, legumes, and whole grains, and low consumption of meat).5 People who adhered to these 4 recommendations had an overall 78% lower risk for development of a chronic condition during an approximately 8-year timeframe.6 Furthermore, in those adhering to the recommendations, there was a 93% reduced risk of diabetes mellitus, an 81% reduced risk of myocardial infarction, and a 36% reduction in the risk of cancer.5

Ample evidence exists to support the avocation of a diet based on the recommendations noted in Table 1.1,5-32 In addition, a whole-food, plant-based diet tends to promote a healthy body mass index, which is associated with, yet again, a lower risk of all common cancers.15 Dietary principles cannot be fully addressed without consideration of caloric density. Caloric density refers to foods that may or may not provide high amounts of vitamins and nutrients, but contain higher levels of calories. High-nutrient foods have fewer calories per pound in contrast to low-nutrient foods.

Table 1. Daily dietary recommendations

<table>
<thead>
<tr>
<th>Decrease or eliminate</th>
<th>Increase or consume heavily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad carbohydrates</td>
<td>Good carbohydrates</td>
</tr>
<tr>
<td>• Refined grains (white bread, crackers)</td>
<td>• Fruits</td>
</tr>
<tr>
<td>• Processed foods (cakes, cookies, chips)</td>
<td>• Vegetables</td>
</tr>
<tr>
<td>• Added/refined sugar (soft drinks, cereals)</td>
<td>• Legumes</td>
</tr>
<tr>
<td>• Processed meats</td>
<td>• Beans/lentils</td>
</tr>
<tr>
<td>• Refined grains</td>
<td>• Whole grains (bread, cereal, pasta)</td>
</tr>
<tr>
<td>• Processed foods (white bread, crackers)</td>
<td>• Natural soy products</td>
</tr>
<tr>
<td>• Refined grains</td>
<td></td>
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<tr>
<td>• Processed foods</td>
<td></td>
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<td>• Refined grains</td>
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</table>

*Processed foods are stripped of nutrients and include unhealthy additives. It is important to remove these from the diet completely.

(Continued on next page.)
patient education regarding the importance of taking medications and appropriate scheduling. Navigators can play an important role as well. Regular telephone or texting conversations to check on a patient’s adherence can not only evaluate the patient for compliance but also serve as a motivator for the patient. Although it would appear intuitive that education for patient and family members about the importance of consistent oral therapy would improve compliance, this has not been fully validated. Reminder letters and telephone calls have demonstrated only a minor increase in adherence rates. Other studies have noted no improvement in patients given additional education materials or increased support services. Going forward, technologic advances such as the widespread use of electronic medical records, sophisticated prescription bottles with built-in reminder timers, and effective pharmacy tracking systems may lead to further improvements. Simplified dosing regimens, as well as seamless access to refills, may also help improve compliance. Clearly, many women are not taking their AET as prescribed, and this remains an issue of major concern. Prescribed medications are useless if the patient does not take them. (See Sidebar: Barriers to Adherence and Compliance.)

LIFESTYLE MANAGEMENT AND BREAST CANCER

In 2014, the American Institute for Cancer Research reported in their latest review of global research that diet, physical activity, and weight management play a major role in survival among patients with breast cancer. Research indicates that a lower BMI and eating a whole-food, plant-based diet (WFPBD), high in fiber and low in fats, improves survival in breast cancer. Maintaining health after a diagnosis foods (Figure 1). A healthy diet should remain in the green zone as much as possible and constitute the bulk of food intake.

Sadly, because profit motives play a large role in the business of health care, the delivery of care and the care of patients is often politicized. Most chronic conditions are influenced by lifestyle and account for more than 75% of health care costs. Since 2009, more than 17% of the US gross national product has been spent on health care, amounting to more than $2 trillion. Few, if any, of these dollars have been spent on identifying the true underlying etiologies of these chronic conditions. Lifestyle changes have taken a backseat to disease treatment. If we continue on the pathway of treating risk factors and developed disease, we will bankrupt the health care system in the near future. Costs for care will continue to escalate; lives will continue to be lost.

It is time for the medical community to intervene and to intervene aggressively. We are not providing the proper treatment when confronting conditions that can be prevented and may even be reversed with lifestyle change and education. Current and future physicians must be trained in lifestyle medicine. The neglect of both the root cause of disease and corrective interventions continues to further the development of chronic conditions and ultimately demise (Figure 2). Lifestyle management courses should be required annual training for all health care employees, optimally as we do annual training for corporate compliance. It is time to prevent disease in all aspects of our lives and the lives of the people we love. It is time to change our health destiny by changing our hearts and minds from an unhealthy lifestyle to a total health lifestyle. It is time to eat healthy, be active, and resolve conflict. The evidence is irrefutable and the message is clear. We are charged with providing patients with the information they need to live a long, healthy life, which can readily be accomplished through lifestyle education. We, as caregivers, owe them that.

Figure 1. Approximate food calories per pound.

| Nutrient-dense foods have fewer calories. High-calorie foods have less nutrients. |

<table>
<thead>
<tr>
<th>Approximate Food Calories Per Pound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables</td>
</tr>
<tr>
<td>Mushrooms</td>
</tr>
<tr>
<td>Fruits</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>Grains</td>
</tr>
<tr>
<td>Whole Grain Bread</td>
</tr>
<tr>
<td>Beans</td>
</tr>
<tr>
<td>Potatoes Flavored</td>
</tr>
<tr>
<td>Pork Chicken</td>
</tr>
<tr>
<td>Beef Fish</td>
</tr>
<tr>
<td>Eggs</td>
</tr>
<tr>
<td>Fried Foods</td>
</tr>
<tr>
<td>Soft Drinks</td>
</tr>
<tr>
<td>Milk</td>
</tr>
</tbody>
</table>

Figure 1. Approximate food calories per pound. Green indicates nutrient-rich foods that should be a major part of a healthy diet; red indicates foods that are low in nutrition and high in calories and should be eliminated completely or consumed in smaller amounts; yellow indicates foods that may be nutrient rich or calorie dense.

Barriers to Adherence and Compliance

| Medication side effects or intolerance |
| Lack of oral parity in health care coverage |
| Poor understanding of importance of therapy |
| Inadequate patient education |
| Complacency |
| Cost of medications |

(Continued from previous page.)
of breast cancer requires a lifestyle transformation that helps fight cancer and prevents the development of other diseases that may lower survival. Thus, all patients should consider developing a lifestyle that includes a focus on the vital signs of health called the Wellness Index (WI).43 (The WI is shown in the Sidebar: The Breast Cancer Wellness Index.)

The goal of the WI is to determine the current state of health and then use the index to identify areas of opportunity to achieve total health during and after treatment. Achieving total health includes a focus on healthy eating, active living, and emotional resilience (HEALER). (See Sidebar: Healthy Eating, Active Living, and Emotional Resilience Goals.) Surviving breast cancer moves one into the HEALER zone, where patients maximize their abilities to prevent cancer recurrence while simultaneously optimizing their ability to treat and prevent chronic diseases such as obesity, DM, hypertension, hyperlipidemia, tobacco and/ or alcohol abuse, and coronary artery disease. The WI appears in two parts. The first part is an objective measure of biometrics. This includes a report on BMI, blood pressure, blood glucose and hemoglobin A1c, and any current history of tobacco use or alcohol abuse. Biometrics is an objective measure of current health status. The second part, HEALER, subjectively assesses what lifestyle changes the patient is making to improve survival.

References


Figure 2. Relationship between lifestyle management and death. The measurement and treatment of high cholesterol, high blood pressure, smoking, and depression are a key strategy to prevent disease and death. Heart attacks, heart failure, strokes, cancer, and cognitive impairment are influenced by unhealthy behaviors and lifestyle. Unhealthy lifestyle choices subsequently lead to endothelial cell injury, endothelial cell dysfunction, and atherosclerosis. Atherosclerosis leads to organ damage and disease that can be prevented and treated through healthy lifestyle interventions. Therefore, basic lifestyle habits—healthy eating, active living, cessation of smoking, and developing emotional resilience—may be a future upstream strategy to help us prevent preventable disease, lower health care costs, and save lives.
HEALER are considered total-health balance factors (Figure 2) because they describe the relationship of our current wellness state and our future lifestyle approaches. Healthy eating, active living, and BMI describe an energy balance that is the relationship between energy consumed (healthy eating), energy expended (physical activity), and energy stored (fat). BMI is defined as weight in kilograms divided by height in meters squared. In general, underweight is a BMI below 20 kg/m², normal weight is a BMI of 21 to 25 kg/m², overweight is a BMI of 25 to 29.9 kg/m², and obesity refers to a BMI above 30 kg/m².456

A positive energy balance results when energy intake exceeds energy expended (BMI increased); negative energy balance results when energy intake is less than energy expended (BMI decreased). Obesity, inactivity, and unhealthy eating are linked to decreased overall and cancer-specific survival in patients with breast cancer. Studies have demonstrated that interventions to maximize healthy eating and active living can improve quality of life and survival in patients with breast cancer.

Obesity
Obesity is associated with an increased risk of postmenopausal breast cancer in population-based studies.457 Obesity at the time of diagnosis may limit the reduction in breast cancer mortality attainable through the detection and treatment of early-stage disease.458 In addition, obesity at diagnosis is associated with inferior outcomes in ER+ operable breast cancers.459 Obesity is a risk factor for breast cancer recurrence and mortality and an important outcome measure for overall health. Maintaining a healthy weight through programs such as HEALER is one of the most important interventions a patient with breast cancer can make to reduce the risk of breast cancer recurrence, mortality, and development of other chronic diseases.

A systematic literature review and meta-analysis of 82 follow-up studies on the relationship between BMI and breast cancer survival was reported in 2014.456 The report included 213,075 survivors of breast cancer and 41,477 deaths (23,182 deaths were attributed to breast cancer).

For each 5 kg/m² increment of BMI before breast cancer diagnosis, less than 12 months after diagnosis, and 12 or more months after diagnosis, increased risks were observed, respectively, of 17%, 11%, and 8% for overall mortality and 18%, 14%, and 29% for breast cancer-specific mortality. The authors concluded that obesity is associated with poorer OS and breast cancer survival regardless of when BMI is ascertained.456

Despite abundant data linking obesity to a poor prognosis in early-stage breast cancer, there have been relatively few studies evaluating the efficacy and potential benefits of weight loss interventions in survivors of breast cancer. In 2002, researchers performed a systematic review of 5687 literature citations to explore associations among survival and/or recurrence and obesity at diagnosis or weight gain after diagnosis of breast cancer. Results of this observational study showed that women with breast cancer who are overweight or gain weight after diagnosis are found to be at higher risk of breast cancer recurrence and death. The authors concluded that weight loss interventions should be considered in the total-health management of patients with breast cancer.460

Data from the Health, Eating, Activity, & Lifestyle Study suggest that increasing physical activity and decreasing body fat may be a reasonable intervention to decrease insulin and leptin levels, thereby potentially influencing breast cancer prognosis.461 Preventing weight gain by regular aerobic exercise in these women may be important in preventing recurrent disease.462 The strongest evidence that physical activity leading to weight loss and weight maintenance is associated with better outcomes of breast cancer comes from the Nurses’ Health Study.463 Weight management with diet and lifestyle changes should be an integral part of the follow-up of women with breast cancer.

Besides BMI, other biometrics are important for health. Women treated for cancer are also at risk of chronic diseases later in life. Controlling blood pressure, cholesterol, and fasting blood glucose/hemoglobin A₁c and avoidance of tobacco and excessive alcohol consumption will help decrease the risk of death caused by chronic disease. For these reasons, women with a breast cancer diagnosis should also monitor and control the other biometrics listed to maintain good health. The HEALER interventions will help maintain a healthy BMI and reduce risks factors associated with the other chronic conditions mentioned.

Epidemiologic evidence shows that the risk of premature death due to coronary artery disease is increased in women who have uncontrolled hypertension, hyperlipidemia, and an elevated hemoglobin A₁c level, and in those who smoke tobacco. The strong association observed between mortality and major cardiovascular risk factors makes the undertaking of multifactorial prevention strategies important. Lifestyle strongly influences the development of high blood pressure, high cholesterol, and DM in women. Therefore, women with uncontrolled risk factors for CVD should be seen by their primary care physician and treatment should be initiated to reduce the risk of CVD.464 Because some studies suggest that all types of alcohol may increase the risk of cancer, women with breast cancer should also limit alcohol intake.465

Women who smoke should stop. The relationship between breast cancer risk and active cigarette smoking remains controversial because of unresolved issues of confounding (alcohol intake) and dose response. To investigate these issues further, researchers analyzed data from 73,388 women in the American Cancer Society’s Cancer Prevention Study II Nutrition Cohort.466 Analyses were based on 3721 patients with invasive breast cancer identified during a median follow-up of 13.8 years. The
results showed that breast cancer rates were higher in current and former smokers than in never smokers. In addition, the data showed that the risk of invasive breast cancer was highest in women who began smoking at an earlier age.466

Because a large portion of the life of a patient with breast cancer may be spent in survivorship, lifestyle interventions could have time to make a difference and should be included in the overall treatment plan of all patients who receive a breast cancer diagnosis. Assessing biometrics will help us understand opportunities for improvement that can be made as described in the next intervention, which includes healthy eating, active living, and developing emotional resilience as it relates to survivorship.

Healthy Eating, Active Living, and Emotional Resilience

Each year breast cancer is diagnosed in more than 240,000 women in the US. A high proportion of these patients are both obese and sedentary.467 Therefore, lifestyle interventions may be needed to improve health outcomes and prognosis. Recent studies demonstrate that weight loss interventions in breast cancer result in significant weight loss at 6, 12, and 18 months after diagnosis.468 A single-variable analysis in 2007 looked at the association between healthy eating, active living, and obesity with breast cancer survival in a prospective study that included 1490 women who underwent treatment of breast cancer.469 The results showed an association between reduced mortality and higher vegetable-fruit consumption, increased physical activity, and a BMI that was neither underweight nor obese.

