Original Research & Contributions

4 Association of Age to Mortality and Repeat Revascularization in End-Stage Renal Disease Patients: Implications for Clinicians and Future Health Policies

10 Emergency Care of Patients with Acute Ischemic Stroke in the Kaiser Permanente Southern California Integrated Health System

14 Risk of Delayed Intracerebral Hemorrhage in Anticoagulated Patients after Minor Head Trauma: The Role of Repeat Cranial Computed Tomography

17 Using Principles of Complex Adaptive Systems to Implement Secondary Prevention of Coronary Heart Disease in Primary Care

25 Low Back Imaging When Not Indicated: A Descriptive Cross-System Analysis

35 Physician Professional Satisfaction and Area of Clinical Practice: Evidence from an Integrated Health Care Delivery System

41 Impact of a Care Directions Activity Tab in the Electronic Health Record on Documentation of Advance Care Planning

49 Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine

54 Family Characteristics Associated with Likelihood of Varicella Vaccination

Special Report

59 Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care

Review Articles

71 Lactation Ketoacidosis: An Unusual Entity and a Review of the Literature

Case Reports

74 PEITC in End-Stage B-Cell Prolymphocytic Leukemia: Case Report of Possible Sensitization to Salvage R-CHOP
Dr Nikravan has enjoyed and practiced medita
tion in a very substantial way. His art, whether
landscape or abstract, is a byproduct of this
practice and is a depiction of moonlight’s
grace and beauty.

On the Cover:
Lunar Love was painted in 2011 by Kamran Nikravan, MD.
This painting is a byproduct of his meditation in a very substantial way. His art, whether landscape or abstract, is a depiction of moonlight’s grace and beauty.
Impact of a Care Directives Activity Tab in the Electronic Health Record on Documentation of Advance Care Planning, Marianne Turley, PhD; Susan Wang, MD; Di Meng, PhD; Michael Kanter, MD; Terhilda Garrido, MPH

A retrospective pre- and postimplementation analysis was conducted in 2012 and 2013 at Kaiser Permanente Southern California among 113,309 patients aged 65 years and older with advance care planning (ACP) opportunities during outpatient or inpatient encounters. Statistically significant differences in documentation rates between patients with and without Care Directives Activity tab use suggest the potential of a standardized location in the electronic health record to improve ACP documentation.

Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine, Muna Beg, MD; Sara Fisher, PharmD; Dana Siu, PharmD, BCPS; Sudhir Rajan, MD; Lawrence Troxell, PharmD; Vincent X Liu, MD, MS

A retrospective, cohort study looked at 77 patients admitted to the adult medical intensive care unit with severe alcohol withdrawal between 1/1/2009 to 10/31/2013. The frequency of dexmedetomidine use (an intravenous central-acting α₂ adrenergic agonist that effectively reduces anxiety among critically ill patients) increased dramatically between 2009 and 2013 (16.7% vs 82.4%). Initiation of dexmedetomidine therapy was associated with significant improvements in Clinical Institute Withdrawal Assessment for Alcohol scores during corresponding 24-hour intervals (14.5 vs 8.5). Benzodiazepine use also decreased. Dexmedetomidine was well tolerated, requiring discontinuation of therapy in only 4 patients (10.5%). Dexmedetomidine use was also associated with significantly longer hospitalizations.

Family Characteristics Associated with Likelihood of Varicella Vaccination. Sheila Weinmann, PhD, MPH; John P Mulloloy, PhD; Lois Drew; Colleen S Chun, MD

The authors identified 88,646 children (between 6/85-12/99) under age 13 years without a history of varicella; 22% were vaccinated during the study period. Varicella vaccination was more likely among children who were born after 1995, were not Medicaid recipients, or had pediatricians as primary clinicians. In the survey-linked cohort, positively associated family characteristics included smaller family size, higher socioeconomic status; and parents who were older, were college graduates, reported excellent health, and received influenza vaccination.

Lactation Ketaacidosis: An Unusual Entity and a Review of the Literature. Sarah Gleeson, MB, BCh, BAO; Eoin Mulvoy, MB, BCh, BA; David E Clarke, MD, FCCP

A 31-year-old woman presented to the hospital with symptoms of nausea, malaise, and emesis. She was breastfeeding her 10-month-old infant. She was found to have severe ketaacidosis. A general review of all causes of ketaacidosis is presented with special emphasis on lactation ketaacidosis.

PEITC in End-Stage B-Cell Prolymphocytic Leukemia: Case Report of Possible Sensitization to Salvage R-CHOP. Arian Nachat, MD; Sam Tuoroff-Ormeyer; Chunnan Liu, MD; Michael McCulloch, LAc, MPH, PhD

A 53-year-old man whose chronic lymphocytic leukemia transformed to end-stage B-cell prolymphocytic leukemia, disqualifying him for allogenic stem cell transplantation, was treated with PEITC (a natural compound from horseradish), followed by salvage R-CHOP chemotherapy, which led to normalized white blood cell count and disease stabilization that requalified him for allogenic peripheral stem-cell transplant therapy. The authors conducted a systematic review to analyze and interpret the potential contribution of PEITC to his unexpectedly favorable R-CHOP response. Following sequential 8 weeks of PEITC/pentostatin and 6 cycles of R-CHOP, the patient received allogenic peripheral blood stem cell transplant on an outpatient basis and remains well at the time of publication with no evidence of CD20+ small B-cells.

Learning to “Swim” with the Experts: Experiences of Two Patient Co-Investigators for a Project Funded by the Patient-Centered Outcomes Research Institute. Michele Robbins; Janice Tute; Clarissa Hsu, PhD

Written from the perspective of two PCORI patient co-investigators, this commentary provides lessons learned and recommendations for incorporating nonscientists into research teams. Specifically, the authors suggest recruiting people with a record of relevant volunteer experience and commitment; establishing a formal application process that provides candidates with details about expectations and responsibilities; and providing comprehensive orientation with ongoing training, encouragement, and support. It is hoped the points in this commentary help research teams that are incorporating patient co-investigators toward a positive and productive experience.

Pigeons in Flight at Boudhanath

Buddhist Stupa in Kathmandu, Nepal

Thomas Sun, MD

Special Report

Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care. Lee D Jacobs, MD; Thomas M Judd, MS; Zulfiqar A Bhutta, MD, PhD

The neonatal, infant, child, and maternal mortality rates in Haiti are the highest in the Western Hemisphere. To create a major change in Haiti’s health care infrastructure, we are implementing two strategies that are unique for low-income countries: development of a countrywide network of geographic “community care grids” to facilitate implementation of frontline interventions, and construction of a centrally located referral and teaching hospital to provide specialty care for communities throughout the country. This hospital strategy will leverage the proximity of Haiti by mobilizing large numbers of North American medical volunteers to provide one-on-one mentoring for the Haitian medical staff.

Special Report

The Blue Lagoon

Daniela Alexandru Abrams, MD

The Dead Sea

Paul Rousseau, MD

Flower Merchant

Bridget Bourgon, PA-C

Pigeons in Flight at Boudhanath

Buddhist Stupa in Kathmandu, Nepal

Thomas Sun, MD

SOUL OF THE HEALER

The Permanente Journal/ Spring 2016/ Volume 20 No. 2

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

89 The Language of Engagement: “Aha!”
Moments from Engaging Patients and Community Partners in Two Pilot Projects of the Patient-Centered Outcomes Research Institute. Ming Tai-Seale, PhD, MPH; Greer Sullivan, MD, MSPH; Ann Cheney, PhD; Kathleen Thomas, PhD; Dominick Frosch, PhD

Compared with people living in the community, researchers often have different frameworks or paradigms for thinking about health and wellness. These differing frameworks are often accompanied by differences in terminology or language. We came to understand how our language and word choices may have been acting as a wedge between ourselves and our community research partners. Patient-centered language can effectively build a bridge between researchers and community partners, as well as enhance cultural competency, and demonstrate being mindful of the social power dynamics between patient and physician.

94 Integrated Strategies to Address Maternal and Child Health and Survival in Low-Income Settings: Implications for Haiti. Zullfiquar A Bhatta, MD, PhD

An overview of child mortality rates in low-income countries is presented, followed by a discussion of evidence-based interventions that can bridge the equity gaps in global health. Finally, the author comments on the companion article in this issue, “Addressing the Child and Maternal Mortality Crisis in Haiti,” and what is needed for that new project to succeed.

96 The Jigsaw Puzzle in the Lunchroom.
John F Steiner, MD, MPH

Members of our Research Department began to bring jigsaw puzzles into the office. Border pieces were sorted, then assembled. Shapes and colors were aggregated. Some days, nothing changed. Some days, whole images emerged. Each puzzle seemed like a multi-authored scientific paper with unknown contributors—no first author, no senior author, no titles and degrees. If we create the right workspace, we will gravitate to shared puzzles. If our instincts are sharp, we will choose the most promising puzzles to solve. If we are patient and persistent, we will solve them.

98 Love and the Value of Life in Health Care: A Narrative Medicine Case Study in Medical Education. Jorge Alberto Martins Pentiado, Jr, MD; Helcia Oliveira de Almeida, MSc; Fábio Ferreira Amorim, MD, PhD; Adriano Machado Facioli, PhD; Eliana Mendonça Vilar Trindade, PhD; Karlo Jozefo Quadros de Almeida, MD

This case study is an example of narrative medicine applied to promote self-awareness and develop humanistic content in medical education. The impact and the human appeal of the narrative lie in the maturity and empathy shown by a student when reporting his dramatic experience during the care given to a mother and a newborn with a rare disease. The narrative approach helped the learner to be successful in bringing out the meanings behind the story, and introspection changed a seemingly scary interaction into a positive experience. This narrative shows how the development of narrative competence can help establish a good physician-patient relationship.

NARRATIVE MEDICINE

Original Article

103 The Role of Clinical Records in Narrative Medicine: A Discourse of Message. John W Murphy, PhD; Jung Min Choi, PhD; Martin Cadeiras, MD

This article is designed to unite theory and practice. The focus of attention is the impact of narrative medicine on clinical records. Specifically important is that records are created through dialogue, whereby patients are able to grow the record through their ability to offer critiques and alternative explanations. Merely allowing patients to peruse their records, through advances in technology, is not sufficient to facilitate this aim. Various theoretical and practical considerations are discussed that may facilitate patient involvement and the creation of more accurate and relevant client records.

109 Melyssa’s Story.
Lee Jacobs, MD

This is a fictionalized account of a potential future scenario, created to dramatize the need for the Bethesda Referral & Teaching Hospital. It is a companion to “Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care,” page 59, and “Integrated Strategies to Address Maternal and Child Health and Survival in Low-Income Settings: Implications for Haiti,” page 94.

111 Tears for the Fallen.
Akhila Pamula, MD

It wasn’t the fact that he was so young, or even that he had died in front of me; it was the fact that he did it on purpose. I had to excuse myself and take a walk—I had 9 hours left in this shift and I had to pull it together.

Copyright © 2016 The Permanente Journal
The Permanente Journal

EDITOR-IN-CHIEF: Tom Janisse, MD, MBA
ASSOCIATE EDITOR-IN-CHIEF: Lee Jacobs, MD

SENIOR EDITORS
Vincent Felitti, MD Preventive Medicine, Book Reviews
Gus M Carmel, MD, FACEP, FAEM Clinical Medicine
Arthur Klitsky, MD Original Articles
Eric Macy, MD Research
Scott Ragon, MD Corridor Consult

ASSOCIATE EDITORS
Mikel Aickin, PhD Biostatistics
James J Annesi, PhD, FAAHB, FTOS, FAPA Community Benefit, Disparities
Marilyn Chow, RN, DNSc, FAAN Cardiology
Ellen Cosgrove, MD Vice Dean, Academic Affairs and Education, University of Nevada, Las Vegas School of Medicine, Las Vegas, Nevada

AMY EAKIN:

LYNETTE LEASURE:

VICTOR LEISURE:

VINEET FELITTI, MD

MAHER A. ABBAS, MD, FACS, FASCRS

Chief, Digestive Disease Institute, Cleveland Clinic, Abu Dhabi, UAE; Professor of Surgery, Cleveland Clinic Lerner College of Medicine at Case Western Reserve University, Cleveland, Ohio

VINCENT FELITTI, MD

Internal Medicine and Geriatrics, The Southeast Permanente Medical Group, Atlanta, Georgia

FABIO FERREIRA AMORIM, MD, PhD

Professor of Medicine, Escola Superior de Ciências da Saúde in the Department of Research and Scientific Communication, Brasilia, Brazil

STANLEY W. ASHLEY, MD

Chief Medical Officer, Brigham and Women’s Hospital; Frank Sawyer Professor of Surgery, Harvard Medical School; Attending Surgeon, Gastrointestinal Cancer Center, Dana Farber Cancer Institute; Chief, General Surgery, Harvard Vanguard Medical Associates, Boston, Massachusetts

THOMAS BODENHEIMER, MD

Professor, Dept of Family and Community Medicine, University of California, San Francisco

BRIAN BUDENHOLZER, MD

Associate Clinical Professor in the Department of Family Medicine at the Brody School of Medicine at East Carolina University, Greenville, North Carolina

ALEXANDER M. CARSON, RN, PhD

Associate Dean of Research and Enterprise at the Institute of Health, Medical Sciences and Society at Glyndwr University in Wrexham, Wales, United Kingdom

RITA CHARON, MD, PhD

Professor of Medicine, Founder and Executive Director of the Program in Narrative Medicine at Columbia University Medical Center, New York, New York

Dan Cherkin, PhD

Senior Research Investigator, Group Health Cooperative, and Affiliate Professor, Dept of Family Medicine and School of Public Health—Health Services, University of Washington, Seattle

Marilyn Chow, RN, DNSc, FAAN

Vice President, Patient Care Services, Kaiser Foundation Health Plan; Associate Clinical Professor, Dept of Community Health Systems, School of Nursing, University of California, San Francisco

Robert R Cima, MD, FACS, FASCRS

Associate Professor of Surgery, Division of Colon and Rectal Surgery; Vice Chairman, Department of Surgery, Mayo Clinic, Rochester, Minnesota

TIERONA LOW DOG, MD

Director, Integrative Medicine Concepts, Pecos, New Mexico; President, My Own Health; Director, Scientific and Regulatory Affairs, Healthy Lifestyle Brands; Tempe, Arizona

Lewis Mehli-Madrona, MD, PhD, MPH

Director of Geriatric Education, Maine Dartmouth Family Medicine Residency; Director of Education and Training, Coyote Institute, Augusta, Maine

MICHEL M. MURR, MD, FACS

Professor of Surgery, Director of Bariatric Surgery, University of South Florida Health Science Center, Tampa, Florida

Sylvestre Quevedo, MD

Department of Medicine and Global Health Rubinsins, University of California, San Francisco

Ilan Rubinfield, MD, MBA, FACS, FCCP

Director, Surgical Intensive Care; Associate Program Director, General Surgery Residency; Henry Ford Hospital, Detroit, Michigan; Assistant Professor of Surgery, Wayne State University School of Medicine, Detroit, Michigan

Marilyn Schlitz, PhD

Ambassador for Creative Projects and Global Affairs, and Senior Scientist, Institute of Noetic Sciences, Petaluma, California

Audrey Shafer, MD

Associate Professor, Dept of Anesthesiology, Co-Director, Biomedical Ethics & Medical Humanities Scholarly Concentration, Stanford University School of Medicine, Palo Alto, California

Mark Snyder, MD

Specialist Leader, Electronic Medical Record Implementation and Physician Adoption; Deloitte Consulting, LLP, McLean, Virginia

Swee Yaw Tan, MBChB (Edin), MRCP (UK), ACSM, FAMS

Senior Consultant Cardiologist, National Heart Centre, Adjunct Assistant Professor Duke National University of Singapore Graduate Medical School, Singapore

William L. Toffler, MD

Professor of Family Medicine; Director of Predoctoral Education, Oregon Health and Sciences University, Portland

Paul Wallace, MD

Senior Vice President and Director, Center for Comparative Effectiveness Research, The Lewin Group, Falls Church, Virginia

The Permanente Press

The Permanente Journal is published by The Permanente Press

3
Association of Age to Mortality and Repeat Revascularization in End-Stage Renal Disease Patients: Implications for Clinicians and Future Health Policies

Ashok Krishnaswami, MD, MAS; Thomas Alloggiamento, MD; Daniel E Forman, MD; Thomas K Leong, MPH; Alan S Go, MD; Charles E McCulloch, PhD

ABSTRACT

Background: The clinical effects of age occur over an age continuum, yet age as a primary predictor is often analyzed using arbitrary age cut-points.

Objective: To assess whether transformation of a continuous variable such as age using a spline function can uncover nonlinear associations between age and cardiovascular outcomes.

Design: Observational retrospective cohort study in 1015 Kaiser Permanente Northern California patients with end-stage renal disease after index coronary revascularization. Age, the primary predictor, was modeled by 5 different techniques: 1) dichotomized at 65 years or older; 2) at 80 years or older (as a sensitivity analysis); 3) categorized as younger than 55 years (reference), 55 to 64, 65 to 74, and 75 years or older; 4) linear (every 5 years) variable; and 5) nonlinear by transformation into a cubic spline. Age categories were changed in a sensitivity analysis.

Main Outcome Measures: Primary and secondary outcomes were all-cause mortality and repeat revascularization, respectively.

Results: Graphical assessment demonstrated that age dichotomized at either 65 years and older or 80 years and older led to loss of information. Categorized age underestimated or overestimated risk at the extremes of age. A sensitivity analysis demonstrated that an arbitrary change in the age category led to a different conclusion. Age modeled linearly adequately represented mortality risk but was suboptimal with repeat revascularization. Only the cubic spline demonstrated the nonlinear association between age and repeat revascularization.

Conclusion: Employing the continuous variable age as a case study, we have demonstrated that the use of flexible transformations, such as spline functions, can unearth clinically meaningful associations that would not have been possible otherwise. Future research should determine whether incorporation of these methods can improve decision making at a population level.

INTRODUCTION

The association of advancing age with cardiovascular diseases and outcomes is often presented on the basis of an arbitrary age cutoff or as age categories. A possible corollary to this is the lack of consensus of what constitutes “old” or “elderly.” There is a growing need to recognize age as a spectrum and to change the current paradigm. The World Health Organization uses the age of 60 years as a cutoff to define “elderly.” In the US, most classifications have subjectively raised this cutoff to age 65 years and have arbitrarily categorized age to define individuals as “young old” (60-74 years), “old old” (75-84 years), and “very old” (≥ 85 years). Unfortunately, these age cutoffs have become standard nomenclature despite the statistical literature clearly noting that cutoffs and categorization of continuous variables such as age is a “bad idea,” “dangerous,” or even “highly problematic,” with total avoidance of such cutoffs suggested. Although the publications of model-based estimates of the relative risk of age dichotomized or categorized continue in the clinical cardiovascular literature, the effect of this practice is unknown.

The importance of avoiding breaking up a continuous variable (by dichotomization or categorization) is demonstrated by the fact that the functional form of continuous variables (age in the current study) has been selected as one of the most important topics to be handled in the STRengthening Analytical Thinking and Reporting of Studies (STReATS) initiative. Using a retrospective observational study design in a cohort of patients with end-stage renal disease (ESRD), we have used the continuous variable age as a meaningful case study example to highlight how arbitrary changes in age categories can dramatically change the perceived relationship of age with an outcome. We expand on this and address whether transformation of the variable age, by spline functions, can improve our understanding of the age continuum. This appreciation should lead to changes in our future perspective of cardiovascular care and health policies toward the older adult.
METHODS

Source Population

Our source population consisted of adult members of Kaiser Permanente Northern California (KPNC), a large integrated health care delivery system. The study population was a cohort of patients with ESRD receiving long-term renal dialysis, who were identified from the Health Plan’s comprehensive ESRD treatment registry. All subjects had undergone an index coronary revascularization procedure by either percutaneous coronary intervention or coronary artery bypass grafting without another concomitant cardiac surgical procedure between January 1, 1996, and December 31, 2008. We identified a coronary revascularization procedure using International Classification of Diseases, Ninth Revision, or Current Procedural Terminology codes for percutaneous coronary intervention or coronary artery bypass grafting (provided on request).

Patients were followed until their death or were censored when they met any of the following criteria: end of the study as of December 31, 2008; renal transplantation; or disenrollment from the Health Plan.

Outcomes, Primary Predictor, and Covariates

The primary outcome for the study was five-year all-cause mortality. The secondary outcome, repeat revascularization, was identified by Current Procedural Terminology codes for revascularization after the index revascularization (provided on request). These were ascertained using standard Health Plan databases as well as state death certificates and Social Security Administration files through December 2008. The KPNC institutional review board approved this study, and informed consent was not obtained because of the observational nature of this study.

The primary predictor was age at the index revascularization and was identified through standard Health Plan databases. Age was modeled in 5 different methods: 1) dichotomized at an arbitrary cutoff of 65 years or older; 2) at 80 years or older (as a sensitivity analysis); 3) categorized into 4 age groups (< 55 [reference], 55-64, 65-74, and ≥ 75 years); 4) as a continuous linear variable with a clinically relevant scale (every 5 years); and 5) after transformation to a restricted cubic spline with 4 knots. The knots for the cubic spline were at 44, 59, 67, and 79 years (5th, 35th, 65th, and 95th percentiles). Cubic splines were used to assess nonlinearity. They are known to have flexible functions and are well suited for this type of analysis.\(^7,10,18-20\) We obtained information on baseline patient demographic and clinical characteristics from the Health Plan’s clinical and administrative databases.

Statistical Analysis

Patient characteristics were initially compared by age categories (< 55, 55-64, 65-74, ≥ 75 years) with \(\chi^2\) analysis for categorical variables and Kruskal-Wallis or analysis of variance for continuous variables. To assess the hazard of mortality or repeat revascularization at 5 years by different modeling techniques of the

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt; 55 years (n = 179)</th>
<th>55-64 years (n = 351)</th>
<th>65-74 years (n = 335)</th>
<th>≥ 75 years (n = 150)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dialysis duration (mean years ± SD)</td>
<td>2.27 ± 2.8</td>
<td>2.16 ± 2.3</td>
<td>2.08 ± 2.14</td>
<td>2.10 ± 1.92</td>
<td>0.0001</td>
</tr>
<tr>
<td>Women (%)</td>
<td>33.0</td>
<td>34.8</td>
<td>39.4</td>
<td>35.3</td>
<td>0.45</td>
</tr>
<tr>
<td>Baseline comorbidities (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>3.4</td>
<td>12.8</td>
<td>17.3</td>
<td>26.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>79.3</td>
<td>82.6</td>
<td>71.9</td>
<td>48.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>78.8</td>
<td>86.9</td>
<td>82.7</td>
<td>82.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.9</td>
<td>93.7</td>
<td>92.8</td>
<td>91.3</td>
<td>0.42</td>
</tr>
<tr>
<td>Heart failure</td>
<td>29.6</td>
<td>39.3</td>
<td>38.5</td>
<td>48.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Liver disease</td>
<td>5.0</td>
<td>6.0</td>
<td>2.7</td>
<td>1.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Lung disease</td>
<td>24.0</td>
<td>23.1</td>
<td>25.1</td>
<td>20.0</td>
<td>0.68</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>34.1</td>
<td>41.6</td>
<td>43.0</td>
<td>51.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Stroke/transient ischemic attack</td>
<td>4.5</td>
<td>6.8</td>
<td>8.1</td>
<td>8.7</td>
<td>0.38</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>39.7</td>
<td>49.0</td>
<td>43.3</td>
<td>41.3</td>
<td>0.15</td>
</tr>
<tr>
<td>Baseline medications (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitor</td>
<td>34.1</td>
<td>36.5</td>
<td>28.9</td>
<td>26.0</td>
<td>0.06</td>
</tr>
<tr>
<td>Angiotensin receptor blocker</td>
<td>11.7</td>
<td>13.4</td>
<td>17.6</td>
<td>12.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>63.7</td>
<td>58.9</td>
<td>58.5</td>
<td>58.0</td>
<td>0.66</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>62.6</td>
<td>67.2</td>
<td>63.3</td>
<td>59.3</td>
<td>0.35</td>
</tr>
<tr>
<td>Diabetes medication</td>
<td>62.6</td>
<td>58.1</td>
<td>53.4</td>
<td>28.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Statin</td>
<td>55.9</td>
<td>53.9</td>
<td>52.8</td>
<td>51.3</td>
<td>0.86</td>
</tr>
<tr>
<td>Coronary revascularization (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>41.9</td>
<td>48.1</td>
<td>47.5</td>
<td>28.7</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>PCI</td>
<td>58.1</td>
<td>51.9</td>
<td>52.5</td>
<td>71.3</td>
<td></td>
</tr>
</tbody>
</table>

\(\text{CABG} = \text{coronary artery bypass grafting}; \text{PCI} = \text{percutaneous coronary intervention}; \text{SD} = \text{standard deviation}.\)
Association of Age to Mortality and Repeat Revascularization in End-Stage Renal Disease Patients: Implications for Clinicians and Future Health Policies

Figure 1. Four standard modeling strategies for the continuous variable age as a function of mortality in the fit of an unadjusted parametric survival regression.

A. Red solid line = age dichotomized ≥ 80 years; red dashed line = age categorized (< 55, 55-64, 65-74, & ≥ 75 years); black dashed line = age as a linear variable; black solid line = age fit as a cubic spline on the log hazard scale.

B. The sensitivity analysis graphically depicts the changes in the red dashed line when there is a change in the age category (< 40, 40-54, 55-69, & ≥ 70 years).

Figure 2. Four standard modeling strategies for the continuous variable age as a function of repeat revascularization in the fit of an unadjusted parametric survival regression.

A. Red solid line = age dichotomized ≥ 80 years; red dashed line = age categorized (< 55, 55-64, 65-74, & ≥ 75 years); black dashed line = age as a linear variable; black solid line = age fit as a cubic spline on the log hazard scale.

B. The sensitivity analysis graphically depicts the changes in the red dashed line when there is a change in the age category (< 40, 40-54, 55-69, & ≥ 70 years).
primary predictor, age, we fit a parametric Weibull survival model (because it enables all models to be graphed on a uniform scale). We then extracted the model-predicted hazard at 5 years with a robust variance estimate that adjusts for within-cluster (facility) correlation. We presented the hazard ratio (HR) both in a tabular format and graphically as a function of age exponentially in the hazard scale. A p value of 0.05 or less was used as the statistical threshold for significance. All statistical analyses were performed using Stata Version 13 software (StataCorp, College Station, TX).

RESULTS

A total of 1015 patients with ESRD underwent an index revascularization at KPNC by either percutaneous coronary intervention or coronary artery bypass grafting between 1996 and 2008. Of the 1015 patients, 17.6% were younger than age 55 years, 34.6% were between age 55 and 64 years, 33.0% were between age 65 and 74 years, and 14.8% were age 75 years or older. The proportion of patients with a history of myocardial infarction, heart failure, and atrial fibrillation increased, whereas the presence of diabetes mellitus and liver disease decreased with age (Table 1). Table 2 shows the unadjusted and risk-adjusted HR and 95% confidence intervals for the 2 outcomes using the different modeling strategies and the sensitivity analysis. Of note, the point estimates for the unadjusted and adjusted HRs were materially similar.

Mortality

Table 2 demonstrates that age dichotomized at 65 years old was associated with a risk-adjusted 5-year HR for mortality of 1.77 (p < 0.0001), whereas age dichotomized at 80 years was associated with an HR of 2.61 (p = 0.001). Compared with the reference age group, all adjusted age categories were significantly associated with mortality: 55 to 64 years (HR = 1.60, p = 0.01), 65 to 74 years (HR = 2.09, p < 0.0001), and 75 years or older (HR = 3.98, p < 0.0001). The trend test for categorized age was statistically significant (p < 0.0001). Age as a continuous variable indicated that for every 5-year increase in age the associated HR for death was 1.25 (p < 0.0001). Age linearized tracked well with the cubic spline method but underestimated the risk compared with the cubic spline above 80 years.

Repeat Revascularization

Table 2 demonstrates that ages dichotomized at 65 and at 85 years were not significantly associated with repeat revascularization. Compared with the reference group, the age category 55 to 64 years was associated with an HR of 0.84 and the age category 65 to 74 years was associated with an HR of 0.63. The age 75 years or older category was associated with an HR of 1.39. Only the unadjusted category 65 to 74 years was statistically significant. The trend test was not significant (p = 0.07). Finally, every 5-year increase in age was associated with a nonsignificant HR of 0.93 (p = 0.3).

Figure 1A demonstrates that age dichotomized at 80 years overestimated the risk compared with categorized age, linear age, and the cubic spline at the lower end of the age spectrum. However, above age 85 years, risk was overestimated compared with the categorized and linearized age but underestimated compared with the cubic spline. This can be considered information loss or bias. Categorized age was able to capture the data relatively well during the “middle” years, but compared with the cubic spline, it underestimated risk above 80 years. Age linearized tracked well with the cubic spline method but underestimated the risk compared with the cubic spline above 80 years.

Table 2. Comparison of effect of three different modeling strategies for the primary predictor, age, on mortality and repeat revascularization

<table>
<thead>
<tr>
<th>Variable</th>
<th>5-year mortality, hazard ratio (95% CI)</th>
<th>Repeat revascularization, hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Risk-adjusted</td>
</tr>
<tr>
<td><strong>Age dichotomized</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 65 years</td>
<td>1.78 (1.47-2.16)</td>
<td>1.77 (1.47-2.15)</td>
</tr>
<tr>
<td>≥ 80 years</td>
<td>2.79 (1.85-4.21)</td>
<td>2.61 (1.49-4.56)</td>
</tr>
<tr>
<td><strong>Age categorized</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 55 years</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>55-64 years</td>
<td>1.60 (1.10-2.32)</td>
<td>1.60 (1.12-2.31)</td>
</tr>
<tr>
<td>65-74 years</td>
<td>2.02 (1.51-2.71)</td>
<td>2.09 (1.60-2.73)</td>
</tr>
<tr>
<td>≥ 75 years</td>
<td>3.92 (2.67-5.77)</td>
<td>3.98 (2.74-5.79)</td>
</tr>
<tr>
<td><strong>Age linearized</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (every 5 years)</td>
<td>1.24 (1.17-1.31)</td>
<td>1.25 (1.18-1.32)</td>
</tr>
<tr>
<td><strong>Sensitivity analysis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 years</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>40-54 years</td>
<td>0.30 (0.08-1.17)</td>
<td>0.27 (0.07-1.09)</td>
</tr>
<tr>
<td>55-69 years</td>
<td>0.57 (0.17-1.95)</td>
<td>0.51 (0.14-1.89)</td>
</tr>
<tr>
<td>≥ 70 years</td>
<td>0.86 (0.24-2.98)</td>
<td>0.80 (0.22-2.94)</td>
</tr>
</tbody>
</table>

* Risk-adjusted model includes sex, year of index revascularization, type of revascularization, duration of dialysis, number of vessels revascularized, and baseline comorbidities.

* For sensitivity analysis, age categories were changed as shown.

Boldface hazard ratios indicate statistical significance; see the text for p values.

CI = confidence interval.
the risk compared with the categorized and the cubic spline method. Categorized age at the aforementioned age categories captured the nadir and the rise of repeat revascularization. However, it underestimated the risk of repeat revascularization compared with the linearized age and the cubic spline in the younger years and just the cubic spline in the older years. Linearized age did not address the nadir around the age of 65 years or the increase in revascularization at either end of the age spectrum. Age transformed to a spline was visually very easy to interpret. This was the only method that overly noted the “reverse” J or U curve; that is, the decrease in the risk of repeat revascularization with advancing age until around the age of 65, after which there was an increase in the risk of revascularization.

Sensitivity Analysis

Last, we performed a sensitivity analysis after arbitrarily changing the cutoff to younger than 40 years, 40 to 54 years, 55 to 69 years, and above 70 years for both outcomes. With a change in the categories, the summary estimates of each category were materially different and in the case of mortality demonstrated an opposite result. In the case of repeat revascularization, a continued downward trend was noted and the rise was not seen (Table 2 and Figures 1B and 2B).

DISCUSSION

The findings from this study demonstrate that dichotomizing age at either of the set ages of 65 or 80 years led to a substantial loss of information, distorted the conclusions, and limited the ability to address outcomes across the age spectrum. A simple change in the age category, as noted by our sensitivity analysis, would have resulted in a different and opposite interpretation. The reliance of a p value would have even further exacerbated the inappropriate interpretation because of residual confounding by known or unknown confounders at each category. We and many other authors recommend avoidance of these methods.7-10,18 When age was treated as a linear variable, it adequately represented mortality risk but was suboptimal with repeat revascularization. Of the 5 methods, only the spline showed the nonlinear association between age and repeat revascularization.