An analysis of 85 studies that included more than 164,000 women worldwide demonstrated that the survival of patients with breast cancer may be associated with healthy eating, active living, and a healthy weight.470 These findings support the recommendation that all survivors of breast cancer eat a WFPBD, maintain a healthy weight, and get regular exercise.471 Research suggests that women who have a healthy weight and are physically active have a better chance of surviving breast cancer. Healthy Eating: On the basis of the aforementioned evidence, women with a breast cancer diagnosis should enroll in a course on lifestyle management. This course should include advice from a WFPBD-trained lifestyle specialist. Consultation should include a discussion on a variety of issues outlined in the Sidebar: The Breast Cancer Wellness Index, including a focus on total health and a WFPBD with a substantial reduction, and possibly complete elimination, of all animal-based foods. The dietary focus should emphasize the importance of fruits, vegetables, whole grains, and legumes as the basis for a healthy diet.472,473 Also included in a WFPBD is the elimination of energy-dense foods such as sugary drinks and processed foods high in added sugar, salt, and fat. These types of foods contain more calories per ounce and increase the risk of weight gain. Low-energy-dense foods, like those found in a WFPBD, allow patients to actually eat more food but consume fewer calories. A WFPBD results in decreased intake of foods that increase the risk of coronary artery disease474 and increased intake of foods that may prevent angiogenesis, or the growth of new blood vessels, to cancer cells.475

A large, multiple-database review (MEDLINE, Embase, and The Cochrane Library) to examine and to quantify the potential dose-response relation between fruit and vegetable consumption and the risk of all-cause, cardiovascular, and cancer mortality was reported in 2014.476 The researchers looked at prospective cohort studies that reported mortality risk estimates by levels of fruit and vegetable consumption. Sixteen prospective cohort studies were eligible in this meta-analysis, with follow-up periods ranging from 4.6 to 26 years in which there were 56,432 deaths (including 11,512 deaths caused by CVD and 16,817 due to cancer) among 833,234 participants. Higher consumption of fruits and vegetables was significantly associated with a lower risk of all-cause mortality. The researchers found that there was a threshold at 5 servings of fruits and vegetables per day, after which the risk of all-cause mortality was not further reduced. The results support current recommendations to increase consumption of fruits and vegetables to promote health and overall longevity. Other studies have shown that a diet rich in fruits and vegetables and low in fat lowers blood pressure and reduces the risk of stroke and type 2 DM.477,480 One meta-analysis of prospective cohort studies demonstrated that increased consumption of fruits and vegetables from fewer than 3 servings per day to more than 5 servings per day is related to a 17% reduction in CVD risk.479

In laboratory studies, many individual minerals, vitamins, and phytochemicals demonstrate anticancer effects, yet evidence suggests it is the synergy of compounds working together in the overall diet that offers the strongest cancer protection. No single food or food component can protect against cancer by itself, but strong evidence shows that a diet filled with a variety of plant foods (vegetables, fruits, whole grains, and beans) helps lower the risk of many cancers. A recent meta-analysis of prospective

Healthy Eating, Active Living, and Emotional Resilience Goals

Healthy eating
- Eat a whole-food, plant-based diet that includes at least 5 servings of fruits and vegetables per day, legumes, and whole grains
- Limit consumption of salty foods and foods processed with salt
- Avoid calorie-dense foods, which include sugary drinks
- Limit consumption of red meats (eg, beef, pork, and lamb) and avoid all processed meats
- Avoid supplements purported to protect against cancer

Active living
- Be physically active for at least 30 minutes 5 days per week
- Limit sedentary habits

Emotional resilience
- Evaluation for depression and treatment of depression, if needed
studies reported that a high intake of fruits and vegetables was associated with a reduction in the risk of breast cancer.491 Further data show that there may be an inverse association between dietary fiber intake and breast cancer risk.492 Finally, reducing dietary fat intake, with a modest influence on body weight, may improve relapse-free survival rates of patients with breast cancer receiving conventional cancer treatment.493

Fruits and vegetables contain large amounts of polyphenols. These nutrients have been shown in epidemiologic studies and meta-analyses to offer some protection against the development of cancers, CVD, and DM.494,495 Polyphenols may fight cancer by inhibiting carcinogenesis.496 For example, resveratrol, found in grapes, has been shown to inhibit the growth of a variety of cancer cells. Studies have shown that resveratrol has the potential to modulate all three stages of carcinogenesis (initiation, promotion, and progression), in both chemically and ultraviolet B-induced skin carcinogenesis in mice, as well as in various murine models of human cancers.497

A number of studies have demonstrated that consumption of polyphenols limits the incidence of coronary artery diseases.498 Atherosclerotic lesions may be present and silent for decades before becoming active and causing cardiovascular events.499 Polyphenols may be protective against CVDs by improving endothelial cell function, inhibiting oxidation of low-density lipoproteins, inhibiting platelet aggregation, and preventing macrophage activation and subsequent thrombosis.489,490

Although the association between breast cancer risk and dietary factors has long been identified, the complex relationship between obesity and breast cancer is poorly understood. Obesity in women presenting with breast cancer may be a marker of unhealthy eating and inactivity. However, recent data suggest that even more important than obesity status, women who eat at least five servings of fruits and vegetables per day have a survival advantage over women who do not.476

Active Living: A prospective observational study to determine whether physical activity among women with breast cancer decreases the risk of death caused by breast cancer compared with more sedentary women has demonstrated the relationship between breast cancer survival and physical activity.491 The study was based on responses from 2987 female registered nurses in the Nurses’ Health Study who were diagnosed with Stage I, II, or III breast cancer. Results showed that women who were inactive had a higher risk of death than women who were physically active. The greatest benefit occurred in women who performed the equivalent of walking 3 to 5 hours per week. The authors concluded that physical activity after a breast cancer diagnosis may reduce the risk of death; thus, women with breast cancer who follow physical activity recommendations may improve their survival.463

Additional studies have shown that women who increased physical activity after a breast cancer diagnosis reduce their overall risk of death by 45%, whereas women who decreased physical activity after diagnosis had a 4-fold greater risk of death.492,493 Other studies suggest that exercise after breast cancer diagnosis may improve overall quality of life494 and DFS.495 Healthy eating and active living interventions for women with breast cancer will require behavior change.496 Therefore, strategies for behavior change should be part of lifestyle management programs designed to improve survival in this population. Finally, physical activity has been shown to improve quality of life and balance of life after a breast cancer diagnosis.497

Emotional Resilience: Depression is a major public health problem and often is undiagnosed and untreated in women with breast cancer.498-500 Untreated, depression can cause amplification of physical symptoms, poor treatment adherence, and increased functional impairment.501,502 Physicians are now more aware of the importance of screening and treating depression while managing a particular chronic disease such as breast cancer.503,504 Important advances include routine depression screening at the time of breast cancer diagnosis,505 as well as early interventions and counseling specifically designed to treat depression in patients with cancer.506,507 Cognitive therapy appears to be particularly helpful in treating depression in patients with breast cancer.508 In addition, cognitive therapy may be used to help women with breast cancer achieve the biometric outcomes and weight loss goals associated with improved survival.509 Tamoxifen is commonly used in the treatment of women with breast cancer. As previously mentioned, certain antidepressants, including paroxetine, fluoxetine, and bupropion, may interfere with the metabolism of tamoxifen and should be avoided. Venlafaxine, desvenlafaxine, and mirtazapine do not appear to affect the metabolism of tamoxifen and may be considered the safer choice for the treatment of depression in patients with breast cancer who are receiving tamoxifen.510

Summary of Lifestyle Recommendations

Diet, physical activity, and weight play a major role in survival among patients with breast cancer.454 Looking at improving long-term survival in breast cancer encompasses a total-health strategy that includes a focus on healthy eating, active living, healthy weight, and emotional resilience.471

Five-year breast cancer survival rates have increased, and a total-health care plan will reduce a woman’s risk of cancer recurrence, new cancer formation, and CVD.497 HEALER is a total-health approach to wellness that includes treating the mind, body, and spirit of a patient with breast cancer. Our long-term goal is to help patients with breast cancer understand the importance of energy balance.518 By helping patients with breast cancer achieve a healthy weight and healthy biometrics, we can maximize their chances for long-term survival.

CONCLUSION

Breast cancer survivorship has become a major issue, particularly in the last decade, as early detection and more effective therapies have led to an ever-increasing number of those transitioning from patient to survivor. These successes present a new challenge to the medical community, which must now deal with the long-term complications of past and current treatment modalities.
Although extremely effective in curative intent, many of these therapies result in long-term side effects. Current therapies, which often include polychemotherapeutic agents, RT, and AET, can challenge the cardiovascular system. Cardiovascular disease remains the number one cause of mortality in women in the US, although breast cancer is the most feared.\(^{31,32}\) Bone strength is affected secondary to prolonged estrogen blockade. As younger patients are receiving a breast cancer diagnosis, the incidence of SPMs is becoming more frequently recognized. Thromboembolism risk increases after a cancer diagnosis, and some therapies increase its risk, resulting in death secondary to embolic events.

Advanced therapies call for extended administration of recently developed oral chemotherapy agents. The medical community has been challenged to enforce a five-year regimen for estrogen blockade, and recent findings suggest that doubling the therapy to ten years may decrease recurrence and increase survival. Adherence and compliance for just five years of oral therapy have been poor, and extending such recommendations to ten years appears to be the next challenge for oncologists.

Lifestyle changes, largely focused on reducing BMI, have been demonstrated to play a significant role in extending OS after breast cancer treatment. HEALER provides a tool for clinicians to evaluate the status of survivors of breast cancer. HEALER also summarizes the proactive role that patients may take to enhance their survival.

There is a well-recognized predicted shortage of oncologists by 2020.\(^{31}\) Therefore, the bulk of long-term care will become dependent on the primary care physician. This shift of care means that these physicians will need to be well educated in the long-term medical issues related to breast cancer treatment. Our intent is to share the present information with all those who will be charged with survivorship care in the coming years.

Disclosure Statement

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

Acknowledgment

The authors wish to acknowledge the assistance of Helene Wolf in the preparation of this manuscript, the assistance of Stephen Beebe in creating the Virchow’s triad figure, and the editorial assistance and support provided by Max L McMullen, ELS.

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

References


The Permanente Journal/ Spring 2015/Volume 19 No. 2
Breast Cancer Survivorship: A Comprehensive Review of Long-Term Medical Issues and Lifestyle Recommendations


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162. US Preventive Services Task Force. Screening

161. Raisz LG. Pathogenesis of osteoporosis:

160. Ralston SH. Genetic determinants of

159. Lane NE. Epidemiology, etiology, and diagnosis

158. Lenihan DJ, Esteva FJ. Multidisciplinary strategy

157. Doyle JJ, Neugut AI, Jacobson JS, Grann VR,

156. Magné N, Védrine L, Chargari C. Impact

155. Moy B, Goss PE. Lapatinib-associated toxicity

154. Magné N, Vieville L, Chargari C. Impact


152. Kanis JA, Borgstrom F, De Laet C, et al. The European

151. Bliziotes MM, Eshleman AJ, Zhang XW,


149. Sengupta PP, Northfelt DW, Gentile F, Zamorano

148. Goddard D, Baru H, Dave B, Migna R,

147. Neiranne S, Khanna A. Comparison and co-location


144. Doyle JJ, Neugut AI, Jacobson JS, Grann VR,

143. Canalis E, Mazziotti G, Giustina A, Bilezikian JP.

142. Saag K. Mend the mind, but mind the bones!

141. Canalies Mazzotti G, Giustina A, Bilezikian JPK.

140. Vetrano DL, Teulucks HG, Abenhiem L,

139. Sluijs TS, Stone KL, et al. Use of antidepressants


133. Roux C, Briot K, Gossesse L, et al. Increase in vertebral


126. Saag K. Mend the mind, but mind the bones:

125. Schneeweiss S, Wang PS. Association

124. Steinbuch M, Youket TE, Cohen S. Oral

123. Castilloux AM, Dorais M, LeLorier J.

122. Clinical and International Breast

121. Canalis E, Mazzotti G, Giustina A, Bilezikian JPK.

120. Mazzotti G, Canalis E, Giustina A, Drug-

119. Pilon D, Castilloux AM, Dorais M, LeLorier J.


116. Canalis E, Mazzotti G, Giustina A, Bilezikian JPK.

115. Vetrano DL, Teulucks HG, Abenhiem L,

114. Sluijs TS, Stone KL, et al. Use of antidepressants


111. Lenihan DJ, Esteva FJ. Multidisciplinary strategy

110. Lanen DJ, Esteva FJ. Multidisciplinary strategy


107. Reisz LG. Pathogenesis of osteoporosis:


102. Reisz LG. Pathogenesis of osteoporosis:

101. L azi A, Castilloux AM, Dorais M, LeLorier J.

100.tribe.167.12.1231.


98. Steinbuch M, Youket TE, Cohen S. Oral

97. Canalis E, Mazzotti G, Giustina A, Bilezikian JPK.

96. Vetrano DL, Teulucks HG, Abenhiem L,

95. Sluijs TS, Stone KL, et al. Use of antidepressants


93. Sluijs TS, Stone KL, et al. Use of antidepressants


91. Sluijs TS, Stone KL, et al. Use of antidepressants

90. Williams JW Jr, Mulrow CD, Chiquette E, et al. Cardiovascular

89. Sluijs TS, Stone KL, et al. Use of antidepressants


87. Sluijs TS, Stone KL, et al. Use of antidepressants

86. Williams JW Jr, Mulrow CD, Chiquette E, et al. Cardiovascular

85. Sluijs TS, Stone KL, et al. Use of antidepressants

84. Williams JW Jr, Mulrow CD, Chiquette E, et al. Cardiovascular

83. Sluijs TS, Stone KL, et al. Use of antidepressants

82. Williams JW Jr, Mulrow CD, Chiquette E, et al. Cardiovascular

81. Sluijs TS, Stone KL, et al. Use of antidepressants


79. Sluijs TS, Stone KL, et al. Use of antidepressants

78. Williams JW Jr, Mulrow CD, Chiquette E, et al. Cardiovascular

77. Sluijs TS, Stone KL, et al. Use of antidepressants

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75. Sluijs TS, Stone KL, et al. Use of antidepressants

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73. Sluijs TS, Stone KL, et al. Use of antidepressants


71. Sluijs TS, Stone KL, et al. Use of antidepressants


A Much Brighter Future

In 50 cases operated upon by what we call the complete method we have been able to trace only three local recurrences [6%] ... In 34 (73%) ... there has never been a local or regional recurrence, 24 are living and 10 are dead. In 43 of 46 cases (93%) there has been no true local recurrence ... . These statistics are so remarkably good that we are encouraged to hope for a much brighter ... future for operations for cancer of the breast.

— Halsted WS. I. The results of operations for the cure of cancer of the breast performed at the Johns Hopkins Hospital from June 1889, to January 1894. Ann Surg 1894 Nov;20(5):497-555
ABSTRACT

Malnutrition is a common and debilitating condition in the acute hospital setting that is associated with many adverse outcomes, including prolonged length of hospital stay, increased readmission rates, and increased mortality. However, malnutrition by definition may be an abnormality in either under- or overnutrition. With obesity rates rising, many patients admitted to the hospital may be overnourished from unhealthy eating habits. Unhealthy eating habits and obesity increase a patient’s risk for cardiovascular events and complications in the hospital setting.

Nutrition risk screening or nutrition reconciliation is an underutilized tool in the hospital that would identify patients with over- and undernutrition. Nutrition intervention or nutrition prophylaxis initiated in the hospital may help reduce hospital days, readmissions, and mortality. Nutrition reconciliation is a new term developed to increase the awareness of nutrition in total health. Nutrition reconciliation means that all patients have their nutritional status reconciled on admission to and discharge from the hospital. Nutrition reconciliation is defined as the process of maximizing health by helping align an individual’s current diet to the diet prescribed for him or her by the health care team. Nutrition prophylaxis is a proactive intervention to prevent a medical complication.