The current study substantiates the premise that age-related results should be presented as a continuous variable rather than grouped into categories.7,9,22 The study findings also bring to the forefront the need to complement linear modeling by searching for nonlinear associations.7,9,22 Although the various specific methods and critiques of assessing nonlinearity are beyond the scope of the current study, application of this method will be very useful for clinicians, accountable care organizations responsible for population management, and clinician researchers interested in studying the effects of age.

The avoidance of cutoffs for continuous variables such as age is well established in the methodologic literature; however, the practice continues in the general cardiovascular literature. It has been clear that this practice overly simplifies or may even distort the relationship of age to an outcome. In fact, dichotomization has been shown to “effectively lose 33% of the data resulting in a serious loss of power in detecting true [associations]” while increasing the Type I error rate.7 Grouping of age into categories brings up issues of multiple hypothesis testing, assumption of equal risk across categories, and difficulty comparing varying cut-points between studies.7 The practice of reporting only significant p values is known to be associated with residual confounding that is not often taken into consideration. More importantly, it fails to address linear and nonlinear associations.

Albeit infrequently, cubic splines have been used in the cardiovascular literature to detect nonlinearity without being the primary focus.19-21 The current work hopes to translate the robust methodologic literature of avoiding cutoffs to a wider audience by having the primary focus aimed toward incorporating nonlinear modeling primarily when age is modeled as the primary predictor. Our unexpected finding of a “reverse” J- or U-shaped curve for repeat revascularization would not have been detected if it were not for using a nonlinear method. However, we do not have a clear understanding of the reason for this finding because the focus of this study was to highlight the use of modeling and did not focus on an attempt to uncover the mechanisms involved. Some have referred to this finding in recurrence risk research as an “index event bias.”24 Further work will need to confirm this finding and assess the possibility of it being an index event bias.

Using our study as an example,7 if one were to ask “What is the risk of repeat revascularization in patients over the age of 80 years?” the answer varies depending on the model used. Only when graphically representing the 4 methods do we appreciate the increase in repeat revascularization after age of 65-70 years using the cubic spline. Although the quantitative extent of this increase as well as specific nuances of modeling splines can and should be debated, this finding would have been completely missed if the focus was the statistical significance of the data from Table 2. Furthermore, if we were to take a health policy stance, one could assume from findings shown in Table 2 that older adults were not being offered repeat revascularization, perhaps because of their advancing age. However, an assessment of nonlinearity shows that this is not the case and avoids potential costly or dangerous policy decisions.

A strength of our study is that the cohort is from a well-defined primary study base of Kaiser Permanente members during the study period. The study has several limitations, however. The methods presented are generalizable, but the cohort-specific findings may be limited to facilities that provide integrated health care similar to KPNC. We specifically did not evaluate how age as a continuous variable modifies the effect or interacts with baseline comorbidities, either individually or by the number of comorbidities27 as well as with indices of frailty.28 We also did not assess how changes in the placement of knots for the cubic spline affected results.

Last, it is important to mention that other methods of nonlinear modeling can be used, such as fractional polynomials, although the focus in the current study was the use of cubic splines.19,20,29

We chose to use cubic splines for the purposes of this study because it has
been well validated and has been used, albeit sporadically, in the cardiovascular literature. These important topics must be addressed in future work as we expand our knowledge in this area and attempt to define a new clinical paradigm for the cardiovascular care of older adults.1

CONCLUSION

It is acceptable to initially present unadjusted outcomes on the basis of age categories. However, subsequent evaluation of risk adjusted, model-based associations between age and cardiovascular outcomes should be graphically shown by both linear and nonlinear methods to complement standard quantitative presentations. Handling age in this manner, rather than by dichotomization or categorization, will most certainly be unnerving to many clinicians and those who are responsible for health policies. However, further research in this area may lead to fundamental changes in our perspective of cardiovascular care and health policies toward the older adult.

Disclosure Statement

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

Acknowledgments

The authors would like to thank Mathew S Maurer, MD, for insight and review of the manuscript. Dr Maurer received no compensation for his contribution.

Dr Krishnaswami was supported by a Kaiser Permanente Community Benefit grant. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

This article was presented as a scientific poster at the American Heart Association’s Quality of Care and Outcomes Research meeting, Baltimore, MD, in June 2013. Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

References


ABSTRACT

Context: Tissue plasminogen activator (tPA) is underutilized for treatment of acute ischemic stroke.

Objective: To determine whether the probability of tPA administration for patients with ischemic stroke in an integrated health care system improved from 2009 to 2013, and to identify predictors of tPA administration.

Design: Retrospective analysis of all ischemic stroke presentations to 14 Emergency Departments between 2009 and 2013. A generalized linear mixed-effects model identified patient and hospital predictors of tPA.

Main Outcome Measures: Primary outcome was tPA administration; secondary outcomes were door-to-imaging and door-to-needle times and tPA-related bleeding complications.

Results: Of the 11,630 patients, 3.9% received tPA. The likelihood of tPA administration increased with presentation in 2012 and 2013 (odds ratio [OR] = 1.75; 95% confidence interval [CI] = 1.26-2.43; and OR = 2.58; 95% CI = 1.90-3.51), female sex (OR = 1.27; 95% CI = 1.04-1.54), and ambulance arrival (OR = 2.17; 95% CI = 1.76-2.67), and decreased with prior stroke (OR = 0.47; 95% CI = 0.25-0.89) and increased age (OR = 0.98; 95% CI = 0.97-0.99). Likelihood varied by Medical Center (pseudo-intraclass correlation coefficient 13.5%). Among tPA-treated patients, median door-to-imaging time was 15 minutes (interquartile range, 9-23 minutes), and door-to-needle time was 73 minutes (interquartile range, 55-103 minutes). The rate of intracranial hemorrhage was 4.2% and 0.9% among tPA- and non-tPA-treated patients (p < 0.001).

Conclusion: Acute ischemic stroke care improved over time in this integrated health system. Better understanding of differences in hospital performance will have important quality-improvement and policy implications.

INTRODUCTION

As US health care reform leads to growth of the accountable care organization model, it is important to understand how these systems perform in the care of patients with ischemic stroke. Integrated health systems, with aligned incentives and efficiencies, function similarly to accountable care organizations. However, aside from the Veterans Health Administration, patterns of acute ischemic stroke care delivery in an integrated health system have not been well described, and other settings have reported underuse of recommended acute ischemic stroke treatment.

This study describes patterns of tissue plasminogen activator (tPA) delivery in an integrated health system (Kaiser Permanente Southern California [KPSC]), which comprises multiple Emergency Departments and hospital systems, and serves approximately 3.8 million members. Our primary objective was to determine whether the probability of tPA administration for patients with acute ischemic stroke in the KPSC system has improved from 2009 to 2013, and to identify predictors of tPA administration. Secondly, we aimed to describe trends in door-to-imaging time and door-to-needle time metrics during the same period, and to describe complication rates among patients treated with tPA. In 2014, the KPSC health care system implemented a telemedicine stroke (“telestroke”) initiative to improve the delivery of ischemic stroke care. This report will provide important baseline performance data to inform future analyses of the telestroke implementation.

METHODS

Data Source and Populations

Structured data from electronic health and administrative records identified all patients presenting to a KPSC Emergency Department between 2009 and 2013 with a primary or secondary diagnosis of ischemic stroke (International Classification of Diseases, Ninth Revision [ICD-9] codes 433.xx, 434.xx, 436). Patients were seen at 1 of 14 KPSC Medical Center Emergency Departments (EDs) of varying size and urbanicity (degree to which a geographic region is urban), 2 of which are academic with inpatient neurology house staff. We excluded patients younger than age 18 years, those with a stroke within 90 days, and those with missing or implausible outcome variables. Human subjects approval was obtained through the KPSC institutional review board.
Outcome Measures

The primary outcome was tPA administration, identified by pharmacy code. Secondary outcome variables were door-to-imaging time and door-to-needle time for tPA delivery. Complications examined were intracranial and gastrointestinal bleeding, defined as ICD-9 codes of 432.xx, 430, 431 and 578.xx. One of the authors (AS) reviewed all patients’ charts in which there was a question about the presence of the outcome variable.

Statistical Analysis

Patient and hospital characteristics were summarized as percentages, means (standard deviation [SD]), or median (interquartile range, [IQR]) as appropriate. Descriptive statistics were used to determine the proportion of patients receiving tPA as well as the mean and median door-to-imaging and door-to-needle times. The annual trend in tPA administration was assessed by ED by plotting the annual proportions by year, separately for each ED.

We used a generalized linear mixed-effects model, with a logit link, to identify patient and hospital predictors of tPA administration. Hospital-level random intercepts were included to account for between-hospital variation in baseline rates of tPA use and to allow for any variation in tPA use caused by unmeasured hospital-level factors. Patient-level covariates included in the model were age, race, sex, prior-year stroke, and Elixhauser comorbidity score. Additionally, the following variables describing the presentation of the patient encounter were included in the analysis: arrival by ambulance, arrival from a skilled nursing facility, arrival during “off-hours” (defined as between 5 pm and 8 am Monday through Friday, or anytime Saturday or Sunday), and year of diagnosis. Variation in rates of tPA administration caused by hospital-level variables was assumed to be captured in the hospital-level random intercept.

A modified version of the multivariable model treated hospital as a fixed effect to assess whether the annual trend in tPA use varied by ED, after adjusting for the relevant patient and presentation characteristics. When necessary, the likelihood ratio test was used to compare the fit of competing models.

Because change in tPA administration varied between hospitals (Figures 1 and 2), we also tested a multivariable model that included a random slope for year of diagnosis, to allow the change in stroke volume over time to vary between EDs, but we found no significant improvement in model fit compared with the final model.

All descriptive analyses were conducted using statistical software (SAS Version 9.3, SAS Institute Inc, Cary, NC). Figures 1 and 2 and multivariable model results were obtained via the R Project for Statistical Computing software package (Free Software Foundation, Boston, MA).

RESULTS

A total of 11,630 patients with ischemic stroke were seen at the 14 KPSC EDs during the 2009 to 2013 study period. Approximately half were women (49.6%); 47.8% of patients were white, 25.4% were Hispanic, 17.5% were black, 8.4% were of Asian or Pacific Island origin, and 0.9% were other races or ethnicities. Comorbidities included diabetes (31.9%), hypertension (63.2%), heart failure (12%), atrial fibrillation (13.9%), and valvular heart disease (8.6%). A minority of patients arrived by ambulance (37.2%).

Of the overall sample, 3.9% of patients were treated with tPA; the proportion of tPA-treated patients increased during the study period from 2.6% in 2009 to 6.4% in 2013.
Table 1. Brain imaging and thrombolytic metrics, 2009 to 2013

<table>
<thead>
<tr>
<th>Metric</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>All years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>2475</td>
<td>2343</td>
<td>2334</td>
<td>2163</td>
<td>2315</td>
<td>11,630</td>
</tr>
<tr>
<td>tPA-treated patients, no. (%)</td>
<td>64 (2.6)</td>
<td>53 (2.3)</td>
<td>87 (3.7)</td>
<td>100 (4.6)</td>
<td>149 (6.4)</td>
<td>453 (3.9)</td>
</tr>
</tbody>
</table>

Door-to-imaging time

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>All years</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients, median minutes (IQR)</td>
<td>58 (35-87)</td>
<td>55 (34-84)</td>
<td>46 (25-79)</td>
<td>47 (23-76)</td>
<td>46 (23-78)</td>
<td>51 (29-81)</td>
</tr>
<tr>
<td>tPA-treated patients, median minutes (IQR)</td>
<td>23 (14.5-28)</td>
<td>16 (8-26)</td>
<td>13 (9-20)</td>
<td>13 (8-22)</td>
<td>15 (9-22)</td>
<td>15 (9-23)</td>
</tr>
</tbody>
</table>

Door-to-needle time

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>All years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minutes, median (IQR)</td>
<td>94 (67-128)</td>
<td>79 (62-112)</td>
<td>74 (58-96)</td>
<td>73.5 (54.5-103.5)</td>
<td>67 (50-89)</td>
<td>73 (55-103)</td>
</tr>
<tr>
<td>Percentage of patients &lt; 60 minutes</td>
<td>20.3</td>
<td>22.6</td>
<td>27.6</td>
<td>32</td>
<td>40.3</td>
<td>31.1</td>
</tr>
</tbody>
</table>

IQR = interquartile range; tPA = tissue plasminogen activator.

(Table 1). In the multivariate analysis, the likelihood of tPA administration was increased for patients presenting in 2012 and 2013 (OR = 1.75; 95% CI = 1.26-2.43; and OR = 2.58; 95% CI = 1.90-3.51, respectively), female sex (OR = 1.27; 95% CI = 1.04-1.54), and arrival by ambulance (OR = 2.17; 95% CI = 1.76-2.67). Conversely, prior stroke and increasing age were associated with a decreased likelihood (OR = 0.47; 95% CI = 0.25-0.89; and OR = 0.98; 95% CI = 0.97-0.99, respectively). Both unadjusted and multivariable-adjusted rates of tPA treatment varied by ED (pseudo-intraclass correlation coefficient, 13.5%; Figures 1 and 2).

The median door-to-imaging time among all patients was 51 minutes (IQR = 29-81 minutes), and among tPA-treated patients was 15 minutes (IQR = 9-23 minutes). The door-to-imaging time improved during the study period from 58 minutes in 2009 to 46 minutes in 2013. The median door-to-needle time was 73 minutes overall (IQR = 55-103 minutes), and 31.1% of patients had a door-to-needle time within the 60-minute guideline-recommended window. The door-to-needle time also improved during the study period (Table 1).

Of the overall sample, 124 patients (1.1%) experienced intracranial bleeding after a primary ischemic stroke diagnosis. Patients who did not receive tPA had a lower rate of intracranial bleeding than those receiving tPA (0.9% vs 4.2%, p = 0.001) but did not have a higher rate of gastrointestinal bleeding (0.4% vs 0.2%, p = 0.55).

**DISCUSSION**

In this analysis of all patients with ischemic stroke in an integrated health system, we found that the probability of tPA administration has improved over time, with concordant improvement in door-to-imaging and door-to-needle times during the same period. Emergency care of acute patients with ischemic stroke is improving in this integrated health system.

This improvement in emergent care of acute ischemic stroke is similar to that observed in larger reports of national trends. Although our overall rate of tPA administration is low, we were limited by our inability to determine patient eligibility for tPA, and it is likely that a substantial portion of the patients in our sample were ineligible for treatment because of a prolonged onset-to-arrival time or other reasons for ineligibility. Furthermore, the rates we report are similar to rates from other hospitals and health systems when the proportion of tPA delivered among all patients with ischemic stroke is reported. 

We found that tPA was less likely to be used in patients with a history of stroke and in those with increased age. We suspect that this reduced likelihood is because of exclusion criteria of tPA in randomized controlled trials, which have excluded patients with recent stroke (within the past 3 months) and patients older than age 80 years.

We found a longer median door-to-imaging time than has been recently reported in other settings. However, one of these reports was isolated to only tPA-treated patients. When we examined door-to-imaging time among tPA-treated patients, our results were similar, with most patients receiving imaging within the guideline-recommended 25-minute window. We also noted that fewer patients in our sample arrived by ambulance than in other reports. Given that ambulance arrival often correlates with stroke severity, this may be an indication that overall stroke severity in our sample was lower than in other reports. Unfortunately, we did not have a measure of stroke severity available in our data to assess this.

It is also important to note that in this integrated health system composed of 14 hospitals of varying size, urbanicity, and academic status, the rate of intracerebral hemorrhage among tPA-treated patients was similar to rates in the randomized controlled trials and larger effectiveness reports.

Our findings confirm that in our integrated health system, delivery of emergency care for patients with acute ischemic stroke is similar to national trends. Yet as Figure 1 illustrates, even in a single integrated system, the delivery of tPA varies widely between hospitals, both with respect to baseline performance and improvement during the study period. Some hospitals showed marked improvement, whereas others remained more static. Thus, it is important to better understand factors that drive differences in stroke care delivery between hospitals and to explore varying approaches to quality-improvement processes to improve care at lower-performing centers and ensure high-quality care across the board.
Our study has several limitations. Because we were unable to determine the time of symptom onset because of inherent limitations of our data, we were unable to define the population of patients eligible for tPA. However, other reports have described rates of tPA administration among all patients with ischemic stroke, and our results can be interpreted in this context. Our use of ICD-9 codes for sample specification and to identify treatment complications may have introduced bias to the sample; however, on a limited chart review by the authors, we found that the ICD-9 codes were appropriately identifying patients with ischemic stroke, and we did not note any change in documentation over the study period to suggest that this would bias the trends we report. We were further limited by our data in our inability to capture the National Institutes of Health Stroke Scale for all patients. Although we were unable to account for stroke severity, we did include the Elixhauser comorbidity index to capture the acuity of patients’ presentation. We were also unable to determine patient eligibility for tPA; thus, it is possible that other factors led to increased tPA utilization. For example, public awareness campaigns may have increased the proportion of patients arriving within the appropriate time window for eligibility, or clinicians may have become more aware of or more comfortable with administration of the treatment. Finally, we may have introduced bias by excluding patients with missing or implausible door-to-imaging times; however, we opted to include only those patients in whom the ED time course and care delivery were consistent with presentation of acute ischemic stroke to avoid the alternative bias of a misspecified sample.

CONCLUSION
In the KPSC integrated health system, acute ischemic stroke care delivery is improving over time, as evidenced by increased rates of tPA delivery and improved door-to-imaging and door-to-needle times. Better understanding of differences in hospital performance in an integrated system will have important implications for quality improvement and policy development.

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

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

References

Apoplexy
This apoplexy, as I take it, is a kind of lethargy, an’t please your lordship; a kind of sleeping in the blood, a whoreson tingling … It hath its original from much grief, from study and perturbation of the brain. I have read the cause of his effects in Galen. It is a kind of deafness.

— Henry IV, Part II, I, ii, 126, William Shakespeare, 1564-1616, English poet, playwright, and actor
ABSTRACT

Context: Patients receiving anticoagulant medications who experience minor head injury are at increased risk of an intracerebral hemorrhage (ICH) developing, even after an initial computed tomography (CT) scan of the brain yields normal findings. Conflicting evidence exists regarding the frequency at which delayed bleeding occurs.

Objective: To identify the frequency of delayed traumatic ICH in patients receiving warfarin or clopidogrel.

Design: We performed a retrospective observational study of adult trauma encounters for anticoagulated patients undergoing head CT at 1 of 13 Kaiser Permanente Southern California Emergency Departments (EDs) between 2007 and 2011. Encounters were identified using structured data from electronic health and administrative records, and then records were individually reviewed for validation of results.

Main Outcome Measures: The primary outcome measure was ICH within 60 days of an ED visit with a normal head CT result.

Results: Our sample included 443 (260 clopidogrel and 183 warfarin) eligible ED encounters with normal findings of initial head CT. Overall, 11 patients (2.5%, 95% confidence interval [CI] = 1.4%-4.4%) had a delayed ICH, and events occurred at similar rates between the clopidogrel group (6/260, 2.3%, CI 1.1%-5.0%) and warfarin group (5/183, 2.7%, CI 1.2%-6.2%).

Conclusion: Trauma patients in the ED who are receiving warfarin or clopidogrel have approximately a 2.5% risk of delayed ICH after an initial normal finding on a head CT.

INTRODUCTION

Emergency medicine currently emphasizes the role of the emergency physician as steward over limited health care resources. Optimizing the use of computed tomography (CT) is a key area of emphasis for emergency physicians to eliminate unnecessary risk and to improve affordability. Targeting this goal, the American College of Emergency Physicians emphasized the use of validated decision rules to guide CT use in the evaluation of Emergency Department (ED) patients with traumatic head injury. Many of these rules have been studied extensively, but all are intended to help assess the initial need for head CT, and few address the needs of specific high-risk groups. Patients receiving anticoagulant medications, such as warfarin or clopidogrel, are one group that could benefit from further investigation. Although imaging in these patients is generally recommended at initial evaluation, there is conflicting evidence regarding the frequency (rates between 0% and 6%) of delayed intracerebral hemorrhage (ICH) and the potential need to repeat CT in this group.

The number of anticoagulated patients visiting EDs is expected to increase with the increasing age of the population. If a substantial percentage of these patients who experience minor head injury are at risk of delayed ICH, they will incur the necessary expense of extended observation or admission, and repeat CT scanning. There is a need to better understand the frequency of delayed bleeding for patients visiting community EDs after head trauma in order to better inform future emergency medicine policies and practices.

The goal of this investigation was to identify the frequency of delayed traumatic ICH in ED patients receiving warfarin or clopidogrel after a normal result of an initial head CT scan.

METHODS

Study Design and Setting

We performed a retrospective observational study of Kaiser Permanente Southern California (KPSC) ED encounters for head injury from 2007 to 2011. Our study uses structured data from KPSC for 13 affiliated community EDs.

Selection of Patients

Structured data routinely collected at KPSC comprising claims data and information from electronic health records were queried to create our sample. Our sample was limited to the following inclusion criteria: ED encounters for trauma (International Classification of Diseases, Ninth Revision [ICD-9] Codes 800-800.06, 802-803.09, 804.01, 804.5, 850-850.12, 850.5, 850.9, 870-873.8, 925.1, 959.01, and 959.09), receipt of a head CT scan (ICD-9: 87.0x and 87.1x; Current Procedural Terminology Codes 0042T, 70450, 70460, 70470, 70480-70482, 70486-70488, and 70494), and currently prescribed warfarin (and had an international normalized ratio above 1.2 on the day of the ED visit) or clopidogrel as listed in our pharmacy records. Patient variables such as demographics, medication (clopidogrel or warfarin), mechanism of injury, initial and follow-up head CT findings, and...
outcome (mortality) were entered into the database by a research assistant. The principal investigator (CS) reviewed the database and, when necessary, patient charts to confirm these variables. We excluded pregnant patients and those with an ICH identified on initial CT. Those who were not KPSC members were also excluded because of inadequate follow-up to identify delayed bleeding.

**Outcome Measures and Follow-Up**

The primary outcome for our study was delayed ICH, with mortality as a secondary outcome. We defined ICH as subarachnoid hemorrhage, subdural hematoma, epidural hematoma, or intraparenchymal hemorrhage or contusion. A delayed hemorrhage was defined as any hemorrhage that was identified within 60 days of an ED encounter for evaluation of head trauma, after analysis of an initial head CT scan had determined no bleeding. Among those patients confirmed to have an initial CT scan with normal results, the medical record was reviewed up to 60 days from the initial trauma to determine if any repeated scans or mortality had occurred. If a patient had an initial normal CT finding, and at a subsequent visit a repeated CT yielded abnormal results, the chart was reviewed to ensure no new trauma had occurred.

The KPSC institutional review board approved the study.

**RESULTS**

**Characteristics of Subjects**

Initially, 1050 subjects were included in the study. However, 559 subjects were excluded because of incomplete data (466 patients did not experience trauma leading to their CT scan, and 93 patients did not have a CT report available), resulting in 491 eligible ED encounters. Of these patients, 290 were receiving clopidogrel, and 201, warfarin. Patients had a mean age of 79.2 years, and 47.5% were female. Among patients with an initial head CT scan, 31% underwent follow-up CT. The median time from initial CT to follow-up CT was 1 day (Table 1).

**Main Results**

Of the 491 encounters, 48 demonstrated ICH on the initial CT scan, leaving 443 patients with an initially normal CT result. Eleven of these 443 patients (2.5%, 95% confidence interval [CI] = 1.4%-4.4%) experienced a delayed ICH: 6 (2.3%, CI 1.1-5.0%) in the clopidogrel group and 5 (2.7%, CI 1.2-6.2%) in the warfarin group (Table 2). Four of the 11 patients with delayed hemorrhages developed would not seek medical attention, and thus such hemorrhages could have been missed in our follow-up.

Of the 11 patients who had ICH observed on subsequent imaging, 4 of them died as a result. This represents a small percentage (0.9%) of the overall group who initially had a normal head CT result after trauma; however, the potential for death is an important consideration when physicians decide who needs further evaluation or follow-up imaging after trauma. As emergency physicians interpret the evidence to guide their management of anticoagulated patients with head trauma, patient outcomes—not radiographic findings—should be most important.

**DISCUSSION**

Our results for delayed hemorrhage show that patients receiving anticoagulant or antiplatelet medications have an overall risk of delayed ICH of 2.5% (2.7% for warfarin and 2.3% for clopidogrel). These results are higher than reported rates of delayed ICH compared with a report in 2012, which showed no patients who were receiving clopidogrel and 0.6% of patients receiving warfarin had delayed bleeding, but are lower than the 6% risk in a smaller prospective study. Numerous factors such as differences in patient demographics or trauma severity may contribute to these differences. Compared with the study by Nishijima and colleagues, 11 our patients had a similar mean age (75 vs 77 years for our study patients). Our study had slightly higher rates of ICH on initial CT (9.8% vs 7.0%), which may indicate that our population had more severe trauma. In addition, our follow-up period was 60 days in an attempt to be more sensitive and capture any delayed bleeding, compared with the former study, which used 14 days.

In our cohort, only 31% of patients had a follow-up CT scan performed. This may reflect that during the study period, it was not standard practice to rescan anticoagulated patients with trauma. For patients who were not rescan, any clinically significant rebleed should be identified during chart review. However, it is possible that patients in whom clinically insignificant hemorrhages developed would not seek medical attention, and thus such hemorrhages could have been missed in our follow-up.

**Table 1. Demographics of 491 adult patients receiving warfarin or clopidogrel and evaluated for head trauma**

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex (%)</td>
<td>47.5</td>
</tr>
<tr>
<td>Age (years)</td>
<td>76.6 (11.9)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>79.2</td>
</tr>
<tr>
<td>Time to follow-up CT (days)</td>
<td>1</td>
</tr>
<tr>
<td>Mean</td>
<td>4.7</td>
</tr>
</tbody>
</table>

*a Evaluated in 1 of 13 Kaiser Permanente Southern California Emergency Departments.
CT = computed tomography; SD = standard deviation.

**Table 2. Computed tomography findings for anticoagulated patients with minor head trauma**

<table>
<thead>
<tr>
<th>CT finding</th>
<th>Clopidogrel (n = 290)</th>
<th>Warfarin (n = 201)</th>
<th>Total (N = 491)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICH on initial CT</td>
<td>30</td>
<td>18</td>
<td>48</td>
</tr>
<tr>
<td>No ICH</td>
<td>254</td>
<td>178</td>
<td>432</td>
</tr>
<tr>
<td>Delayed ICH</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
</tbody>
</table>

CT = computed tomography; ICH = intracranial hemorrhage.
allow for informed and shared decision making between a physician and an anticoagulated patient who has a head injury and a normal initial head CT finding. Physicians have not yet established an agreed-on risk threshold; for some, 2.5% is too high a risk to omit repeated imaging, whereas for others this may be a small risk to warrant the costs, inconvenience, and risks associated with further observation and repeated imaging.

As with the need for repeat imaging, there are currently no consensus guidelines to recommend the timing of patient follow-up or when the patient can resume anticoagulant therapy. For those who do not receive repeat imaging, we recommend follow-up within 24 to 48 hours, and we generally advise that patients discontinue anticoagulant medications until they can be reevaluated. Given that delayed hemorrhage can occur more than 24 hours after the initial injury, the potential risks of restarting warfarin or clopidogrel therapy should be weighed carefully with the indication for the medication.

Our study has some important limitations. The study was retrospective, which inherently creates the possibility of selection bias. In addition, because of the retrospective nature of the study and the limitations of the program that we used to select subjects, a large percentage of subjects were excluded from the study because they either had missing CT data (because the initial scan was performed at a non-Kaiser Permanente facility) or, on chart review, were identified as not having minor trauma. This may have resulted in sampling or exclusion bias.

### CONCLUSION

In our sample, patients receiving warfarin or clopidogrel who experience minor head trauma and have normal findings of initial CT have approximately a 2.5% risk of development of ICH and a 0.9% risk of death caused by delayed ICH. ❍

### Disclosure Statement

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

### Acknowledgments

This study was supported by a Kaiser Permanente Regional Research Committee grant. Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

### References


ABSTRACT

Context: Primary care practice.

Objective: To test whether the principles of complex adaptive systems are applicable to implementation of team-based primary care.

Design: We used complex adaptive system principles to implement team-based care in a private, five-clinic primary care practice. We compared randomly selected samples of patients with coronary heart disease (CHD) and diabetes before system implementation (March 1, 2009, to February 28, 2010) and after system implementation (December 1, 2011, to March 31, 2013).

Main Outcome Measures: Rates of patients meeting the composite goals for CHD (blood pressure < 140/90 mmHg, low-density lipoprotein cholesterol level < 100 mg/dL, tobacco-free, and using aspirin unless contraindicated) and diabetes (CHD goal plus hemoglobin A\textsubscript{c} concentration < 8%) before and after the intervention. We also measured provider and patient satisfaction with preventive services.

Results: The proportion of patients with CHD who met the composite goal increased from 40.3% to 59.9% (p < 0.0001) because documented aspirin use increased (65.2%-97.5%, p < 0.0001) and attainment of the cholesterol goal increased (77.0%-83.9%, p = 0.0041). The proportion of diabetic patients meeting the composite goal rose from 24.5% to 45.4% (p < 0.0001) because aspirin use increased (77.0%-97.6%, p < 0.0001). Increased percentages of patients meeting the CHD and diabetes composite goals were not significantly different (p = 0.2319). Provider satisfaction with preventive services delivery increased significantly (p = 0.0017). Patient satisfaction improved but not significantly.

Conclusion: Principles of complex adaptive systems can be used to implement team-based care systems for patients with CHD and possibly diabetic patients.

INTRODUCTION

Despite the burden that cardiovascular diseases place on Americans\textsuperscript{1} and clear evidence that team-based health care improves control of cardiovascular risk factors,\textsuperscript{2-10} many medical practices have not adopted this innovation. A classic trial to reduce cardiac surgical mortality provides clues about the components that make practice improvement interventions successful. Nearly 20 years ago the Northern New England Cardiovascular Disease Study Group showed that surgical outcomes could be improved with a simple 3-component intervention: feedback of outcome data, training in continuous quality improvement techniques, and site visits to other Medical Centers.\textsuperscript{11} Even though the surgeons were not provided with detailed process improvement instructions, the intervention was associated with a 24% reduction in in-hospital mortality.\textsuperscript{11} The authors suggested that, along with the 3 prongs of the intervention, giving each care team the autonomy to change their operations as they saw fit led to the rapid decline in mortality.

In his appendix to Crossing the Quality Chasm,\textsuperscript{12} Plsek\textsuperscript{13} suggests that, rather than using the principles of mechanical systems to try to improve health care, innovators should employ the principles of complex adaptive systems. The behavior of mechanical systems (eg, automobiles) can always be predicted if the system is described in adequate detail. The same is not true for complex adaptive systems like human social interaction because people are autonomous. Although the behavior of complex adaptive systems cannot be predicted using the rules that apply to mechanical systems, simple rules can suffice. For example, the behavior of flocks of birds, schools of fish, and herds of mammals can be explained with just three rules: avoid collisions, attempt to match velocity, and attempt to stay close to the nearest neighbor.\textsuperscript{14}

Kottke and colleagues\textsuperscript{15} have hypothesized that only five conditions need to be met to create value in health care. These conditions are: 1) the stakeholders agree on a set of mutual, measurable goals for the health system; 2) the extent to which the goals are being achieved is reported to the public; 3) resources are available to achieve the goals; 4) stakeholder incentives, imperatives, and sanctions are aligned with the agreed-on health system goals; and 5) leaders among all stakeholders endorse and promote the agreed-on health system goals.
When these conditions are met, the stakeholders will organize themselves to perform. This observation is consistent with the reported experience of the Northern New England Cardiovascular Disease Study Group.11

The goal we set was to test whether a group practice that comprises 5 privately owned primary care clinics would implement systems of team-based care if we used the principles of complex adaptive systems to design the intervention. We defined success as the satisfaction of 3 objectives. The first objective was that, relative to patients with Type 2 diabetes mellitus, the care system would increase the proportion of patients with coronary heart disease (CHD) who satisfy a composite measure (blood pressure < 140/90 mmHg, low-density lipoprotein [LDL] cholesterol level < 100 mg/dL, no use of tobacco, and taking at least 81 mg/day of aspirin unless contraindicated).