Mandatory nutrition reconciliation and nutrition prophylaxis is not widely performed in most hospitals. Such an intervention may help our patients by improving their short- and long-term health. In addition, nutrition reconciliation and nutrition prophylaxis may allow for a more effective use of resources to prevent a preventable disease.

INTRODUCTION

The nutritional status of Americans has been studied and shows some disturbing trends, with some Americans being undernourished while most Americans are overnourished.1 In addition, there are Americans who eat unhealthy diets that, if not modified over time, may lead to overnutrition, obesity, and chronic disease.2 A startling number of patients admitted to the hospital suffer from protein energy malnutrition and obesity. These conditions are associated with unhealthy eating habits and food insecurity. Nutrition assessment and intervention during an admission to the hospital may represent an opportunity to educate all patients about the importance of healthy eating and increase awareness of interventions to help treat short-term effects of undernutrition and long-term effects of overnutrition.3,4

Reducing avoidable readmissions to the hospital has been a focus of Medicare as a target for cost reduction. Researchers have shown that nine of the top ten primary diagnosis-related groups causing readmission were associated with malnutrition.5 Therefore, a focus on nutrition may be a new approach in addressing avoidable hospital readmission rates.6 Although most of the care that prevents readmission to the hospital occurs after discharge, the process to prevent readmission starts in the hospital. We have previously reported that a bundle of elements initiated before and after discharge from the hospital is correlated with reduced readmission rates.7 Examples include medication reconciliation and venous thromboembolism prophylaxis.

Medication reconciliation has been shown to be an important intervention to reduce avoidable readmissions.8 Schnipper et al9 reported that pharmacist medication review and counseling were associated with a lower rate of preventable adverse drug events after hospital discharge. The adverse effects of not reconciling medications at the time of discharge from the hospital have been well documented.10 Other studies have shown that medication reconciliation decreased readmission rates at 7, 14, and 30 days after discharge, with statistical significance at 7 and 14 days.11

Deep vein thrombosis and pulmonary embolism after hospitalization is an example of an avoidable high-cost and potentially life-threatening readmission to the hospital.12 Venous thromboembolism prophylaxis is now a national guideline intervention to prevent thrombosis and embolism during hospitalization.13 On admission to the hospital, patients are risk stratified for deep vein thrombosis risk. If the risk is high they are given blood-thinning agents to prevent deep vein clots during their hospital stay. A recent study showed that venous thromboembolism prophylaxis was associated with a decrease in readmissions to the hospital.14

Hospital readmission is a frequent and costly event that is associated with gaps in care.5 Rates of readmission can be reduced with the implementation of more reliable systemic interventions. Information learned from bundling elements such as medication reconciliation and venous thromboembolism prophylaxis to reduce readmission rates could be applied to nutrition. Recent meta-analysis suggests that readmission rates can be significantly reduced by prophylactic identification and treatment of older patients who have been diagnosed to have protein energy malnutrition.15

Education, screening, and nutrition intervention may be the most cost-effective and efficient way to reduce avoidable readmissions to the hospital.16 However, for adequate nutrition to have an impact on health, one must also address food

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availability, food choice, and eating habits as separate but complementary aspects of over- or undernutrition. Nutrition prophylaxis is an important preventive activity that would be appropriate for adaptation to most chronic illness or prevention treatment regimens.

Nutrition reconciliation and nutrition prophylaxis in the hospital and at discharge may lead to both decreased hospital costs and improved patient care. However, few hospitals are looking at nutrition as a cost-effective intervention to prevent an avoidable return to the hospital. A hospital-based program aimed at screening and treating patients with nutrition issues could follow the programs that have been instituted for medication reconciliation and venous thrombosis prophylaxis. These programs used two basic concepts: 1) screen for high-risk patients and 2) provide prophylaxis treatment to prevent complications. In the next sections we will define malnutrition and then propose two interventions to be performed on all patients admitted to the hospital: 1) nutrition reconciliation and 2) nutrition prophylaxis.

MALNUTRITION

*Malnutrition* is common and by definition is any imbalance in nutrition. There are several *International Classification of Diseases* codes for malnutrition including mild, moderate, and severe protein-calorie malnutrition. Although typically thought of as a lack of something, current thoughts include the fact that malnutrition can develop as a consequence of under- or overnutrition. In the hospital, undernutrition is associated with increased morbidity and mortality. In the outpatient setting, overnutrition can result in chronic diseases such as obesity, diabetes, high blood pressure, and coronary artery disease. Obesity is now a major public health preventable disease, and efforts to screen and educate the general public are an important first step to preventing negative consequences of this disease.

The nutritional status of older Americans reflects disturbing trends, especially in the Medicare population. A study by Meals on Wheels of America indicates that 5.7% of older Americans are at risk for food insecurity, hunger, and malnutrition. Other studies have shown that undernutrition is present in up to 72% of elderly patients admitted to the hospital. In 2011, researchers reported that body mass index (BMI) showed a relationship with readmission for patients both above and below the normal weight range. The authors concluded that pre- and posthospital interventions should consider targeting nutritional status.

The causes and types of malnourishment in the elder population are varied, both physiologic and psychological in nature, and may lead to protein energy malnutrition. The phrase *anorexia of aging* has been used by many to describe the decreased food intake of old age. Compromised metabolism caused by underlying chronic disease, natural processes, and immobility contribute to poor nutrition among this population. The presence of protein energy malnutrition has been shown to be a risk factor for elderly admitted to the hospital and for subsequent readmission. In effect, if a patient has protein energy malnutrition at hospitalization, their overall outcome has been shown to be poor. Malnutrition can affect every system in the body, resulting in impairment of wound healing, in increased risk of infections and pressure ulcers, in decreased respiratory and cardiac function, in poorer outcomes of chronic lung diseases, in increased risk of cardiovascular and gastrointestinal disorders, in poorer physical function, and in mortality.

Patients who leave the hospital in an undernourished state also have a high mortality rate. Patients with a history of weight loss and low BMI were found to have a 1-year post-discharge mortality risk of 24% compared with 7% in the control group. Similar findings were reported for undernourished patients discharged from the hospital with a diagnosis of stroke. Several meta-analyses have also demonstrated reduced mortality in patients receiving optimized nutrition care. An analysis of 11 studies found significantly lower mortality rates among hospitalized patients receiving oral nutritional supplements compared with control patients. In addition, nutrition intervention that provides nurse visits and free meals to elderly patients upon discharge reduced readmission rates from 23% to 7.6%.

**NUTRITION RECONCILIATION**

Despite the high prevalence of undernutrition in geriatric patients and overnutrition in the general adult population, nutrition-related problems are rarely recognized and treated in the hospital. To improve outcomes, routine screening and

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<th>Table 1. Screening tools available on the Internet</th>
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<td>Malnutrition Universal Screening Tool (MUST)</td>
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interventions should be implemented to help all patients admitted to the hospital. In 2013, the Alliance to Advance Patient Nutrition published a consensus report that suggested hospitals update the current clinical practices to include more rigorous nutrition screening for patients admitted to the hospital who may be over- or undernourished.

Nutritional issues before or during hospitalizations may cause complications but often receive limited attention. Unfortunately undernutrition, which is a significant risk factor for poor outcomes, continues to go unrecognized and untreated in many hospitalized patients. The Joint Commission has recognized the negative impact of malnutrition in hospitals and has made nutritional assessment, support, and ongoing reassessment an integral and essential part of current accreditation. Even when there is a documented nutrition assessment in the medical chart, there may be a delay in physician implementation of a nutritional intervention that may help a patient heal from the disease that required admission to the hospital. A recent review demonstrated that nurses who care for patients during the entire hospital stay are not required to screen for, to educate about, or to treat malnutrition.

As we enter a new era of health care delivery, it is time to prevent preventable diseases and to identify opportunities to reduce the high cost of hospital care. Malnutrition is a preventable disease. Effective management of malnutrition requires early detection and intervention. Validated screening tools have been developed for nutrition (Table 1) but are underutilized in the hospital. Hospitalized patients, regardless of their weight, may suffer from undernutrition associated with inflammation or infection. Patients at risk for undernutrition include patients with an acute illness, poor appetite, and weight loss. Nutrition reconciliation is a new term developed to increase the awareness of the important role nutrition plays in total health. Nutrition reconciliation means that all patients have their nutritional status reconciled on admission to and on discharge from the hospital. With widespread use of electronic medical records (EMRs), it is now possible to implement screening and billable treatment protocols for malnutrition as we do for medication and venous thrombus prevention. Nutrition reconciliation is defined as the process of maximizing health by helping align an individual’s current diet to the diet prescribed for him or her by the health care team. There are two issues in identifying a patient’s current diet. The first is identifying patients who are undernourished. The second is identifying patients who are overnourished or not eating a healthy diet.

Nutrition Reconciliation and Nutrition Prophylaxis: Toward Total Health

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<th>Table 2. Proposed nutrition reconciliation screening tool</th>
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<th>Table 3. Proposed nutrition reconciliation risk stratification</th>
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<td><strong>High risk for unhealthy eating</strong></td>
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NUTRITION PROPHYLAXIS

Systematically identifying patients who are malnourished and intervening before they develop a preventable disease, get admitted to the hospital, or develop nutrition-related complications during a hospital visit will reduce overall cost of care.
After the patient has completed nutrition reconciliation we can begin nutrition prophylaxis.

Nutrition prophylaxis is a proactive intervention to prevent medical complications from malnutrition. Nutrition prophylaxis is designed to screen and treat preventable disease. As mentioned above, the three risk groups outlined in Table 3 represent potential risk groups for interventions that may prevent complications inside and outside the hospital while helping to reverse or prevent a chronic disease.

Undernutrition

Nutrition intervention for malnourished patients is a low-risk, cost-effective strategy to improve quality of care, prevent preventable disease, and lower overall health care costs. It is estimated that more than one-third of medical patients in the hospital are undernourished.18 If the nutrition problem is not addressed, undernourished patients may experience a further decline in nutrition and further progression of an illness before discharge from the hospital. Undernutrition is associated with many adverse outcomes, including depression of the immune system, impaired wound healing, muscle wasting, longer lengths of hospital stay, higher treatment costs, and increased mortality.18

Many of the adverse outcomes influenced by undernutrition are potentially preventable. Data from several recent studies show that undernutrition can influence hospital readmission rates and reduce health care costs.15,44,45 Undernourished patients may benefit from oral nutritional supplements. A large Cochrane systematic review of 24 studies involving 6225 patients aged 65 years and older at risk for malnutrition demonstrated fewer complications (eg, pressure sores, deep vein thrombosis, and respiratory and urinary infections) among patients receiving oral nutritional supplements compared with routine care.46 In a prospective study conducted at the Johns Hopkins Hospital, nutrition screening involving a team approach to address malnutrition and earlier intervention reduced the length of hospital stay by an average of 3.2 days in severely malnourished patients.47

A recent retrospective analysis used information from more than 1 million adult inpatient cases found in the 2000-2010 Premier Perspectives Database maintained by the Premier Healthcare Alliance—representing a total of 44 million hospital episodes from across the US or approximately 20% of all inpatient admissions in the US.48 Within this sample, oral nutritional supplements reduced length of hospital stay by an average of 2.3 days.48

One of the commonly used treatments for undernutrition is oral nutritional supplements. Systematic reviews and meta-analyses have documented the effects of oral nutritional supplements on clinical outcomes. In 2013, Stratton et al15 reported the results of systematic review of nine randomized controlled studies and meta-analysis on the effects of oral nutritional supplements on hospital readmissions. This study showed that oral nutritional supplements significantly reduce hospital readmissions, particularly in older patient groups. Although oral supplementation is one avenue for improvement of nutritional status, providing adequate and appropriate food in the form of meals can also be a sustainable method for enhancing patient nutrition at home.

Overnutrition and Unhealthy Eating

Although less of a risk for complications during an admission, identification of and treatment of patients who eat an unhealthy diet may prevent short- and long-term complications. Obesity and unhealthy eating are risk factors for chronic

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<th>Table 4. Solutions for lower-income individuals</th>
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<td>Older Americans Act Nutrition Program</td>
<td><a href="http://nutritionandaging.fiu.edu/DANP_Toolkit/toolkit%20update%2012.7.06.pdf">http://nutritionandaging.fiu.edu/DANP_Toolkit/toolkit%20update%2012.7.06.pdf</a></td>
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<td>Home-delivered meals (Meals on Wheels and Mom’s Meals)</td>
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<td><a href="http://www.momsmeals.com">www.momsmeals.com</a></td>
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<td>Medicaid waiver and other government programs</td>
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<td>Managed Long-Term Services and Supports</td>
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<td>Program of All-Inclusive Care for Elderly</td>
<td><a href="http://www.medicare.gov/your-medicare-costs/help-paying-costs/pace/pace.html">www.medicare.gov/your-medicare-costs/help-paying-costs/pace/pace.html</a></td>
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disease. Researchers have reported that disease risk for hypertension, type 2 diabetes, and coronary artery disease as well as related costs increase with increased BMI.9

Because patients admitted to the hospital are at risk for unhealthy eating, as is the general population, successful nutrition prophylaxis including educational components for obesity and consumption of foods that are inappropriate for the disease state will help reduce future disease burden and cost. Once identified for being at risk for overnutrition and unhealthy eating, patients could receive initial education during the hospital stay and follow-up planning at discharge on the benefits of healthy weight and healthy eating.

With the changing health care environment, high-quality, cost-effective preventive care is important. Automated proactive nutrition assessment and intervention are critical steps to reduce current and future hospital complications and cost. The prevention and treatment of hospital malnutrition offer a tremendous opportunity to optimize the overall quality of patient care, improve clinical outcomes, and reduce costs.

Nutrition prophylaxis should follow immediately after nutrition reconciliation has been completed and a nutrition diagnosis has been obtained. Nutrition prophylaxis could follow the steps outlined in the Sidebar: Steps in a Nutrition Prophylaxis Plan. Nutrition prophylaxis should be person focused and address particular issues related to the importance of the diet and health of the individual. Most patients admitted to the hospital suffer from a chronic disease. A general diet that has reported health benefits is the Dietary Approach to Stop Hypertension (DASH) diet; this could be a universal healthy diet for all patients admitted to the hospital.10 This general diet can be used to teach patients the benefit of healthy eating. Additional teaching could also help patients with disease-specific dietary needs such as diabetes (low carbohydrate diet) and kidney disease (low phosphorus and low potassium diet).

While in the hospital, patients are in a controlled environment. Once they leave the hospital, they are at risk for returning to their unhealthy eating habits. This is why nutrition reconciliation will be required at the time of discharge and also when the patient returns to a primary care physician for a posthospital follow-up appointment. After discharge from the hospital it is important to ensure that the nutrition discharge plan meets the health condition needs the patient learned about in the hospital. This plan should be convenient, tailored to patient preferences, and affordable. If patients are not able to prepare healthy meals when they return home, they may want to consider paying for meals that are healthy and meet their nutrition needs, such as a home meal delivery service (see Sidebar: Mom’s Meals NourishCare Program). Other options for low-income individuals include government- or managed-care-funded programs that provide supplemental nutrition to low-income individuals (Table 4). Some states include funds for home-delivered meals as part of their Medicaid package.

**DISCUSSION**

With policy changes in the US health care system pushing for a greater focus on high-quality and affordable care, there’s an urgent need to address the ongoing issue of avoidable readmissions to the hospital. Addressing hospital malnutrition and ensuring that medical nutrition therapy intervention occurs should play a critical role in patient care.16

Physicians and nurses should initiate the nutrition reconciliation process at the time of admission so dietitians can start evaluation and treatment shortly after admission. This process requires little time if questions are clearly outlined in the EMR, as we currently do for venous thromboembolism prophylaxis. In the hospital, the decision point for reconciliation is primarily focused on undertreatment to identify patients who may benefit most from nutrition supplementation. Patients identified as overnourished or who have unhealthy eating habits may benefit from education. We recommend that hospital leadership consider developing a culture of healthy eating for all patients admitted to the hospital. Hospital food should be aligned with the food we are asking our patients to eat when they leave the hospital.31

The proposed nutrition reconciliation screening tool outlined in Table 2 has not been validated. The questions in Table 2 were taken from the many validated tools outlined in Table 1. However, the basic questions are a tool to help physicians identify patients admitted to the hospital who may benefit from nutrition prophylaxis. For example, not all patients with an elevated BMI are unhealthy.32 Some obese patients may eat a healthy diet and exercise regularly. These patients may have a lower incidence of chronic disease and
In March 2014, the Tulane University School of Medicine in New Orleans, LA, announced that the university was adding an unconventional course to its curriculum. Medical students now take cooking classes in addition to their usual training. The idea behind this “culinary medicine” program is to encourage physicians to use food to prevent or to cure illnesses. Most medical students in the US receive on average 20 hours of nutritional education even though diet may be the cause of many modern Western diseases. Lifestyle management, including a healthy diet, may be able to prevent diseases such as diabetes while significantly reducing overall health care costs. Training physicians to cook, however, takes nutritional education to a whole new level. Not only will physicians be able to explain which foods are best to eat, but they will also understand how to prepare them. Tulane medical students prepare for teaching future patients by offering free cooking classes to New Orleans residents—a mutually beneficial arrangement for everyone who shares that food. Fortunately, the culinary medicine model seems to be catching on. Two other medical schools have licensed the curriculum and are adding it to their courses. Ideally all medical schools will adopt this best practice.

a higher survival rate than some patients who are not obese but do not eat a healthy diet. The purpose of this article is to help physicians understand the potential benefits of nutrition reconciliation in the hospital that may eventually be applied to the clinic setting as a vital sign of health. Applying the principles discussed in this article will involve collaborative efforts among members of an interdisciplinary health care team, including physicians, nurses, social workers, and dietitians, with the full support of hospital administrators. Everyone, including the patient, has a role in supporting nutrition interventions. Team members, including nurses and physicians, have a responsibility to be involved in nutrition care.

The principles proposed in this article are an opportunity for hospitals and physicians to begin the work needed to make nutrition reconciliation and nutrition prophylaxis a reality. Our goal would be that hospitals develop a person-focused nutrition culture in which nutrition care is a priority for physicians, employees, and patients. All patients should be screened for malnutrition and interventions applied when indicated. With the widespread use of the EMR it should be possible to develop an application to ensure that nutrition reconciliation occurs on admission and discharge and is aligned with nutrition prophylaxis during and after the time the patient spends in the hospital.

Follow-up, monitoring, and creating a nutrition care plan for discharged patients is paramount because malnutrition is not cured when patients leave the hospital. The nutrition care plan should be incorporated into nutrition education for patients and caregivers as well as communicated to physicians who follow up with the patient after discharge (see Sidebar: Tulane University School of Medicine). The nutrition care plan should be part of the patient’s EMR and reviewed each time the patient sees a physician. Unidentified malnutrition heightens the risk of adverse complications and of avoidable cost of care.

CONCLUSION

Social issues play a key role in health and are also a very important cause of under- and overnutrition. During hospitalization, the physician must also consider reversible nutrition concerns and nutrition issues that may occur as part of natural aging. Social workers, dietitians, and nurses must advocate together for policy changes in their hospitals and Regions to resolve community issues related to food insecurity and overnutrition. In addition, end-of-life issues are also important when looking at malnutrition in the sick elderly. Physicians can help patients and families understand that undernutrition associated with comorbidities may be an opportunity to discuss end-of-life issues and advance care planning. In summary, malnutrition is a preventable disease that can be cured by an organized systemwide program of nutrition reconciliation and nutrition prophylaxis that focuses not just on a disease but on the person with a disease.

Disclosure Statement

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

Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

References


30. Moore T, Conlin PR, And J, Sweeney LP, DASH (Dietary Approaches to Stop Hypertension) diet is effective treatment for stage 1 isolated systolic hypertension. Hypertension 2001 Aug;38(2):155-6. DOI: http://dx.doi.org/10.1161/01.HYP.38.2.155.


This painting was inspired by the Nigerian women who were captured by Boko Haram, bathed and dressed in bright clothing, and then sold into slavery.

Dr Brunner is a retired Pediatrician and former Chief of Service at the South Bay Medical Center in Harbor City, CA.
BACKGROUND

This report on the First International Congress on Whole Person Care is based on the experiences of two of the authors while attending the conference. (The first-person accounts are authored by Gary Huffaker, MD.) It was held in Montreal, Quebec, Canada, October 17-20, 2013, and sponsored by McGill University. David Petrie, MD, FRCP, first informed me of the conference in early 2013, and in collaboration with several others from the Integral Health and Medicine Center, we developed a poster that was ultimately accepted by the conference for presentation.

I had attended many medical conferences previously, mostly in my specialty fields of ophthalmology and pediatric ophthalmology. Since retiring from full-time practice and obtaining an MA in Integral Theory from John F Kennedy University, the conferences I chose to attend began to “morph” into the broader fields of medicine (general medicine, cardiology, medical ethics) as I attempted to see my chosen field from a wider perspective. I had exchanged my “microscope” of pediatric ophthalmology for the “telescope” of integral theory and was searching for meetings that could satisfy my more inclusive interests. When Dr Petrie suggested that we prepare a poster for this conference on the basis of our studies at John F Kennedy University, my interest was piqued. Perhaps, I hoped, this event would satisfy my developing needs for a humanistic meeting with other physicians and caregivers who were likewise committed to a “big picture” perspective on medicine.

Our studies in Integral Theory had emphasized the importance of taking multiple perspectives in all areas of human inquiry. The Four Quadrant Model of Ken Wilber (Figure 1) is just the beginning of a systematic approach from several perspectives suggested by Integral Theory. Interiors (thoughts, intentions, will) of both physician and patient are as important as the exteriors (the measurable parameters, such as lab results) that we often emphasize. Collective cultural and social mores anchor and affect medicine in ways that we may be likely to overlook (society’s customs as well as the systems of health care delivery and support).

CONFERENCE HIGHLIGHTS

The opening public lecture by Gregory Fricchione, MD, Director of the Division of Psychiatry and Medicine at Massachusetts General Hospital, was based on his book Compassion and Healing in Medicine and Society. Titled “A New Vision for Healthcare in the 21st Century,” the lecture began by emphasizing a distinction between sickness and suffering. He defined sickness as dysfunction of the body and suffering as primarily a psychological and mental experience. Although technologic medicine is skilled at addressing sickness, it is not so well suited to psychological suffering. He argued that suffering may be seen as a reaction to the trauma of “separation” that occurs when the emotional salience of illness becomes so overwhelming that it results in a “splitting” of patient mental wholeness into disconnected fragments. The solution, he claimed, comes through “attachment,” a repair of disconnection that may be mediated by the skilled physician. The deep and salutary relationship that is provided by the caregiver can restore the patient...
to wholeness, regardless of the course of the disease itself. This “attachment solution to the detachment problem,” as he put it, can be facilitated by many different modalities, but the strength of the physician’s emotional connection to the patient is key to its implementation. His excellent book was available at the congress (see Sidebar: Books Written by Conference Presenters).

Another highlight was the presentation by Craig Hassed, MD, a family physician and faculty member at Monash University in Melbourne, Australia and a leader in mindfulness training for medical students and physicians. He spoke on “Mindfulness and the Use of Self in Healthcare Practice.” He outlined his rationale for the exercise of mindfulness in medicine, describing the advantages it provides to both practitioner and patient. The cost of not being mindful—not fully present—often leads to the waste of time, an increase in accidents, and less ability to communicate effectively. He related that his experiences have demonstrated the value of mindfulness in reducing stress and anxiety, increasing resilience and peace of mind, enhancing cognitive performance, and improving relationships between patients and their caregivers. In a later session, he emphasized how distracting multitasking can be for physicians and how tempting it is to engage in it. He advised simple acceptance of the most important task of the moment and accomplishing it before taking on a second assignment—for example, discontinuing work on an e-mail when the telephone rings with an important call.

Rita Charon, MD, PhD, internist and world expert on Narrative Medicine, is Professor of Clinical Medicine and Director of the Program in Narrative Medicine at Columbia University College of Physicians and Surgeons. She had several presentations at the conference related to her pioneering work in teaching physicians and medical students how to use narrative means to enhance access to inner intentions and feelings. Using a painting by 20th-century abstract artist Mark Rothko entitled “Summoned,” she elicited a correspondence between art and narrative. The abstract image on the screen consisted of two panels, one of black and one of grey. Reflection upon the image eventually conveyed to me an understanding of choice in art—this (panel) and/or that (panel), a kind of digital language. Any narrative may also be seen as a choice of words, vehicles that cannot fully convey the meaning of an event but that are skillfully yet arbitrarily chosen to engender the feelings that the narratologist (Dr Charon’s term) wishes to emphasize. In so doing, the words become representative of emotional elements that invite “affiliation” by the reader, who identifies with the story. Later Dr Charon shared that her teaching goals not only have been in teaching physicians to write narrative medicine, but also have sought to create better readers in her audience (“to deliver to the writer a good reader!”).

Tom Hutchinson, MB, FRCP(C)’s topic was “Healing Healthcare.” Nephrologist and Palliative Care physician, he is the Director of McGill Programs in Whole Person Care. And what is “whole person care”? It is the skillful application and combination of traditional “curing” of disease with “healing,” the restoration of wholeness that Dr Fricchione had mentioned. Moving from suffering to integrity and wholeness is the hallmark of healing, regardless of the outcome of the disease process. It is a shift from an external focus to an internal one. Although curing is the province of science, healing is more accurately seen as the domain of art. Accordingly, it is important to spend “friendly” time with the patient, never losing sight of the need of every human for hope. Cultivating an open-minded presence creates the space in which patient needs and expectations can be verbalized and physician approaches to whole person care maximized. Medicine must never be forced to choose between academic, scientific skills and people skills. If health care is to thrive in the 21st century, we must insist on both!

One of the plenary sessions was “Professionalism, Altruism and Self-Care in Clinical Practice,” with Richard Cruess, MD; Sylvia Cruess, MD; and Dr Hassed. Drs Richard and Sylvia Cruess are members of the faculty of the McGill University School of Medicine. An imaginary situation was created for the discussion that involved a patient “of yours” who had just begun experiencing chest pain and was being evaluated by a competent colleague who was on call at the time. The dilemma for you, as the patient’s regular physician, resulted as you happened to be leaving your office early to attend your daughter’s high school graduation at the very time of the patient’s admission. To provide reassurance, you decided to stop by the hospital briefly to speak to the patient. Quite unexpectedly the patient insisted that you stay with her. She was very frightened and found your presence comforting in this moment of need. What should you do? How could your daughter’s graduation, important as it may be, compete with the life-and-death issues your patient was now facing? And yet how could you skip your own daughter’s graduation, an event that would perhaps be remembered her entire life

### Books Written by Conference Presenters

as a kind of abandonment? Did the fact that your colleague who was evaluating her was highly competent change your decision in any way? After all, it was your presence, not your skill, that the patient seemed to need most. When must professional obligations be abandoned in favor of personal? In this case, the physician with the dilemma went to her daughter’s graduation. But the variety of opinions in panel and audience indicated that such decisions are never easy to negotiate yet necessary to reflect upon.

During one of the evening sessions, the film Flight from Death: The Quest for Immortality was shown. In this film death anxiety was presented as a root cause of many of our behaviors on a psychological, spiritual, and cultural level. Many years ago, I read a mind-altering book titled The Denial of Death, by Ernest Becker.\(^3\) I still remember writing “Wow!” at the book’s conclusion. It is the work of this book that served as the basis for the later investigations presented in the film. Sheldon Solomon from the Department of Psychology at Skidmore College, who had done many of the follow-up studies, was interviewed in the film and appeared in person for a discussion immediately after its presentation. In the book, Ernest Becker contended that humanity’s capacity for symbolic thought enables us to create what he termed “immortality projects” that help us deny our inevitable demise. These of course vary in their capacity to provide a sense of immortality, but who can forget Mahler’s Fifth Symphony as an example of music that will last forever? The research at Skidmore College indicated that the more aware of death or demise a person becomes, the more intolerant and projective their death defenses also become. Reminders of our own mortality result in “mortality salience” and create more defensive reactions as, for example, we saw after the events of 9/11. Even physicians, when reminded of their own mortality, can become more single-minded about keeping their patients alive in order to assure their own death fears. As physicians, the more aware we are of the power of mortality salience, the more mindful we will become of the challenge for us to face death and demise with courage and fortitude, as we know and accept its inevitability. Ernest Becker’s book and this fine film are highly recommended to the reader.

**POSTER PRESENTATION**

Our poster, titled “Integral Medicine: Treating the Whole—Patient, Provider, Health Care System,” was developed by a team of five authors at the Integral Health and Medicine Center, including Olga Jarrin, RN, PhD; Baron Short, MD; Joel Kreisberg, DC, CCH; David Petrie, MD; and Gary Huffaker, MD. Over several months, we attempted to present Integral Theory in a poster form that would demonstrate the capacity of the theory to inform whole person care. Perhaps the “Purpose” section of the poster summarizes the main point best: “Integral Medicine is an approach to health, disease and healing that invites multiple perspectives and modes of inquiry to synergistically support health for patients, providers and health care systems.” Using Ken Wilber’s Four Quadrants’ (Figure 1) and developmental models, we showed that a coherent set of perspectives could be developed that were able to address the “big picture” of health, healing, and wholeness.