The second objective was that the system would be associated with increased satisfaction among both patients and staff. The third objective was that the financial impact of the system would be positive or neutral for the practice. We also collected qualitative data from providers during the implementation period so that we could better understand the process that the clinics experienced as they implemented their systems.

In this article, we report the results of the first two objectives. Regarding the third objective, we were unable to generate a revenue stream that offset the cost of the team-based care system. We are in the process of preparing a detailed report. Finally, the results of the qualitative analysis demonstrate that the task of implementing team-based care is complex. Among other tasks, roles must be defined and individuals must learn how to work in teams; patient registry and clinical data retrieval technology must be developed and implemented; and care processes for previsit planning and between-visit care management must be defined and implemented. Success requires an ongoing effort of creation, revision, retraining, and reinforcement.16

Figure 1. Trial evaluation design.a

* Dates are presented as month/day/year.

CHD = coronary heart disease; DM = diabetes mellitus; dx = diagnosis; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.
METHODS

The HealthPartners Institute for Education and Research institutional review board approved the study as Protocol 09-132.

Clinical Setting

We conducted the study in a for-profit primary care practice of 46 primary care physicians and advanced care providers who care for small town and rural patients as well as a commuter population in western Wisconsin. The practice is made up of 5 clinics in 3 divisions (1 division has a main practice site and 2 satellite clinics). Each division has its own administrator and Clinical Services Manager. Physicians own and govern the practice. Clinic assistants, primarily certified medical assistants, support the providers during patient visits to increase work flow efficiency. A few months before we began our trial, the practice created a new position of care coordinator in all its divisions to coordinate the care of patients who might benefit from follow-up services. The practice also implemented an electronic medical record system at about the same time. The clinics had already used continuous quality improvement methods to innovate, and in 2013, all 3 divisions achieved National Committee for Quality Assurance Medical Home accreditation.

Patient Management System

We took three concepts into account when we designed the implementation process: 1) health services delivery systems are complex adaptive systems, not mechanical systems\(^1\); 2) adoption of any system of care requires adaptation and reinvention\(^2\);\(^3\); and 3) the long-term survival of any system of care requires that a new process, at a minimum, does not threaten the viability of the overall system. We accepted the long-term financial success of the practice to be its driving force as prima facie evidence that the physicians in the group knew the fundamentals of designing care delivery systems; they did not need guidance at that level.

Therefore, rather than provide the clinics with an operational structure that we expected them to implement in parallel with their other care processes, our only firm requests were that they use the study resources to improve their Minnesota HealthScores vascular disease quality scores\(^4\) and hire a registered nurse (RN) Care Manager to coordinate the team-care program. Although we paid her salary with grant resources, the RN Care Manager was a clinic employee who reported to one of the Clinical Services Managers and a lead primary care physician; she did not report to the investigators. Otherwise, the clinics could use or modify existing care processes to the extent they wished but could also develop new processes as they believed necessary. Although each of the five clinics shared information and worked to develop common treatment goals, they were free to implement the processes that best fit their existing procedures.

The clinics used the concepts of the medical home\(^5\) and the chronic care model\(^6\) to develop their patient care systems. The systems’ personnel were composed of the RN Care Manager, information technology staff, and clinic assistant care coordinators. These care coordinators supported providers in the following tasks: developing treatment protocols and processes; verifying the accuracy of patient data; reviewing the lists of patients who were not at goal with the responsible provider; and developing and carrying out care and follow-up plans. The RN Care Manager rotated to a different clinic every month, but care coordinators and providers from all five clinics could contact her by phone and e-mail during the trial. The RN Care Manager also helped the care coordinators refine patient education and counseling techniques, identify resources for patients (eg, smoking cessation options), address barriers to care that the patients were facing (eg, transportation, paying for medications), and helped refine and revise clinic systems (eg, previsit planning, after-visit care, between-visit follow-up, and team communications).

For some tasks, the system development teams were able to use existing clinic care and information technology systems; for other tasks, however, they needed to develop new protocols, processes, and capabilities. For example, they needed to develop protocols for hypertension, lipid management, and tobacco use cessation. The clinics also needed to develop previsit planning and postvisit follow-up protocols. All protocols needed to be approved by clinic leaders.

All patients were assigned to provider panels. This allowed the staff to generate quarterly provider-specific lists of patient names and risk factor levels that could be reviewed with each provider to develop treatment and follow-up plans. These plans were then implemented by the care coordinators and the RN Care Manager.

Evaluation Design

We tested the hypothesis that the patient management system would increase the proportion of patients who met goals for controlling their risk factors. To do so, we reviewed the medical records of independent random samples of patients who received care in the 12 months before the system was implemented and during the 12-month period that started 6 months after each clinic implemented its care system (Figure 1). We excluded the first 6 months of the implementation period from the evaluation because we considered it an early learning period. We compared the differences in the 2 samples of patients with CHD with 2 randomly selected samples of diabetic patients who were treated during the same periods. We selected patients with diabetes as the reference group because, with the exception of hemoglobin A1c concentration, their chronic care management goals are identical. Patients who had both CHD and diabetes were included in our sample of patients with CHD. To ensure that a primary care provider had an opportunity to take corrective action if a patient was not at goal, we required that patients in all 4 samples have 2 or more primary care visits during each evaluation period.

The preimplementation evaluation period was March 1, 2009, to February
The postimplementation evaluation period was December 1, 2011, to March 31, 2013. The postimplementation period was greater than 1 year because implementation was staggered in the 5 clinics. Applying prespecified exclusion rules to the 1202 patients identified for the postimplementation sample, we excluded 3 patients because of a diagnosis of dementia, 3 patients because they died during the observation period, 5 patients because they resided in a nursing home, 4 patients because they did not have 2 or more primary care visits in the postimplementation period, and 149 patients because they did not have CHD or diabetes diagnosis codes. The final postimplementation CHD sample comprised 551 patients, and the final postimplementation diabetes sample comprised 485 patients.

To test whether the new system would improve provider satisfaction with the delivery of preventive services, we invited all primary care providers and administrative staff who provided primary care services to complete a survey before implementation. After system implementation, we invited the individuals who had completed the preimplementation survey to complete it again.

Activities Undertaken by Participating Clinics to Implement Ischemic Vascular Disease Management Systems

<table>
<thead>
<tr>
<th>Related to patient care delivery</th>
<th>Related to staff education and training, and tool development</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop and/or revise a previsit planning form</td>
<td>Develop a frequently asked questions document that answers questions about IVD and addresses the goals, coding, and similar care improvement project topics</td>
</tr>
<tr>
<td>Adopt hypertension, hyperlipidemia, and tobacco treatment protocols</td>
<td>Train clinical services staff to use the previsit planning tool, registry, and patient education materials</td>
</tr>
<tr>
<td>Create a rapid medication titration protocol</td>
<td>Conduct training for tobacco use cessation intervention</td>
</tr>
<tr>
<td>Develop protocols for proactive between-visit contacts with patients</td>
<td>Provide in-service training for the clinical services staff regarding pathophysiology of IVD and risk factors</td>
</tr>
<tr>
<td>Create a care coordinator’s patient summary tool that includes treatment goals, medication and medical history, and record of communications with the patient</td>
<td>Develop tip sheets and quizzes for use by clinical services staff</td>
</tr>
<tr>
<td>Create protocols for care coordinator’s team communications regarding blood pressure rechecks and referral to registered nurse Care Manager</td>
<td>Develop patient education materials, door posters, tobacco use cessation folders, and similar products</td>
</tr>
<tr>
<td>Develop an ischemic vascular disease (IVD) report card for patients</td>
<td>Related to information technology</td>
</tr>
<tr>
<td>Conduct a monthly meeting with a consulting cardiologist to review care plans</td>
<td>Create an IVD registry</td>
</tr>
<tr>
<td>Create protocols to provide drug samples, referrals to the free clinic, transportation services, etc</td>
<td>Update the registry twice weekly</td>
</tr>
<tr>
<td>Provide comparison of attainment of IVD goal before and after program implementation</td>
<td>Modify and maintain the electronic health record to ensure data accuracy regarding patient status, provider attribution, aspirin documentation, blood pressure recording, and diagnostic coding</td>
</tr>
<tr>
<td>Provide repeated comparisons of diabetes mellitus and IVD goal achievement</td>
<td>Provide monthly, unblinded IVD report cards for all providers</td>
</tr>
<tr>
<td>Provide monthly, unblinded IVD report cards for all providers</td>
<td>Periodically report project updates to clinic services staff</td>
</tr>
<tr>
<td>Periodically report project updates to clinic services staff</td>
<td>Review reports and care plans with physicians and clinic services staff at team meetings</td>
</tr>
</tbody>
</table>
to evaluate the main trial outcomes. Two trained nurses abstracted the data from the patients’ medical records. Because the clinics had not yet instituted an electronic medical record system at the beginning of the study, the nurses abstracted the preintervention data from paper charts. The clinics implemented an electronic medical record system (Cerner Corp, North Kansas City, MO) in May 2010; thus, we collected postimplementation data from electronic records.

We defined the primary outcomes for patients with CHD and patients with diabetes according to the goals of the Minnesota Community Measurement. Patients with CHD had to meet a composite measure comprising the following criteria to be considered at goal: systolic blood pressure under 140 mmHg and diastolic blood pressure below 90 mmHg, LDL cholesterol less than 100 mg/dL, no tobacco use, and taking aspirin unless contraindicated. Patients with diabetes had to meet a composite measure comprising the same criteria plus a hemoglobin A1c level less than 8%.

To document the reliability of the data extraction process from the electronic records, the 2 nurse abstractors extracted the same data from the records of 50 patients. Kappa statistics for the comparison between the electronically extracted data and the data extracted by the nurses were as follows for systolic blood pressure, diastolic blood pressure, LDL cholesterol, tobacco use, and hemoglobin A1c, respectively: 0.82, 0.82, 0.86, 0.81, and 0.91. Kappa statistics for interrater reliability between the 2 chart auditors were 0.86, 1.00, 0.89, 0.82, and 0.87 for the same 5 data elements, respectively.

**Statistical Analysis**

We used statistical analysis software (SAS Version 9.3, SAS Institute, Cary NC) to generate all descriptive statistics (means, standard deviations, and proportions) and multivariable analyses. To compare differences between periods and subgroups, we used the Student t-test for continuous data and the χ² test for categorical data. We used a difference-in-differences analysis to compare differences in blood pressure and LDL cholesterol between the CHD and diabetic pre- and postimplementation samples.

We employed a series of mixed model logistic regressions to compute predicted probabilities of binary outcomes (whether or not at goal for each component of the composite measure) and ordinal outcomes (the composite care score). We used an interaction term for time and condition (CHD, diabetes) to test our hypothesis that the increase in the proportion of patients satisfying the CHD composite measure would be greater than the increase in the proportion of patients satisfying the composite diabetes measure.

For our analysis of the provider survey, we compared individual item responses before and after implementation. For our analysis of the patient survey data, we also compared preimplementation responses with postimplementation responses.

**RESULTS**

**Risk Factor Changes**

We identified 23 components that the clinics developed as they implemented their care management systems (see Sidebar: Activities Undertaken by Participating Clinics to Implement Ischemic Vascular Disease Management Systems). Nine were directly related to the delivery of patient care; 5 were related to training and supporting providers and staff; 6 were related to staff education and

---

### Table 1. Demographic characteristics and visit frequency of independent samples of patients with coronary heart disease and diabetes before and after implementation of care systems

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coronary heart disease</th>
<th>Diabetes</th>
<th>CHD vs DM p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (n = 485)</td>
<td>Post (n = 509)</td>
<td>Pre vs post p value</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>63.6 (7.6)</td>
<td>64.2 (7.7)</td>
<td>0.2033</td>
</tr>
<tr>
<td>Age category, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49 years</td>
<td>6.2</td>
<td>6.4</td>
<td>0.2857</td>
</tr>
<tr>
<td>50-59 years</td>
<td>24.7</td>
<td>19.9</td>
<td>35.2</td>
</tr>
<tr>
<td>60-69 years</td>
<td>45.8</td>
<td>48.2</td>
<td>36.9</td>
</tr>
<tr>
<td>70-75 years</td>
<td>23.3</td>
<td>25.5</td>
<td>13.2</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>75.7</td>
<td>74.3</td>
<td>0.6471</td>
</tr>
<tr>
<td>Women</td>
<td>24.3</td>
<td>25.7</td>
<td>48.0</td>
</tr>
<tr>
<td>Medical history, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>76.0</td>
<td>77.3</td>
<td>0.6212</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>82.9</td>
<td>87.2</td>
<td>0.0530</td>
</tr>
<tr>
<td>Visit frequency, mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any primary care visit during observation period</td>
<td>8.5 (6.1)</td>
<td>7.6 (4.6)</td>
<td>0.0546</td>
</tr>
<tr>
<td>Any visit to other services during observation period</td>
<td>0.6 (2.6)</td>
<td>0.3 (1.4)</td>
<td>0.2607</td>
</tr>
</tbody>
</table>

CHD = coronary heart disease; DM = diabetes mellitus; post = postimplementation; pre = preimplementation; SD = standard deviation.
training and tool development; and 3 were related to information technology needs.

On average, patients in the CHD samples were older than patients in the diabetes samples, and the ratio of men to women was greater in the CHD sample than in the diabetes samples. (Table 1). More than 96% of the patients in each of the samples were white. Although the diagnosis of hypertension was equally prevalent for the patients with CHD and the patients with diabetes, the diagnosis of hyperlipidemia was more prevalent among the patients with CHD. On average, the patients with CHD had more primary care visits and more visits to other services than did the patients with diabetes.

The only significant difference in biometric characteristics between the preimplementation and postimplementation CHD samples was a mean LDL cholesterol level that was nearly 7 mg/dL lower in the postimplementation sample (Table 2). Diastolic blood pressure was the only significantly different biometric parameter between the two samples of patients with diabetes. There were no significant biometric differences in differences among the 4 samples.

The proportion of patients in the CHD postimplementation sample who met the LDL cholesterol goal was significantly higher than the proportion in the preimplementation CHD sample (Table 3). The proportion of patients who met the LDL cholesterol goal was the same for both samples of patients with diabetes. The proportions of patients who were documented to be taking aspirin unless contraindicated were significantly higher in both postimplementation samples. The proportion of patients satisfying the composite score criterion was significantly higher in the postimplementation sample of patients with CHD relative to the preimplementation sample. The same was true for the two samples of patients with diabetes. The difference in LDL before vs after implementation was the only difference between the samples of patients with CHD and the samples of patients with diabetes.

**Survey Results**

**Providers**

Of the 290 providers who were invited to complete the preimplementation survey, 231 (79.8%) responded. We invited the 231 baseline respondents to complete the same survey after implementation, and 205 individuals (88.8%) responded. The only difference between preimplementation and postimplementation responses was the level of satisfaction with the way preventive services were currently being provided in the respondent’s clinic. The proportion of providers who indicated that they were satisfied or very satisfied increased from 59.5% before implementation to 74.3% after implementation (p = 0.0017).

**Patients**

A total of 760 patients with a CHD code were randomly selected to be

### Table 2. Biometric characteristics of independent samples of patients with coronary heart disease and diabetes before and after implementation of care systems

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Coronary heart disease</th>
<th>Diabetes</th>
<th>p value: change in CHD vs change in DM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (n = 511)</td>
<td>Post (n = 529)</td>
<td>p value</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg), mean (SD)</td>
<td>122.8 (13.8)</td>
<td>124.1 (13.4)</td>
<td>0.1658</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg), mean (SD)</td>
<td>71.7 (8.9)</td>
<td>72.5 (9.3)</td>
<td>0.2526</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL), mean (SD)</td>
<td>87.7 (35.8)</td>
<td>80.9 (28.3)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Hemoglobin A&lt;sub&gt;1c&lt;/sub&gt;, mean (SD)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

**Table 3. Percentage of patients with coronary heart disease and diabetes whose parameters were at goal before and after program implementation**

<table>
<thead>
<tr>
<th>Goal parameter</th>
<th>Coronary heart disease</th>
<th>Diabetes</th>
<th>p value: change in CHD vs change in diabetes parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre (n = 511)</td>
<td>Post (n = 529)</td>
<td>p value</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>86.6</td>
<td>86.8</td>
<td>0.9239</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>77.0</td>
<td>83.9</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>65.2</td>
<td>97.5</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Tobacco-free</td>
<td>79.7</td>
<td>81.1</td>
<td>0.5562</td>
</tr>
<tr>
<td>Hemoglobin A&lt;sub&gt;1c&lt;/sub&gt;</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Composite score criterion</td>
<td>40.3</td>
<td>59.9</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

*Composite score for patients with coronary heart disease comprises blood pressure under 140/90 mmHg, low-density-lipoprotein cholesterol level below 100 mg/dL, daily aspirin therapy unless contraindicated, and tobacco-free status. Composite score criterion for patients with diabetes encompasses the same 4 components plus a hemoglobin A<sub>1c</sub> concentration below 8%.

**CHD = coronary heart disease; LDL = low-density-lipoprotein; NA = not applicable; post = postimplementation; pre = preimplementation.**
surveyed before implementation of the new system. Of these, 27 were found not to actually have a diagnosis of CHD; 6 were deceased; 95 returned the survey without completing it or refused to complete it when contacted by telephone; 38 were unable to complete the survey; and 139 could not be contacted or did not return the survey. Responses from 455 patients were included in the preimplementation survey analysis.

Four hundred fifty-five eligible patients were invited to take the postimplementation survey. One patient was a duplicate and 3 were ineligible patients; 19 patients refused; 4 no longer received care from the clinics; 3 were unable to complete the survey; 4 were in assisted living or nursing homes; 6 were deceased; and 98 could not return the survey. The postimplementation survey analysis comprised the responses of 320 patients.

The proportion of patients who reported that they were satisfied or very satisfied with the preventive services that they received increased from 79.6% to 92.4%, and the proportion rating the overall health care received as good, very good, or excellent increased from 96.3% to 99.0%. However, neither of these differences, nor any other pre- or postimplementation comparison, was statistically significant.

**DISCUSSION**

Using the principles of complex adaptive systems, we were able to help five private primary care clinic sites organize themselves to provide team-based care for their patients with CHD. Both LDL cholesterol control and aspirin documentation improved whereas patient satisfaction with their preventive services remained high and provider satisfaction with delivery of preventive services increased. However, the system did not generate sufficient revenue to offset the cost of team-based care.

These facts are evidence that the principles of complex adaptive systems can be used to implement nurse-led team-based care in a private primary care practice. As with the trial conducted by the Northern New England Cardiovascular Disease Study Group,¹¹ the clinicians themselves were able to locally develop and apply the systems and procedures that they needed to succeed. Analyses of large numbers of efforts to diffuse innovations suggest that autonomy to adapt an intervention to fit local conditions is necessary for success.¹⁸,¹⁹

Despite the fact that the composite scores of patients with CHD were not improved relative to the improvement in composite scores of patients with diabetes, there is other evidence of success: LDL cholesterol levels were significantly lower in the postimplementation sample of patients with CHD, a difference that did not occur between the two samples of patients with diabetes. Documentation of aspirin use also increased, but it did so both among patients with CHD and among patients with diabetes. Documentation of aspirin was responsible for the significant improvement in the composite scores. It is possible that hypertension control did not improve because of a ceiling effect. Even before team-based care, blood pressure control for patients in this practice was outstanding relative to the Healthcare Effectiveness Data and Information Set’s national average and that in other medical groups.²⁴

Our trial has several limitations. Randomizing several clinics to intervention and control groups would have been a stronger study design. However, this was not an option for us. Although there is considerable evidence that a complex adaptive system strategy will succeed in other settings, this is not assured. Migration to an electronic record system and hiring of the RN Care Manager could have confounded the results. In fact, we believe that the RN Care Manager role was crucial to the results because the nurse was the communication and organizing node in the center of physicians, clinical care coordinators, and informatics. She also had time free from patient care that allowed her to work on system development. It is notable that one of the clinics hired the RN Care Manager in a new position of Quality Nurse after funding for the trial ended.

Because the patients with diabetes were treated by the same care teams that treated the patients with CHD, we do not know whether the improvement in aspirin documentation in both groups was caused by contamination by the newly implemented patient management system or whether it was due to another cause. We also believe that most of the change in documentation of aspirin use was simply change in documentation. If we were to consider only our primary hypothesis that the increase in the proportion of patients meeting the composite measure would be greater for patients with CHD than for diabetic patients, we would need to conclude that the study failed. However, we believe that there is still much to be learned from this trial.

**CONCLUSION**

We believe that the organization of care systems and the improvement in care for patients with CHD documents that the principles of complex adaptive system science and diffusion of innovations can be used to implement team-based care in private primary care practices. As the Northern New England Cardiovascular Disease Study Group demonstrated almost 20 years ago, once the goals of care are agreed on and a few other conditions are met, it is not necessary to supply clinicians with detailed operational protocols and processes. When the conditions are met, clinicians themselves have the skills, training, and professionalism that are required to implement systems that ensure high-quality care for patients who have chronic conditions.

**Disclosure Statement**

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

**Acknowledgments**

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

**References**

Using Principles of Complex Adaptive Systems to Implement Secondary Prevention of Coronary Heart Disease in Primary Care


The Root of Life

The heart is the root of life and causes the versatility of the spiritual faculties.

The heart influences the face and fills the pulse with blood.

— The Yellow Emperor’s Classic of Internal Medicine, Bk 3 Sect 9, Huangdi, c 2704 BC-2598 BC, known as the Yellow Emperor, a legendary Chinese sovereign and culture hero
Low Back Imaging When Not Indicated: A Descriptive Cross-System Analysis

Rachel Gold, PhD, MPH; Elizabeth Esterberg, MS; Celine Hollombe, MPH; Jill Arkind, MPH; Patricia A Vakarcs; Huong Tran, MS; Tim Burdick, MD, MSc; Jennifer E DeVoe, MD, DPhil; Michael A Horberg, MD, MAS, FACP, FIDSA

ABSTRACT

Context: Guideline-discordant imaging to evaluate incident low back pain is common.

Objective: We compared rates of guideline-discordant imaging in patients with low back pain in two care delivery systems with differing abilities to track care through an electronic health record (EHR), and in their patients’ insurance status, to measure the association between these factors and rates of ordered low back imaging.

Design: We used data from two Kaiser Permanente (KP) Regions and from OCHIN, a community health center network. We extracted data on imaging performed after index visits for low back pain from June 1, 2011, to May 31, 2012, in these systems. Adjusted logistic regression measured associations between system-level factors and imaging rates.

Main Outcome Measures: Imaging rates for incident low back pain using 2 national quality metrics: Clinical Quality Measure 0052, a measure for assessing Meaningful Use of EHRs, and the Healthcare Effectiveness Data and Information Set measure “Use of Imaging Studies for Low Back Pain.”

Results: Among 19,503 KP patients and 2694 OCHIN patients with incident low back pain, ordered imaging was higher among men and whites but did not differ across health care systems. OCHIN’s publicly insured patients had higher rates of imaging compared with those with private or no insurance.

Conclusion: Rates of ordered imaging to evaluate incident low back pain among uninsured OCHIN patients were lower than in KP overall; among insured OCHIN patients, rates were higher than in KP overall. Research is needed to establish causality and develop interventions.

INTRODUCTION

Low back pain is a common reason for US primary care visits.1-3 Patients seeking primary care for low back pain often receive x-rays and other imaging studies, but such imaging rarely improves care and can incur unnecessary radiation exposure and costs.4-12

Several national quality guidelines recommend that clinicians not order imaging tests for nonspecific low back pain. One Clinical Quality Measure (CQM) that is a metric of “Meaningful Use” of electronic health records (EHR), per the Centers for Medicare and Medicaid Services (CMS), is “Percentage of patients with a primary diagnosis of low back pain who did not have an imaging study ... within 28 days of diagnosis.”13,14 The National Committee for Quality Assurance’s Healthcare Effectiveness Data and Information Set (HEDIS) includes a similar measure.15 Nevertheless, clinical practice often diverges from these guidelines.10 In data representing 440 million visits for spine-related care, 17% were associated with subsequent radiography.11

Research suggests possible reasons for this guideline-discordant care.12 For example, physicians may be unaware of the guidelines, not trust them, or think they do not apply to the case at hand. They may order imaging for low back pain to appear to be “doing something,” or from fear of litigation.16-21 Health system-level factors that may influence these physician behaviors include local practice customs; incentives to follow guidelines (or, conversely, to provide care that patients request); time restraints; and access to automated reminders in the EHR, counseling materials, and radiology services.16-21

The purpose of these analyses was to generate hypotheses for further exploration and development of interventions. To that end, we explored several patient- and system-level factors potentially affecting guideline-discordant imaging for low back pain. We compared imaging rates in two care systems divergent in their ability to provide integrated care and track patient care with a unified EHR, and in their patients’ insurance status. We hypothesized that the fully integrated managed care system with sophisticated EHR communication functions would have lower rates of imaging for incident low back pain, compared with a system without these resources.

This study was reviewed by the Kaiser Permanente (KP) Northwest institutional review board by expedited review on July 7, 2013, and verified to be exempt from institutional review board review.

Rachel Gold, PhD, MPH, is an Investigator in the Science Program at the Center for Health Research and an Investigator for the Practice-Based Research Network for OCHIN, Inc, in Portland, OR. E-mail: rachel.gold@kpchr.org. Elizabeth Esterberg, MS, is a former Research Analyst in the Science Program at the Center for Health Research in Portland, OR. E-mail: elizabeth.esterberg@kp.org. Celine Hollombe, MPH, is Project Manager in the Science Program at the Center for Health Research in Portland, OR. E-mail: celine.h.hollombe@kpchr.org. Jill Arkind, MPH, is a Research Associate for OCHIN, Inc, in Portland, OR. E-mail: arkind@ochin.org. Patricia A Vakarcs is a Research Analyst for OCHIN, Inc, in Portland, OR. E-mail: vakarcs@ochin.org. Huong Tran, MS, is a Research Analyst for Utility of Care Data Analysis for the Kaiser Foundation Health Plan in Oakland, CA. E-mail: marie.h.tran@kp.org. Tim Burdick MD, MSc, is the Chief Research Officer for the Practice-Based Research Network for OCHIN, Inc, in Portland, OR. E-mail: burdick@ochin.org. Jennifer E DeVoe, MD, DPhil, is the Chief Clinical Research Informatics Officer for OCHIN, Inc, and an Associate Professor of Family Medicine at Oregon Health and Science University in Portland, OR. E-mail: devoej@ohsu.edu. Michael A Horberg, MD, MAS, FACP, FIDSA, is the Executive Director of Research and Community Benefit for the Mid-Atlantic Permanente Research Institute in Rockville, MD. E-mail: michael.horberg@kp.org.
Methods

Care Delivery Systems
Kaiser Permanente

Kaiser Permanente (KP), one of the nation’s largest managed care organizations, provides integrated care to its members. The organization’s Epic EHR (Epic Systems Corp, Verona, WI) captures all aspects of patient care delivered at or billed to KP. Members of KP can subscribe to plans with different levels of coverage; these analyses include members with standard plans (in which all medical care is delivered at KP facilities), or with point-of-service plans. In both plans, KP is the insurer. Point-of-service plans allow members to obtain care at non-KP facilities, although attendance at KP facilities is encouraged. For KP standard members, most imaging procedures are performed at KP sites that share an EHR with the primary care physician. It is more common for KP point-of-service members to receive imaging at non-KP facilities, which do not share this EHR.

We used data from 2 KP Regions differing in degree of regional market saturation (indicating likelihood that members sought care at non-KP settings, if no KP facility was nearby). These Regions extend across 5 states and in 2012 served approximately 1 million unique patients (488,269 members in 1 Region; 480,386 in the other).

OCHIN, Inc

Originally called the Oregon Community Health Information Network but now serving many states, OCHIN is a nonprofit organization that provides health information technology support to safety-net community health centers (CHCs). OCHIN is not an integrated or managed care system, but rather a network of autonomous primary care ambulatory CHCs sharing a single, linked Epic EHR. At the time of analysis, OCHIN served more than 450 primary care CHCs in 17 states. Most OCHIN CHCs refer patients to external care providers for imaging. These analyses included data from 87 OCHIN member CHCs in 3 states (Oregon, Washington, and California), with 156,190 unique patients served in 2012; one-fourth of these CHCs offer on-site imaging.

Cross-System Comparison

We calculated rates of patients with low back pain who received orders and/or procedures for imaging as discordant with the CQM quality metric (described later, in the Outcome Measures section) in these two systems. We compared rates in KP’s population (privately insured; EHR data available in an integrated managed care system) and OCHIN’s population (mostly uninsured or publicly insured; EHR data available in a nonintegrated system) to assess whether integrated care, use of a systemwide EHR, and patients’ insurance status were associated with system-level rates of guideline-discordant imaging for noncomplicated, incident low back pain.

Both systems use an Epic EHR; the same query was used to extract comparable data as possible. We extracted data on imaging subsequent to index visits occurring from June 1, 2011, to May 31, 2012. Data from June 1, 2010, to May 31, 2011, were used to identify persons meeting study exclusion criteria (described in the Outcome Measures section) and prior care utilization; data from June 1, 2012, to December 31, 2012, were used for follow-up. Extracted data included ordered imaging, referrals, received imaging, diagnoses, and demographic characteristics as available.

All KP data were extracted from KP’s Epic EHR Clarity database and the Decision Support Services National Value Tracker datamart (which provides data about medical services provided to KP members, including external claims). All OCHIN data were extracted from OCHIN’s Epic EHR Clarity database, which contains data on care received, and patient demographics and insurance status. Few OCHIN CHCs offer on-site imaging; imaging procedures are often externally referred, and results are scanned or hand-entered into the EHR when and if the patient is returned to the referring site. To validate the OCHIN data on received imaging, we conducted a manual chart review of 50 randomly selected study patients to ensure that we collected all available relevant EHR data.

Outcome Measures

Our outcome measures were rates of imaging for incident low back pain based on 2 national quality metrics: CQM 0052, one of a set of measures for assessing care systems’ Meaningful Use of EHRs, and the HEDIS measure “Use of Imaging Studies for Low Back Pain.” Both metrics assess “Percentage of patients with a primary diagnosis of low back pain who did not have an imaging study (plain x-ray [film], MRI [magnetic resonance imaging], CT [computed tomography] scan) within 28 days of diagnosis.” 13-15,22,23 The following parameters apply to both metrics except as noted:

• Numerator: Persons who did not receive imaging (plain x-ray, magnetic resonance imaging, or computed tomography imaging) within 28 days of an index visit. (Here, we present the inverse of this metric—the percentage of patients who did have an imaging study within 28 days of index low back pain visit—to explore guideline-discordant imaging.)

• Denominator: Persons aged 18 to 50 years who had an index visit, defined as the first primary care outpatient visit or Emergency Department (ED) encounter not resulting in hospitalization with a principal diagnosis of low back pain, according to International Classification of Diseases, Ninth Revision (ICD-9) codes (in the next paragraph), in the measurement year.

• ICD-9 codes identifying a low back pain index visit: Both metrics: 724.2 (Lumbago); 724.5 (Backache, unspecified); the HEDIS measure also includes 721.3 (Lumbosacral spondylolisthesis without myelopathy); 722.10, 722.32, 722.52, and 722.93 (Disc disorder of the lumbar region); 724.02 and 724.03 (Spinal stenosis, lumbar region); 724.3 (Sciatica); 724.6 (Disorders of sacrum); 724.70 and 724.79 (Other or unspecified disorder of coccyx); 738.5 (Other acquired deformity of back or spine); 739.3 and 739.4 (Nonallopatic lesions of lumbar/sacral region); and 846.0, 846.1, 846.9, and 847.2 (Sprain of lumbar/sacral region).