In the conclusion, we stated, “Treating the whole person becomes more than simply including body, mind and spirit. The whole person includes multiple epistemological ways of knowing.” By acknowledging and using these different perspectives and methods, interacting with the patient becomes a complex tapestry of involvement, offering new ways to love, heal, and cure.
Sol Duc Falls is located deep in the rain forest on the Olympic Peninsula in Washington. This photograph captures the tranquil motion of the Sol Duc River and a glimpse of the beauty of Olympic National Park.

Dr. Shenson is an Internist at Mt. Scott Medical Office in Clackamas, OR. More of his photography may be viewed at: www.davidshenson.com.
Changing Medicine and Building Community: Maine’s Adverse Childhood Experiences Momentum

Leslie Forstadt, PhD; Sally Cooper, MD; Sue Mackey Andrews

ABSTRACT
Physicians are instrumental in community education, prevention, and intervention for adverse childhood experiences. In Maine, a statewide effort is focusing on education about adverse childhood experiences and ways that communities and physicians can approach childhood adversity. This article describes how education about adversity and resilience can positively change the practice of medicine and related fields. The Maine Resilience Building Network brings together ongoing programs, supports new ventures, and builds on existing resources to increase its impact. It exemplifies the collective impact model by increasing community knowledge, affecting medical practice, and improving lives.

PHYSICIANS AND ADVERSE CHILDHOOD EXPERIENCES
Fifty physicians sit in a darkened room, listening to an atypical grand rounds presentation. Rather than a focus on the latest in medical treatment or an in-depth case study, the topic is “What You Should Know about Adverse Childhood Experiences” (ACEs). For the next 75 minutes, the physicians learn about the ACE Study, complete the ACE questionnaire, and respond to an invitation to integrate the information into their medical practice. No specific recommendations and guidelines are articulated, but the question-and-answer session is ripe with ideas, questions, and uncertainty about next steps.

The ACE Study, by Vincent Felitti, MD, and Robert Anda, MD, MS,1 was published in the late 1990s and was a collaboration between the Centers for Disease Control and Prevention in Atlanta, GA, and Kaiser Permanente in San Diego, CA. The study found that early childhood experiences correlated with adult health and behavior outcomes. Ten types of childhood adversity were included in an intake questionnaire: emotional, physical, and sexual abuse; emotional and physical neglect; and five types of family dysfunction—a mother treated violently, a mentally ill parent, an alcoholic (or other substance-abusing) parent, losing a parent through abandonment or divorce, and a family member in prison.

In this study of 17,471 insured Americans, a score between 0 and 10 (called the ACE score) was determined on the basis of the 10 categories of early childhood adversity described in the preceding paragraph. A score of 1 indicated that the person had experienced at least 1 event in the selected category. No additional numbers were added even if there were multiple occurrences in a single category. For example, the experience of physical abuse and an alcoholic parent would equal a score of 2, even if there had been multiple occurrences of physical abuse and/or more than 1 alcoholic parent. Almost two-thirds of the participants in the ACE Study reported experiencing at least 1 ACE. As the number of ACEs increased, so did the risk of heart disease, cancer, obesity, depression, and autoimmune disorders.

The ACE Study findings are supported by more recent research on childhood toxic stress and trauma. The list of potential stressors is longer than 10, and the potential long-term impacts are infinite. A growing collection of evidence related to ACEs and other childhood stressors is available: ACEs have an impact on health and substance use,2 mental health,3 health care utilization,4 psychotropic medication use,5 and autoimmune disease.6 The overarching point is made: the impact of trauma in childhood is lasting. The long-term effects are seen in the health status and behavior of adults. What happens in childhood lays a foundation for multigenerational illness, adversity, and disparity.

If trauma represents one side of the coin, the antidote for trauma is resilience. An accompanying and powerful body of research is building about resilience and the capacity of humans to thrive in the face of traumatic life events.7 Resilience is the ability to respond to experiences, fostered by the clinicians, teachers, friends, family, and community in one’s life.8 Support from others, referrals as needed, and the simple act of having a trusted provider listen nonjudgmentally and with compassion can provide support. Then, if needed, patients can be referred to additional services they believe would support them. The patients’ own insights about personal motivation on their journey toward health and well-being are both respected and reinforced by their clinicians. This interaction between medical professional and patient does not change the past experiences of the patient; however, it can change their experience moving forward.

NATURAL QUESTIONS
During the question-and-answer period of the grand rounds, response is mixed. Clinicians want to help, yet there is a finite amount of time with patients. There is skepticism as to the amount of training needed to delve into the patient’s childhood experiences.

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http://dx.doi.org/10.7812/TPP/14-169
In one corner, there is a collective overwhelmed sigh at the thought of adding one more task to a full and overburdened plate. In another corner, there is a glimmer of curiosity and bubbling ideas about how to implement the information. Many of the questions center on unfamiliarity with the ACE Study and corresponding uncertainty about how best to use the information.

The first results of the ACE Study were published 15 years ago, with 100s of articles published since then, and yet the study remains unknown to many in the medical profession. The ACE Study found that many of the seemingly destructive behaviors of patients (eg, smoking, overeating, or promiscuity) were, in fact, ways that patients were self-medicating in response to trauma and stress.

Jeffrey Brenner, MD, a family physician and MacArthur Fellow from Camden, NJ, comments, “In my training … I was told not to pull up the lid on something you didn’t have the time and training to deal with.” However, he acknowledges that the lack of awareness of the ACE Study and the unwillingness of physicians to understand the effects of trauma reflect a failure of the profession. He believes “we need more trauma victims to publicly discuss how their early life experiences have impacted their life and their health and we need more physicians to talk publicly about the importance of this issue. We also need research on ways to bring ACE scores into routine primary care.”

One way to bring ACEs and trauma into medical practice is to change the conversation. In the column, “Protecting Children from Toxic Stress,” journalist David Bornstein articulates this change. As physicians understand the science of ACEs, toxic stress, and brain plasticity, Bornstein believes we should change the question from “What’s wrong with the person?” to “What happened to the person?” and “What’s the best response?” The ACE score provides language for conversation, but the score itself does not predict the degree of resilience of an individual; deciphering resilience becomes the work of the treatment team and the individual.

There is also a need to calm the fear of opening a Pandora’s box. In a 2007 commentary, Edwards et al proposed that because of the association between trauma and health, the practice of medicine might, in fact, be improved if physicians understand and incorporate identification of the signs and impacts of trauma into their medical practices. When physicians learn about the impacts of trauma in general, and the experiences of their patients in particular, this understanding can lead to improvements in relationships with patients, adherence to medical protocols, and health outcomes. The ACE score is one way to provide a common language in that it facilitates the process of referrals for services for children and adults with complex needs, particularly those individuals with challenges that are affecting their health and their ability to participate effectively in their own health care in a functional and sustainable way. The ACE score can help clinicians ask different questions that address the complexity of an individual’s case.

Following is a sample of ways that ACEs and resilience can be incorporated into medical practices. Some of these methods, where noted, are being explored in Maine.

• A Maine psychologist, Mark Rains, PhD, consults with physicians and other professionals who are interested in engaging patients in conversation. He has developed a nonspecific type of ACE inquiry that focuses on strengths and introduces the ACE survey in a simple and straightforward manner. Without asking for extensive detail, or even needing to know the specific categories of ACEs, one can ask questions such as “How did what you experienced in childhood affect you?” and “Are you still bothered by any of the things that happened to you?” and “If you are no longer bothered, how has this happened?”

• Maine obstetricians are beginning to have ACE-specific conversations with expectant families by incorporating ACEs and the Protective Factors (parental resilience, social connections, concrete support in times of need, knowledge of parenting and child development, and social and emotional competence of children). In these conversations, physicians ask about preparation and readiness for the birth, what parenting practices the expectant parents have experienced that they will use with their child, and, conversely, what they will change and what supports they need. This ongoing dialogue helps to provide support, validation, and resources to parents through the relationship that the physician has cultivated by asking, “What happened to you that may affect your parenting?”

• In the pediatric practice of San Francisco’s Nadine Burke Harris, MD, children are screened for various types of adverse experiences that increase their risks of long-term health problems associated with ACEs. The treatment model is multidisciplinary in the primary care setting and includes home visits to support families where they are. The treatment provides a “complete spectrum of response,” working with both primary prevention and secondary care and includes, as well as goes beyond, protocols and tools for early detection.

• Philadelphia pediatrician Kenneth Ginsburg, MD, focuses on finding strengths in his adolescent patients by focusing on the future and on small steps toward reaching personal goals. He “flips” the trauma story, finding the dedication, ingenuity, and creativity of people to overcome their challenges and demonstrate resilience in daily life. Dr Ginsburg co-edited a comprehensive curriculum titled “Reaching Teens,” which is based on his strengths-based approach to working with teens.

• The Center on the Developing Child at Harvard University in Cambridge, MA, provides a variety of videos and research-based materials explaining the damaging impact of toxic stress on the developing brain. The resources are effective tools for personal and professional development, and facilitate meaningful conversations with parents about their important role in promoting resilience in their children.

• Maine is incorporating supports at home to assist with patient follow-through, attachment, and skill building through strong relationships between the physician community and Early Head Start, the Public Health Nursing Program, and Maine Families. These evidenced-based
programs provide home visiting services to expectant families and those with young children. Their parenting curricula and additional resources and referrals complete the circle of support that is essential to ensure adequate protective factors for all children and their parents. This community-based approach integrates education and prevention, and professionals are trained to make referrals in the community when interventions are needed.

CASE IN POINT
At the Edmund N Ervin Pediatric Center at Maine General Medical Center in Waterville and Augusta, ME, the staff provides programs incorporating trauma-informed care into every aspect of the clinical process. The ACE survey provides a common language for the Pediatric Rapid Evaluation Program (PREP), which provides evaluation to all children on entry into the custody of the Department of Health and Human Services, from five counties in Maine. All children in this clinic start with one point on the ACE survey because of their separation from their family of origin. Most also have been exposed to physical violence, sexual abuse, neglect, and a family member’s mental health and/or substance abuse issues. The goal for the PREP team, which consists of a child psychologist and a pediatrician, is to provide a baseline assessment of the child’s medical, educational/developmental, emotional, and physical needs on entry into foster care.

One important purpose is to help clinicians identify the child’s strengths in addition to his/her needs. Teamwork and knowledge of where to refer patients are key. The medical professional who may be the expert in heart disease or family medicine is greatly empowered when the resources for referral for treatment of substance abuse, domestic violence, and mental health issues are within reach. Better yet, the fears about Pandora’s box can be abated with the confidence in being part of a team, with referral within reach.

Teamwork starts with relationships built through opportunities across disciplines to come together and develop protocols that include response and referral strategies. This is true at Maine General Medical Center, where the PREP team coordinates and collaborates to provide care among staff from multiple disciplines in the clinic (psychology, social work, developmental pediatrics, psychiatry, speech therapy, physical therapy, occupational therapy) as well as primary care physicians in the community. Referrals are bidirectional, allowing for identification of needs and pathways for access to services at multiple points of entry into the system of care. It is essential that every contact point and process in the system is trauma-informed. Even the most apparently insignificant interaction with a clinician in the medical system is an opportunity to promote resilience.

MAINE’S MOMENTUM
The grand rounds presentation was successful. Many of the physicians signed up for future communications about training sessions, and some started exploring ways to incorporate ACEs and resilience in conversation with their patients. In addition, there was resounding support for a Part 2 training to practice and share specific strategies.

Grand rounds are one of many educational offerings about ACEs and resilience in Maine thanks to the Maine Resilience Building Network (MRBN), a multisector collaborative using the collective impact process. A variety of stakeholders are engaged in exploring how ACEs and resilience can be applied “on the ground” through practice and skill building. Educational presentations similar to the grand rounds are tailored to different audiences and range from a 45-minute brief session to a 6-hour intensive workshop, with a variety of individually structured opportunities in-between. The offerings have expanded to a 3½-hour workshop on ACEs and resilience called the ACEs Summit. The MRBN is creating a “menu” of opportunities that are cumulative in content, are informed by participant evaluation, and engage statewide partners such as THRIVE, Maine Behavioral Health Organization, and the Maine Chapter of the American Academy of Pediatrics. This “menu” currently includes the Summit; a skill-building seminar on resilience promotion called “Bring it On”; a self-care/trauma prevention seminar; and technical assistance in administration of the ACEs screening tool in multiple formats for medical, health care, early care and education, and community-based organizations.

In the first 2 years since the MRBN formed, the network has grown to more than 50 sites around the state. The overall purposes of the MRBN are to create community conversations, increasing awareness of ACEs and resilience among Maine citizens, and to provide collegial support among professionals from multiple disciplines in Maine. To do this, there are public education sessions, conferences, grand rounds, trainings in agencies, regular network meetings, and a Web site at www.maineaces.org. These efforts increase the understanding that what happens in childhood affects adulthood, and correspondingly, the way adults present at physicians’ offices and the way they act in schools, social service agencies, or even in the grocery store might relate to experiences from childhood.

Among professionals, the MRBN functions as a support group and think tank for new projects, and as a facilitator for planning projects that involve the whole state of Maine. For some of the nonprofit organizations involved, the educational work is sometimes “in-house” to educate all professionals in a single organization.

The value of the MRBN is bringing together practitioners from multiple fields to talk about how to educate about ACEs. Each meeting (about five per year) begins with an orientation for new members, including an overview of the ACE Study. The remainder of the meeting flows in two directions: 1) what people are doing independently and 2) what collective projects can involve everyone. The
efforts of some regions, such as the ACEs screening with expectant parents and families with young infants, serve as powerful examples of local capacity building. As the MRBN continues to establish a foundation statewide, both horizontal collaboration with other statewide entities and state agencies, and lateral collaboration with local county collaboratives, early childhood staff, physician teams, and behavioral health and human service agencies occur.

SHARING THE MOMENTUM

Maine’s accomplishments are possible partially because of the rural nature of the state, which has a population of more than one million people. Members of the MRBN believe it is possible for every town, family practice, and school to be educated about ACEs and the power of community members to build resilience. Each state, city, and town has its own strengths and barriers. A committed group of individuals can create the momentum and garner the type of financial resources necessary to establish a foundation for incorporating ACEs in medical homes.

The MRBN’s presentations and Summits are the core of the momentum’s success. These venues provide opportunities for professionals to reflect, to talk to one another, and to strategize about changing practice. In response to demand and to continue the momentum, the next step is developing ongoing technical assistance for professionals to have the support they need once they choose to implement changes in practice. This multifaceted approach will build confidence as professionals begin talking about ACEs and resilience.

\* A site is defined as a local or statewide project or initiative related to ACEs. A site might include an annual conference, a training for home visitors, or development of an agencywide policy related to ACEs and resilience. All sites are developing efforts to educate and make change about ACEs and resilience on a large or small scale, short or long term, and in isolation or partnership. All sites are part of the statewide Maine Resilience Building Network.