• Inclusion criteria: In KP, persons continuously enrolled in the Health Plan 180 days before through 28 days after...
### Table 1. Subjects’ characteristics at index visit for low back pain, by study group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>KP*</th>
<th>OCHIN*</th>
<th>p value (χ²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients aged 18-50 years with LBP visit June 1, 2011 to May 31, 2012</td>
<td>36,735</td>
<td>6214</td>
<td></td>
</tr>
<tr>
<td>Excluded</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evidence of prior LBP</td>
<td>5651</td>
<td>2333</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Evidence of cancer diagnosis</td>
<td>3259</td>
<td>274</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Evidence of neurologic diagnosis</td>
<td>642</td>
<td>73</td>
<td>0.001</td>
</tr>
<tr>
<td>Evidence of recent trauma</td>
<td>2135</td>
<td>407</td>
<td>0.023</td>
</tr>
<tr>
<td>Evidence of IV drug use</td>
<td>262</td>
<td>238</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Included in analyses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eligible patients with Clinical Quality Measure LBP index visitΔ</td>
<td>19,503</td>
<td>2694</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>11,305 (58.0)</td>
<td>1510 (56.1)</td>
<td>0.059</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-30</td>
<td>5817 (29.8)</td>
<td>980 (36.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>31-40</td>
<td>6090 (31.2)</td>
<td>859 (31.9)</td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>7596 (39.0)</td>
<td>855 (31.7)</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>7807 (40.3)</td>
<td>1605 (59.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Black</td>
<td>4121 (21.1)</td>
<td>336 (12.5)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>2020 (10.4)</td>
<td>576 (21.4)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>997 (5.1)</td>
<td>55 (2.0)</td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>4558 (23.4)</td>
<td>122 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Utilization in 6 months before index visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean number of visits</td>
<td>2.8 (4.0)</td>
<td>3.3 (5.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>0 visits</td>
<td>6045 (31.0)</td>
<td>1101 (40.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1 visit</td>
<td>3859 (19.8)</td>
<td>359 (13.3)</td>
<td></td>
</tr>
<tr>
<td>2+ visits</td>
<td>9599 (49.2)</td>
<td>1234 (45.8)</td>
<td></td>
</tr>
<tr>
<td>LBP index diagnosis source, KP only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal</td>
<td>19,345 (99.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>External</td>
<td>158 (0.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Payment source, OCHIN only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td>NA</td>
<td>325 (12.1)</td>
<td>NA</td>
</tr>
<tr>
<td>Medicare</td>
<td>NA</td>
<td>116 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>984 (36.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>1268 (47.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other/unknown</td>
<td>1 (0.04)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Federal poverty level, OCHIN only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% or less</td>
<td>NA</td>
<td>1869 (69.4)</td>
<td>NA</td>
</tr>
<tr>
<td>101%-150%</td>
<td>NA</td>
<td>244 (9.1)</td>
<td></td>
</tr>
<tr>
<td>150%-200%</td>
<td>NA</td>
<td>83 (3.1)</td>
<td></td>
</tr>
<tr>
<td>200% or more</td>
<td>NA</td>
<td>133 (4.9)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>NA</td>
<td>365 (13.4)</td>
<td></td>
</tr>
<tr>
<td>Index CHC with onsite imaging, OCHIN only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>1670 (62)</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>NA</td>
<td>1024 (38)</td>
<td></td>
</tr>
<tr>
<td>Follow-up at KP sites</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All follow-up care at KP sites</td>
<td>17,590 (90.2)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Any follow-up care at non-KP sites</td>
<td>1913 (9.8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Data are presented as no. (%) unless indicated otherwise.

* All subsequent data reflect this population.

CHC = community health center; IV = intravenous; LBP = low back pain; KP = Kaiser Permanente; NA = not applicable.
the index visit; in OCHIN, any person with a claim or encounter during the measurement year.

- **Exclusion criteria:** Patients with a diagnosis clinically indicating imaging (cancer, recent trauma, intravenous drug abuse, neurologic impairment) in the last 180 days. See CQM definitions for details.

Using these criteria, we assessed rates of persons confirmed to have received an imaging procedure. There were substantial cross-system differences in how we could identify received imaging. In KP’s data, it was primarily identified in clinical results entered into the EHR at or after the radiology visit, and/or in billing data; in OCHIN’s data, received imaging was identified primarily through the presence of scanned imaging results. Because of these differences and because we were interested in assessing physician behaviors (ie, imaging orders), we also looked at each system’s rates of persons for whom imaging was ordered. There were minimal cross-system differences in how ordered imaging was identified. Ordered or received imaging occurring more than once on a given day was considered a single event.

**Analysis**

Our primary analyses included persons with an index low back pain visit from June 1, 2011, to May 31, 2012. We described the populations at the index visit, and persons excluded from analyses per the CQM/HEDIS criteria, comparing the included populations via χ² tests. We calculated rates of the outcome measures overall and stratified them by baseline factors: age; sex; care utilization in the last 6 months; ICD-9 code associated with the index visit; insurance status at index visit (OCHIN only); and whether the index or any follow-up visits were at non-KP facilities (KP only).

We conducted adjusted logistic regressions of the association between these factors and low back pain imaging rates in three models:

1. in both groups, including a variable for group, adjusted for baseline factors differing between study groups
2. in OCHIN only, adjusted for insurance status at index visit and for whether the index visit was at a CHC with on-site imaging

### Table 2. Differences in unadjusted rates of imaging across study groups (percentage)a)

<table>
<thead>
<tr>
<th>Factors</th>
<th>KP, no. with an index visit = 19,503</th>
<th>OCHIN, no. with an index visit = 2694</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any imaging in 28 days after index visit</td>
<td>Imaging ordered or received</td>
<td>Ordered onlyb</td>
</tr>
<tr>
<td></td>
<td>17.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Any imaging in 28 days after index visit by:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-30</td>
<td>16.7</td>
<td>0.1</td>
</tr>
<tr>
<td>31-40</td>
<td>16.6</td>
<td>0.2</td>
</tr>
<tr>
<td>41-50</td>
<td>18.0</td>
<td>0.1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Female</td>
<td>15.9</td>
<td>0.1</td>
</tr>
<tr>
<td>No. of visits 6 months before index visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18.1</td>
<td>0.1</td>
</tr>
<tr>
<td>1</td>
<td>16.3</td>
<td>0.1</td>
</tr>
<tr>
<td>2+</td>
<td>16.9</td>
<td>0.1</td>
</tr>
<tr>
<td>Insurer at index visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Medicaid/Medicare</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Commercial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index clinic has imaging</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>Data not available</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Index visit at KP site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17.2</td>
<td>0.1</td>
</tr>
<tr>
<td>No</td>
<td>12.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Follow-up all at KP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16.4</td>
<td>0.1</td>
</tr>
<tr>
<td>No</td>
<td>24.5</td>
<td>0.1</td>
</tr>
</tbody>
</table>

a Population as defined by Clinical Quality Measure #0052.
b Subsets of those ordered or received.
KP = Kaiser Permanente; NA = not applicable.
3. in KP only, including a variable for whether the index and/or all follow-up visits took place at KP facilities or external sites, and adjusted for KP Region.

Because OCHIN’s data do not include information on ED visits, our cross-system analyses included only persons whose index visit was an in-person primary care encounter. Then, in KP patients only, we conducted secondary analyses of ordered and received imaging rates among patients whose index visit was in an ED vs a primary care setting, further stratified into KP primary care sites, non-KP primary care sites, KP-run EDs, and EDs not in the KP system. All analyses were performed in SAS Version 9.3 (SAS Institute Inc, Cary, NC).

RESULTS

Sensitivity analyses showed little difference in outcomes when we used the CQM vs HEDIS measure definitions, so all presented results are based on the CQM measure, for brevity. Using this definition, 19,503 KP patients and 2694 OCHIN patients were identified.

Table 1 shows how the study groups differed in terms of baseline age, race-ethnicity, and number of recent visits. Table 2 shows unadjusted rates of imaging ordered or received.

Cross-System Analysis

Ordered Imaging

Table 3 shows the odds of a patient with incident low back pain having any imaging ordered in the 28 days after the index visit, according to adjusted logistic regression. There was no significant difference between KP and OCHIN. Men were significantly more likely than women, and white patients were significantly more likely than black or Hispanic patients, to have imaging ordered.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Both groups (N = 22,197)</th>
<th>KP only (n = 19,503)</th>
<th>OCHIN only (n = 2694)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ordered, %</td>
<td>Odds ratio,</td>
<td>Ordered, %</td>
</tr>
<tr>
<td></td>
<td></td>
<td>adjusted (95% CI)</td>
<td></td>
</tr>
<tr>
<td><strong>Group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KP</td>
<td>16.9</td>
<td>Reference</td>
<td>NA</td>
</tr>
<tr>
<td>OCHIN</td>
<td>16.7</td>
<td>0.97 (0.87-1.08)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18.1</td>
<td>Reference</td>
<td>18.5</td>
</tr>
<tr>
<td>Female</td>
<td>15.9</td>
<td>0.87 (0.81-0.94)</td>
<td>15.7</td>
</tr>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-30</td>
<td>16.4</td>
<td>Reference</td>
<td>16.4</td>
</tr>
<tr>
<td>31-40</td>
<td>16.6</td>
<td>1.02 (0.93-1.12)</td>
<td>16.4</td>
</tr>
<tr>
<td>41-50</td>
<td>17.4</td>
<td>1.09 (1.00-1.19)</td>
<td>17.6</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18.6</td>
<td>Reference</td>
<td>18.2</td>
</tr>
<tr>
<td>Black</td>
<td>14.2</td>
<td>0.73 (0.66-0.80)</td>
<td>14.7</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14.3</td>
<td>0.74 (0.65-0.83)</td>
<td>15.6</td>
</tr>
<tr>
<td>Asian</td>
<td>18.4</td>
<td>0.99 (0.84-1.17)</td>
<td>18.3</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>16.9</td>
<td>0.89 (0.81-0.97)</td>
<td>16.8</td>
</tr>
<tr>
<td><strong>Utilization 6 months before index visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 visits</td>
<td>17.2</td>
<td>Reference</td>
<td>17.8</td>
</tr>
<tr>
<td>1 visit</td>
<td>16.5</td>
<td>0.96 (0.87-1.06)</td>
<td>16.0</td>
</tr>
<tr>
<td>2+ visits</td>
<td>16.7</td>
<td>1.01 (0.93-1.10)</td>
<td>16.6</td>
</tr>
<tr>
<td><strong>Follow-up at KP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal only</td>
<td>NA</td>
<td>16.3</td>
<td>Reference</td>
</tr>
<tr>
<td>Any external</td>
<td>21.9</td>
<td>1.44 (1.29-1.62)</td>
<td></td>
</tr>
<tr>
<td><strong>Payment source at index visit</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>NA</td>
<td>NA</td>
<td>13.2</td>
</tr>
<tr>
<td>Medicare/Medicaid</td>
<td>NA</td>
<td>22.4</td>
<td>1.53 (1.21-1.94)</td>
</tr>
<tr>
<td>Commercial</td>
<td>11.1</td>
<td>0.64 (0.43-0.95)</td>
<td></td>
</tr>
<tr>
<td><strong>Index CHC has imaging</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Data not available for non-KP sites</td>
<td>Data not available for non-KP sites</td>
<td>17.6</td>
</tr>
<tr>
<td>Yes</td>
<td>15.1</td>
<td>1.05 (0.84-1.32)</td>
<td></td>
</tr>
</tbody>
</table>

*Population as defined by Clinical Quality Measure #0052. Boldface on odds ratios and confidence intervals indicates significant difference.

*Also adjusted for KP Region.

*Boldface on odds ratios and confidence intervals indicates significant difference.

CHC = community health center; CI = confidence interval; KP = Kaiser Permanente; NA = not applicable.
Low Back Imaging When Not Indicated: A Descriptive Cross-System Analysis

Received Imaging
Rates of received imaging were significantly lower at OCHIN than at KP (Table 4). Older patients were significantly more likely than younger patients, men more likely than women, and white patients more likely than black or Hispanic patients, to receive imaging. There was no significant difference in prior utilization patterns.

In both systems, approximately half of patients had no care utilization in the 28 days after the index visit (Table 5), and 76% to 80% had no visit associated with low back pain in that time; 16% were issued only 1 imaging order during the 28-day follow-up, and very few had more than 1 order.

Kaiser Permanente-Only Analysis
Ordered Imaging
Differences by sex and race-ethnicity seen in the KP data were similar to those in the cross-system analyses. Patients receiving any follow-up care in the 28 days after the index visit at a non-KP facility were significantly more likely to have imaging ordered.

Received Imaging
Differences in demographic characteristics were similar to those in the cross-system analyses of received imaging. Patients who had any follow-up care at a non-KP facility were significantly more likely to receive imaging than those who did not.

Site of Care
Eight percent of persons with index visits at a KP-run ED (n = 591) had subsequent ordered or received imaging; 23% of those at a non-KP ED (n = 1210); 17% of those at a KP-run primary care setting (n = 19,345); and 13% of those at a non-KP primary care setting (n = 158). Adjusted results were similar. Compared with patients with index visits at KP-run primary care sites, those seen at non-KP primary care sites, KP-run EDs, or non-KP EDs had significantly lower adjusted

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All groups (N = 22,197)</th>
<th>KP only (n = 19,503)</th>
<th>OCHIN only (n = 2694)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Received, %</td>
<td>Odds ratio, adjusted (95% CI)</td>
<td>Received, %</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KP</td>
<td>17.1</td>
<td>Reference</td>
<td>NA</td>
</tr>
<tr>
<td>OCHIN</td>
<td>14.0</td>
<td>0.78 (0.69-0.87)</td>
<td>NA</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18.0</td>
<td>Reference</td>
<td>18.8</td>
</tr>
<tr>
<td>Female</td>
<td>15.7</td>
<td>0.86 (0.80-0.93)</td>
<td>15.8</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-30</td>
<td>15.9</td>
<td>Reference</td>
<td>16.6</td>
</tr>
<tr>
<td>31-40</td>
<td>16.3</td>
<td>1.03 (0.94-1.13)</td>
<td>16.4</td>
</tr>
<tr>
<td>41-50</td>
<td>17.6</td>
<td>1.13 (1.04-1.24)</td>
<td>17.9</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18.2</td>
<td>Reference</td>
<td>18.5</td>
</tr>
<tr>
<td>Black</td>
<td>14.2</td>
<td>0.73 (0.66-0.80)</td>
<td>14.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14.1</td>
<td>0.75 (0.66-0.85)</td>
<td>15.7</td>
</tr>
<tr>
<td>Asian</td>
<td>18.5</td>
<td>0.99 (0.84-1.17)</td>
<td>18.3</td>
</tr>
<tr>
<td>Other/unknown</td>
<td>17.0</td>
<td>0.88 (0.80-0.97)</td>
<td>16.9</td>
</tr>
<tr>
<td>Utilization 6 months before index visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 visits</td>
<td>17.1</td>
<td>Reference</td>
<td>18.0</td>
</tr>
<tr>
<td>1 visit</td>
<td>16.3</td>
<td>0.95 (0.85-1.05)</td>
<td>16.2</td>
</tr>
<tr>
<td>2+ visits</td>
<td>16.6</td>
<td>1.00 (0.92-1.09)</td>
<td>16.8</td>
</tr>
<tr>
<td>Follow-up at KP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal only</td>
<td>NA</td>
<td>Reference</td>
<td>NA</td>
</tr>
<tr>
<td>Any external</td>
<td>24.5</td>
<td>1.68 (1.50-1.88)</td>
<td>NA</td>
</tr>
<tr>
<td>Payment source at index visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>NA</td>
<td>Reference</td>
<td>NA</td>
</tr>
<tr>
<td>Medicare/Medicaid</td>
<td>NA</td>
<td>NA</td>
<td>19.1</td>
</tr>
<tr>
<td>Commercial</td>
<td>9.5</td>
<td>0.73 (0.48-1.10)</td>
<td>9.5</td>
</tr>
<tr>
<td>Index CHC has imaging</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>NA</td>
<td>Reference</td>
<td>NA</td>
</tr>
<tr>
<td>Yes</td>
<td>13.6</td>
<td>1.24 (0.98-1.58)</td>
<td></td>
</tr>
</tbody>
</table>

*Population as defined by Clinical Quality Measure #0052.
*Also adjusted for KP Region.
Boldface on odds ratios and confidence intervals indicates significant difference.
CHC = community health center; CI = confidence interval; KP = Kaiser Permanente; NA = not applicable.
odds ratio (OR) of having ordered imaging (OR = 0.38, 95% confidence interval [CI] = 0.22-0.67; OR = 0.22, 95% CI = 0.14-0.33; and OR = 0.20, 95% CI = 0.15-0.28, respectively). (Non-KP physicians cannot place orders in the KP EHR, so imaging at non-KP sites was identified via billing records and could only be counted as received.) Compared with patients with index visits at a KP primary care site, those with visits at a non-KP primary care site or at a KP ED had lower odds of receiving imaging (OR = 0.51, 95% CI = 0.31-0.83 and OR = 0.42, 95% CI = 0.31-0.57, respectively); results not shown. Those with index visits at non-KP EDs had higher odds of receiving imaging (OR = 1.51, 95% CI = 1.29-1.76).

OCHIN-Only Analysis

Ordered Imaging
Only 15% of uninsured and 13% of privately insured patients received imaging orders, compared with 26% of those with public insurance; the regression results were similar. White OCHIN patients had significantly higher adjusted odds of having imaging ordered than did black or Hispanic patients. Patients with public insurance coverage at the index visit had significantly higher odds of having imaging ordered than uninsured patients did; persons with private coverage had lower odds than did uninsured patients.

Received Imaging
Older OCHIN patients had higher odds than did younger patients of receiving imaging. Race-ethnicity and insurance-based differences in the odds of receiving imaging were similar to the odds of having imaging ordered, except the difference between privately insured and uninsured patients in odds of receiving imaging was not significant.

Site of Care
Sixteen percent of patients seen at CHCs with on-site imaging (n = 22 clinics, 1024 patients), and 21% of those seen at CHCs without on-site imaging (n = 65 clinics, 1670 patients) had any ordered or received imaging. "Ordered-only" imaging rates were higher in CHCs without (6%) than in those with (3%) on-site imaging. On-site imaging at the index visit at the CHC did not significantly affect the adjusted odds of ordered imaging, but the odds of receiving imaging were greater. Payment source may drive this difference: roughly half of uninsured and commercially insured patients were seen at clinics with onsite imaging, but only 14% of publicly insured patients were.

DISCUSSION

The overall rates of guideline-discordant imaging for incident low back pain reported here align with those reported previously. System-level and individual-level factors appear to influence these rates. We expected ordered imaging rates to be lower in KP, hypothesizing that KP’s managed care organizational structure could support centralized communication about care guidelines and about any needed follow-up, and provide financial incentives for guideline compliance, more feasibly than in OCHIN’s CHCs, which are not centrally managed. However, we found that these cross-system differences were not seen until we considered patients’ insurance status. OCHIN’s uninsured and privately insured patients—47% and 12% of the study population, respectively—appear to drive OCHIN’s overall imaging order rates; KP’s imaging order rate is 53% lower (17% vs 26%) than that in OCHIN’s publicly insured population. Uninsured patients may not be able to afford recommended care and thus may decline certain services; similarly, OCHIN’s privately insured patients may face unaffordable copayments. Imaging order rates are highest among OCHIN’s publicly insured patients, possibly because of fewer cost barriers. Thus, although in some situations unaffordable copayments may yield guideline-discordant care, in terms of ordering imaging for evaluation of low back pain, they may lead to more guideline-concordant care by providing a disincentive to getting imaging.

Rates of received imaging were significantly lower at OCHIN (14%) than KP (17%). Insurance coverage distribution has a role here as well, perhaps because patients do not follow-up on ordered imaging to avoid payments. Care integration is involved. In KP’s managed care system, most patients receive imaging at the facility where the index visit occurs, but for many OCHIN patients, filling imaging orders requires travel, probably affecting rates of received imaging. Furthermore, in OCHIN CHCs, imaging results may be mailed back to the primary care physician, then scanned into the EHR, weeks after the imaging is performed, if ever. Thus, our findings may underestimate imaging procedures actually received in the OCHIN population, but the differences in availability of imaging results reflect the EHR information available to physicians.

Rates of ordered or received imaging were almost 50% higher among KP patients who had any follow-up care at a non-KP facility, and they remained significantly higher in

Table 5. Ordered imaging during a 28-day follow-up perioda

<table>
<thead>
<tr>
<th>Parameter</th>
<th>KP, no. (SD)</th>
<th>OCHIN, no. (SD)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Denominator</td>
<td>19,503</td>
<td>2694</td>
<td></td>
</tr>
<tr>
<td>Visits in follow-up period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean no. of visits</td>
<td>1.0 (1.4)</td>
<td>1.1 (1.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>0 visits</td>
<td>9687 (49.7)</td>
<td>1283 (47.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1 visit</td>
<td>4887 (25.1)</td>
<td>622 (23.1)</td>
<td></td>
</tr>
<tr>
<td>2+ visits</td>
<td>4929 (25.3)</td>
<td>789 (29.3)</td>
<td></td>
</tr>
<tr>
<td>LBP-coded visits in follow-up period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean no. of LBP-related visits</td>
<td>0.6 (2.2)</td>
<td>0.2 (0.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>0 visits</td>
<td>14,731 (75.5)</td>
<td>2178 (80.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1 visit</td>
<td>2845 (14.6)</td>
<td>413 (15.3)</td>
<td></td>
</tr>
<tr>
<td>2+ visits</td>
<td>1927 (9.9)</td>
<td>103 (3.8)</td>
<td></td>
</tr>
</tbody>
</table>

Ordered imaging

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3286 (16.9)</td>
<td>449 (16.7)</td>
<td></td>
</tr>
<tr>
<td>1 ordered image</td>
<td>3077 (15.8)</td>
<td>431 (16.0)</td>
<td>0.046</td>
</tr>
<tr>
<td>2+ ordered images</td>
<td>211 (1.1)</td>
<td>18 (0.7)</td>
<td></td>
</tr>
</tbody>
</table>

a Population as defined by Clinical Quality Measure #0052.
KP = Kaiser Permanente; LBP = low back pain; SD = standard deviation.

The Permanente Journal/ Spring 2016/ Volume 20 No. 2
adjusted analyses. This may reflect the lack of a single EHR system shared by KP and non-KP sites, resulting in non-KP physicians lacking access to certain medical history data or to information on imaging guidelines.

In both KP and OCHIN, white patients had significantly higher rates of ordered and received imaging, compared with black and Hispanic patients. This may be explained by socioeconomic or cultural differences in patients’ demand for imaging for evaluation of low back pain. Some previous research found differences between white and nonwhite patients in ordered or received imaging related to low back pain,26-27 whereas some did not.11

Although these analyses were exploratory, several strategies for improving implementation of care quality guidelines are implied. Managed care systems may choose to charge higher copayments for guideline-discardant care. Administrators may consider implementing strategies to facilitate physicians following imaging guidelines; for example, EHR reminders and decision-support tools can be effective at changing physicians behaviors.28-31 Another option might involve continuing medical education related to guidelines, or coaching physicians in how to dissuade patients who demand guideline-discardant care.32 Administrators could also support improved data sharing with external care providers. Health educators could inform patients about imaging guidelines.33

Our ability to collect data on received imaging differed across the two care systems; we were less able to identify received imaging in OCHIN, reflecting cross-system differences in the data available to providers in the EHR. However, rates of ordered imaging may more accurately indicate how physician actions align with care guidelines. Finally, these exploratory analyses cannot establish causation.

CONCLUSION

Rates of guideline-discardant imaging for evaluation of incident noncomplicated low back pain may be affected by the following criteria: 1) patient’s ability to afford copayments, 2) whether the imaging service is performed at the same location as a primary care visit, 3) whether data on ordered or received imaging are available in real time, and 4) where follow-up care occurs. Research is needed to establish the causal relationships between patient-level and system-level factors and adherence to treatment guidelines, and to develop system-level interventions that can decrease rates of guideline-discardant imaging for low back pain.

Disclosure Statement

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

Acknowledgments

We wish to thank Craig Mosbaek for suggesting higher copayments for guideline-discardant care. We also wish to thank Michael S Johnson, PhD, at the Kaiser Foundation Health Plan, Portland, OR, for his help in developing this article.

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

References

Low Back Imaging When Not Indicated: A Descriptive Cross-System Analysis


We Want to Know

If the Roentgen rays, that are way ahead,
Will show us in the simple note,
How, when we ask our best girl to wed,
That lump will look in our throat.

If the cathode rays, that we hear all about,
When the burglar threatens to shoot,
Will they show us the picture without any doubt,
Of the heart that we feel in our boot.

If the new x-rays, that the paper do laud,
When the ghosts do walk at night,
Will show ‘neath our hat to the world abroad
How our hair stands on end in our fright.

If the wonderful, new, electric rays,
Will do all the people have said,
And show us quite plainly, before many days,
Those wheels that we have in our head.

If the Roentgen, cathode, electric, x-light,
Invisible! This of that!
Can ever be turned on the Congressman bright
And show him just where he is at.

Oh, if these rays should strike you and me,
Going through us without any pain,
Oh, what a fright they would give us to see
The mess which our stomachs contain!

— Homer C Bennett, American X-ray Journal, 1987
The Blue Lagoon
acrylic paint on canvas

Daniela Alexandru Abrams, MD

This original, gallery-style painting of a water lily was painted on a 16" x 20" canvas with acrylic paint.

Dr. Alexandru Abrams is a Neurosurgeon at the University of California, Irvine School of Medicine. More of her work can be seen in previous issues of The Permanente Journal.
ABSTRACT

Context: For health care reform to succeed, health care systems need a professionally satisfied primary care workforce. Evidence suggests that primary care physicians are less satisfied than those in other medical specialties.

Objective: To assess three domains of physician satisfaction by area of clinical practice among physicians practicing in an established integrated health system.

Design: Cross-sectional online survey of all Southern California Permanente Medical Group (SCPMG) partner and associate physicians (N = 1034) who were primarily providing clinic-based care in 1 of 4 geographically and operationally distinct Kaiser Permanente Southern California Medical Centers.

Main Outcome Measures: Primary measure was satisfaction with one’s day-to-day professional life as a physician. Secondary measures were satisfaction with quality of care and income.

Results: Of the 636 physicians responding to the survey (61.5% response rate), on average, 8 in 10 SCPMG physicians reported satisfaction with their day-to-day professional life as a physician. Primary care physicians were only minimally less likely to report being satisfied (difference of 8.2-9.5 percentage points; p < 0.05) than were other physicians. Nearly all physicians (98.2%) were satisfied with the quality of care they are able to provide. Roughly 8 in 10 physicians reported satisfaction with their income. No differences were found between primary care physicians and those in other clinical practice areas regarding satisfaction with quality of care or income.

Conclusion: It is possible to create practice settings, such as SCPMG, in which most physicians, including those in primary care, experience high levels of professional satisfaction.

INTRODUCTION

Health care reform sets the US on a path toward a health care system that is more patient-centered and more coordinated and that delivers more value per dollar spent. Getting to such a system cannot occur without the active engagement and involvement of all physicians, particularly those practicing in primary care. One of the many reasons for this is because health care reform requires the willingness of all physicians to accept and to work to improve new models of care delivery such as medical homes as well as various forms of value-based purchasing. Primary care physicians (PCPs) are being additionally relied on to spearhead the formation of medical homes and to take the lead in coordinating patient care in accountable care organizations.

The active engagement and the involvement required by physicians to help ensure the success of health care reform are worrisome when considered against the backdrop of physician satisfaction. For example, a national study using survey data collected in 2011 found that 45.8% of physicians studied reported at least 1 symptom of burnout, 37.8% screened positive for depression, and fewer than half of physicians either “agreed” or “strongly agreed” that their work leaves them enough time for their personal and/or family life schedule. Although prior studies, including a 2013 RAND report, have examined physician satisfaction, we sought to add to the literature by examining satisfaction by area of clinical practice among physicians practicing in an established integrated health care system. We partnered with the Southern California Permanente Medical Group (SCPMG)—the physician group that provides care to Kaiser Permanente Southern California (KPSC) members—because it is an organization that reflects a model of care promoted by health care reform and is one that has made considerable investments promoting both quality of care and physician professional satisfaction.
As health care reform continues to unfold, more practice settings may look like SCPMG. As such, we believe our results are relevant to medical students assessing the pros and cons and potential satisfaction of various career paths, and more broadly to policy makers wondering what physician satisfaction might look like as our health care system evolves toward that envisioned in the Affordable Care Act.8

**METHODS**

**Design**

We conducted a cross-sectional online survey of physicians. Our survey was developed by the authors at the RAND Corporation (Santa Monica, CA) in Fall 2011 with the goal of engaging physicians on the broad topic of health care value, including physician satisfaction. Of the 28 questions in our survey, 3 were dedicated to physician satisfaction and 7 were designed to gather physician demographics. The survey took approximately 15 minutes to complete. Our study was approved by the institutional review boards at both the RAND Corporation and KPSC.

**Setting and Participants**

SCPMG is a 6000-physician Medical Group composed of all major specialties that has an exclusive contract to provide medical services across 14 hospitals and more than 200 medical office buildings for the 3.7 million members of the Kaiser Foundation Health Plan in Southern California. The physicians surveyed practice care in a closed, integrated delivery system. SCPMG is a general partnership that self-governs and elects its own leaders. For our study, all SCPMG partner and associate (partner-track) physicians (N = 1034) who were primarily providing clinic-based care in 1 of 4 geographically and operationally distinct KPSC Medical Centers were invited to participate in the survey.

**Measures**

We divided physician satisfaction into three domains: day-to-day professional life, quality of care, and income. Day-to-day professional life was our primary measure. This captures the ultimate physician outcome that is a function of many factors, including organizational features such as staffing ratios, health system contexts such as the professional liability environment, and work perceptions such as the quality of care one is able to provide. Our secondary measures were designed to capture information on work perceptions that contribute to overall professional satisfaction: satisfaction with quality of care and satisfaction with income. Our approach followed the physician satisfaction conceptual framework recently developed by the RAND Corporation.6

The survey-item stems for our three measures were as follows: 1) “Thinking about your own satisfaction with your day-to-day professional life as a physician, would you say you are …”; 2) “Thinking about the quality of care you are able to give patients now, would you say you are …”; and 3) “Thinking about your income in 2012, would you say you are ….” Participants were asked for each to choose one of seven response levels ranging from “extremely satisfied” to “extremely dissatisfied.”

We dichotomized each measure for use in our multivariable analysis by categorizing “extremely satisfied” to “some what satisfied” as “satisfied” and all other responses (ranging from “neither satisfied nor dissatisfied” to “extremely dissatisfied”) as “unsatisfied” following an approach used in prior studies.11,12

**Procedures**

To allow for comparing PCPs with physicians working in other areas of clinical practice, we asked physicians to self-identify as practicing in “primary care,” “medical specialty,” “general surgery or surgical subspecialty,” or “other.” Additional demographic data such as sex and years of postgraduate training were also collected in the survey. RAND Corporation was provided with SCPMG administrative data for all physicians invited to take the survey, to supplement the survey-based demographic data and to allow for comparisons between survey respondents and nonrespondents.

A 7-step process was used to recruit participants from September through November 2013. Step 1 was an e-mail endorsing the survey from each of the 4 Area Medical Directors, followed by an e-mail from regional medical leadership in Step 2. In Step 3, eligible physicians were e-mailed an invitation to participate, which included an encrypted link to the survey hosted on a RAND Survey Research Group server. Steps 4 through 7 involved a series of reminder e-mails to complete the survey, to help maximize the response rate. Survey invitations and reminders were all co-signed by the site-specific Area Medical Directors, the SCPMG regional leader, and the RAND principal investigator. Physicians invited were promised full confidentiality with their responses to the survey and with their response status, both of which were available only to the RAND team. As a token of appreciation and to motivate participation, $25 Amazon gift cards were provided to physicians who submitted a complete survey.

**Data Analysis**

Descriptive statistics were used to characterize physicians invited to participate in the survey and to summarize survey responses. Tests of statistical significance (t-tests for continuous variables and χ² tests for categorical variables) were used to compare physician responses by area of clinical practice and to compare survey respondents with nonrespondents.

Multivariable logistic regression analysis was used to estimate the adjusted proportion of physicians satisfied for each satisfaction measure. Independent variables were selected using the physician satisfaction conceptual model previously developed by RAND.6

To illustrate the impact of physician characteristics on our satisfaction measures, we generated predicted probabilities for each physician characteristic in our regression model. These probabilities were calculated by averaging the predictions across all individuals responding to the survey, producing an average marginal effect. The t-tests were used to compare predicted probabilities of satisfaction across the levels of each characteristic analyzed. Pearson correlation coefficients were used to measure the strength and direction
of the linear relationship between our satisfaction measures; these are expressed as \( \phi \) coefficients because our satisfaction measures were dichotomous.

**RESULTS**

Surveys were completed by 636 of the 1034 physicians invited to participate, for an overall response rate of 61.5%. The characteristics of survey respondents, overall and by area of clinical practice, are shown in Table 1. Table 2 compares the characteristics of survey respondents with those of nonrespondents. The distribution of physicians across the 7 response levels for each of our primary and secondary satisfaction measures is shown in Figure 1. Results of our multivariable regressions can be found in Tables 3 and 4. Because of a lack of variation in the responses to our quality measure—98.2% of physicians reported being satisfied with the quality of care they are able to provide patients—we were unable to perform our planned regression analysis for this measure.

Overall, 83.6% of physicians reported being satisfied with their day-to-day professional life (Table 1). The predicted probabilities for being satisfied with day-to-day professional life found satisfaction to vary between areas of clinical practice, age categories, and medical school type (Figure 2). Compared with physicians working in primary care, medical specialists and general surgeons or surgical subspecialists were on average found to be 8.2 percentage points \((p = 0.03)\) and 9.5 percentage points \((p = 0.02)\), respectively, more satisfied with their day-to-day professional life. These absolute differences in professional satisfaction by area of clinical practice were similar in magnitude to those between the physician age categories and type of medical school attended. We found the youngest physicians in our sample (those aged 30-39 years) to be

<table>
<thead>
<tr>
<th>Table 1: Characteristics of SCPMG physicians responding to survey, overall and by area of clinical practice&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physician responses</strong></td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>No. (%)</td>
</tr>
<tr>
<td>Sex, no. (%)</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Age (years), no. (%)</td>
</tr>
<tr>
<td>30-39</td>
</tr>
<tr>
<td>40-49</td>
</tr>
<tr>
<td>50-59</td>
</tr>
<tr>
<td>60-69</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
</tr>
<tr>
<td>Medical school type, no. (%)</td>
</tr>
<tr>
<td>Public</td>
</tr>
<tr>
<td>Private</td>
</tr>
<tr>
<td>International</td>
</tr>
<tr>
<td>Years since medical school, mean (SD)</td>
</tr>
<tr>
<td>Years of postgraduate training, mean (SD)</td>
</tr>
<tr>
<td>Average total hours per week working as an SCPMG physician, mean (SD)</td>
</tr>
<tr>
<td>Physician satisfaction, mean percentage (SD)</td>
</tr>
<tr>
<td>Satisfied with day-to-day professional life</td>
</tr>
<tr>
<td>Satisfied with quality of care</td>
</tr>
<tr>
<td>Satisfied with income in 2012</td>
</tr>
<tr>
<td>SCPMG partner status, no. (%)</td>
</tr>
<tr>
<td>Associate</td>
</tr>
<tr>
<td>Partner</td>
</tr>
<tr>
<td>KPSC site, no. (%)</td>
</tr>
<tr>
<td>Site 1</td>
</tr>
<tr>
<td>Site 2</td>
</tr>
<tr>
<td>Site 3</td>
</tr>
<tr>
<td>Site 4</td>
</tr>
</tbody>
</table>

<sup>a</sup> Percentages may not total to 100 because of rounding.

<sup>b</sup> Source: authors’ analysis of SCPMG survey data.

KPSC = Kaiser Permanente Southern California; SD = standard deviation; SCPMG = Southern California Permanente Medical Group.
Physician Professional Satisfaction and Area of Clinical Practice: Evidence from an Integrated Health Care Delivery System

9.9 percentage points more likely to be satisfied with their professional life than those aged 40 to 49 years (p < 0.01), 13.0 percentage points likelier vs those aged 50 to 59 years (p < 0.01), and 16.7 percentage points likelier vs those aged 60 to 69 years (p = 0.02). Graduates of international medical schools were roughly 10 percentage points (p = 0.02 for both) more likely to be satisfied with their professional life vs those from both public and private US medical schools.

Although 83.9% of physicians reported satisfaction with their income—a proportion nearly identical to that for professional life satisfaction—income satisfaction was not found to vary by any physician characteristics other than age (Figure 3). Physicians aged 60 to 69 years were, on average, 13.4 percentage points (p < 0.01) more likely to be satisfied vs those aged 40 to 49 years.

The correlation between the satisfaction with the perceived quality of care physicians are able to give patients now and one’s day-to-day professional life as...
Physician Professional Satisfaction and Area of Clinical Practice: Evidence from an Integrated Health Care Delivery System

a physician was positive and statistically significant ($\phi = 0.30; p < 0.01$), as was the correlation between satisfaction with one's income and satisfaction with one's day-to-day professional life as a physician ($\phi = 0.17; p < 0.01$). No significant association was found between the quality and income satisfaction measures ($\phi = -0.02; p = 0.60$).

DISCUSSION

We found that among the SCPMG physicians responding to our survey, roughly 8 in 10 PCPs, 9 in 10 medical specialists, 9 in 10 general surgeons or surgical subspecialists, and 9 in 10 physicians working in another discipline (listed as “other” on the survey) reported satisfaction with their day-to-day professional life. These results provide strong evidence that nearly all physicians—regardless of area of clinical practice—can be professionally satisfied, at least in SCPMG’s closed, integrated delivery system. This finding is likely of interest to medical students weighing the pros and cons of different career paths.

The high levels of satisfaction reported for one's day-to-day professional life may in part be driven by the high levels of satisfaction observed for the perceived ability to provide high-quality care and satisfaction with personal income as shown by Friedberg et al. Although we could not formally estimate the magnitude of these relationships through regression analyses, our correlation coefficients between our primary and secondary satisfaction measures support this hypothesis.

We thought it best to study SCPMG physicians because they practice in a setting encouraged by health care reform that differs in a number of ways from more traditional fee-for-service practice settings. Such practice-setting differences are particularly important to note if they may differentially promote physician satisfaction. For example, SCPMG physicians are all salaried, which may promote physician satisfaction by providing greater income stability and reduced income-related anxiety compared with typical fee-for-service compensation arrangements in which income is in large part a function of volume of services.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area of clinical practice</td>
<td></td>
</tr>
<tr>
<td>Primary care (reference)</td>
<td></td>
</tr>
<tr>
<td>Medical specialty</td>
<td>0.611* (0.297)</td>
</tr>
<tr>
<td>General surgery or surgical subspecialty</td>
<td>0.740* (0.342)</td>
</tr>
<tr>
<td>Other</td>
<td>0.502 (0.486)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Men (reference)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>-0.221 (0.253)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>30-39 (reference)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>-0.897* (0.357)</td>
</tr>
<tr>
<td>50-59</td>
<td>-1.102* (0.393)</td>
</tr>
<tr>
<td>60-69</td>
<td>-1.319* (0.500)</td>
</tr>
<tr>
<td>Medical school type</td>
<td></td>
</tr>
<tr>
<td>Public (reference)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>-0.054 (0.254)</td>
</tr>
<tr>
<td>International</td>
<td>0.924* (0.443)</td>
</tr>
<tr>
<td>SCPMG partner status</td>
<td></td>
</tr>
<tr>
<td>Associate (reference)</td>
<td></td>
</tr>
<tr>
<td>Partner</td>
<td>0.308 (0.343)</td>
</tr>
<tr>
<td>Total hours per week working as an SCPMG physician (divided by 10)</td>
<td>-0.166 (0.112)</td>
</tr>
<tr>
<td>KPSC site</td>
<td></td>
</tr>
<tr>
<td>Site 1 (reference)</td>
<td>-0.189 (0.375)</td>
</tr>
<tr>
<td>Site 2</td>
<td>-0.425 (0.378)</td>
</tr>
<tr>
<td>Site 3</td>
<td>-0.689* (0.352)</td>
</tr>
<tr>
<td>Site 4</td>
<td>3.010* (0.730)</td>
</tr>
<tr>
<td>Intercept</td>
<td>558</td>
</tr>
<tr>
<td>Observations</td>
<td></td>
</tr>
</tbody>
</table>

* Dependent variable was satisfaction with day-to-day professional life as a physician; logistic regression model was used.
* $p < 0.05$.
* $p < 0.01$.
* $p < 0.1$.

Table 2. Characteristics of physicians invited to complete survey, by response status

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Respondents</th>
<th>Nonrespondents</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (%)</td>
<td>636 (61.5)</td>
<td>398 (38.5)</td>
<td></td>
</tr>
<tr>
<td>Sex, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>268 (42.1)</td>
<td>163 (41.0)</td>
<td>0.71</td>
</tr>
<tr>
<td>Men</td>
<td>368 (57.9)</td>
<td>235 (59.0)</td>
<td></td>
</tr>
<tr>
<td>Age (years), no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>199 (31.3)</td>
<td>96 (24.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>40-49</td>
<td>225 (35.4)</td>
<td>157 (39.4)</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>147 (23.1)</td>
<td>84 (21.1)</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>65 (10.2)</td>
<td>61 (15.3)</td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>45.9 (9.2)</td>
<td>47.1 (9.2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Medical school type, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>263 (41.4)</td>
<td>138 (34.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Private</td>
<td>270 (42.5)</td>
<td>195 (49.0)</td>
<td></td>
</tr>
<tr>
<td>International</td>
<td>103 (16.2)</td>
<td>65 (16.3)</td>
<td></td>
</tr>
<tr>
<td>Years since medical school, mean (SD)</td>
<td>18.5 (9.6)</td>
<td>19.9 (9.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>SCPMG partner status, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Associate</td>
<td>154 (24.2)</td>
<td>68 (17.1)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Partner</td>
<td>482 (75.8)</td>
<td>330 (82.9)</td>
<td></td>
</tr>
<tr>
<td>KPSC site, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site 1</td>
<td>149 (23.4)</td>
<td>99 (24.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>Site 2</td>
<td>172 (27.0)</td>
<td>89 (22.4)</td>
<td></td>
</tr>
<tr>
<td>Site 3</td>
<td>139 (21.9)</td>
<td>107 (26.9)</td>
<td></td>
</tr>
<tr>
<td>Site 4</td>
<td>176 (27.7)</td>
<td>103 (25.9)</td>
<td></td>
</tr>
</tbody>
</table>

* Percentages may not total to 100 because of rounding.
* p values were generated using two-sample t tests for continuous variables and $\chi^2$ tests for categorical variables.
* Source: authors’ analysis of SCPMG survey data.
* SCPMG = Southern California Permanente Medical Group; KPSC = Kaiser Permanente Southern California; SCPMG = Southern California Permanente Medical Group.
provided; this hypothesis is consistent with the recent RAND physician satisfaction study.8 The eligibility of all full-time SCPMG physicians to become partners over time may create a sense of ownership, which may also promote satisfaction vs fee-for-service settings and other settings in which physicians are employed (but are not partners). The nearly unanimous satisfaction with quality of care among the physicians responding to our survey may not come as a surprise given the longstanding commitment and efforts by SCPMG leadership to create high-quality systems of care that lead in the nation, according to the National Committee for Quality Assurance.4,13,14

We found no relationship between physicians’ self-reported number of hours worked and day-to-day professional satisfaction (see regression results in Table 3), an area in which prior studies have produced mixed findings.15 However, our study may not have been able to detect a relationship between hours worked and satisfaction because of the limited variation in hours worked among the physicians responding to our survey (Table 1). Future work could investigate whether equality in the number of hours worked may create a sense of equity and thereby serve as one way to promote physician professional satisfaction.

Reasonable work hours and likewise the high levels of both care quality and day-to-day professional satisfaction reported by the physicians responding to our survey may be attributable in part to SCPMG’s well-developed infrastructure for engaging and supporting physicians.5 In fact, in a recent study, organizational interventions aimed at improving communication and workflow, and initiating quality-improvement projects to address clinician concerns—interventions that largely reflect processes already in place in SCPMG—were found to reduce PCPs’ burnout and dissatisfaction.16 How such characteristics of SCPMG may affect the satisfaction of non-PCPs is unknown.

Our key result—that professional satisfaction varies minimally across the 4 areas of clinical practice defined in our study—is difficult to contrast with prior studies because of how specialties are demarcated, the choice of specialty for the reference group, the variation of specialties included, and the exact definitions of professional satisfaction used.17 A few articles important to note include a 2012 study by Chen and colleagues,18 who examined career satisfaction among PCPs and found those in pediatrics to be marginally more satisfied compared with those in internal medicine. An older article found physicians in geriatric internal medicine, neonatal-perinatal medicine, dermatology, pediatrics and “all other specialties” to be between 104% (geriatric internal medicine) and 27% (“all other specialties”) more likely to be satisfied vs family practice (the reference category); no other specialties examined had higher satisfaction with statistical significance.12 The article also examined the likelihood of being dissatisfied vs family practice; the only specialties that were lower (with statistical significance) vs family practice were otolaryngology and rhinology, obstetrics and gynecology, ophthalmology, orthopedic surgery, and internal medicine with the likelihood of dissatisfaction ranging from 78% more likely (otolaryngology) to 22% (internal medicine).12 Leigh and colleagues,17 in a follow-up in 2009 to their earlier article on physician career satisfaction,12 again examined career satisfaction across specialties. The only specialties found to have greater satisfaction with statistical significance compared with family practice (their reference group), were pediatric emergency medicine, geriatric medicine, other pediatric subspecialty, neonatal-perinatal medicine, internal medicine and pediatrics, pediatrics, dermatology, and child and adolescent psychiatry. The specialties that were less likely with statistical significance to be satisfied vs family practice were obstetrics and gynecology, nephrology, pulmonary critical care medicine, and neurologic surgery.

To help frame the implications of our study in the context of health care reform promoting models of care reflective of SCPMG, we sought to contrast our findings with prior studies of physicians practicing in settings similar to SCPMG. The most relevant studies identified were reviewed by Scheurer and colleagues,15 who found evidence that physicians practicing in health maintenance organizations and those paid based on capitation may be less satisfied. Although somewhat relevant, health maintenance organization and capitation in these prior studies have a very different meaning because the physicians studied were not practicing in

### Table 4. Multivariable regression: satisfaction with income in 2012

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient (standard error)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area of clinical practice</td>
<td></td>
</tr>
<tr>
<td>Medical specialty (reference)</td>
<td>-0.336 (0.290)</td>
</tr>
<tr>
<td>General surgery or surgical sub specialty</td>
<td>-0.372 (0.323)</td>
</tr>
<tr>
<td>Other</td>
<td>-0.680 (0.430)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Men (reference)</td>
<td>0.297 (0.253)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>30-39 (reference)</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>-0.327 (0.306)</td>
</tr>
<tr>
<td>50-59</td>
<td>0.222 (0.378)</td>
</tr>
<tr>
<td>60-69</td>
<td>0.876 (0.607)</td>
</tr>
<tr>
<td>Medical school type</td>
<td></td>
</tr>
<tr>
<td>Public (reference)</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>-0.236 (0.261)</td>
</tr>
<tr>
<td>International</td>
<td>-0.197 (0.362)</td>
</tr>
<tr>
<td>SCPMG partner status</td>
<td></td>
</tr>
<tr>
<td>Associate (reference)</td>
<td></td>
</tr>
<tr>
<td>Partner</td>
<td>0.264 (0.303)</td>
</tr>
<tr>
<td>Total hours per week working as an SCPMG physician (divided by 10)</td>
<td>0.0977 (0.122)</td>
</tr>
<tr>
<td>KPSC site</td>
<td></td>
</tr>
<tr>
<td>Site 1 (reference)</td>
<td></td>
</tr>
<tr>
<td>Site 2</td>
<td>-0.336 (0.290)</td>
</tr>
<tr>
<td>Site 3</td>
<td>-0.247 (0.371)</td>
</tr>
<tr>
<td>Site 4</td>
<td>-0.480 (0.349)</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.529 (0.715)</td>
</tr>
</tbody>
</table>

* Dependent variable was satisfaction with income in 2012; logistic regression model was used.
* p < 0.05.
* Source: authors’ analysis of SCPMG survey data.
* KPSC = Kaiser Permanente Southern California.
* SCPMG = Southern California Permanente Medical Group.
closed, integrated care delivery systems, as were SCPMG physicians. We thus conclude that there is hope that, as our health care system evolves to look more like the model of care practiced within SCPMG, attaining the high levels of physician satisfaction found in our study may be possible in other settings.

We believe our results should provide hope to both medical students and physicians that practice settings do exist where nearly all physicians across all areas of clinical practice are satisfied not only with their day-to-day professional life but also with their compensation and perceived ability to provide care that is of high quality. Physicians also ought to take from our results that if trying to prioritize professional satisfaction, they should consider both the quality of care they believe they will be able to deliver and the compensation they are being offered. The positive correlation we found between satisfaction with the perceived ability to provide quality care and one’s day-to-day professional life points toward a potential benefit of practices giving their physicians the flexibility needed to provide care they perceive as being of high quality.

As health care reform continues to unfold, physician satisfaction should be actively monitored. In this way, the models of care being implemented across the US can be refined in ways that maintain physician satisfaction, particularly among PCPs, while at the same time moving our system toward care that is provided consistently, with high quality and at reasonable cost for all Americans.

CONCLUSION
Our results demonstrate that there are groups of physicians practicing medicine in settings where nearly all physicians across all areas of clinical practice (including primary care) report satisfaction with their day-to-day professional life as a physician. Because the success of health care reform depends largely on PCPs’ efforts to maximize their professional satisfaction are required. We hope our findings encourage organizations, including SCPMG, to continue monitoring the satisfaction of their physicians and to strive to create practice settings where physicians across all areas of clinical practice can experience high levels of professional satisfaction.

The National Committee for Quality Assurance (NCQA) is a private, nonprofit organization dedicated to improving health care quality. The NCQA accredits and certifies a wide range of health care organizations. It also recognizes clinicians and practices in key areas of performance. The NCQA Healthcare Effectiveness Data and Information Set (HEDIS) is the most widely used performance measurement tool in health care.

Disclosure Statement
Mr Caloyeris is currently an employee and shareholder of Amgen Inc, Thousand Oaks, CA, but was not at the time the study was conducted. Dr Kanter is a Southern California Permanente Medical Group (SCPMG) partner; Ms Ives and Dr Kim are SCPMG employees. The authors have no other conflicts of interest to disclose.

Acknowledgments
Development and proof-of-concept work for the survey used in this study was funded through a donation to the RAND Corporation by David Richards and by SCPMG. The implementation of the survey in SCPMG, including data analysis and manuscript preparation, was funded through a donation to the RAND Corporation by David Richards. We thank all the SCPMG physicians who participated in our survey for taking the time to share their thoughts with us; without them, our study would not have been possible. We also thank the RAND Survey Research Group. We appreciate the SCPMG leadership for partnering with us on this study, allowing us to implement our survey among physicians in their medical group.

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

References
This photograph was taken during a chance discovery while walking in the woods outside of Charleston, SC. The rusting, dying boat could only hint at its history and the voyages it had taken in the Charleston Harbor and beyond. The title suggested itself.

Dr Rousseau is a Professor of Internal Medicine and a Physician in the Department of Palliative Care at the Wake Forest University School of Medicine in Winston-Salem, NC.
ORIGINAL RESEARCH & CONTRIBUTIONS

Impact of a Care Directives Activity Tab in the Electronic Health Record on Documentation of Advance Care Planning

Marianne Turley, PhD; Susan Wang, MD; Di Meng, PhD; Michael Kanter, MD; Terhilda Garrido, MPH

ABSTRACT
Context: To ensure patient-centered end-of-life care, advance care planning (ACP) must be documented in the medical record and readily retrievable across care settings.

Objective: To describe use of the Care Directives Activity tab (CDA), a single-location feature in the electronic health record for collecting and viewing ACP documentation in inpatient and ambulatory care settings, and to assess its association with ACP documentation rates.

Design: Retrospective pre- and postimplementation analysis in 2012 and 2013 at Kaiser Permanente Southern California among 113,309 patients aged 65 years and older with ACP opportunities during outpatient or inpatient encounters.

Main Outcome Measures: Providers’ CDA use rates and documentation rates of advance directives and physician orders for life-sustaining treatments stratified by CDA use.

Results: Documentation rates of advance directives and physician orders for life-sustaining treatments among patients with outpatient and inpatient encounters were 3.5 to 9.6 percentage points higher for patients with CDA use vs those without it. The greatest differences were for orders for life-sustaining treatments among patients with inpatient encounters and for advance directives among patients with outpatient encounters; both were 9.6 percentage points higher among those with CDA use than those without it. All differences were significant after controlling for yearly variation (p < 0.001).

Conclusion: Statistically significant differences in documentation rates between patients with and without CDA use suggest the potential of a standardized location in the electronic health record to improve ACP documentation. Further research is required to understand effects of CDA use on retrieval of preferences and end-of-life care.

INTRODUCTION
Advance care planning is a process in which patients make decisions about their future health care in consultation with clinicians, family, and important others. The main goal of this planning is to allow patients to continue to participate in shared decision making should they become incapable of making care decisions. The overarching aim is to provide patient-centered care in all circumstances, especially those in which patients can no longer express their goals and preferences or advocate for themselves. To achieve these goals, advance care planning activities must be documented in the medical record and readily retrievable in any setting in which patients receive care. Signed documents such as advance directives and standardized, state-approved physician or medical orders for life-sustaining treatments (POLSTs) provide a legal foundation for tailoring treatments to patient preferences.

Only 18% to 30% of the total US adult population has completed advance directives, and just 1 in 3 chronically ill patients has a documented advance directive. The percentage of older adults completing advance directives is unclear. Population-based estimates are in the range of 5% to 15%. Conversely, interviews with health care proxies suggest that as many as 70% of adult decedents older than age 60 years may have some form of advance directive. Substantial racial-ethnic disparities exist in rates of completion of advance directives.

Regardless of the proportion of older adults completing advance directives and having POLSTs, documentation of preferences is problematic. In a recent study, agreement between hospitalized elderly patients’ expressed preferences for end-of-life care and documentation in the medical record was only 30%; for example, 28% of elders preferred only comfort measures at the end of life, but just 5% of all documented treatment goals reflected this preference. Similar findings among community-dwelling vulnerable elders were obtained in a secondary analysis of data from 2 related studies; only 15% to 47% of 800 elders who reported completing an advance directive and giving it to a health care clinician had corresponding documentation in the medical record. Agreement between expressed and documented preferences may be affected by the fact that a substantial proportion of older adults completing advance directives may not fully understand these documents.

Advanced care documentation must be readily accessible to clinicians. A recent study assessed the documentation of advance care planning discussions and decisions in the electronic health records (EHRs) of more than 60,000 ambulatory care patients aged 65 years and older. Variable locations rendered retrieval difficult, and the authors concluded that a
standardized location was necessary to ensure quick retrieval of needed information. Similarly, information related to advance care planning is located inconsistently in the Kaiser Permanente (KP) EHR, KP HealthConnect. When 50 KP Southern California (KPSC) physicians and medical assistants who were experienced EHR users were asked to locate advance care planning documentation, they looked in multiple locations in 35% of searches. Twenty-three percent of physicians and 72% of medical assistants were unable to locate advance care planning documentation within 2 minutes. When they located advance care planning documentation, even these experienced users required up to 19 seconds to do so (unpublished data, 2011 Dec 8-9).

Multiple strategies are required to improve advance care planning and ensure that care is patient-centered: facilitating clinician-patient discussions; improving documentation rates; and readily retrieving documented patient preferences, including information about health care proxies or surrogate decision makers, from the medical record. Systematic programs that include clinician support for engaging patients in and conducting advance care planning conversations over time can improve the proportion of patients who engage in discussions about advance care planning and the quality of those conversations. However, KP recognized that challenges related to documenting and retrieving patient preferences transcended conversations about advance care planning.

From June 2009 to November 2012, a KP interregional workgroup designed, built, and implemented a new functionality in the EHR for recording and viewing documentation of patients’ advance care planning across settings in a single, easily accessible location. The Care Directives Activity tab (CDA) is embedded into the Epic software (Epic Systems Corp, Verona, WI) on which the EHR is based. The purpose of this study was to assess patterns of CDA use and the impact of CDA use on documentation rates of advance directives and POLSTs.

**METHODS**

**Setting and Design**

KPSC is 1 of 7 Regions of KP, which, with its 9.6 million members, is among the largest not-for-profit integrated care delivery systems in the US. Of the approximately 3 million patients KPSC cares for, 668,000 are 65 years of age or older. An integrated EHR is available in all KPSC care settings. It includes comprehensive clinical information (demographics, documentation from all provider types, problem and medication lists, and discharge summaries), computerized order entry for medications, laboratory tests, radiology, consultation, and nursing care, results (eg, laboratory, radiology, and consultation) management, point-of-care decision support, and secure messaging between clinicians and with patients.

We conducted a retrospective observational study, assessing documentation rates of advance directives and POLSTs before and after CDA implementation in the KPSC Orange County Service Area in November 2012. We defined the preimplementation period as January 2012 to October 2012 and the postimplementation period as January 2013 to October 2013.
Impact of a Care Directives Activity Tab in the Electronic Health Record on Documentation of Advance Care Planning

Population

We examined documentation rates of advance directives and POLSTs among unique KPSC patients aged 65 years and older. Although younger patients may benefit from advance care planning, we limited our study to older patients because we assumed they were more likely to need end-of-life care. For inclusion, patients had to have at least 1 ambulatory care or inpatient encounter during the study period; we also assumed that documentation of advance care planning was more likely among patients with face-to-face interactions with clinicians that represented opportunities for advance care planning conversations. Between 2009 and 2012, for KPSC patients aged 65 years and older with at least 1 ambulatory care or inpatient visit, average annual rates of new documentation in the EHR of advance directives and POLSTs were 3.1% and 1.4%, respectively.

Intervention

Accessible in all inpatient and outpatient care settings, CDA is a single EHR tab used for documenting and viewing activities of advance care planning and patient preferences. Figure 1 displays the top-level summary view across settings, which contains an overview of end-of-life care preferences and activities, including documentation of advance directives and POLSTs, and links to subpages:

- current and historical code status
- the POLST: whether on file, in process, or not completed, with a hyperlink to scanned documents (Figure 2)
- advance directives: whether on file, in process, or not completed, with a hyperlink to scanned documents
- surrogate and protected health information: contact information for a designated health care surrogate, individuals excluded from surrogate decision making, and individuals with whom protected health information can and cannot be shared
- advanced illness care: value- and religion-based treatment preferences, end-of-life goals, preferred location for advanced illness care, and preferences for specific treatments (eg, mechanical ventilation, transfusion of blood or blood products, and intravenous nutrition and hydration)
- blood product declaration: any blood transfusion or infusion, no blood transfusions or infusions, and nonblood medical management (eg, nonblood volume expanders)
- palliative and hospice care: start dates and care team.

Advance directives and POLSTs are completed and signed on paper by patients and clinicians, centrally scanned, and stored in a single location in the enterprise data warehouse. Hyperlinks to electronic versions then appear in the CDA in the patient's EHR. Hyperlinks to documents may also appear elsewhere in the patient's record, but the CDA is the single consistent location for hyperlinks to advance directives and POLSTs across all patient records.

Implementation of the CDA was accompanied by on-site trainings for selected departments with an anticipated high need for documentation of advance care planning; approximately 150 clinicians (physicians, nurse practitioners, and physician assistants) participated. Webinars introducing the CDA were available to all clinicians and were recorded for later viewing.

Outcome Measures

We measured CDA use, which we defined by the following clinician actions: clicking on the tab in a patient's EHR to launch the summary page or clicking to view information or perform activities in one of the CDA sections. Clinicians' CDA use was linked to an encounter occurring in either the ambulatory care or inpatient setting in the postimplementation period; if patients had multiple encounters during the postimplementation period, CDA use was linked to the first encounter. Patients with CDA use in each setting were examined separately, and those with CDA use in both settings were included in each encounter-based group.

We also measured rates of filed advance directives and POLSTs before and after implementation of the CDA. We defined a filed document as one completed by the patient and/or his/her clinician or health care proxy, signed, returned to the clinician, and linked as a scanned version to a patient's EHR. This sequence was indicated by a document's presence in the enterprise data warehouse. Documentation filing was not linked to a patient encounter because it could occur outside of an encounter (eg, if a member mailed in an advance directive).

Statistical Analysis

We tabulated the number of encounters in ambulatory care and inpatient settings among the study population in which clinicians used the CDA in the patient's EHR during the postimplementation period. To evaluate filed documentation rates, we tabulated the number of times that new or updated advance directives and POLSTs were filed in patients'
EHRs during the pre- and postimplementation periods, comparing filing rates before and after implementation and, in the postimplementation period, with and without CDA use. We assessed the statistical significance of differences in documentation rates and controlled for temporal trends with Mantel-Haenszel $\chi^2$ tests using statistical software (SAS Version 9.2, SAS Institute, Cary, NC). The KPSC institutional review board approved this study.

RESULTS

In the preimplementation period, 56,251 patients were included in the study population; 43,057 unique patients (76.5%) had 1 or more ambulatory care visits and 13,194 (23.5%) had an inpatient encounter. In the postimplementation period, 57,058 patients were included in the study population; 47,145 unique patients (82.6%) had 1 or more ambulatory care encounters and 9913 (17.4%) had an inpatient encounter. In the postimplementation period, among patients with ambulatory care and inpatient encounters, 464 (1%) and 764 (7.8%), respectively, had CDA use.

Documentation Rates

Among patients with ambulatory care encounters, documentation rates of advance directives in the pre- and postimplementation periods were 3.3% (n = 1401) and 3.0% (n = 1431), respectively (p = 0.06, Table 1). Among patients with an inpatient encounter, documentation rates of advance directives were 5.8% in both periods (p = 0.91).

For POLSTs, filed documentation rates were higher in the postimplementation period in both care settings. Documenta
tion rates of POLST were also higher for patients with CDA use than among patients without it. For patients with ambulatory care encounters, advance directive documentation rates were 12.5% (n = 58) and 2.9% (n = 1373) for CDA use and no CDA use, respectively (p < 0.001, Table 2). Compared with patients without CDA use, patients with CDA use in ambulatory care were nearly 5 times as likely to file an advance directive (odds ratio [OR] = 4.71; 95% confidence interval [CI] = 3.56-6.24). For patients with inpatient encounters, advance directive documentation rates were 9.0% (n = 69) and 5.5% (n = 504) for CDA use and no CDA use, respectively (p < 0.001). Compared with inpatients without CDA use, inpatients with CDA use were more likely to file an advance directive (OR = 1.70; 95% CI = 1.31-2.22).

Documentation rates of POLSTs in both care settings were higher among patients with CDA use than among patients without it. For patients with ambulatory care encounters, POLST documentation rates were 8.2% (n = 38) and 1.7% (n = 814) for CDA use and no CDA use, respectively (p < 0.001). Compared with patients without CDA use, patients with CDA use in ambulatory care were more likely to file a POLST (OR = 2.90; 95% CI = 1.62-5.15).

In the pre- and postimplementation periods, filing rates among patients with inpatient encounters in the pre- and postimplementation periods were 1.2% (n = 505) and 1.8% (n = 852), respectively (p < 0.001). Documentation rates among patients with inpatient encounters in the pre- and postimplementation periods increased from 2.0% (n = 262) to 4.2% (n = 419), respectively (p < 0.001).

Use of Care Directives Activity Tab

We stratified documentation rates for patients with and without CDA use in the postimplementation period to examine associations between CDA use and documentation rates (Table 2). Filed documentation rates of advance directives and POLSTs in both care settings were higher among patients with CDA use than among patients without it. For patients with ambulatory care encounters, advance directive documentation rates were 12.5% (n = 58) and 2.9% (n = 1373) for CDA use and no CDA use, respectively (p < 0.001, Table 2). Compared with patients without CDA use, patients with CDA use in ambulatory care were nearly 5 times as likely to file an advance directive (odds ratio [OR] = 4.71; 95% confidence interval [CI] = 3.56-6.24). For patients with inpatient encounters, advance directive documentation rates were 9.0% (n = 69) and 5.5% (n = 504) for CDA use and no CDA use, respectively (p < 0.001). Compared with inpatients without CDA use, inpatients with CDA use were more likely to file an advance directive (OR = 1.70; 95% CI = 1.31-2.22).