Disclosure Statement

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

Acknowledgment

Thank you to Marjorie Withers for her review and insights on early versions of the manuscript.

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

Disclaimer

The views expressed in this article are a reflection of the authors and not an official position of the institutions employing the authors.

References

Spring 2015
CME Evaluation Program

Section A.

Article 1. (page 15) Big Data, Mini registries: A Rapid-Turnaround Solution to Get Quality Improvement Data into the Hands of Medical Specialists

The approach to population management of specialty care differs from population management of primary care in that:
- [ ] a. the volume of patients is smaller
- [ ] b. knowledge of the disease and its management is held by fewer clinicians
- [ ] c. specialty care is more costly than primary care
- [ ] d. patients visit specialty care less frequently than they visit primary care

For lower-volume conditions, information technology used for population management should be designed with the skill set of the end user in mind. Which of the following skill sets are important?
- [ ] a. computer programming
- [ ] b. statistical modeling
- [ ] c. medicine
- [ ] d. health care management

Article 2. (page 28) Alcohol Intake, Beverage Choice, and Cancer: A Cohort Study in a Large Kaiser Permanente Population

In this Kaiser Permanente study, heavy drinkers were at higher risk for each of the following except:
- [ ] a. esophageal cancer
- [ ] b. breast cancer
- [ ] c. pancreatic cancer
- [ ] d. colorectal cancer
- [ ] e. melanoma

Defining light-moderate drinking as 2 drinks per day or less, which of the following statements is false:
- [ ] a. light-moderate drinkers were at higher risk of cancer
- [ ] b. light-moderate drinkers taking preponderantly liquor, but not wine or beer, had higher cancer risk
- [ ] c. underreporting appeared to play a role in the relationship of light-moderate drinking to cancer
- [ ] d. for persons over the age of 50 years, total mortality was lower among light-moderate drinkers than among abstainers
- [ ] e. advice to patients about light-moderate drinking needs to be individualized according to specific risks and benefits

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?

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<th>Objective 1</th>
<th>Objective 2</th>
<th>Objective 3</th>
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<td>[ ] Integrate learned knowledge and increase competence/confidence to support improvement and change in specific practices, behaviors, and performance.</td>
<td>[ ] 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.</td>
<td>[ ] 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.</td>
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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
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Date
CASE REPORTS

Ruptured Intracranial Lipoma—A Fatty Outburst in the Brain

Vinod Chaubey, MD; Ganesh Kulkarni, MD; Lovely Chhabra, MD

ABSTRACT

Intracranial lipomas are rare congenital lesions that occur because of abnormal differentiation of embryogenic meninges. These lipomas are usually seen incidentally on brain imaging performed for another reason, and they are usually asymptomatic and do not require treatment. We present a case of ruptured intracranial lipoma, discovered in an elderly patient presenting with dizziness and after falling.

CASE STUDY

A 94-year-old man presented after 2 falls during a 1-week period. Each fall was preceded by dizziness. The patient denied any loss of consciousness, abnormal body movements, headache, tinnitus, diplopia, palpitations, or chest pain. His medical history was significant for hypertension and chronic kidney disease. On examination, his vitals were within normal limits, including orthostatic blood pressure response. The oral mucosa was dry. Chest, cardiovascular, and abdominal examinations were unremarkable. Neurologic examination showed lethargy and absence of focal weakness/numbness or nystagmus. Laboratory testing, including hemogram and basic metabolic panel, was unremarkable except for evidence of acute kidney injury (creatinine, 2.2 mg/dL; baseline, 1.5 mg/dL). A computed tomography (CT) scan of the brain without contrast revealed numerous foci of likely fat deposits, estimated by densitometry (-13 Hounsfield units), within the suprasellar cistern, ambient cisterns, left cerebellar subarachnoid space, and left temporal horns. This finding was confirmed by noncontrast magnetic resonance imaging of the brain, which showed bright spots on T1-weighted imaging in the suprasellar cistern (A), ambient cisterns (B), left cerebellar subarachnoid space, and left temporal horns. This finding was confirmed by noncontrast magnetic resonance imaging of the brain, which showed bright spots on T1-weighted imaging and low signal intensity on fat saturation imaging in similar locations as previously noted on the CT scan (Figure 1). A review of a brain CT scan performed 2 years earlier was suggestive of a lipoma in the suprasellar region (Figure 2). Intravenous hydration with normal saline was given for mild dehydration, and this also resolved the acute kidney injury. Physical therapy was initiated. The patient's dizziness improved significantly in 48 hours, and he was discharged with close neurology follow-up. To our knowledge, this is the first reported case of ruptured intracranial lipoma.

Figure 1. Magnetic resonance imaging of the brain showing bright spots on T1-weighted images in the suprasellar cistern (A), ambient cisterns (B), left cerebellar subarachnoid space, and left temporal horns.

Figure 2. Computed tomography scan of the brain suggestive of lipoma in the suprasellar cistern. The dashed arrow indicates an intracranial lesion (determined by negative Hounsfield units).

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DISCUSSION

Intracranial lipomas are usually discovered in asymptomatic patients as an incidental finding on neuroimaging or during postmortem examination. They are considered rare tumors with incidence estimated at 0.06%-0.46% of all intracranial tumors.1 Intracranial lipomas are congenital malformations resulting from abnormal persistence and maldifferentiation of the meninx primitiva during the development of the subarachnoid cisterns.2 Approximately 45% of intracranial lipomas occur in the pericallosal region, making it the most common location, followed by the quadrigeminal cistern (25% of occurrences) and suprasellar cistern areas (15% of occurrences).3,4 The clinical manifestations of lipomas are nonspecific and depend on lipoma location. Epilepsy is the most common symptom in supratentorial lipomas and occurs in about 50% of cases of callosal lipomas.5 Intracranial lipomas located near the brainstem may cause ataxia, hydrocephalus, gaze palsies, and trochlear nerve paralysis. In the pediatric population, they are associated with nonspecific neurologic complaints: headache, dizziness, seizures, or global psychomotor delay, which affects language and gross psychomotor skills.6 Intracranial lipomas have a characteristic appearance on unenhanced CT scans, with low attenuation. Calcifications are often present in interhemispheric lipomas, most commonly within a fibrous capsule surrounding the lipoma. On magnetic resonance imaging, intracranial lipomas present with a high signal on T1-weighted images and intermediate/low signal on T2-weighted spin-echo sequences.6,7 Intracranial lipomas are managed conservatively, as with our patient.8 Attempts at resection are associated with high mortality.9

Our patient presented with nonspecific dizziness and associated falls. It is unclear what caused these symptoms, as well as whether the dizziness and falls were the cause or the result of the ruptured intracranial lipoma. Lipomatous density/signal spots were seen in the suprasellar region and superior cerebellar surface. We theorize that these spots resulted from the rupture of the lipoma seeding the subarachnoid space. It is prudent to be cognizant of the fact that ruptured lipomas can be seen on imaging for fall and dizziness evaluation. The diagnosis of intracranial lipoma can be made confidently with magnetic resonance imaging, with 100% specificity.10

Disclosure Statement

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

References


Key Points

1. Intracranial lipomas are mostly congenital and form because of an abnormal differentiation of the meninx primitiva.
2. The clinical manifestations of lipomas are nonspecific and depend on their location. Epilepsy is the most common symptom of supratentorial lipomas and occurs in about 50% of cases of callosal lipomas.
3. Intracranial lipomas are often managed conservatively, and attempts at resection are associated with high mortality.
Atrial Fibrillation and Cor Triatriatum Sinister: A Case Report

Hoa Jeannie Tran, MD; Robert Gordon, MD; Thomas Alloggiamento, MD, MS; Sukhvinder Kaur Nagi, MD, PhD; Ashok Krishnaswami, MD, MAS

Perm J 2015 Spring;19(2):e105-e106
http://dx.doi.org/10.7812/TPP/14-182

ABSTRACT
A 29-year-old man presented with palpitations, shortness of breath, and orthopnea. After being admitted, he progressed to cardiogenic shock and respiratory failure, which required ventilator support and cardioversion. Subsequent evaluation revealed a fibromuscular membrane across the left atrium, requiring urgent corrective surgery. This case report highlights the importance of identifying and treating the relatively rare cor triatriatum.

CASE REPORT
A 29-year-old man presented to the ambulatory clinic after 4 days of palpitations, shortness of breath, and orthopnea. Electrocardiography revealed atrial fibrillation with a rate of 181 beats per minute and a chest x-ray consistent with pulmonary edema. The patient was transferred to the Emergency Department and became progressively dyspneic. The initial attempt at controlling his heart rate by using a standard regimen of intravenous beta-blockers and calcium-channel blockers was ineffective. His condition subsequently deteriorated and progressed to cardiogenic shock and respiratory failure, which required ventilator support and cardioversion. His condition subsequently deteriorated and progressed to cardiogenic shock and respiratory failure, which required ventilator support and cardioversion. Subsequent evaluation revealed a fibromuscular membrane across the left atrium, requiring urgent corrective surgery. This case report highlights the importance of identifying and treating the relatively rare cor triatriatum.

The patient underwent urgent corrective cardiac surgery with resection of the fibromuscular septum to address the CTS, placement of a Number 30 Carpentier-Edwards Physio annuloplasty ring (Carpentier-Edwards, Irvine, CA) to address the dilatation of the mitral annulus, and a CryoMaze procedure to address the atrial fibrillation (Figures 2 and 3). The patient was postoperatively prescribed oral warfarin. A follow-up transthoracic echocardiogram 1 year after surgery demonstrated normal left ventricular systolic function and appropriate functioning of the mitral valve. Eighteen months after surgery, the patient remained asymptomatic and in normal sinus rhythm and was able to stop taking oral anticoagulant therapy.

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DISCUSSION

Cor triatriatum is a rare congenital cardiac anomaly represented by the development of a thick fibromuscular membrane that divides the left atrium (sinister) or the right atrium (dexter) into 2 chambers.\(^1,2\) CTS is much more common and occurs in approximately 0.1% to 0.4% of patients with congenital heart disease, whereas cor triatriatum dexter occurs in less than 8% of all cor triatriatum patients. CTS has a higher prevalence in males with a 1.5:1 male-to-female ratio. CTS is usually diagnosed in childhood; however, some cases, such as the one reported here, may present in adulthood.\(^3,5\)

According to a simple classification by Loeffler\(^6\) in 1949, there are three groupings of CTS. These are based on the size and number of fenestrations in the fibromuscular membrane. Group 1 has no fenestration, Group 2 has one or a few tiny fenestrations, and Group 3 has a single wide opening.\(^6\) Adults usually present as Group 3 because the other two groups become symptomatic early in life and are associated with a high early mortality.\(^7\)

When CTS is diagnosed in adulthood, the patient may be asymptomatic with diagnosis made incidentally, or the patient may present with dyspnea, orthopnea, or hemoptysis.\(^1,3,8\) It is thought that patients become symptomatic owing to gradual fibrosis of the fenestrations in the fibromuscular membrane as well as development of valvular insufficiency and atrial arrhythmias.\(^4\) Classically, CTS is found in isolation; however, azygous CTS is associated with other anomalies, including secundum-type atrial septal defect, anomalous partial pulmonary venous connection, or mitral regurgitation, as in our patient’s case.\(^1,9\)

CONCLUSION

The clinical features of CTS mimic mitral stenosis because of flow obstruction across the membrane, leading to an increase in pulmonary pressures and subsequently causing arrhythmias such as the atrial fibrillation found in our patient.\(^10\) On auscultation of the heart, one might appreciate a diastolic murmur similar to the diastolic murmur of mitral stenosis. However, the lack of an opening snap or a loud first heart sound distinguishes CTS from mitral stenosis. Surgical intervention involving removal of the fibromuscular membrane is usually reserved for cases with severe obstruction and has been shown to provide significant symptomatic relief as well as mortality benefit.\(^3,11,12\)

References

Rare Case of Myocardial Infarction in a 19-Year-Old Caused by a Paradoxical Coronary Artery Embolism

Jonathan Kei, MD, MPH; Jennifer Kiss Avilla, MD; Jeffrey J Cavendish, MD

ABSTRACT
Chest pain visits to the Emergency Department among the young adult population are rarely caused by cardiac etiologies. This case focuses on a 19-year-old man who developed an inferior ST-segment elevation myocardial infarction as a result of a previously undetected large atrial septal defect. This cardiac anomaly facilitated the transport of a paradoxical embolism that occluded the right coronary artery. This rare case highlights the importance of a thorough evaluation to rule out cardiac-related chest pain in young adults, despite the low incidence in this population.

INTRODUCTION
Coronary artery disease (CAD) remains the number one cause of death in the US, and chest pain is one of the most common reasons patients go to the Emergency Department (ED) for medical care. The vast majority of chest pain evaluations occur in the adult population; however, chest pain visits among young adults (younger than age 35 years) are not uncommon. The leading causes of chest pain among teens and young adults are idiopathic, musculoskeletal, pulmonary, gastrointestinal, anxiety, and drug-related in origin. Although cardiac-related chest pain is uncommon and rarely caused by myocardial infarction (MI) in this age group, identifying high-risk individuals during their ED visits is critical.

CASE REPORT
A 19-year-old man presented to the ED with 3 hours of constant chest pressure. He described the pain as 8 out of 10 on the pain scale, located in the substernal area and radiating throughout his entire chest. The pain started suddenly at rest and he denied any associated symptoms. The patient did not use tobacco but admitted to occasionally smoking marijuana. He also denied other drug use, including cocaine or methamphetamines. There was no associated trauma. According to the patient, he had had a cardiac murmur since he was a child, but it was never fully evaluated.

On physical examination, vital signs were stable with a temperature of 36.4°C, blood pressure 128/74 mm Hg, pulse 58 beats/min, respiratory rate 18 breaths/min, and pulse oximetry 98% on room air. The patient appeared moderately distressed. His cardiovascular examination revealed a regular rhythm and a 2/6 systolic murmur. Pulmonary examination demonstrated clear breath sounds bilaterally. The rest of his examination, chest radiograph, and laboratory results (including complete blood count, chemistries, and troponin) were unremarkable.

Initial electrocardiogram (ECG) showed sinus bradycardia at 52 beats/min and 5 mm ST-segment elevations in leads II, III, and aVF with reciprocal ST-segment depressions in V1-V2 (Figure 1). This ECG was consistent with an ST-segment elevation MI, and he was immediately given an aspirin, nitroglycerin, and morphine for his pain. A heparin bolus was given and the patient was transferred for emergent cardiac catheterization.

Upon initial fluoroscopy of the cardiac silhouette, the right ventricle appeared enlarged. Coronary angiography revealed complete occlusion of the two terminal branches of the right coronary artery. There were dual posterior descending artery branches, both having evidence of clot and abrupt closure (Figure 2). The patient was then given a bolus and infusion of eptifibatide. Coronary angioplasty, stenting, and aspiration thrombectomy were considered but, owing to the small caliber and the very distal location of the occluded arteries, these therapies were felt to carry more risk than benefit.