Documentation rates of POLST were also higher for patients with CDA use than for those without it. For patients with ambulatory care encounters, POLST documentation rates were 8.2% (n = 38) and 1.7% (n = 814) for CDA use and no CDA use, respectively (p < 0.001). Compared with patients in ambulatory care with no CDA use, patients with

| Table 1. Documentation of advance directive and physician order for life-sustaining treatments before and after implementation of Care Directives Activity tab |
|---|---|
| **Document** | **Unique members with ambulatory care encounters (N = 90,202)** | **Unique members with inpatient encounters (N = 23,107)** |
| | **Pre-CDA (n = 43,057)** | **Post-CDA (n = 47,145)** | **Pre-CDA (n = 13,194)** | **Post-CDA (n = 9913)** |
| Advance directive filed, no. (%) | 1401 (3.25) | 1431 (3.04) | 758 (5.75) | 573 (5.78) |
| p value of difference | 0.06 | 0.91 |
| POLST filed, no. (%) | 505 (1.2) | 852 (1.8) | 262 (2.0) | 419 (4.2) |
| p value of difference | < 0.001 | < 0.001 |

CDA = Care Directives Activity tab; POLST = physician order for life-sustaining treatments.

| Table 2. Documentation of advance directive and physician order for life-sustaining treatments with and without use of Care Directives Activity tab |
|---|---|
| **Document** | **Unique members with ambulatory care encounters (N = 47,145)** | **Unique members with inpatient encounters (N = 9913)** |
| | **CDA use (n = 464)** | **No CDA use (n = 46,681)** | **CDA use (n = 764)** | **No CDA use (n = 9149)** |
| Advance directive filed, no. (%) | 58 (12.5) | 1373 (2.9) | 69 (9.0) | 504 (5.5) |
| p value of difference | < 0.001 | < 0.001 |
| POLST filed, no. (%) | 38 (8.2) | 814 (1.7) | 100 (13.1) | 319 (3.5) |
| p value of difference | < 0.001 | < 0.001 |

CDA = Care Directives Activity tab; POLST = physician order for life-sustaining treatments.
CDA use were 5 times more likely to file a POLST (OR = 5.03; 95% CI = 3.58-7.05). Documentation rates among patients with inpatient encounters were 13.1% (n = 100) and 3.5% (n = 319) for CDA use and no CDA use, respectively (p < 0.001). Compared with inpatients with no CDA use, inpatients with CDA use were 4 times more likely to file a POLST (OR = 4.17; 95% CI = 3.28-5.29).

**DISCUSSION**

In the pilot study reported here, we found statistically significant associations between clinicians’ CDA use and higher rates of filed advance directives and POLSTs. Patients with CDA use were 1.7 to 5.0 times more likely to file advance directives and POLSTs than were those without CDA use.

Strengths of our report include that it is, to the best of our knowledge, the first describing the use of a standardized location in an EHR for documenting advance care planning. In addition, we assessed the use of CDA in a large metropolitan population and compared preexisting documentation rates with those after implementation. Limitations of our report include the potential impact of unmeasured factors on our findings. For instance, we did not adjust CDA use rates for factors known to have an impact on advance care planning, such as race and literacy, although we have no reason to believe that patients with and without CDA use differed in ways that would have influenced our findings. Although the CDA is intended to improve both the documentation and retrieval of advance care planning preferences, this study addressed only the first. Advance care planning is also a concern for younger patients with terminal conditions; we did not assess the use of the CDA among this population. We did not assess the impact of clinician participation in a limited number of trainings provided on CDA use, and implementation itself may have drawn attention to the need for advance care planning that played a role in increased documentation rates. We cannot distinguish between the effects of increased awareness and the availability of the CDA or assess the impact of CDA implementation throughout KPSC in July 2013.

The rate of CDA use was low at 1% to 7.8%. Following regional rollout, we conducted a survey of KPSC clinicians to ascertain reasons for nonuse. Among more than 800 respondents, 74% indicated that they used the CDA rarely or not at all because they did not know what it was or where it was located in the EHR, and 41% indicated that they did not know how it fit into clinical workflows. Nevertheless, low use rates were associated with statistically significant increases in POLST documentation rates for the entire study population. Subsequent efforts to promote broader use have included incentives to document advance care planning on the tab for providers in selected specialties, a short educational video posted on a regional continuing education Internet portal, and embedding documenting advance care planning preferences on the tab into workflows for an advance care planning process adopted regionally.

Statistically significant differences in documentation rates between patients with and without CDA use point out the potential of a standardized location in the EHR to affect rates of advance care planning documentation for older adults. We cannot assert a causal relationship from our findings. However, we speculate that a single easily accessible location for these documents may engender confidence among clinicians that the effort required to obtain them will be well spent because advance care planning documentation will be available when needed. It is also possible that a standardized location helps clinicians identify patients who need to complete advance care planning documents.

A centralized location provides a clear and efficient process for documenting patient care preferences; KPSC clinicians across inpatient and outpatient settings used the CDA in the same way. Our findings suggest that the CDA facilitated advance care planning documentation that was relevant to the care setting. In the inpatient setting, differences in documentation rates were more pronounced for POLSTs than for advance directives; the opposite was true in ambulatory care.

The documentation of patient care preferences is pivotal to ensuring patient-centered care at the end of life. The CDA is one approach to doing so. Other efforts are under way across KP to facilitate advance care planning via patient engagement, shared decision making, and documentation. Attention must also be paid to providing advance care planning processes that are sensitive to beliefs and values common in racial-ethnic groups that influence decision making at the end of life.

Our report offers early evidence that a systematic approach is beneficial to documenting care preferences. As we successfully engage more patients in advance care planning, we anticipate that benefits will accumulate. Ongoing work examines how to adapt the CDA to systematic advance care planning programs.

Standardized documentation of preferences in the EHR is necessary, but not sufficient, for ensuring that end-of-life care is patient-centered. An important concern not addressed here is the quality of advance care planning conversations, particularly in terms of informed consent and an ongoing dialogue that addresses patients’ changing circumstances. The retrieval of advance care planning documents when they are needed is also a key step in ensuring patient-centered care, and adherence to the patient values and goals they reflect is essential. Evidence exists that even among patients with documented advance care planning preferences, care may not reflect their goals and values. A current quality-improvement project at KP goes beyond facilitating advance care planning documentation to examine concordance between patients’ documented preferences and the end-of-life care they receive.

**CONCLUSION**

Use of the CDA in the EHR was associated with statistically significant increases in documentation rates of advance directives and orders for life-sustaining treatments. Our study will help improve patient-centered end-of-life care.

Among more than 800 respondents, 74% indicated that they used the CDA rarely or not at all because they did not know what it was or where it was located in the EHR, and 41% indicated that they did not know how it fit into clinical workflows.
Disclosure Statement

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

Acknowledgments

We thank the Kaiser Permanente Southern California physicians and medical assistants for participating in the Care Directives Activity pilot study, and Tim Morse, MBA, and Laura Johnson, MPH, for project management. Heather Qian, MBA, provided management support, and Jenni Green, MS, assisted with writing and editing. Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

References


Honor

A good death does honor to a whole life.

— Petrarch, 1304-1374, Italian Renaissance poet and scholar
Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine

Muna Beg, MD; Sara Fisher, PharmD; Dana Siu, PharmD, BCPS; Sudhir Rajan, MD; Lawrence Troxell, PharmD; Vincent X Liu, MD, MS

Perm J 2016 Spring;20(2):49-53
http://dx.doi.org/10.7812/TPP/15-113

ABSTRACT

Context: Studies suggest that dexmedetomidine—an intravenous central-acting \(\alpha_2\)-adrenergic agonist that effectively reduces anxiety among critically ill patients—is being used in patients with severe alcohol withdrawal. However, evidence supporting its use is limited, and it is not approved for this indication.

Objective: To assess the effect of dexmedetomidine on severe alcohol withdrawal symptoms and to compare its use with benzodiazepines alone.

Design: A retrospective, cohort study of 77 patients admitted to the adult medical intensive care unit with severe alcohol withdrawal between January 1, 2009, and October 31, 2013.

Main Outcome Measures: The difference in lorazepam equivalents and Clinical Institute Withdrawal Assessment for Alcohol scores in the 24 hours before and after initiation of dexmedetomidine therapy.

Results: The frequency of dexmedetomidine use increased dramatically between 2009 and 2013 (16.7% vs 82.4%; \(p = 0.01\)). Initiation of dexmedetomidine therapy was associated with significant improvements in Clinical Institute Withdrawal Assessment for Alcohol scores over corresponding 24-hour intervals (14.5 vs 8.5; \(p < 0.01\)). Benzodiazepine use also decreased, but the difference was not statistically significant at 24 hours (\(p = 0.10\)). Dexmedetomidine was well tolerated, requiring discontinuation of therapy in only 4 patients (10.5%). Dexmedetomidine use was associated with significantly longer hospitalizations (\(p < 0.01\)). Benzodiazepine use also decreased, but the difference was not statistically significant (24 hours (\(p = 0.10\)). Dexmedetomidine was well tolerated, requiring discontinuation of therapy in only 4 patients (10.5%). Dexmedetomidine use was associated with significantly longer hospitalizations (\(p < 0.01\)).

Conclusion: Dexmedetomidine initiation was associated with a reduction in short-term alcohol withdrawal symptoms in patients in the intensive care unit, with only a few patients experiencing adverse events. However, its use was also associated with longer hospitalizations. Further research is necessary to evaluate whether dexmedetomidine is efficacious or cost-effective in severe alcohol withdrawal.

INTRODUCTION

Nearly 1 in 10 US adults meets the criteria for an alcohol use disorder, a condition that contributes to an estimated 79,000 deaths and $224 billion in societal costs each year. Alcohol dependency also results in approximately 500,000 annual episodes of alcohol withdrawal that require pharmacologic treatment. Alcohol withdrawal syndrome is characterized by adrenergic symptoms such as tremor, agitation, anxiety, and tachycardia. In severe cases, withdrawal can result in seizures, respiratory failure, and delirium tremens—a condition associated with inhospital mortality of 5%.

Benzodiazepines are currently first-line therapy for treatment of alcohol withdrawal. However, treatment with benzodiazepines may increase the risk of respiratory depression and sedation, especially in patients with liver dysfunction. There is also growing concern that benzodiazepines may worsen delirium and the mortality rate in hospitalized patients; therefore, recent guidelines recommend against using benzodiazepines as first-line sedatives in critical illness. Prior studies suggest that dexmedetomidine—an intravenous central-acting \(\alpha_2\)-adrenergic agonist that effectively reduces anxiety among critically ill patients—is being used in patients with severe alcohol withdrawal.

However, the evidence supporting its use is limited, and it has not received approval from the US Food and Drug Administration for this indication.

We evaluated all episodes of severe alcohol withdrawal requiring admission to the intensive care unit (ICU) from January 1, 2009 to October 31, 2013, at Kaiser Permanente Santa Clara Medical Center in Santa Clara, CA. We also compared the baseline characteristics, hospital course, and outcomes of patients who received benzodiazepines alone versus those who also received dexmedetomidine.

Among patients with severe alcohol withdrawal, we evaluated whether dexmedetomidine initiation was associated with improved symptom control on the basis of Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-Ar) scores and decreased benzodiazepine use.

METHODS

The Kaiser Permanente institutional review board approved this retrospective study and waived the need for informed consent.

Subject Identification

We conducted a retrospective cohort study of patients with severe alcohol withdrawal who were admitted to the adult medical ICU at Kaiser Permanente...
Santa Clara Medical Center, a 327-bed community hospital with 30 ICU beds. We identified patients using International Classification of Disease, Ninth Revision diagnosis codes of 291.0, 291.3, and 291.81 for ICU admissions between January 1, 2009, and October 31, 2013. We excluded patients with a diagnosis of seizures unlikely to have resulted from alcohol withdrawal (Codes 780.31, 780.39, 345.0, 345.1, and 345.4-345.9). From this initial cohort, we excluded patients without alcohol withdrawal confirmed on manual chart review, those with brief ICU stays (< 20 minutes), those receiving dexmedetomidine therapy for diagnoses besides alcohol withdrawal, and those with incomplete documentation (Figure 1). Finally, we excluded patients with fewer than 5 CIWA score assessments documented in the medical record because these patients were believed to have less severe withdrawal symptoms. The CIWA score quantifies the severity of alcohol withdrawal on a scale of 0 through 67, with higher scores indicating more severe symptoms.\textsuperscript{13} Our CIWA-Ar assessment is included in the Sidebar: Clinical Institute Withdrawal Alcohol Scale, Revised (CIWA-Ar) and Lorazepam Dosing Protocol Used at the Kaiser Permanente Santa Clara Medical Center, available online at www.thepermanentjournal.org/files/Spring2016/CIWA-Ar-Sidebar.pdf.

In our ICU setting, the Richmond Agitation Sedation Scale (RASS) is assessed in all patients at 4-hour intervals unless patients are receiving sedative medications, in which case RASS is assessed hourly. Thus, regarding intubated patients, if sedation was lightened to a RASS of 0 to -3, CIWA-Ar was assessed and lorazepam dosed accordingly. If the patient was sedated with RASS of -4, CIWA-Ar was not assessable, and thus lorazepam was dosed according to physician discretion. Patients’ self-reported alcohol intake was estimated using nurses’ and physicians’ documentation in the medical record.

In our cohort, we grouped patients on the basis of whether they were treated with benzodiazepines alone or with benzodiazepines plus dexmedetomidine during their entire ICU stay. Dexmedetomidine therapy was not directed by a protocol.

Patient Characteristics and Treatment

We recorded patients’ baseline characteristics as well as their alcohol use and withdrawal history; we standardized self-reported alcohol intake on the basis of the National Institute of Alcohol Abuse and Alcoholism standard drink equivalent chart\textsuperscript{14} The ethanol level was first assessed at hospital admission. Delirium tremens information was obtained any time during the hospital course when the patient exhibited this sign. We evaluated patients’ CIWA-Ar scores and quantified the timing and dosage of benzodiazepines and dexmedetomidine administered throughout the entire hospitalization. We standardized the doses of different benzodiazepines by converting all benzodiazepines into estimated lorazepam equivalents (Table 1)\textsuperscript{15-18} At our center, a standardized CIWA-Ar protocol is used to administer symptom-based benzodiazepines with additional dosages of benzodiazepines administered on the basis of physician clinical judgment. For all patients in the ICU, dexmedetomidine is administered without a bolus and is titrated to a sedation target.

Analysis

Our primary outcome was the difference in lorazepam equivalents and CIWA-Ar scores in the 24 hours before and after the initiation of dexmedetomidine therapy. In secondary analysis, we compared the 30-day mortality and lengths of stay between patients receiving dexmedetomidine and benzodiazepines versus those receiving benzodiazepines alone. We reported variables as number (percentage) or median (interquartile range) and compared groups with the Wilcoxon signed rank test (paired) as well as the Wilcoxon rank sum test (unpaired). We considered a p value of < 0.05 to be statistically significant.

RESULTS

Baseline Patient Characteristics

We identified 38 patients treated with benzodiazepines and dexmedetomidine and 29 patients treated with

![Figure 1. Flowchart of patients included in and excluded from study. CIWA = Clinical Institute of Withdrawal Assessment; ICU = intensive care unit.](Image 259x490 to 540x675)

<table>
<thead>
<tr>
<th>Table 1. Benzodiazepine equivalent conversions to lorazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Lorazepam</td>
</tr>
<tr>
<td>Diazepam</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
</tr>
<tr>
<td>Midazolam</td>
</tr>
<tr>
<td>Clonazepam</td>
</tr>
<tr>
<td>Oxazepam</td>
</tr>
</tbody>
</table>
benzodiazepines alone who met entry criteria. Most characteristics between groups were not significantly different, with most patients in both groups having prior hospitalizations because of alcohol withdrawal (Table 2). However, patients treated with benzodiazepines alone were more likely to report multidrug abuse (34.5% vs. 5.3%; \( p = 0.02 \)) compared with patients treated with benzodiazepines and dexmedetomidine. The frequency of combined therapy for alcohol withdrawal increased dramatically over time from 16.7% (\( n = 1 \)) in 2009 to 82.4% (\( n = 14 \)) by 2013 (\( p = 0.01 \)).

Cohort Comparison
Patients treated with combination therapy, compared with single-agent therapy, were more likely to have presented with severe alcohol withdrawal marked by delirium tremens (44.7% vs. 20.7%; \( p = 0.02 \); Table 3). They were also more likely to have had a concomitant medical condition requiring critical care (23.7% vs. 10.3%; \( p = 0.04 \)). However, they were less frequently admitted directly to the ICU from the Emergency Department, as evidenced by a longer elapsed time between hospital and ICU admission (1.1 vs. 0.3 days; \( p < 0.01 \)). Most patients ultimately receiving dexmedetomidine did not receive it within the first 24 hours of hospitalization. In total, patients treated with combination therapy received significantly more benzodiazepines during their hospital course compared with those treated with single therapy (100.5 mg vs. 37.0 lorazepam equivalent units; \( p < 0.01 \)). Hospital and ICU length of stay (8.9 days vs. 4.7 days; \( p < 0.01 \)); and 2.9 days vs. 1.4 days, \( p < 0.01 \), respectively) were also significantly higher in patients receiving combination therapy (\( p < 0.01 \) for both) compared with benzodiazepine alone, whereas mortality was not statistically different between groups (2.6% vs. 6.9%; \( p = 0.56 \)).

Effectiveness and Safety of Dexmedetomidine
The initiation of dexmedetomidine was associated with significant improvements in mean CIWA scores during corresponding 24-hour intervals (14.5 vs. 8.5; \( p < 0.01 \); Figure 2, Table 3). Although overall benzodiazepine use also decreased, the difference was not statistically significant at 24 hours (\( p = 0.10 \); Figure 3). However, some patients experienced substantial reductions in benzodiazepine use after initiation of combination therapy; for example, 31.6% of patients experienced at least a 50% reduction in benzodiazepine use. Two patients had a reduction in lorazepam dose greater than 100 mg, whereas another patient required no additional

### Table 2. Baseline patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Benzodiazepines alone (n = 29)</th>
<th>Benzodiazepines plus dexmedetomidine (n = 38)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (interquartile range)</td>
<td>51.0 (44-63)</td>
<td>54.5 (44.8-59.5)</td>
<td>0.89</td>
</tr>
<tr>
<td>Women</td>
<td>7.0 (24.1)</td>
<td>5.0 (13.2)</td>
<td>0.56</td>
</tr>
<tr>
<td>Previous hospitalizations for alcohol withdrawal</td>
<td>17.0 (58.6)</td>
<td>21.0 (55.3)</td>
<td>0.52</td>
</tr>
<tr>
<td>Multidrug abuse</td>
<td>10.0 (34.5)</td>
<td>2.0 (5.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Intubated</td>
<td>6.0 (20.7)</td>
<td>10.0 (26.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Self-reported alcohol intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinks per day (interquartile range)</td>
<td>11.0 (5.0-22.0)</td>
<td>12.0 (11.0-18.3)</td>
<td>0.32</td>
</tr>
<tr>
<td>Number of patients with data</td>
<td>29.0 (100)</td>
<td>35.0 (92.1)</td>
<td></td>
</tr>
<tr>
<td>Year of hospitalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2009</td>
<td>5.0 (17.2)</td>
<td>1.0 (2.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>2010</td>
<td>8.0 (27.6)</td>
<td>4.0 (10.5)</td>
<td></td>
</tr>
<tr>
<td>2011</td>
<td>7.0 (24.1)</td>
<td>6.0 (15.8)</td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>6.0 (20.7)</td>
<td>13.0 (34.2)</td>
<td></td>
</tr>
<tr>
<td>2013 (until Oct 31)</td>
<td>3.0 (10.3)</td>
<td>14.0 (36.8)</td>
<td></td>
</tr>
</tbody>
</table>

* Values are expressed as median number (percentage) unless otherwise indicated.

### Table 3. Patient hospitalization characteristics: utilization and mortality

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Benzodiazepines alone (n = 29)</th>
<th>Benzodiazepines plus dexmedetomidine (n = 38)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital admit time to ICU admit time, days</td>
<td>0.3 (0.2-0.6)</td>
<td>1.1 (0.4-1.7)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Direct admission to ICU from ED, no. (%)</td>
<td>21.0 (72.4)</td>
<td>20.0 (52.6)</td>
<td>0.88</td>
</tr>
<tr>
<td>Hospital length of stay, days</td>
<td>4.7 (3.5-8.9)</td>
<td>8.9 (6.1-12.0)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>ICU length of stay, days</td>
<td>1.4 (0.6-2.3)</td>
<td>2.9 (1.8-5.4)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Delirium tremens, no. (%)</td>
<td>6.0 (20.7)</td>
<td>17.0 (44.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Reason for ICU admission, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol withdrawal alone</td>
<td>16.0 (55.2)</td>
<td>25.0 (65.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Alcohol withdrawal plus medical condition</td>
<td>3.0 (10.3)</td>
<td>9.0 (23.7)</td>
<td></td>
</tr>
<tr>
<td>Medical condition alone</td>
<td>10.0 (34.5)</td>
<td>4.0 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Ethanol level: not measured, no. (%)</td>
<td>11.0 (37.9)</td>
<td>15.0 (39.5)</td>
<td>0.43</td>
</tr>
<tr>
<td>Ethanol level: measured, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 0.3% (coma)</td>
<td>7.0 (24.1)</td>
<td>6.0 (15.8)</td>
<td>0.19</td>
</tr>
<tr>
<td>0.08%-0.3%</td>
<td>5.0 (17.2)</td>
<td>2.0 (5.3)</td>
<td></td>
</tr>
<tr>
<td>0.01%-0.08% (legal limit)</td>
<td>1.0 (3.5)</td>
<td>3.0 (7.9)</td>
<td></td>
</tr>
<tr>
<td>&lt; 0.01% (unmeasurable)</td>
<td>5.0 (17.2)</td>
<td>12.0 (31.2)</td>
<td></td>
</tr>
<tr>
<td>Lorazepam equivalents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Throughout ICU stay, mg</td>
<td>37.0 (16-85.5)</td>
<td>100.5 (48.8-193.1)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Patients with data, no. (%)</td>
<td>29.0 (100)</td>
<td>38.0 (100)</td>
<td></td>
</tr>
<tr>
<td>30-day mortality, no. (%)</td>
<td>2.0 (6.9)</td>
<td>1.0 (2.6)</td>
<td>0.56</td>
</tr>
<tr>
<td>30-day mortality related to alcohol withdrawal, no. (%)</td>
<td>1.0 (3.4)</td>
<td>1.0 (2.6)</td>
<td></td>
</tr>
</tbody>
</table>

* Values are expressed as median (interquartile range) unless otherwise indicated.

A 50% reduction in lorazepam dose greater than 100 mg, whereas another patient required no additional.
Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine

Over time at our center, the concomitant use of dexmedetomidine and benzodiazepines increased dramatically, such that by 2012, more than two-thirds of ICU patients with alcohol withdrawal were treated with combination therapy. At the same time, we found that length of stay was significantly longer among patients treated with combination therapy compared with those treated with benzodiazepines alone. However, because of our retrospective study design, we could not determine whether this difference resulted from dexmedetomidine treatment itself or from residual confounding based on patient characteristics or the timing and initiation of therapy between groups.

The evidence supporting the use of dexmedetomidine in alcohol withdrawal is limited. To our knowledge, there is only 1 prospective study of dexmedetomidine use in alcohol withdrawal. Mueller et al randomized assigned 24 patients with CIWA scores of 15 or higher despite at least 16 mg of lorazepam over a 4-hour period to 1.2 μg/kg/h (high dose), 0.4 μg/kg/h (low dose), or placebo. The authors found that dexmedetomidine at either dose had a short-term benzodiazepine-sparing effect. However, this effect was no longer significant when evaluated over the total duration of hospitalization. Interestingly, dexmedetomidine administration also resulted in a slightly increased hospital length of stay, albeit not statistically significant. Furthermore, there were more cardiovascular side effects compared with benzodiazepine use alone. Smaller retrospective studies show similar findings to those of our study, suggesting that initiation of dexmedetomidine therapy was associated with reduced symptoms, benzodiazepine requirements, hypertension and tachycardia, and minimal side effects. Other reports also suggest that dexmedetomidine is effective in benzodiazepine-refractory alcohol withdrawal.

Because of the adrenergic etiology of alcohol withdrawal syndrome, centrally acting α-agonists have the potential to help control symptoms. The proposed mechanism of action is presynaptic α-agonistic activity, which prevents the further release of norepinephrine, thereby reducing anxiety, tachycardia, and tremor associated with alcohol withdrawal. The importance of dexmedetomidine use in comparison with standard-of-care benzodiazepine use is twofold. Because dexmedetomidine does not act on γ-aminobutyric acid receptors such as benzodiazepines, it does not suppress respiration; nor does it cause a decline in neurologic status, thus also reducing the risk of respiratory depression. The α-agonist activity of dexmedetomidine also makes it an appealing choice because it targets a separate pathway, which can increase the chance of treatment success.

Despite these potential benefits, dexmedetomidine also has limitations. Many patients experience cardiovascular side effects; for example, in large-scale studies of critically ill patients receiving lorazepam after initiation of dexmedetomidine therapy. Dexmedetomidine was well tolerated, with 4 (10.5%) of the patients requiring discontinuation of therapy because of hypotension or bradycardia.

**DISCUSSION**

In this study, we found that the initiation of dexmedetomidine was associated with a significant reduction in alcohol withdrawal symptoms. Dexmedetomidine use was also associated with minimal side effects, with only 10% of patients requiring discontinuation of therapy because of adverse events.

### Table 4. Usage and effects of dexmedetomidine

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number</th>
<th>Mean ± CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of patients</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>CIWA score 24 hours before initiation</td>
<td>14.5 (9.3-17.3)</td>
<td></td>
</tr>
<tr>
<td>CIWA score 24 hours after initiation</td>
<td>8.5 (5.5-11.2)</td>
<td></td>
</tr>
<tr>
<td>Duration of dexmedetomidine, hours</td>
<td>37.4 (21.1-126.7)</td>
<td></td>
</tr>
<tr>
<td>Lorazepam equivalents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equivalents 24 hours before initiation</td>
<td>21.0 (5.0-56.9)</td>
<td></td>
</tr>
<tr>
<td>Equivalents 24 hours after initiation</td>
<td>11.0 (3.3-33.3)</td>
<td></td>
</tr>
<tr>
<td>Time to initiation, days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From ICU admission</td>
<td>0.3 (0.1-1.1)</td>
<td></td>
</tr>
<tr>
<td>From hospital admission</td>
<td>1.7 (0.9-2.1)</td>
<td></td>
</tr>
<tr>
<td>From last drink (approximate)</td>
<td>2.5 (1.3-4)</td>
<td></td>
</tr>
<tr>
<td>Reason for discontinuation, no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Improvement of withdrawal symptoms</td>
<td>20.0 (52.6)</td>
<td></td>
</tr>
<tr>
<td>Extubation</td>
<td>7.0 (18.4)</td>
<td></td>
</tr>
<tr>
<td>Hypotension/bradycardia</td>
<td>4.0 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Death/transfer from hospital</td>
<td>4.0 (10.5)</td>
<td></td>
</tr>
<tr>
<td>Evaluation of mental status</td>
<td>3.0 (7.9)</td>
<td></td>
</tr>
</tbody>
</table>

* Values expressed as median (interquartile range) unless otherwise indicated.

**CI = confidence interval.**
Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine

dexmedetomidine, approximately 25% experienced hypotension and 5% experienced bradycardia. This may be a less important issue among patients with alcohol withdrawal who are hypertensive. Also, the relatively high cost of dexmedetomidine may limit its cost-effectiveness, especially because its impact on resource utilization (length of stay) and mortality were equivalent to, or worse than, benzodiazepine therapy alone. According to standardized pricing data, the average wholesale price of a 400 μg/100 mL vial of dexmedetomidine is $41.88 compared with $0.89 for a 2 mg/mL vial of lorazepam. Thus, a daily infusion of 0.8 μg/kg/h for a 70-kg patient could purchase roughly 320 mg of lorazepam.

This study has several limitations. First, the study was performed at a single center and may reflect unique practice patterns and patient case mix, limiting generalizability. Second, although we included data from five years, we were able to capture only a modest population of patients with severe alcohol withdrawal, also limiting the power of our statistical analyses. Third, the study is vulnerable to confounding by indication because the initiation, titration, and discontinuation of dexmedetomidine and benzodiazepines were not controlled. For example, we noted several baseline differences between the cohorts, including differences in the severity of withdrawal symptoms and comorbid illness, the year in which they were treated, the disparity in the incidence of polysubstance abuse, and differences in the time of dexmedetomidine use. In addition, it is clear that the study captured patients during a period in which the use of dexmedetomidine was changing dramatically. Thus, in several patients treated with dexmedetomidine, alcohol withdrawal was not the primary diagnosis for ICU patients. Finally, we did not account for the use of other neurotropic agents, including antipsychotics, anticonvulsants, and pain medication, that can affect the progression of alcohol withdrawal and are increasingly used in ICU settings.

CONCLUSION

Dexmedetomidine initiation was associated with a reduction in short-term alcohol withdrawal symptoms in ICU patients, with only a fraction of patients experiencing adverse events. However, dexmedetomidine was associated with increases in both hospital and ICU length of stay. Given the increasing use of dexmedetomidine in patients with severe alcohol withdrawal, further research is necessary to determine whether its use is efficacious and cost-effective.

Disclosure Statement

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

Acknowledgments

This study was funded by The Permanente Medical Group and Kaiser Foundation Hospitals and Health Plan. Vincent Liu also was supported by National Institutes of Health Award K23 GM-11-2018. The funding sources had no involvement in study design, analysis and interpretation of data, writing the report, or the decision to submit the article for publication. Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

References


The Permanente Journal/ Spring 2016/ Volume 20 No. 2

ORIGINAL RESEARCH & CONTRIBUTIONS
ABSTRACT

**Context:** The introduction of the varicella vaccine as a routine pediatric immunization in the US, in 1995, provided an opportunity to assess factors associated with uptake of new vaccines in the member population of the Kaiser Permanente Northwest (KPNW) Health Plan.

**Objective:** Identify factors associated with varicella vaccination in the KPNW population in the first five years after varicella vaccine was introduced.

**Design:** A retrospective cohort of children under age 13 years between June 1995 and December 1999, without a history of varicella disease, was identified using KPNW automated data. Membership records were linked to vaccine databases. Cox regression was used to estimate likelihood of varicella vaccination during the study period in relation to age, sex, primary clinician’s specialty, and Medicaid eligibility. For a subset whose parents answered a behavioral health survey, additional demographic and behavioral characteristics were evaluated.

**Main Outcome Measure:** Varicella vaccination.

**Results:** We identified 88,646 children under age 13 years without a history of varicella; 22% were vaccinated during the study period. Varicella vaccination was more likely among children who were born after 1995, were not Medicaid recipients, or had pediatricians as primary clinicians. In the survey-linked cohort, positively associated family characteristics included smaller family size; higher socioeconomic status; and parents who were older, were college graduates, reported excellent health, and received influenza vaccination.

**Conclusion:** Understanding predictors of early varicella vaccine-era vaccine acceptance may help in planning for introduction of new vaccines to routine schedules.

INTRODUCTION

The introduction of the varicella vaccine as a routine pediatric immunization in the US, in 1995, provided an opportunity to assess factors associated with uptake of new vaccines in the member population of the Kaiser Permanente Northwest (KPNW) Health Plan. For the first few years after its introduction, the varicella vaccine was available to Health Plan members, but it was not consistently promoted by clinicians, particularly for older children. During this time, parent choice was a major determinant of whether a child was vaccinated against varicella.

After the varicella vaccine was introduced, vaccination coverage increased more slowly than expected across the US (34% among children 19-35 months of age in 1997-1998), with wide geographic variation. Parents’ concerns, lack of information about the vaccine, and beliefs that clinical varicella was not an illness to be concerned about are thought to have influenced vaccine acceptance. Several nonfamilial factors undoubtedly influenced the likelihood of varicella vaccination in the KPNW pediatric population. In 1995, the US Centers for Disease Control and Prevention (CDC) recommended that the vaccine be routinely administered to children between 12 and 18 months of age and to older children lacking a history of varicella infection. In 1998, varicella vaccination of 1-year-olds was incorporated into the childhood immunization status measure of the national Healthcare Effectiveness Data and Information Set (HEDIS), and in 1999, varicella vaccination for 2-year-olds was adopted as a regional performance measure for KPNW. Also in 1999, varicella vaccination was a major determinant of whether a child was vaccinated particularly for older children. During this time, parent choice members, but it was not consistently promoted by clinicians, particularly for older children. During this time, parent choice was a major determinant of whether a child was vaccinated against varicella.

Several nonfamilial factors undoubtedly influenced the likelihood of varicella vaccination in the KPNW pediatric population. In 1995, the US Centers for Disease Control and Prevention (CDC) recommended that the vaccine be routinely administered to children between 12 and 18 months of age and to older children lacking a history of varicella infection. In 1998, varicella vaccination of 1-year-olds was incorporated into the childhood immunization status measure of the national Healthcare Effectiveness Data and Information Set (HEDIS), and in 1999, varicella vaccination for 2-year-olds was adopted as a regional performance measure for KPNW. Also in 1999, varicella vaccination was a major determinant of whether a child was vaccinated particularly for older children. During this time, parent choice was a major determinant of whether a child was vaccinated against varicella.

During the early and mid-1990s, KPNW annually surveyed its adult members to collect information on demographics and health behaviors; a 2% to 3% random sample of the member population was mailed a questionnaire to gather information on health status, medical history, health services utilization, and behavioral risk factors. We linked this parent-provided survey information with automated vaccination data on the survey respondents’ children to identify demographic and parental factors associated with varicella vaccination from 1995 to 1999. This project was undertaken as a part of the CDC’s Vaccine Safety Datalink, a project that studies the safety, effectiveness, and use of vaccines.
METHODS

Study Population

Using automated membership records, we identified 114,865 Health Plan members who were under age 13 years on June 1, 1995, or who were born after that date and were at least 1 year old by the last day of 1999. Of these, 3,447 had at least 1 parent who had completed a Health Plan member survey from 1991 to 1996; if both parents responded to the survey, we randomly selected data from one parent. For each child, we defined an observation period that began at the child’s first birthday, date of entry into the Health Plan, or date of first vaccine availability (June 1, 1995), whichever was later, and extended through December 31, 1999, date of leaving the Health Plan, date of varicella diagnosis, or date of varicella vaccination, whichever was earlier. Children with varicella disease or varicella vaccination before this period were excluded (Table 1), leaving 88,646 total study members. Of these, 2,300 members were in the cohort linked to the membership survey information.

Data Sources

Vaccination dates were obtained from KPNW’s automated vaccination database. In addition to vaccines administered by KPNW, this database captured non-KPNW vaccinations for which written documentation was available. In a study of the reliability of the KPNW automated vaccination data, Mullooly et al found 83% to 92% agreement between automated vaccination data and vaccine information abstracted from medical records for common childhood vaccines. History of varicella disease was recorded in the automated vaccination database as a contraindication for varicella vaccine. We found 83% to 92% agreement between automated vaccination data and vaccine information abstracted from medical records for common childhood vaccines. Varicella diagnoses for the years 1995 to 1999 were obtained from the Health Plan’s electronic medical record system and from inpatient, Emergency Department, and telephone advice databases. This project was approved by the KPNW institutional review board.

Analysis

We used Cox regression survival models to estimate the likelihood of varicella vaccination. Follow-up was measured in days after cohort entry. Start of follow-up was June 1, 1995, for Health Plan members 12 months of age or older on that date; the child’s first birthday (eligible age for the vaccine) for children younger than 12 months on June 1, 1995; or date of entry into the Health Plan for children aged 2 years and older who were not in the Health Plan on June 1, 1995. Subjects without vaccination were removed from the analysis on the date of varicella diagnosis, Health Plan termination, or end of the study period (December 31, 1999), whichever was earlier. The maximum follow-up interval was 4 years, 7 months (June 1, 1995-December 31, 1999).

Covariates available for both the linked and unlinked cohorts included age group, sex, clinician specialty (Family Practice vs Pediatrics), and Medicaid eligibility (a surrogate for socioeconomic status [SES]). The cohort linked to the Health Plan membership survey had additional categorical variables available to analyze, including race; number of children in the family; family income; self-reported SES; and parent’s age, education, marital status, self-reported health status, history of depression, and current cigarette smoking.

To perform the Cox regression models, we created the following analytic variables to examine demographics: race (nonwhite vs white), number of children in the family (1, 2, or 3 or more), self-reported lower SES vs middle or higher SES, annual family income (less than $20,000; $20,000 to 49,999; or $50,000 or more per year), parent education.

### Table 1. Number of study subjects by age group and medically identified varicella and varicella vaccination during observation period

<table>
<thead>
<tr>
<th>Age group</th>
<th>Survey-linked and unlinked cohorts combined</th>
<th>Survey-linked cohort only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. after exclusions&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Median observation time, days</td>
</tr>
<tr>
<td>Group no.</td>
<td>Birth date range&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Born June 1, 1998-December 31, 1998</td>
<td>1916</td>
</tr>
<tr>
<td>2</td>
<td>Born June 1, 1997-May 31, 1998</td>
<td>4027</td>
</tr>
<tr>
<td>3</td>
<td>Born June 1, 1996-May 31, 1997</td>
<td>4633</td>
</tr>
<tr>
<td>4</td>
<td>Born June 1, 1995-May 31, 1996</td>
<td>5474</td>
</tr>
<tr>
<td>5</td>
<td>Born June 1, 1994-May 31, 1995</td>
<td>6322</td>
</tr>
<tr>
<td>7</td>
<td>Born June 1, 1992-May 31, 1993</td>
<td>19,564</td>
</tr>
<tr>
<td>8</td>
<td>Born June 1, 1991-May 31, 1992</td>
<td>25,594</td>
</tr>
<tr>
<td>9</td>
<td>Born June 1, 1990-May 31, 1991</td>
<td>14,515</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>88,646</td>
</tr>
</tbody>
</table>

<sup>a</sup> Includes relationship to date of first availability of varicella vaccine on June 1, 1995.

<sup>b</sup> Subjects with varicella disease or varicella vaccine before observation period were excluded: 26,219 in survey-linked and unlinked cohorts combined and 1147 in survey-linked cohort only.
(high school graduate or less, some college, or college graduate), parent age (30 years or more vs younger than 30 years), and single-parent marital status (divorced/widowed/never-married) vs married. We also created variables to describe parental health status and health behaviors: parent's influenza vaccine ("flu shot") in previous year (yes vs no), parent's health status (less than excellent health vs excellent health), parent's current cigarette smoking (yes vs no), and parent's history of depression (yes vs no).

We divided the children in our study population into age groups relative to the date of first availability of varicella vaccine and computed risk ratios for each age group before combining age groups where appropriate. Because vaccine receipt was much more common among younger children, we used dummy variables to adjust for age group in all regression models. We also used a time-dependent covariate for Calendar Year 1998 (yes/no) and another time-dependent covariate for Calendar Year 1999 (yes/no) to take into account increased clinician influence on likelihood of varicella vaccination (because of changes in guidelines and staff evaluation criteria). Because factors influencing vaccination for children turning 1 year old after the vaccine was introduced might be different from factors influencing vaccination in older children, we created the following groups: children turning 1 year old after the date of vaccine introduction (Groups 1-5—the younger stratum), children 12 to 23 months old on the date of vaccine introduction (Group 6), and children 2 years of age and older on the date of vaccine introduction (Groups 7-9—the older stratum). We then ran 2 separate multivariable models. Group 6 was the reference group for both models.

### RESULTS

In the total subject population (linked plus unlinked cohorts), the child's age group was strongly associated with likelihood of vaccination. Using children 12 to 23 months old on June 1, 1995, as the reference group (Age Group 6), the relative likelihood of vaccination during the observation period increased to 1.5 for children turning 1 year old during the following year (Age Group 5), and to 2.2, 4.1, 8.6, and 11.9 respectively, in the subsequent 1-year age groups (Table 2). Children less than 1 year old on June 1, 1995, were the most likely to be vaccinated. Children older than 1 year on June 1, 1995, were much less likely than the 1-year-olds to be vaccinated during the study period: 2- to 4-year-olds (Age Group 7) were only half as likely to be vaccinated, whereas 5- to 9-year-olds (Age Group 8) were only one-fifth as likely, and the oldest age group (Age Group 9) was less than one-tenth as likely. The child's sex was not associated with vaccination status.

Family and clinician characteristics also affected the likelihood of child vaccination in the total subject population. Medicaid eligibility was associated with lower rates of vaccination in both the younger and older age strata (risk ratio [RR] = 0.8 for Age Groups 1-6 and Age Groups 6-9) and in every age group (results not shown). Children with family practitioners as their primary care clinicians were much less likely to receive the vaccine than were children with pediatricians as primary clinicians; this was more pronounced among older children (RR = 0.36, 95% confidence interval [CI] 0.31-0.41) than among younger children (RR = 0.56, 95% CI 0.48-0.66).

We were able to examine additional family characteristics in the cohort linked to the member survey. In this cohort, family factors were more strongly related to risk of vaccination in the older age stratum than in the younger (Table 3); however, the larger number of subjects in this stratum improved statistical power for comparisons. In both the older and younger age strata, the presence of 3 or more children in the family was associated with a lower likelihood of vaccination compared with families with only 1 child. Before multivariable adjustment, self-reported low SES and Medicaid eligibility were associated with lower likelihood of vaccination than higher SES and no Medicaid eligibility in both age strata. Children with parents aged 30 years or older and with parents who were college graduates were more likely to be vaccinated than were children of younger and less well-educated parents. If the parent did not get a flu shot in the year before the member survey, the child’s likelihood of receiving the varicella vaccine was lower than in families in which the parent did get a flu shot. In the older age stratum, vaccination was more likely if family income was high and less likely if the parent was currently single or reported less than excellent health status, current cigarette use, or history of depression.

In the linked cohort, as in the total subject population, use of a family practitioner rather than a pediatrician as the primary clinician was associated with a reduced relative likelihood of vaccination. There were only 16 subjects in the

---

**Table 2. Family characteristics related to likelihood of varicella vaccination, survey-linked and unlinked cohorts combined**

<table>
<thead>
<tr>
<th>Population</th>
<th>Characteristic</th>
<th>Risk ratio*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Groups 1-5* (N = 28,973)</td>
<td>Age Group 6</td>
<td>1.0</td>
<td>Reference</td>
</tr>
<tr>
<td></td>
<td>Age Group 1</td>
<td>11.9</td>
<td>11.0-12.8</td>
</tr>
<tr>
<td></td>
<td>Age Group 2</td>
<td>8.6</td>
<td>8.1-9.1</td>
</tr>
<tr>
<td></td>
<td>Age Group 3</td>
<td>4.1</td>
<td>3.9-4.4</td>
</tr>
<tr>
<td></td>
<td>Age Group 4</td>
<td>2.2</td>
<td>2.0-2.3</td>
</tr>
<tr>
<td></td>
<td>Age Group 5</td>
<td>1.5</td>
<td>1.4-1.6</td>
</tr>
<tr>
<td></td>
<td>Male vs female child</td>
<td>1.0</td>
<td>0.96-1.0</td>
</tr>
<tr>
<td></td>
<td>Family practitioner vs pediatrician</td>
<td>0.56</td>
<td>0.48-0.66</td>
</tr>
<tr>
<td></td>
<td>Medicaid vs other insurance</td>
<td>0.81</td>
<td>0.78-0.84</td>
</tr>
</tbody>
</table>

| Age Groups 6-9* (N = 66,274) | Age Group 6 | 1.0 | Reference |
| | Age Group 7 | 0.52 | 0.49-0.55 |
| | Age Group 8 | 0.18 | 0.17-0.19 |
| | Age Group 9 | 0.07 | 0.06-0.08 |
| | Male vs female child | 0.99 | 0.94-1.0 |
| | Family practitioner vs pediatrician | 0.36 | 0.31-0.41 |
| | Medicaid vs other insurance | 0.79 | 0.73-0.84 |

* Adjusted for age group and time-dependent covariates for the years 1998 and 1999.
* See Table 1 for age group characteristics.
CI = confidence interval.
younger age stratum who regularly visited family practitioners, so statistical power for that comparison was poor, but the risk ratio was similar to that of the larger group.

When covariates of interest were combined into a multivariate regression model, the factor most strongly related to vaccination in the younger age stratum, other than age group, was number of children in the family (Table 3). The primary clinician’s specialty was also strongly related, although statistical power was poor because of small numbers in the family practitioner category. Income, education, and SES were less influential in the multivariate model than in the univariate models. Medicaid status was not included in this model because it was highly correlated with SES.

In the multivariate model for the older age stratum, as in the younger age stratum, the primary clinician’s specialty and the number of children in the family were strongly related to vaccination (Table 3). In addition, vaccination was positively associated with high family income, excellent parental health status, and parent’s receipt of a flu shot and was negatively associated with parental history of depression. Variables that were less influential in the multivariate model than the univariate models included single-parent status, history of cigarette smoking, parent’s education level, and self-reported SES.

DISCUSSION

We found several factors to be related to the likelihood of varicella vaccination in our pediatric population. One consistent relationship was with clinician specialty; children cared for by family practitioners were only about half as likely to be vaccinated as were patients of pediatricians. A large retrospective cohort study previously reported a similar finding for compliance with the routine second varicella vaccination dose among four- to six-year-olds. A 1996 survey of physicians in Rochester, NY, found that the physicians most likely to offer the varicella vaccine were pediatricians. Our results are also consistent with those of parent surveys conducted by Taylor and Newman and Freeman and Freed, in which clinicians powerfully influenced parental decisions to accept the varicella vaccine.

Clinician specialty differences in vaccination practices could be addressed by a systemwide vaccine in-reach strategy such as a nurse reviewing the child’s immunization record at every medical or dental office visit and flagging the chart for the clinician with immunizations needed. Another helpful tool is access to the routine childhood immunization schedules, either electronically or as a pocket card, for each clinician seeing children.

Family demographics and health factors were also related, especially in children older than 1 year on date of vaccine introduction. For the older children particularly, lower vaccination rates were associated with poorer parent health as reflected in reporting depression, less than excellent health, or lack of health awareness as reflected in cigarette smoking or not getting a flu shot. The consistently inverse relationship between number of children in the family and immunization, independent of family income or parent education, may be related to parental experience with uncomplicated varicella; the highly contagious nature of varicella makes it likely that children in larger families had more opportunities for

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Age Groups 1-6* (N = 664)</th>
<th>Age Groups 6-9* (N = 1817)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk ratio (95% CI)*</td>
<td>Multivariable adjusted risk ratio (95% CI)*</td>
</tr>
<tr>
<td>Family practitioner vs pediatrician</td>
<td>0.46 (0.19-1.1)</td>
<td>0.35 (0.12-1.1)</td>
</tr>
<tr>
<td>Nonwhite vs white</td>
<td>1.4 (0.99-1.9)</td>
<td>1.1 (0.73-1.6)</td>
</tr>
<tr>
<td>2 children in family vs 1</td>
<td>0.81 (0.62-1.1)</td>
<td>0.87 (0.64-1.2)</td>
</tr>
<tr>
<td>3 or more children in family vs 1</td>
<td>0.76 (0.56-1.1)</td>
<td>0.65 (0.46-0.91)</td>
</tr>
<tr>
<td>Self-reported low socioeconomic status</td>
<td>0.85 (0.69-1.0)</td>
<td>1.0 (0.74-1.3)</td>
</tr>
<tr>
<td>Medicaid recipient</td>
<td>0.76 (0.56-1.0)</td>
<td>Not in model</td>
</tr>
<tr>
<td>Family income &lt; $20K vs $20K-$49K</td>
<td>1.1 (0.76-1.5)</td>
<td>1.3 (0.85-2.0)</td>
</tr>
<tr>
<td>Family income ≥ $50K vs $20K-$49K</td>
<td>1.2 (0.93-1.5)</td>
<td>1.1 (0.84-1.5)</td>
</tr>
<tr>
<td>Parent college graduate vs high school or less</td>
<td>1.3 (1.0-1.7)</td>
<td>1.2 (0.85-1.6)</td>
</tr>
<tr>
<td>Parent aged 30 years or older vs &lt; 30 years</td>
<td>1.2 (0.99-1.5)</td>
<td>1.2 (0.93-1.5)</td>
</tr>
<tr>
<td>Parent flu shot previous year (no vs yes)</td>
<td>0.80 (0.61-1.0)</td>
<td>0.83 (0.61-1.1)</td>
</tr>
<tr>
<td>Parent health (not excellent vs excellent)</td>
<td>0.95 (0.85-1.1)</td>
<td>0.91 (0.80-1.0)</td>
</tr>
<tr>
<td>Parent smokes cigarettes</td>
<td>0.88 (0.67-1.2)</td>
<td>1.1 (0.79-1.5)</td>
</tr>
<tr>
<td>Parent history of depression</td>
<td>0.85 (0.59-1.2)</td>
<td>0.88 (0.59-1.3)</td>
</tr>
<tr>
<td>Single parent</td>
<td>0.95 (0.74-1.2)</td>
<td>0.98 (0.70-1.4)</td>
</tr>
</tbody>
</table>

* See Table 1 for age group characteristics.

† Each model contained dummy variables for all age groups except the reference group (Age Group 6) and time-dependent covariates for calendar years 1998 and 1999 (both yes/no).

‡ Each model contained dummy variables for all age groups except the reference group (Age Group 6), time-dependent covariates for calendar years 1998 and 1999 (both yes/no), and the other variables listed in the table.

CI = confidence interval; flu shot = influenza vaccination; K = 0.00.
exposure to the disease. The more often that parents observe uncomplicated varicella in the family, the less likely they may be to contact the medical system for care or advice about varicella or to immunize their children to prevent disease. Parental perception that varicella is a mild disease is common; a phone survey about varicella vaccination of 14- to 17-month-olds performed 18 months after Canada licensed the vaccine revealed that 90% of parents perceived varicella as a benign disease. The inverse relationship between family size and varicella immunization was also described in a study from a health care organization in Israel; investigators reported that children in families with 3 or fewer children were significantly more likely to be vaccinated than those in larger families.

Studies of public acceptance of other pediatric vaccines have found that likelihood of vaccination is lower in single-parent families, families with larger numbers of children, families with young primary caregivers, and families of lower SES. These studies’ results are similar to ours, although only one was conducted in a prepaid Health Plan. A strategy to improve immunization uptake among these families could include a text message or e-mail appointment reminder sent to parents with information including which immunizations are due. Offering to immunize siblings who accompany their patients at the office visit may also help clinicians encourage more parents to vaccinate their children.

A limitation of this study is that a fairly large proportion of varicella disease is not reported to the medical system (approximately 30% in this Health Plan), and so some children who were not candidates for varicella vaccination because of a history of varicella are included in this analysis. For the analyses linked to the membership survey, we had educational and health information on 1 parent only. Some of the survey information was old (up to 8 years old) and may not have accurately described the current situation of the family during the study period. These member surveys were designed to collect information on demographics, health behaviors, and satisfaction with health services, but they did not ask specific questions about knowledge and attitudes on vaccines. Because our study population belonged to a prepaid Health Plan, the weak association we found could not be to a prepaid Health Plan, the weak association we found.

Strengths of this study include the large number of subjects, the relatively complete automated immunization database, and the access to self-reported personal information on the family that was collected separately from information on vaccine status.

The incorporation of varicella vaccination into KPNW’s clinical guidelines and performance measures, combined with state requirements for varicella vaccination for school entry (Oregon in 2000 and Washington in 2008) have likely reduced parental reluctance to vaccinate in this population. However, understanding parental factors related to vaccine acceptance will help focus educational efforts with the introduction of new routine immunizations in the future. In addition, identification of clinician specialty differences in vaccination practices will help health care organizations improve procedures and staff education to increase vaccine coverage.

Disclosure Statement

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

This research was supported by the Centers for Disease Control and Prevention Vaccine Safety Datalink, Task Order 0967-047, Contract 200-0967, Atlanta, GA.

Acknowledgments

The authors wish to thank the following contributors to this work: Terry Kimes and Karen Riedlinger, MT, MPH, for computer programming support; Jill Mesa for study coordination; and Jill Pope and Stephanie Irving, MS, for editorial assistance.

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

Family Characteristics Associated with Likelihood of Varicella Vaccination

References

Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care

Lee D Jacobs, MD; Thomas M Judd, MS; Zulfiqar A Bhutta, MD, PhD

ABSTRACT
The neonatal, infant, child, and maternal mortality rates in Haiti are the highest in the Western Hemisphere, with rates similar to those found in Afghanistan and several African countries. We identify several factors that have perpetuated this health care crisis and summarize the literature highlighting the most cost-effective, evidence-based interventions proved to decrease these mortality rates in low- and middle-income countries.

To create a major change in Haiti’s health care infrastructure, we are implementing two strategies that are unique for low-income countries: development of a countrywide network of geographic “community care grids” to facilitate implementation of frontline interventions, and the construction of a centrally located referral and teaching hospital to provide specialty care for communities throughout the country. This hospital strategy will leverage the proximity of Haiti to North America by mobilizing large numbers of North American medical volunteers to provide one-on-one mentoring for the Haitian medical staff. The first phase of this strategy will address the child and maternal health crisis.

We have begun implementation of these evidence-based strategies that we believe will fast-track improvement in the child and maternal mortality rates throughout the country. We anticipate that, as we partner with private and public groups already working in Haiti, one day Haiti’s health care system will be among the leaders in that region.

INTRODUCTION: THE HAITI CRISIS
Child and Maternal Mortality Rates
The World Health Organization (WHO), US Agency for International Development, United Nations International Children’s Emergency Fund (UNICEF), and other international agencies have published several years of annual child, neonatal, and maternal (CNM) mortality rates for countries around the world. Although the rates and annual trends are important in understanding the extent of a country’s problems, a comparison of the results with regional countries adds valuable information to the understanding of the magnitude of a crisis. This is especially true when one compares Haiti’s mortality rates with those of other countries in the Caribbean.

According to UNICEF, Haiti has the highest mortality rates for infants, children under age 5 years, and pregnant women in the Western Hemisphere.1 (For an explanation of terms, see Sidebar: Definitions.) There were an estimated 265,000 live births in Haiti in 2013,2 underscoring the magnitude of the number of deaths in each CNM category per year.

Neonatal Mortality Rate
In Haiti, of all the deaths of children under 5 years of age, 34% died in the neonatal period, with approximately 90% of these deaths occurring in the first week of life.3 In 2013, there were an estimated 6800 neonatal deaths in Haiti on the basis of a neonatal mortality rate of 25 per 1000 live births, which was unchanged since 2010.1,3 This rate is much higher than the annual mortality rate in other Caribbean countries, including the Dominican Republic’s rate of 16 per 1000.4

Infant Mortality Rate
Haiti’s infant mortality rate was 55 per 1000 live births in 2013,1,4 which means that 75% of childhood deaths occur before a child’s first birthday. This rate was at least twice any other Caribbean country and much higher than the neighboring country, the Dominican Republic (21/1000). Haiti’s infant mortality rate is most certainly the highest in the Western Hemisphere,2 and is more in line with the 2013 reported rates of Liberia (54/1000) and Ghana (53/1000).4

Child Mortality Rate
In 2013 there were more than 20,000 deaths in children under age 5 years.2 The child mortality rate in Haiti in 2013 was 73 per 1000 compared with other Caribbean countries, which had an average rate of 15.2,5 Of the 75% of childhood deaths that occur before the first year of age, 34% occur during the neonatal period; the remaining 25% of childhood deaths occur between the first and fifth birthdays.6

Maternal Mortality Ratio
In 2013, the maternal mortality ratio in Haiti was 380 per 100,000 live births, with more than 1000 maternal deaths; this ratio was, unfortunately, not greatly different from the 2010 mortality ratio of 350.3 The ratio of 380 was much...
higher than the average of regional Caribbean countries (68) and similar to the rates of Rwanda (320), Sudan (360), and Afghanistan (400).\textsuperscript{3}

**Causes of Child, Neonatal, and Maternal Deaths**

To determine the most appropriate interventions to confront this crisis, it is important for us to first understand the various contributing factors to these unacceptably high mortality rates in Haiti. A literature review of the various causes of the CNM mortality in low- and middle-income countries suggests that multiple factors usually contribute to the mortality rates. Overall, the diseases listed are almost universally preventable and treatable, and the causative situations are generally correctable.

**Poverty**

One reason may seem obvious: poverty.\textsuperscript{4} Haiti is the poorest country in the Western Hemisphere and one of the poorest in the world.\textsuperscript{5} Although the factors contributing to the high CNM death rates in Haiti are complex, it will become apparent that poverty is a contributing factor for each specific cause as they are assessed. The effect of poverty is best illustrated by contrasting Haiti and the Dominican Republic, two countries sharing the same island with populations of similar sizes. As mentioned earlier, all the CNM mortality rates are much lower in the Dominican Republic than in Haiti. Almost as dramatic is the comparison of the economic measures of both countries, in which the Dominican Republic has one of the most robust economies in the region as opposed to Haiti, which is at the bottom of the scale.\textsuperscript{6}

**Neonatal and Infant Causes**

According to the WHO, more than 80% of all global neonatal deaths are caused by preterm birth complications, newborn infections, and birth asphyxia.\textsuperscript{6,7} Complications arising from preterm births are now the leading cause of neonatal mortality worldwide. In 2012, prematurity was a cause in 17% of childhood deaths under 5 years old and in approximately 35% of all neonatal deaths.\textsuperscript{8} Haiti’s preterm birth rate in 2010 was 14.1%, ranking it 19th among countries with the highest preterm birth rates, similar to Bangladesh and Liberia. During the same period, the Dominican Republic’s preterm birth rate was 10.8%, ranking it much lower (79th) among all countries.\textsuperscript{9} We are not aware of any Haitian neonatal mortality data based on gestational age.

The WHO has defined low birth weight as the *weight at birth of less than 2500 g (5.5 lb).*\textsuperscript{10} Infants weighing less than 2500 g are approximately 20 times more likely to die than heavier babies.\textsuperscript{9} In Haiti, the average percentage of low-birthweight infants in 2008 to 2012 was 23%, and during the same period in the Dominican Republic the percentage of low birth weight was 11%. These percentages from both countries were unchanged from 2000 assessments.\textsuperscript{1}

In low- and middle-income countries, the major contributors to the death of infants from 28 days to 1 year are birth asphyxia, injuries, low birth weight, malnutrition, infectious diseases such as diarrhea and pneumonia, and poor home sanitation.\textsuperscript{11} These occur more often in children born in remote rural areas or in poor households, or to a mother with limited education. These demographic factors result in children who are undernourished, have vitamin and iron deficiencies, and do not receive appropriate immunizations.\textsuperscript{12}

**Child Causes**

Injuries are by far the most common cause (66%) of death in children aged 1 to 5 years, followed by pneumonia (11%) and diarrheal diseases (8%).\textsuperscript{13} The lack of availability of pneumonia treatment in Haiti is one explanation for children dying at such an appalling rate compared with other Caribbean countries.\textsuperscript{1,13} The percentage of children younger than age 5 years with suspected pneumonia taken to appropriate health care practitioners reached 31% in 2006 and 38% in 2012. The same year, only 46% of children younger than age 5 years with suspected pneumonia received antibiotics.

**Maternal Causes**

Most maternal deaths occur during childbirth and the first week post partum.\textsuperscript{14,15} Worldwide in low- and middle-income countries, 5 factors contribute to 80% of maternal deaths: heavy bleeding after birth, hypertension, infections, obstructed labor, and unsafe abortions.\textsuperscript{16}

In 2013, the WHO published regional maternal mortality rates for the Caribbean,\textsuperscript{1,7} identifying the most common causes of maternal death as hemorrhage (23%) and hypertension (22%). However, the situation is different in Haiti, where the primary cause of maternal death is preeclampsia/eclampsia (37.5%), with hemorrhage the second cause (22%).\textsuperscript{5} In a WHO analysis, Bilano and associates\textsuperscript{17} studied 276,388 mothers and their infants in low- and middle-income countries to determine the prevalence and risk factors associated with preeclampsia and eclampsia. They identified 3 major risk factors: chronic hypertension, obesity, and severe anemia (hemoglobin level < 7.0 g/dL). Although we are not aware of the overall rates of anemia in Haitian pregnant women, obesity rates are less than regional averages.\textsuperscript{1} However, Haitian women do have a significantly higher rate of high blood pressure compared with other Caribbean countries (33% vs 26.3% in 2008).\textsuperscript{1} This observation has obvious ramifications when determining which screening risk factors are used to lower maternal mortality in Haitian women.
Infectious Diseases

Human immunodeficiency virus (HIV), malaria, and tuberculosis are common infectious causes of child and maternal mortality in Haiti. According to UNICEF, infection with HIV is much more prevalent in Haiti than in other countries in the region. It estimates that 5.6% of Haitians aged 15 to 49 years, including about 19,000 children, live with HIV or acquired immune deficiency syndrome, and antiretroviral drugs are in short supply. In 2012, there were 78,000 women living in Haiti with HIV compared with 22,000 in the Dominican Republic. According to the CDC, 4330 HIV-positive pregnant women were identified in Haiti in 2012, and 83% had antiretroviral therapy initiated.

Malaria in pregnancy contributes to substantial perinatal morbidity and mortality. Chloroquine-sensitive Plasmodium falciparum malaria is endemic in Haiti, resulting in a high rate of transmission. In Haiti in 2012, few households had insecticide-treated mosquito nets, with only an estimated 9% of pregnant women sleeping under a protective net.

The incidence rate of tuberculosis in Haiti from 2010 to 2014 was 206 cases per 100,000, basically unchanged over the past decade. During the same timeframe, the incidence rate in the Dominican Republic was 60 per 100,000.

Geographical isolation: As reflected in the Sidebar, Haiti is the third largest country in the Caribbean. The main population density, Port-au-Prince, is distributed. Approximately 45% of Haitians live in rural areas,1,25 as opposed to 30% of the Dominican Republic’s population residing in rural areas. Rural residents have limited access to basic health care and to qualified medical facilities.1

In rural areas in Haiti, less than half of the households have access to improved sources of drinking water, contrasted with 88% in urban areas. One-third of the households must travel 30 or more minutes to access drinking water.2 Also in rural areas, 38% of households have no toilet facilities compared with only 7% in urban areas.12 Only 11% of people in the Haitian countryside have access to energy compared with 63% in the country’s cities.26 Not surprisingly, UNICEF reports disparities of urban and rural populations for the prevalence of underweight children and diarrhea treatment.1 Children living in rural Haiti have a 46% greater chance of dying before their fifth birthday than their counterparts in urban areas.6

Haiti Demographics

| Population: 10,573,000, with 2.3 million people (21%) living in the metropolitan area of the capital, Port-au-Prince.1 Overall, the population living in urban areas is 55% (regional average, 80%).2 |
| Size: Haiti’s 27,560 square km is approximately the size of Vermont, which has a population of 626,000.3 Haiti is the third largest country in the Caribbean; only the Dominican Republic and Cuba are larger. |
| Administrative Division: The country is subdivided into 10 departments (provinces), each having a capital city. |
| Income: Haiti is a poor country, ranking 168 of 187 on the United Nations Human Development Index.4 |
| Transportation: More than half of the highways are unpaved. From Port-au-Prince, it takes approximately 4 hours to drive the 245 km to Cap-Haitian, a city on the northern coast of Haiti, and approximately 3 hours to drive the 200 km from Port-au-Prince to Les Cayes, a city to the south. There are 15 airports throughout the country, 10 of which are paved. The main international airport is located just outside and north of Port-au-Prince. Flying time from Miami is 1.5 hours and from Atlanta is less than 3 hours. |

Cost barrier: As noted earlier, poverty is a major contributing factor and most certainly adversely affects access. The evidence suggests that the financial barrier to health care is one of the most important obstacles for pregnant women needing access to obstetric care. In Haiti, 47% of the population lack access to health care primarily because of financial or geographic barriers, and 50% of households say they had not accessed health services when needed because of the high costs associated with services. If a pregnant woman cannot pay for a midwife or a physician, she will most likely be delivering the baby at home without any skilled assistance, resulting in the large number of births without a skilled attendant present as noted later in this section.

Transportation: Motorized transport in rural areas of this mountainous country is almost nonexistent. Most roads are in poor condition, and only 5% of rural Haitians have access to a paved road.

Inadequate Health Care Facilities
The earthquake of January 12, 2010, had terrible consequences for the Haitian society and for the Haitian health sector. Sixty percent of the Haitian state infrastructure was destroyed, including more than 50 health institutions with losses and damage in the health sector that exceeded 200% of annual expenditure in health from all sources.

Even before the earthquake, the number and quality of health care facilities were inadequate to care for a population exceeding 10 million. Over the years, we have learned from our visits to hospitals that a major contributing factor for the CNM deaths in Haiti is a major shortage of neonatal, pediatric, and adult intensive care units. Probably no other observation underscores the poor condition of the Haiti health care system than the dire shortage of neonatal intensive care units. Despite the very high rates of prematurity, lifesaving neonatal care is almost completely unavailable to the vast number of babies needing intensive assistance, especially when they are born in rural Haiti.