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Rare Case of Myocardial Infarction in a 19-Year-Old Caused by a Paradoxical Coronary Artery Embolism

After cardiac catheterization, a trans-thoracic echocardiogram revealed a large secundum atrial septal defect (ASD) measuring 2.9 cm with bidirectional shunting (Figure 3). The initial cardiac markers, including troponin, were normal. Serial cardiac markers showed a peak creatine kinase of 1521 IU/L and peak myoglobin of 32.5 ng/mL. The patient was monitored over the next 48 hours with no dysrhythmias noted. Aspirin 81 mg daily, metoprolol 25 mg twice daily, and warfarin were initiated. The patient was discharged on hospital day 3 with a referral to cardiothoracic surgery, as the nature and size of the ASD was not amenable to percutaneous repair. Six weeks after MI, the patient underwent uneventful surgical repair of his ASD (Figure 4) and recovered with no additional sequelae.

DISCUSSION

Coronary artery embolism has been shown to cause acute MI in the setting of an existing ASD, tissue or mechanical valve replacement, and atrial fibrillation.4–7 Congenital defects of the atrial septum are common and account for approximately 7% of all congenital heart disorders.8 Most ASDs less than 6 mm in diameter close spontaneously and rarely require surgical correction.9 The patient in this case had a known cardiac murmur but it had never been fully evaluated. It was not until after the MI that the ASD was discovered on echocardiography. Like many individuals with ASDs, this patient was asymptomatic for years. As a result, the MI was the first time he became aware of his cardiac defect. Studies show that transthoracic and even more sensitive transesophageal echocardiography can be used quite effectively to diagnose cardiac sources of embolization.10

Figure 2. Right coronary angiogram showing embolism to the terminal right coronary artery with two posterior descending artery branches (indicated by arrows) having evidence of clot and abrupt closure.

Figure 3. Transesophageal echocardiogram image showing a large secundum atrial septal defect (ASD) measuring 2.9 cm with bidirectional shunting between the right atrium (RA) and the left atrium (LA).

Figure 4. Transesophageal echocardiogram image showing a repaired atrial septal defect (ASD) and resolution of the bidirectional shunt between the right atrium (RA) and left atrium (LA).
On presentation to the ED, the patient had a clearly abnormal ECG with ST-segment elevations in multiple contiguous leads. Although musculoskeletal, psychological, and other noncardiac etiologies are often attributed to chest pain in the teen population, it is critical that emergency physicians consider cardiac causes in these patients. This case report reinforces the common practice of performing ECGs on all patients with chest pain regardless of their age.

One of the main challenges in the recognition of cardiovascular-related chest pain is the age-related differences in the pediatric and young adult population compared with adults. When one is evaluating chest pain in young patients, their risk factors, clinical presentations, and prognoses can vary from those of the typical older patients who present with the same chief complaint.12-14

MI in young patients (younger than age 35 years), although rare, has been described in the literature. Cases of atherosclerotic MI occur predominantly in men, and important risk factors include smoking, positive family history of MI, hypertension, and familial hyperlipidemia.15 Nonatherosclerotic etiologies, such as drug-induced coronary artery spasm, can cause MI in young patients with cocaine being the most common culprit.16 Unlike the previous examples that occur predominantly in males, spontaneous coronary artery dissection is a very rare cause of acute coronary syndrome in young otherwise healthy patients, with a striking predilection for the female sex.17 Coronary embolism, coronary vasospasm, Tokotsubo cardiomyopathy, hypercoagulable states, trauma, arterial inflammatory (autoimmune) conditions, and very rarely myocarditis can all produce ECG findings that mimic acute MI.

Detailed history taking and comprehensive physical examinations may help elucidate a cardiac cause for chest pain in young adults. In these patients where cardiological-related causes are on the differential, an ECG should be performed at a minimum and chest radiographs may be useful. Studies looking at the most effective way to evaluate chest pain in young adults and pediatric patients suggest that a careful history, physical examination, screening ECGs, and targeted echocardiograms are the best way to identify serious causes of chest pain and can reduce the number of unnecessary studies.18 The cardiac murmur heard on the initial physical examination was a very important physical finding. In the setting of acute chest pain in a young patient with a new or undocumented murmur, an ECG should be obtained. Although this case highlights the importance of always ruling out cardiac-related chest pain in young patients and teens, no matter how uncommon it may be in this population, it is just as important to pay careful attention to the details of routine examinations. If the murmur in this patient had been picked up earlier by his primary physician and if he had been further evaluated with an ECG, this case of MI might have been avoided.

CONCLUSION
This case describes the rare event of an ST-segment elevation MI in a 19-year-old man who presented to an ED. Although MI-related chest pain is rare in the young adult population, it must always be considered because it has the potential for poor outcomes if not promptly recognized./disclosure

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

Acknowledgment
Mary Corrado, ELS, provided editorial assistance.

References

The Permanente Journal/ Spring 2015/ Volume 19 No. 2

CASE REPORTS

Rare Case of Myocardial Infarction in a 19-Year-Old Caused by a Paradoxical Coronary Artery Embolism
CASE STUDY

A 14-year-old boy with no significant medical history presented to the Emergency Department (ED) for evaluation with 3 months of generalized headache. He had seen his primary care physician for the same problem a few weeks earlier, and the ibuprofen he was told to take had not seemed to improve his symptoms. The patient reported his headaches had increased in intensity and frequency, with associated lightheadedness, in the 2 weeks before presentation to the ED. The patient denied drug or alcohol use and stated that he never got headaches. He also denied any fevers, neck stiffness, shortness of breath, abdominal pain, diarrhea, visual changes, focal weakness, or speech disturbances. However, nausea and vomiting started a day before presenting to the ED. The patient’s mother witnessed the patient having a syncopal episode upon standing, which led her to bring him to the ED.

On arrival, the patient was afebrile and his blood pressure, pulse, respiratory rate, and oxygenation were all normal. Physical exam found the patient was in no acute distress, his neck was supple, and his cranial nerves were grossly intact, including normal pupils. In addition, he had 5/5 strength bilaterally in his upper and lower extremities, a normal gait, and normal cerebellar function. The rest of his physical examination was unremarkable, and there was no family history of central nervous system processes. Laboratory test results, including complete blood count and basic metabolic panel, were all normal.

Although the patient had a normal physical exam, the clinical features in his history of a chronic progressive headache pattern and associated vomiting in the context of never getting headaches, along with a lack of response to outpatient medical therapy, suggested the possibility of an intracranial mass or bleed. We obtained a computed tomography scan of his brain without intravenous contrast, which showed a large extra-axial cystic lesion causing mass effect with effacement of the right lateral ventricle and brain shift to the left (Figures 1 and 2). We diagnosed the lesion as an arachnoid cyst and admitted the patient to the hospital.

Magnetic resonance imaging of the brain was performed during his hospitalization and confirmed the diagnosis of an arachnoid cyst. Because of the associated symptoms, size of the cyst, and mass effect seen in this case, the patient underwent
endoscopic fenestration of the arachnoid cyst during his hospital stay. The neurosurgery was uneventful and reconfirmed the diagnosis of a primary arachnoid cyst. The patient fully recovered with no further sequelae.

DISCUSSION

Localized within the layers of the arachnoid membrane, arachnoid cysts are benign lesions that are prevalent in about 1% to 2% of both pediatric and adult populations.1-2 Sixty percent to 80% of these malformations are diagnosed in patients under 16 years of age3 with the largest proportion recognized in the first 2 years of life.4 Primary arachnoid cysts result from developmental abnormalities arising in the brain and spinal cord during the early weeks of gestation.5 Secondary arachnoid cysts, however, are more rare and develop as a result of head injury, meningitis, or tumors, or as a complication of brain surgery.6

The vast majority of individuals with arachnoid cysts remain asymptomatic throughout their lifetime, though expanding cysts that exert mass effect on the brain may produce clinical symptoms and ultimately require surgical intervention. Associated symptoms may include headache, nausea and vomiting, seizures, hearing and vision disturbances, vertigo, and difficulties with balance and walking. Computed tomography and magnetic resonance imaging are the preferred modalities for diagnosis. Surgical decompression and removal of these cysts can be done with a burr hole, craniotomy, shunt placement, or endoscopic fenestration depending on the size and location of the cyst.7

Headaches in the pediatric population tend to be self-limited and of benign origin.7 However, physicians should always be aware of concerning clinical features such as a sudden severe headache, persistent nausea or vomiting, a worsening progressive pattern of symptoms, altered mental status, ataxia, and papilledema, which may indicate severe intracranial pathology requiring more emergent neuroimaging and intervention.8

Disclosure Statement

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

References

BOOK REVIEW

40 Years in Family Medicine
by Joseph E Scherger, MD, MPH

Review by Robert W Hogan, MD

Joseph Scherger, MD, MPH, has provided those of us who enjoy his writing with a 426-page soft cover, self-published monograph consisting primarily of a compilation of previously published works. The title suggests an autobiographical work, and as the reader proceeds through the timeline in the work, it becomes clear that in a sense 40 Years in Family Medicine is not exactly an autobiography, at least in the conventional sense. This is an impressive collection of short pieces, written by a very distinguished clinician-scholar.

The work begins with an essay first published in 1975, written while Dr Scherger was a medical student. It pertains to his observations about preceptorship in Family Medicine.

As one proceeds through the book, the voice of the author matures and takes on a futurist dimension, going beyond describing which particular foment is roiling the Family Medicine waters of the moment (and over the years there have been many) toward visions of what medical practice in the primary care or Family Medicine domains will be like in a not-too-distant future. In the role of futurist, Dr Scherger has proven to be remarkably prescient.

There are glimpses of the author’s struggles, for example, “I was not a natural writer.” Perhaps, but if so, Dr Scherger has more than overcome any impediment with diligence and intelligence and well-expressed insight.

Family Medicine developed as a reform movement. Born in the aftermath of the socially tumultuous 1960s in an optimistic time when change for the better seemed possible in all things, idealism was widely embraced and respected. Arguably our current era has developed into a time of cynicism. Perhaps Family Medicine should be thought of as a reactionary movement—too much idealism at the start, which then led to missteps, disappointments, and retrenchment.

Dr Scherger’s book is beyond a chronicle of personal development. By virtue of having practiced from the earliest years of Family Medicine and having been close to the universities throughout much of his career, his commentaries reflect a sort of intellectual chronicle. For a person “not a natural writer,” Dr Scherger’s essays illustrate how thoughtful commentary on the discourse of the day over time becomes a de facto history.

Dr Scherger is clearly one of the most distinguished members of an entire generation of family practitioners, having been present at the beginning of the movement in the 1970s, and still being present and participating in clinical practice, academic affairs, and senior leadership roles almost too numerous to count. He has maintained a stream of cogent insightful commentary over a period of four decades.

I was personally influenced by some of the early greats in Family Medicine, including the charismatic Eugene Farley, MD; Jack Froom, MD; and Paul Frame, MD, and by having either heard or read Ted Phillips, Gayle Stevens, and others cited in Dr Scherger’s book. Back in the day, as a student, my peers were most awed by “Triple Threat” physicians, gifted individuals who easily moved between the roles of clinician-teacher-researcher.

Dr Scherger’s book documents his status as something more, a quadruple threat—physician clinician, physician administrator, physician leader, and physician author/futurist. Students in the field, budding leaders in Family Medicine, young academic family physicians wishing to understand how the field grew and developed, policy makers, and anyone else who aspires to comprehend the origins and development of Family Medicine as a discipline should have a well-thumbed copy of this book on their bookshelf.
WORKPLACE VIOLENCE IN THE EMERGENCY DEPARTMENT: GIVING STAFF THE TOOLS AND SUPPORT TO REPORT

INTRODUCTION

Workplace violence (WPV) is defined as any act or threat of physical violence, harassment, intimidation, or other disruptive behavior that occurs at the work site and may cause physical or emotional harm.1,2 Health care professionals are among the workers at highest risk for WPV.1,2 According to a 2007 report of the US Bureau of Labor Statistics, WPV occurs more often in health care and social assistance industries than in any other workforce sector, accounting for 60% of all nonfatal assaults.1,3 Such events are routinely underreported to health care supervisors and administration because the perception among health care workers is that violence is the norm (ie, an expected part of the job) and because workers fear the response they may receive when reporting these events.4-5

A 2004 study that included 6300 Minnesota registered nurses (RNs) and licensed practical nurses, from a variety of practice settings, identified the rate of physical or nonphysical attacks against nursing staff as 52 per 100 persons per year.4 In this study, patients represented the most common source of the violent attacks. The effect of violent behavior and the forms of WPV are substantial in negatively affecting staff morale and compromising health care delivery and efficiency.6-8 Nursing staff most often reported WPV-induced anger, frustration, fear, stress, and irritability, with 13% of staff reporting long-term difficulty with these symptoms following an event.4 Other long-term problems identified include chronic pain, disability, and flashbacks.4

The Emergency Nurses Association (ENA) recently presented a position statement that identifies WPV as a serious occupational hazard for emergency nurses. Health care organizations have a responsibility to provide a safe environment for employees, as well as for the public.7 According to the ENA and the Occupational Safety and Health Administration, WPV can be prevented, or the risk at least minimized, when employers take the necessary precautions. They advocate an interdisciplinary approach to WPV prevention and implementation of a zero-tolerance policy to help achieve the goal of resolving WPV.1,2 This effort is aided by the implementation of safety training specific to the emergency setting, expected reporting of violent behavior through an established reporting process, a culture change that supports reporting incidents and, when applicable, reporting to law enforcement without reprisal.1 Key to the success of the process is the establishment of a clearly understood and facile system for reporting violent incidents.1

LOCAL PROBLEM AND INTENDED IMPROVEMENT

Emergency Departments (EDs) are a high-risk area for WPV from patients and visitors directed toward staff members. Factors aiding in this are 24-hour accessibility, a high-stress environment, and lack of visible or trained security staff.7 Patients and associated family members or visitors are the most common instigators of violence, for reasons including pain, stress, lack of privacy, and
long wait times. With fear, anxiety, substance abuse, or mental illness, a volatile environment can be created within the ED.

In this 64-bed level 1 trauma center, there are approximately 72,000 patient visits annually. Of the approximately 150 nurses on staff, no one was reporting the violent events occurring. Before the implementation of this quality-improvement (QI) project in 2012, zero staff incident reports had been filed using the current process. According to the initial survey results, ED staff did not understand what acts constitute WPV or how to report the events, and reported feeling a lack of support from nursing leadership to report the events that did occur.

The project sought answers to these primary questions: do staff perceive violence as part of the job within the ED, and are staff aware of what acts constitute WPV? Other goals were to increase staff awareness of WPV and to develop a simplified process for reporting and evaluating these events within a supportive and nonjudgmental culture of safety with zero tolerance for violence. The project has the intent of improving personal safety and job satisfaction. This effort aligns with initiatives of the ENA and the Occupational Safety and Health Administration. The project also supports the medical center’s commitment to safety, which is considered integral to achieving the inherent goal of medical professionals: to provide safe, quality patient care.

DATA ANALYSIS METHODS

This project was a QI activity, was monitored closely by clinically responsible professionals, and abided by the Health Insurance Portability and Accountability Act and other constraints to protect staff privacy. As a QI project in ordinary operations, this initiative was not classified as research on human participants and did not need institutional review board approval.

This QI project was initiated in the ED at a large academic, level 1 trauma center in the upper Midwest. In spring 2012 a work group comprised of staff nurses and a nurse manager was formed to evaluate the current state of awareness and perception of WPV. This work group used the Emergency Department Assessment Tool provided by the ENA to evaluate the structural and functional status of the ED as it relates to safety and security.

The Survey

A staff survey was then developed on the basis of the ENA’s Emergency Department Violence Surveillance Study. The intent of the survey was to gather data regarding the nursing staff’s exposure to and perception of WPV. The 19-question online survey sought to assess the perceptions of RNs and patient care assistants (PCAs) regarding safety and violence in the workplace, exposure to violence, perceptions of preparedness in the event of violence, and knowledge of when and how to report violent events.

The survey contained questions regarding the amount of verbal and physical abuse staff experience in the ED. It listed examples of physical and verbal violence, asking staff to indicate which examples they believed constituted WPV, whether they personally had experienced the examples described, and whether they would report it to hospital security or law enforcement personnel. The staff were asked whether they thought WPV from patients or visitors was simply “part of the job” in the ED and how they perceived the amount of violence in the ED over the previous year. The staff also were asked whether they had been instructed to report physical or verbal abuse regardless of severity and whether they knew what acts of WPV directed toward health care providers could be prosecuted.

The survey was sent electronically in spring 2012, using the program SurveyMonkey (Palo Alto, CA), to the RNs and PCAs working within the ED before the introduction of interventions related to WPV. Participation was voluntary and was solicited through e-mail announcements before and during the open survey time. The same survey was sent to all RN and PCA staff approximately one year later to evaluate postintervention changes.

The Educational Program

When the initial survey results were compiled, the project team created an educational program for the staff, which was delivered approximately two months later. This education included a review of the initial data captured by the survey, factual representation of what acts constitute WPV, a review of the reporting tool created, and information on how to report violent incidents. The educational program for WPV was presented by the project team members through lecture and PowerPoint (Microsoft, Redmond, WA) presentation at the departmental practice committee meeting and the departmental professional development days. All staff were encouraged to attend these meetings. Staff were paid for their time;

<table>
<thead>
<tr>
<th>Responses to the Question: “Is WPV Part of the Job in the Emergency Department?”</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial survey staff comments</strong></td>
</tr>
<tr>
<td>• We cannot control others, just our response</td>
</tr>
<tr>
<td>• Part of the job, up to a point</td>
</tr>
<tr>
<td>• WPV should never be tolerated</td>
</tr>
<tr>
<td>• Comes with the job, things can be done to prevent it from happening or keep staff safe when it does happen</td>
</tr>
<tr>
<td>• This has been an accepted way for too long</td>
</tr>
<tr>
<td>• I shouldn't feel that way, but it goes on enough that I'm getting desensitized to it</td>
</tr>
<tr>
<td>• I feel that there is a lot more that could be done in order to keep ourselves and our patients safe</td>
</tr>
<tr>
<td><strong>Follow-up survey staff comments</strong></td>
</tr>
<tr>
<td>• It is tolerated to help the flow of the ED</td>
</tr>
<tr>
<td>• It should not be considered part of the job by anyone</td>
</tr>
<tr>
<td>• I feel the culture in the ED provides a feeling of it being not a big deal when it happens</td>
</tr>
<tr>
<td>• I do not tolerate it and will inform the patient politely on that matter</td>
</tr>
<tr>
<td>• The presence of WPV is unavoidable in the population we see</td>
</tr>
<tr>
<td>• Since the start of my career, I thought this was a part of my job; however, the increase of mental health issues, drugs, and gang-related behaviors have increased so that now I feel that it is NOT a part of my job and I will not tolerate it</td>
</tr>
<tr>
<td>• I think it is because it does happen. But I don’t think it should be tolerated like it is</td>
</tr>
</tbody>
</table>

ED = Emergency Department; WPV = workplace violence.
however, the meetings were not mandatory. The education was also communicated through personal staff interactions by the project team and via e-mail, which is considered the standard within the institution for distribution of educational material. To facilitate ongoing competency, a question related to WPV was added to the yearly mandated competency examination of the emergency nurses. At the end of the educational program, the expectation of all staff to complete the reporting tool with each event was clearly communicated.

The Reporting Tool

In an attempt to successfully capture violent events, the WPV project team identified the current reporting process as a barrier: staff are required to navigate through a cumbersome online reporting process, which often requires 15 to 20 minutes to complete. Therefore, during the creation of the informal reporting tool, the WPV project team knew the tool must be concise, easy to use, and easy to find, in contrast to the current staff incident reporting process. This tool was not intended to replace the current process, which remains the formal reporting process for the institution. The tool provides staff a simplified way to report events in real time, aiding staff and nursing leadership in completing the formal report at a later time, outside of the acute crisis period.

The tool identifies the patient name, medical record number, date the incident occurred, and a brief description of the incident, taking approximately 1 to 2 minutes to complete. This mechanism of reporting would permit the staff to complete the report in a timely fashion, creating the least amount of disruption to workflow and patient care. For ease of locating what acts constitute WPV and educational reinforcement, specific WPV actions were listed on the back of the reporting form. The form was placed at the charge nurse desk and in the behavioral health area of the ED. The tool was printed on brightly colored paper for ease of identifying the correct form.

Table 1. Percentage of staff reporting verbal and physical abuse

<table>
<thead>
<tr>
<th>Type of abuse</th>
<th>Initial survey, %</th>
<th>Follow-up survey, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 times</td>
<td>21</td>
<td>19</td>
</tr>
<tr>
<td>1-10 times</td>
<td>70</td>
<td>79</td>
</tr>
<tr>
<td>&gt;10 times</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Physical abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 times</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>1-10 times</td>
<td>25</td>
<td>15</td>
</tr>
<tr>
<td>&gt;10 times</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. Respondent answers to the question: “Is WPV part of the job in the Emergency Department?”

<table>
<thead>
<tr>
<th>Response</th>
<th>Initial survey, % (n = 154)</th>
<th>Follow-up survey, % (n = 203)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>55.8</td>
<td>24.2</td>
</tr>
<tr>
<td>No</td>
<td>44.2</td>
<td>75.8</td>
</tr>
</tbody>
</table>

WPV = workplace violence.

RESULTS

The initial survey was sent to the entire 154-member nursing care team and was completed by 108 RNs and 6 PCAs, resulting in a 74% response rate. A follow-up survey was sent to 203 nursing staff approximately one year later. Of note, staff size increased by 49 members between the initial and follow-up surveys. The follow-up survey was completed by 112 RNs and 8 PCAs, resulting in a 59% response rate. Table 1 represents a comparison between the initial and follow-up survey results, denoting the percentage of staff who experienced verbal and physical abuse within the preceding month of survey distribution.

On the initial survey, more than half the staff perceived WPV to be part of the job; on the follow-up survey, the number of staff perceiving violence as part of their job was reduced by more than half, as indicated in Table 2. Initial and follow-up staff comments regarding why they feel WPV is part of the job within the ED are included in the Sidebar: Responses to the Question: “Is WPV Part of the Job in the Emergency Department?”

Staff response on how they perceived the amount of violence in the ED during the preceding year is reflected in Figure 1. Although in the follow-up survey fewer staff felt violence had increased, more staff felt violence had remained the same. A small portion of the staff felt violence had decreased in the follow-up survey.

In the initial survey, for the 16 examples of physical violence, approximately 91% of staff respondents indicated that they considered the examples to be WPV. The follow-up survey showed the same results. In the initial survey, for the 8 examples of verbal violence, approximately 75% of staff indicated they considered those examples to be WPV. In a follow-up survey, those results were essentially unchanged. The staff were asked if they had formally reported WPV when they experienced it. Figure 2 depicts an increase in the formal reporting process after intervention.

Examples of physical violence given to the staff in the survey included biting, hair pulling, getting hit/punched/slapped, being hit by a thrown object, and being kicked, pinched, pushed/shoved, scratched, sexually assaulted, shot/shot at, spit on/at, stabbed, and voided on/at by any patient, whether sober, intoxicated by drugs or alcohol, or mentally ill. Examples of verbal violence included in the survey were being harassed with sexual language/innuendo, sworn/cursed at, threatened with physical harm, verbally intimidated, yelled/shouted at, and called names by any patient, whether sober, intoxicated by drugs or alcohol, or mentally ill.

In the initial survey when staff were asked whether they had been instructed to report physical or verbal abuse regardless of severity, 40% of respondents reported “yes,” 47% reported “no,” and 13% reported “sometimes.” On the follow-up survey, 76% reported “yes,” 15% reported “no,” and 9% reported “sometimes.” The responses for why staff did not report WPV in the initial survey are shown in the Sidebar: Initial Survey Responses to the Question: “Why do ED Staff Members Not Report Workplace Violence?” There continued to be a small percentage after intervention who chose not to
Workplace Violence in the Emergency Department: Giving Staff the Tools and Support to Report

Survey responses included: “fear,” “too much work,” “nothing ever happens,” “they should be used to it,” “it is an ED area—anything can happen.” These results demonstrate the need for further education.

When staff were asked whether they knew what acts of WPV directed toward health care providers could be prosecuted, on the initial survey, 65% of the staff reported “yes” and 35% reported “no.” On the follow-up survey, 78% of the staff reported “yes” and 22% reported “no.”

**DISCUSSION**

Globally, as noted in the research literature, and locally, as shown by the internal survey completed by the emergency nurses and PCAs, violence is an ongoing problem within the ED. More than half of the staff working in our ED perceives WPV to be part of their job. Of these staff members, 75% were verbally assaulted in the month before the survey, and 25% acknowledged some form of physical abuse during this same time. Knowledge gaps were addressed, as 40% of the ED staff did not know what acts constituted WPV, and more than 67% admitted they had not reported previous acts of violence that occurred within the ED. In the follow-up survey results, more than 77% of the staff knew which acts were considered WPV, and more important, the number of staff who considered those same acts to be part of their job was cut in half. This change in perception is considered the greatest success of this project.

The endorsement from ED leadership to report WPV incidents, both internally via the WPV reporting tool as well as to law enforcement, was a crucial step in the process. A challenging aspect during project implementation was found to be staff concern regarding staff and patient confidentiality when reporting to law enforcement and the legal process. Support from ED leadership and education was found to be the most helpful in alleviating these concerns. The ED leadership team receives all WPV incident reports and follows up individually with each employee involved in WPV to ensure his or her well-being, provide support to the person reporting in an effort to change unit culture, and establish a follow-through with the institutional reporting process when applicable. Each staff member who reports a WPV incident receives leadership support, and therefore the behavior of continued reporting is reinforced.

After the reporting tool was created and implemented, and ED leadership began following through with each incident report, the ED staff perceived a decrease of violence within the ED during the year between the initial survey and follow-up survey. After the ED staff were given the education, support, and tool to report these incidences, the ED staff began reporting those violent incidents that occurred within the ED. Before the implementation of this project, no staff incident reports related to WPV were filed in 2012, even though staff indicated on the initial survey that WPV was present. The number of WPV reports filed after project implementation was promising as more than 50 reports were filed in 2013.

Three of the reports filed to law enforcement by nursing staff were published in local news sources, including the local newspaper and local television news channel. These articles highlighted the charges filed, ranging from misdemeanor assault charges to felonies, and the circumstances of the charges. Slapping, kicking, spitting at, biting, and verbally threatening to kill a nurse and his children were examples for each.
shared in the news reports. Although once identified as a barrier to reporting, the publication of these violent events was accepted with positive reactions from staff in the hopes of increasing awareness to the public that violence in the ED would not be tolerated.

The emergency nurses and PCAs collectively acknowledged violence was not to be tolerated in the ED and violence was no longer part of their job. Assessing knowledge gaps, providing education, creating a brief reporting tool, and acquiring the support of the ED leadership were imperative to move this sensitive issue into the forefront for the safety of staff and patients alike.

Limitations

This project does have notable limitations. The initial survey was sent to all staff working in the ED. The follow-up survey was also sent to all staff members working in the ED approximately one year later. Whether the staff had participated in the initial survey as well was not assessed; neither were staff turnover rates because they were not considered a deterrent in participating in the follow-up survey. The educational program was not ongoing; therefore, the 49 new staff members hired within that year may not have had the same level of education/awareness as those who participated in the initial survey.

The project was performed at only one location, which limited the sample size and possibly narrowed the viewpoints that could have been addressed if studying multiple EDs. The data were collected through a convenience sample of ED staff, and participation was elective. The return rates for the survey were encouraging, nearing 70%; however, the sample size continued to be relatively small at 114 and 120 responses to the pre- and post-surveys. These limitations may have hindered the project, we acknowledge, and the results may not be generalizable to other EDs nationally.

CONCLUSION

Violence in the ED has been traditionally tolerated as part of the job. When given the tools and support to report these violent incidents, staff realized a decreased tolerance for the violence. By means of assessment of the current state, thorough education, and a concise reporting tool, the project team has empowered their peers to identify the issues and patterns within the patient population and to commit to an environment structured around zero tolerance and holding patients accountable for their behavior. With these tools in place, the reporting of violent incidents increased, with some incidents leading to criminal prosecution as supported by Minnesota statute 609.2231. This statute indicates that persons who inflict bodily harm on a health care provider within a hospital ED are guilty of a felony and could be imprisoned or made to pay a substantial fine, or both. The accumulation of these events is leading toward a zero-tolerance culture for WPV within the ED. Violence within our ED is no longer tolerated as part of the job.

Disclosure Statement

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

Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

References


5. Guidelines for preventing workplace violence for health care & social service workers [Internet]. Washington, DC: United States Department of Lab-394.


Initial Survey Responses to the Question: “Why Do ED Staff Members Not Report Workplace Violence?”

• Feel nothing happens
• Too much work, part of the job, people are afraid
• Part of the job, nobody cares
• We think it’s part of the job, intimidated to do so
• We fear retaliation, feel it’s part of the job
• Takes too much time, too busy, happens too much
• I didn’t know we were supposed to until recently
• Not sure of how to do it
• Fear of not being supported by leadership
• You slowly get used to dealing with it
• Daily occurrence, the sheer number of reports would keep us from patient care
• Management does not care, and security does not encourage the reporting

ED = Emergency Department