Health Care Practitioners—Inadequate Numbers and Training
The health workforce has been identified as the key to effective health services because the shortage of health workers in developing countries is the most important constraint to attaining improvement in maternal health to reduce child mortality.
In Haiti, there is a tremendous undersupply of physicians and other health professionals. The number of physicians, nurses, and midwives is 4 per 10,000 population, which is far below the WHO recommendation of 23 doctors, midwives, and nurses per 10,000 population. When contrasted with the regional average, the numbers are even more striking. Per 10,000 population, Haiti has less than 1 physician (regional, 20.8) and less than 1 nurse and midwife (regional, 45.8). There are no data for pediatric and obstetric physician specialists.

In our experience, physicians in Haiti are extremely capable and very interested in learning. However, their training has been very limited, with little outside influence. As we have learned from our onsite assessments, inadequate equipment and insufficient supplies of medication further compromise their practices. To produce the larger numbers of trained medical personnel needed to improve care, Haiti and partner organizations must undertake interventions to support high-quality medical, nursing, and allied health schools and resident programs, as a means to offset the brain drain and support national needs.

The problem of a shortage of trained medical personnel is exacerbated by the large exodus of professionals to Canada and to the US, a fact that has frustrated the health care leaders working in Haiti to improve conditions. Later in this article, we will address how this Haitian diaspora, estimated to be more than 1.5 million Haitians, can be a valuable part of the solution to fast-track improvements in this country’s health care.

Low Percentage of Skilled Attendants at Deliveries

Industrialized countries in the early 20th century halved the maternal mortality rate by providing professional midwifery care at childbirth. The importance of births attended by skilled health personnel is considered a key indicator for improvements in maternal health.

As mentioned earlier, in Haiti in 2012, only 37% of deliveries had a skilled attendant present; this remains basically unchanged in 2016. The average of other Caribbean countries was 94% in 2012. If the poorest 20% of pregnant Haitian mothers are considered, only 9.6% will have a skilled attendant at birth compared with 78% of the richest 20%. The low rate of attendant-assisted births in Haiti is even more striking when the 2008 to 2012 percentages of skilled attendant rates are subdivided into urban births (59.4%) and the extremely low percentage for rural births (24.6%). It is not difficult to understand why the neonatal and maternal death rates in Haiti are so high when one understands that 63% of countrywide deliveries and 75% of deliveries in rural settings were not attended by a provider skilled in obstetrics (physician, nurse, or nurse-midwife).

Low Percentage of Prenatal and Postnatal Visits

Of pregnant women in Haiti, 40% do not have an antenatal care visit before their fourth month of pregnancy. Over all of Haiti in 2012, the percentage of mothers receiving antenatal care (at least 4 visits) was 67%. The regional average was 86% for postnatal care within 2 days of delivery. During the 41 days after giving birth, 61% of women did not have a postnatal checkup.

High-Risk Deliveries in Nonqualified Health Facilities

Only 25% of women deliver in institutions, with 78.2% of women in the richest quintile delivering in health centers vs 5.9% of women in the poorest quintile. Most facilities are in urban areas, and even if mothers could make it to a facility, most facilities are generally not staffed or equipped adequately to provide the necessary obstetric care for complicated deliveries.

STRATEGIES TO ADDRESS THE CRISIS

These statistics make it easy to understand why the CNM mortality rates are so much higher in Haiti than in other countries in the region. Although the situation is complex, it is clear that major changes are needed and must happen soon if the country is to successfully address this crisis and to improve the overall quality of medical care in the country. There are challenges to making these changes happen, yet studies suggest that with coordinated and collaborative efforts addressing each step of care, fewer children and mothers will die.

To address the child and maternal health crisis, for the past 2 years Bethesda Referral & Teaching Hospital, Inc (BRTH), has been implementing 2 primary strategies: 1) construction of a 225-bed central referral and teaching hospital that will provide specialty care for communities throughout the country and 2) development of countrywide community care grids, a network of defined geographic populations, to facilitate the implementation of frontline interventions.

Central Referral Hospital

BRTH, a private, not-for-profit specialty teaching hospital, will be centrally located in the new Port Lafito in close proximity to the international airport and Port-au-Prince to facilitate transfers from across the country. Although there are capable hospitals in Haiti, most focus on primary and emergency care. To address the unacceptably high Haitian CNM mortality rates, BRTH will focus in the initial phase on maternal and child specialty health care, and subsequent phases will include medical and surgical subspecialties.

BRTH will provide access to care for high-risk infant and maternal patients throughout all of Haiti. It will support the implementation of evidence-based community interventions countrywide through innovative community care grids (described in the next section). Additionally, high-risk obstetric and pediatric patients will be triaged and transported from the community network to the hospital as necessary. An extensive communication network, transportation capabilities, and state-of-the-art telemedicine will facilitate the movement and care of patients.

The uniqueness of this model is that the BRTH staff will consist at any one time of more than 100 North American short-term health care volunteers providing one-on-one mentoring for physicians, midwives, and nurses from the Haitian medical community. This type of one-on-one teaching approach is not being used elsewhere in Haiti, to our knowledge.
To provide lodging for the visiting North American medical volunteers, the construction plans will include an adjoining guest hotel. As the need for visiting North American teachers diminishes over the years, the hotel will be converted to hospital beds, providing a cost-effective basis for future hospital expansion.

Improvement of the overall knowledge and procedural skills of the health care practitioners and enhancement of the specialty care referral infrastructure should improve health care in Haiti by any measurement.

The site for the hospital, Port Lafito, is a new, private economic zone covering more than 404 hectares (1000 acres) of oceanfront land developed 19.2 km (12 miles) north of Port-au-Prince. This project is a $145 million investment that includes a new port for container ships and a large industrial-free zone and business park, as well as 24-hour security; a residential area and country club will be included in later phases. The developers anticipate that the manufacturing zone will generate up to 20,000 new jobs by 2020. Clearly, this mixed-use development is one of the most exciting things to happen to Haiti in recent memory.

This new project is owned and developed by the GB Group from Miami, one of the leading private industrial groups in the Caribbean. The chairman is Gilbert Bigio, a Haitian from one of the most respected families in Haiti. Mr Bigio, his family, and the GB Group understand the potential impact of BRTH and for that reason have generously donated 8.1 hectares of valuable property in the port area for construction of the hospital. BRTH and the GB Group are forming a strong partnership because both organizations have the same vision of expediting improvements in the quality of life for all Haitians.

Program Guiding Principles

The following principles will provide direction and ensure the successful implementation of the strategies:

Partnerships

A strong partnership with the Haitian community is essential. Since 2013, we have involved the Haitian medical, political, and social leadership in the development of this plan. The response from the Haitian leaders has been overwhelmingly positive. We believe that our partnership with them is essential because Haitians want to be, and should be, involved in resolving this crisis in their country. Also important are effective partnerships between BRTH and North American health care organizations, governmental agencies, and nonprofit organizations—a critical factor for success of the entire BRTH project that will be discussed later.

Inclusion

As are many other hospitals in Haiti, BRTH is a nonprofit Christian organization that highly values volunteers, employees, and patients of all faiths and ethnicities. It will take a large team of compassionate, talented medical volunteers to confront this crisis in Haiti, and so are all needed and all are welcome.

Evidence-Based Holistic Care

The care processes and policies of BRTH will be in accordance with US standards and to the level required by accreditation agencies such as the Joint Commission International. We will strive to provide medical care whose basis is strong clinical evidence while considering the total need of patients including the physical, emotional, social, and spiritual.

Safety and Security

The hospital and guest hotel will be constructed in accordance with earthquake building codes and consider safety and security as prime design criteria. The GB Group has provided us with a tremendously secure site at Port Lafito, away from the population density of Port-au-Prince but centrally located. We plan to have intense security for entrance onto the hospital grounds as well as a high level of security throughout the hospital. We have port security outside and then security to enter the compound. Overall, we will provide employees and patients a secure environment and be able to offer volunteers a safe and meaningful experience.

Countrywide Interventions

These interventions will reflect the primary objective, which is to create partnerships to improve maternal and child health care in all of the departments of Haiti, regardless how distant from Port-au-Prince.

Financial Responsibility

Remuneration for hospital care will be based on a sliding-scale fee schedule, enabling care for referred patients to be provided without charge for those with no or limited income. However, we do not want to undermine the economics of local hospitals and practitioners. We will always support our hospital partners in Haiti by making certain that our financial approaches and general operations do not compromise their revenue or the revenue of individual practitioners in Haiti.

Adaptability

Because our model is unique, ambitious, and complex, the interventions we deploy must be regularly assessed and adjusted accordingly.

Fast-Tracking Improvements in Child, Neonatal, and Maternal Mortality

In this article, we have identified the major underlying factors for the high death rates of children and mothers in Haiti. The literature is clear; if mortality rates for neonates, children, and mothers in low- and middle-income countries are to decrease, it is essential that major improvements be achieved throughout the entire health system. Interventions must be implemented across the entire sector of care starting in the home, then in the community in each department, and finally extending to a functional referral facility. As stated by Bhutta et al: “There is not a simple and straightforward intervention, which by itself will bring maternal mortality significantly down; and it is commonly agreed that the high maternal mortality can only be addressed if the health system is effective and strengthened.” We envision that BRTH, along with private- and public-sector partnerships in the community care grid network, will strengthen the health care infrastructure in Haiti by
implementing interventions that will address the primary contributing factors identified in this article.

The following are the six major interventions that BRTH is implementing:
1. implement evidence-based interventions in the community
2. develop community care grids
3. increase the number and skills of health care professionals
4. provide affordable, high-quality health care
5. leverage communications and technology
6. transport patients to the hospital.

**Implement Evidence-Based Interventions in the Community**

Although the literature is not robust in identifying evidence-based interventions, there are sufficient data from several meta-analyses to understand the complexities of the problem, to identify proven interventions, and to propose strategies for low- and middle-income countries such as Haiti. We are implementing only evidence-based interventions that have been proved to be cost-effective, are culturally relevant, and can be deployed successfully. Frontline community interventions include preconception and prenatal maternal care, delivery care, and postpartum maternal, neonatal, and infant care.

The Sidebar: Evidence-Based Interventions lists evidence-based interventions based on several meta-analyses. The major improvements in child survival since 1990 are partly attributable to affordable, evidence-based interventions against the leading infectious diseases, use of insecticide-treated mosquito nets, rehydration treatment of diarrhea, nutritional supplements, and therapeutic food.

**Package of Interventions:** Although the value of several interventions has been validated over time by several studies, it is important to emphasize that to lower mortality rates in children and mothers, implementation of multiple interventions together (a “package”) make much more of an impact than a single intervention. An example of a package of interventions is a World Bank study presented multiple key countrywide factors necessary for reducing mortality rates:

- increased availability of a skilled birth attendant
- increased availability of healthcare facilities to provide skilled birthing care
- appropriate service costs for the setting
- strong policy guidance for delivery of care
- a functional referral system, beginning with practitioners at the community level
- accountability for practitioners’ performance

**Essential Obstetric Care:** Essential (or emergency) obstetric care is another example of a package of interventions that, when implemented with prenatal interventions, has proved to be extremely effective in preventing mother and infant mortality and for that reason must be a component of any strategy to reduce CNM mortality. Campbell and Graham underscore the importance of this package: “Capacity to provide adequate and timely emergency obstetric care is, however, the minimum standard a health system is ethnically obliged to provide to begin to address maternal mortality.” The six components of essential obstetric care are listed in the Sidebar:

- Evidence-Based Interventions (under Childbirth).
- Most of the capabilities on this list are not available at departmental health care facilities in rural Haiti, making it imperative that, when indicated, children and mothers can be transferred to a fully qualified central facility that can provide essential obstetric care.

**Develop Community Care Grids**

To assist departments throughout Haiti in implementing necessary interventions and to address the top 3 causative factors—accessibility barriers, the low percentage of skilled attendants, and the low percentage of prenatal visits—we have created a countrywide networking and community training approach that we call community care grids. Beginning with Haiti’s 10 departments, we have divided the country into geographic, population-based “grids.” Departments will be subdivided into additional grids as indicated by population densities or geographic impediments. We anticipate that around 20 grids will eventually be identified. These grids will enable us to collaborate at the local level to implement home-based and community-based interventions, to maximize the outreach strategies, and to facilitate timely referrals to BRTH.

**Coordinators:** To support this strategy, BRTH will hire, train, and oversee community care grid coordinators for each of the geographic grids. The coordinators’ responsibilities will be as follows:

- To identify community leaders, including public health officials, church clergy, medical leaders (physicians, midwives, nurses), nongovernmental organizations (NGOs), and any government agencies active in the community within their assigned grids. All these individuals and organizations together will form the community care team
- To define, in consultation with the local community care team, the geographic border of the grid as well as population estimates
- To assess the CNM capabilities of the local health care system, including the capability of the local health facilities, the availability of medical personnel, and the level of financial barriers to service
- To facilitate a collaborative process with the community care team to identify and to prioritize the best strategy for comprehensively deploying the frontline CNM package of interventions in their community
- To assist the community care team members in identifying high-risk individuals (initially pregnant or new mothers and children) as well as to provide the health care professionals with details about how to refer patients to BRTH for specialty care
- To coordinate the appropriate level of care for each patient by facilitating the referral of patients to BRTH or to other locations when the hospital is at capacity or when primary care and medical and surgical specialty services are not available in Phase 1 at BRTH.

We believe that this community grid strategy will provide the foundation for implementing the evidence-based...
interventions targeted to families, local communities, and departments throughout Haiti. We intend to build on the work already being done by the Minister of Health's office, by several North American NGOs, and by Haitian medical personnel. To better understand how to best implement this approach, this year we have invested in the development of five pilot grid sites representing large and small communities as well as suburban Port-au-Prince and areas more remote from the city. In addition to defining the borders and population of each grid, these pilots have included CNM-related health surveys and screenings to support the interventions listed in the Sidebar: Evidence-Based Interventions. Such assessments have been done sporadically in Haiti in the past but not with the frequency and with the data elements that we will be compiling over the years in these five pilots. Additionally, we are creating a process with each pilot site's community care team that would establish more accurate health care data, including such basic information as reliable birth and death documentation. We believe these baseline data will be indispensable in assessing the value of community interventions.

**Funding:** BRTH is committed to providing the income for the grid coordinators because they will be part of the hospital staff. Additionally, since it is important for the overall mission of the hospital, BRTH will provide the telemedicine capability for each department. All other funding will come from the public- and private-sector organizations and individuals making up each community care team. We believe that individuals and institutions will be more likely to contribute funds to an NGO or church when the organization is able to demonstrate a cohesive plan to implement proven communitywide

---

**Evidence-Based Interventions**

For all stages of care, there is “strong evidence” for the capacity to move patients emergently, urgently, and electively to the nearest equipped medical facility.

<table>
<thead>
<tr>
<th>ANTENATAL CARE PACKAGE</th>
<th>CHILDBIRTH</th>
<th>POSTDELIVERY (NEWBORN)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screenings:</strong></td>
<td>• skilled birth attendants</td>
<td>• immediate assessment and stimulation</td>
</tr>
<tr>
<td>• identify high-risk pregnancy on the basis of age (adolescent screening)</td>
<td>• delayed cord clamping</td>
<td>• topical ophthalmic antibiotic drops</td>
</tr>
<tr>
<td>• laboratory screens: urine analysis “dip-stick” and sexually transmitted infections: human immunodeficiency virus (HIV) and syphilis</td>
<td>• neonatal resuscitation</td>
<td>• chlorhexidine baths: hygienic cord and skin care</td>
</tr>
<tr>
<td>• identify high risk for preeclampsia and eclampsia: hypertension and anemia</td>
<td>• active management of the third stage of labor</td>
<td>• kangaroo care (skin-to-skin contact)</td>
</tr>
</tbody>
</table>

**Nutritional Supplementation**

- multiple micronutrients: vitamin A, iron, zinc, etc
- balanced protein and energy supplements for severely malnourished women (body mass index < 20 kg/m²)

Dietary folic acid and iodine replacement incorporated into general community health food programs will be provided before conception and not as prenatal replacement. Calcium replacement will be considered in the future after an analysis of dietary calcium data in Haiti is completed.

**Immunizations**

- hepatitis B (depending on the prevalence)
- tetanus

**Case Management**

- hypertension
- diabetes
- prevention of mother-to-child transmission of HIV (including breastfeeding choices)
- preeclampsia and eclampsia: low-dose aspirin for prevention
- malaria protection: insecticide-treated bed nets and case management

**Essential Obstetric Care**

- availability of parenteral antibiotics, oxytocics, and anticonvulsants
- facilities for manual removal of the placenta
- facilities for removal of retained products of conception if necessary
- assisted vaginal delivery
- facilities for blood transfusion
- facilities for cesarean delivery

**Case Management**

- antenatal corticosteroids in preterm labor in facilities
- magnesium sulfate for eclampsia
- antibiotics in cases of premature rupture of the membranes
- induction of labor for pregnancies lasting 41 weeks or longer

**Infants and Children Younger Than Age Five Years**

- exclusive breastfeeding for six months, then continued with complementary feeding
- WASH (water, sanitation, and hygiene) interventions

**Nutritional Supplementation**

- therapeutic feeding for severe acute malnutrition

**Immunizations**

- polio
- tetanus
- pneumococcal
- rotavirus
- measles

**Case Management**

- management of diarrhea with oral rehydration solutions
- antimalarial medication as needed
- treatment of moderate-acute malnutrition
- vitamin A supplementation from six months of age
- antibiotics for treatment of pneumonia

---


interventions to save children and mothers. The challenge has not been the lack of funds; these interventions are not expensive when contrasted with the amount of money now being invested by North Americans throughout Haiti.

Collaboration: A critical success factor for this intervention will be the networking and collaboration of NGOs. In a report on low- and middle-income countries that successfully accelerated improvement in CNM care, Presern and associates noted that the one approach they all had in common was creating strong partnerships between governmental agencies and NGOs. The only way improvements in Haiti can be fast-tracked throughout the country will be through the networking and collaboration of large international organizations and foundations, as well as the smaller North American churches and other NGOs in the community in which they are working. Most of the North American NGOs work in outlying regions to provide valuable support to communities such as the building and equipping of clinics, schools, and orphanages, while also providing episodic medical and optical clinics. Although the exact number of NGOs and other humanitarian organizations working in Haiti is uncertain, the number ranges from several hundred to more than 1000.

During the summer months, planes to and from Haiti carry hundreds of short-term humanitarian workers from all over North America. In our experience, however, most of these North American churches and other NGOs work almost completely in isolation without coordinated strategies. Although their contributions fill major gaps in rural settings, there is almost no communication or large-scale networking efforts across these various entities, and collaboration and sharing of resources is extremely uncommon.

Because not all NGOs have a good record of working together, an important question is why would they work together on community care grid teams. Many North Americans who have been involved in ministry in Haiti are probably aware of an infant or a mother who has died of a preventable illness, including birth complications, or children dying of infections. When NGOs realize how the proposed community grid strategies will save the lives of mothers and babies, including the lifesaving care available at BRTH, we believe that for the first time these North American churches and organizations will have a compelling reason to come together and collaborate.

Increase the Number and Skills of Health Care Professionals

The inadequate number and training of health care practitioners must be reversed to accomplish and sustain improvements in mortality rates. No other intervention will succeed until there are adequate numbers of high-quality, accessible Haitian-trained physicians, nurses, midwives, and other health care personnel. For this reason, BRTH will focus on training and employment to ensure the sustainability of quality and accessible medical care well into the future.

As a specialty teaching hospital, there will be extensive learning opportunities for Haitian health care personnel, including, but not limited to, physicians, midwives, nurses, nurse practitioners, residents, and students from all disciplines. Also included in training will be x-ray and laboratory technicians, hospital administrators, hospital food preparation, security, and maintenance personnel.

For this training to occur, there must be a strong partnership between BRTH and the Haitian medical community. We have involved leaders from hospitals, medical schools, and the Minister of Health’s office to understand their needs and plan together on how best to partner.

Training Approach: Our objective is to provide direct supervision and teaching of both cognitive and procedure skills for Haitian community physicians, midwives, medical students and residents, nurses, and other hospital personnel. Training at BRTH will be defined as one-on-one instruction and supervision, an approach not generally used in Haiti. The training will be based on established curriculum jointly developed by Haitian and North American educational leaders. Additionally, we intend to partner with present medical, nursing, and pharmacology schools in Haiti to provide educational opportunities.

Bethesda Recertification Program: To maximize educational efforts that will sustain health care improvement throughout Haiti, we plan for the primary teaching target group to be practicing community physicians, midwives, and specialty nurses. They will be invited to participate in BRTH’s medical education recertification program. It has been our experience that the Haitian medical community has always been receptive to outside high-quality teaching and that it values such educational certification opportunities.

Components of the recertification program include the following:

- For most physicians, midwives, and nursing specialists the duration of involvement to receive the certification will be two years
- There will be a minimum weekly four-hour commitment, for which time the practitioner will be paid
- Recertification tests include written and practical examinations after the first year and a final examination after the completion of two years
- Updates will be offered to those professionals completing recertification through special educational events offered in the future
- The Haitian physicians and nursing specialists on BRTH’s staff will either be enrolled in the certification program or, at a later time, have completed it.

We believe that with intensive training, along with the availability of quality employment opportunities, the number of skilled health care professionals will increase to a level necessary to provide high-quality CNM coverage throughout the country. However, there must be good employment opportunities or these trained practitioners will consider leaving Haiti. It is our experience that Haitians do not want to leave, but with the lack of work they may believe they have no choice. In fact, we have learned from interviews during our needs assessment that many Haitian-American practitioners would like to return to Haiti if conditions improve. We will provide training and job opportunities at BRTH, and only
then will the exodus from Haiti to the US and Canada stop being such a drain on the Haitian health care system.

A critical success factor for this intervention will be North American volunteers: This intervention is dependent on the participation of large numbers of North American short-term volunteer physicians, midwives, specialty nurses, and other health care personnel. We have made the assumption that most North American health care individuals would like to use their skills to provide service to those in need, whether in their community or around the world, especially if their skills can be applied with meaningful results. Although primary care physicians and nurses have opportunities through several volunteer organizations to serve overseas, this is not the case for specialists. There are very limited opportunities for physician specialists such as neonatologists, obstetricians, and surgeons to use their skills outside their practices. The same is true for midwives and specialty nurses, such as neonatal nurses and pediatric intensive care unit nurses. BRTH will provide just such a high-quality, safe, and meaningful teaching experience for North Americans to make a difference in Haiti. We believe that North American health care professionals from all disciplines and practices will want to be involved in such an endeavor that will have a positive and major impact on the health condition of Haitians. Plus, the opportunity is so close to home.

**Provide Affordable, High-Quality Health Care**

As identified above, the underlying poverty in Haiti is a major barrier for mothers and children in accessing health care. As a short-term solution, the community care team will take steps to make certain that cost will not be a barrier to care and that services will be provided regardless of the ability to pay.

The long-term solution to removing the financial barrier is a robust economy with employment opportunities. Although the employment numbers at BRTH will be well below the large number at the Port Lafito industrial zone, we do anticipate hiring between 900 and 1400 local Haitians, to enhance the community economy while providing occupational training in hospital-related work skills.

As identified, another major causative factor to the CNM mortality rates is a very low percentage of deliveries occurring in qualified health facilities. To increase this percentage, in addition to the community care grid strategy, we will focus on two interventions: 1) leverage communications and technology and 2) transport patients to the hospital.

**Leverage Communications and Technology**

The Bethesda Communications Center at the hospital will be the central hub for the flow of information from the many community care grids throughout the country. A communication center will be staffed around the clock to receive phone calls for requests for care from community care team members. The staff will identify and triage specialty needs, and, if appropriate, patients from these grids will be referred to BRTH for the appropriate care.

We will leverage state-of-the-art telemedicine capabilities from any location in the country to provide an “e-consult” with colleagues at BRTH or with experts across North America. Real-time telemedicine assessments, such as ultrasonography and cardiac assessments, will help determine the most appropriate interventions for mothers and infants.

**Transport Patients to the Hospital**

As outlined in the Sidebar: Haiti Demographics, the mountainous terrain, poor highway infrastructure, and lack of affordable transportation provide obstacles to children and mothers reaching the best facility for care. Even if there were well-equipped and well-staffed neonatal intensive care units located centrally in the Port-au-Prince area, most neonates born in the rural areas would still not be able to access this care because of transportation challenges.

For this reason, we will have vehicles and contracted air transportation available to transport children, newborns, and pregnant and postpartum mothers to the hospital for lifesaving care. On the basis of information received by the Bethesda Communications Center, supplemented as necessary by telemedicine-generated clinical data, it will be determined whether the patient needs to be transported to the BRTH or to another appropriate hospital. Depending on the urgency of the situation, transportation will be deployed to bring patients to the hospital. We believe that with planning, coordination, and experience, we can achieve a door-to-door time that will meet most of the patients’ needs.

**Perceptions of Corruption and the Impact on the Hospital**

When we tell our Bethesda story, it does not take long before we are asked about how we deal with corruption in Haiti, a question that is usually followed by comments related to misuse of earthquake relief funds. We must address this question because individuals and organizations considering donating their time and money will want to know how BRTH plans to move forward in a country with these concerns.

Transparency International is a nonpartisan, independent group that each year publishes a “corruption perceptions index” for 175 countries, ranking each on the basis of public perceptions of corruption obtained from survey data and interviews. The higher the score, the greater the public perception of corruption. The 2014 index ranking for Haiti was 161 of 175, ranking it among the most corrupted countries in the world. In contrast, the Dominican Republic’s corruption perceptions index was 115 and Puerto Rico’s was 31.

So how does BRTH, as a large nonprofit organization dependent on philanthropic donors, thrive in such an environment? First, BRTH’s stateside corporation holds all assets, ensuring that funds go directly to the hospital operations. As part of the organizational structure, there is a Haitian NGO created to provide administrative management of the hospital, but complete governance and control of finances resides in the US. Second, there is a major layer of protection from the influences of corruption by having BRTH located in the privately owned Port Lafito. The importance of our partnership with the GB Group cannot be underestimated when it comes to being sheltered from unnecessary public-sector interference.
Finally, we will always promote and operate with values that are incompatible with corruption. When it comes to our relations with community hospitals, and as we partner with the public sector in the grids, our intolerance for bribery, nepotism, and other forms of corruption will be obvious to all. This was true three years ago when we wrote the first prospectus on BRTH in which we emphasized one of our major values: “we will be ethical and honest in all of our transactions.” We will be clear; we intend to confront corruption at every opportunity.

Status of Plans
After years of planning, and now having several major partners joining this venture, we anticipate that funding will be in place within a year to support construction on the hospital and guest hotel. To make this happen, it will take the philanthropic efforts of individuals, corporations, and organizations who share our vision for saving mothers and children in Haiti—beginning as soon as possible.

Meanwhile, we are moving ahead on several fronts. We are meeting regularly with our architect and interviewing contractors, and we have started the implementation of the community care grids by working in five grid pilots. Additionally, we are participating in conferences and meetings to mobilize North Americans, including physicians, midwives, and nurse specialists, and we are taking steps to involve Haitians in the North American Haitian diaspora.

CONCLUSION
The situation in Haiti is grim. The death rates for newborns, mothers, and children are at crisis proportions with no objective evidence that the mortality rate is improving or any reason to believe that it will.

On the basis of the data presented in this article, we can anticipate that the planned new hospital, along with the many partnerships developed through the countrywide community care grid network, will be a major impetus for fast-tracking the needed improvements in Haiti’s health care system.

As a demonstration project, BRTH will provide valuable information for international organizations such as the WHO, UNICEF, US Agency for International Development, the World Bank, and other organizations as they consider the most cost-effective, countrywide approaches for improving the health care infrastructures of low- and middle-income countries.

The strength of this approach is that it leverages several important realities:
• the excitement and support for this project from the Haitian medical and political communities
• the opportunity for North American specialty physicians, midwives, and nurses to use their skills in a meaningful way
• the proximity of Haiti to the US—for many, just a brief plane flight away
• the meaningful and sustainable opportunity to improve the skills of the Haitian workforce.

Most importantly, the lives of babies, children, and mothers will be saved.

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

Acknowledgments
We wish to thank Marat Turgunbaev, MD, MPH, MBA, for his research assistance.

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

References
37. Goodburn E, Campbell O. Reducing maternal mortality in the developing world: sector-wide approaches may be the key. BMJ 2001 Apr 14;322(7291):917-20. DOI: http://dx.doi.org/10.1136/bmj.322.7291.917.

The Children's Bill of Rights

The proper shelter, nutrition, clothes, education, and health measures be provided each child to assure that each, with maturity, can assume the full responsibilities of adulthood and citizenship.

— The Children's Bill of Rights; Billy F Andrews, MD
The Permanente Journal/ Spring 2016/ Volume 20 No. 2

Lactation Ketoacidosis: An Unusual Entity and a Review of the Literature

Sarah Gleeson, MB, BCh, BAO; Eoin Mulroy, MB, BCh, BAO; David E Clarke, MD, FCCP

ABSTRACT
A 31-year-old woman presented to the hospital with symptoms of nausea, malaise, and emesis. She was breastfeeding her 10-month-old infant. She was found to have severe ketoacidosis. The patient was not in diabetic ketoacidosis or alcoholic ketoacidosis; nor had she ingested any toxins. After she was admitted to the hospital, received intravenous fluids, and stopped breastfeeding, her symptoms resolved. She was found to have lactation ketoacidosis, an uncommon condition in humans. A review of all causes of ketoacidosis is presented with special emphasis on lactation ketocacosis.

CASE PRESENTATION
A 31-year-old woman who was 10 months postpartum and was breastfeeding presented to the Emergency Department with nausea, fatigue, vertigo, malaise, and 1 episode of emesis. She had been well until 20 hours earlier when her symptoms began somewhat suddenly and progressed in severity such that she sought treatment in the Emergency Department. She denied having fever, chills, or diarrhea and reported having consumed nothing out of the ordinary; no one else in her household was ill. She had not ingested or used any illicit substances, alcohol, or over-the-counter or prescription medications in the days preceding her presentation. Her medical history included mild asthma, for which she took no medications on a regular basis. She had an ectopic pregnancy 6 years earlier and hyperemesis gravidum 7 years ago when pregnant with her first child. She was breastfeeding her second child, a 10-month-old daughter. She had 2 hospital admissions in the preceding 3 months, with symptoms similar to those at current presentation. In each case, she was given intravenous fluids, her symptoms quickly resolved, and she was discharged from the hospital the following day. No cause was established for her illness in either of her prior hospital admissions.

On physical examination, she appeared ill but was not in acute distress. She was alert and fully oriented. Her temperature was 35.8°C, respiration rate was 16/min, heart rate was 92/min, blood pressure was 157/125 mmHg, and oxygen saturation was 100% breathing room air. Results of her physical examination revealed no abnormalities of her head or neck. She had clear breath sounds, normal heart tones and no murmurs, and a soft nontender abdomen. She had no abnormalities of the extremities or nervous system.

Results of the arterial blood gas analysis showed the following values: pH, 7.26; partial pressure of carbon dioxide, 31 mmHg; bicarbonate (HCO₃⁻), 13.5 mmol/L; base excess, -12.11 mmol/L; lactate, 1.0 mmol/L; chloride, 98 mmol/L; and serum ketones, ++. The remainder of her laboratory examinations revealed these values: sodium, 140 mmol/L; potassium, 3.8 mmol/L; urea, 7.9 mmol/L; creatinine, 0.7 mmol/d (normal value = 0.6-1.3 mmol/d); glucose, 3.8 mmol/L (normal value = 3.9-6.1 mmol/L); hemoglobin A₁c, 30 mmol/mol (normal value = < 42 mmol/mol); salicylate, < 0.04 mmol/L; and sodium, 145 g/L (normal value = 135-145 g/L) white blood cells, 12.1 × 10⁹/L; and neutrophils, 10.6 × 10⁹/L. Urinalysis revealed ketones at ++++. Thyroid-stimulating hormone and cortisol levels were normal. An electrocardiogram demonstrated sinus rhythm. Her serum anion gap was calculated to be 32.3 mmol/L ([Na⁺ + K⁺] – [Cl⁻ + HCO₃⁻]) (reference range, 12-18 mmol/L). Her osmolar gap was normal.

A review of her two prior hospital presentations that year revealed that, on both occasions, she had an increased anion gap metabolic acidosis with positive ketones and normal blood glucose readings.

For this current illness, she was admitted to the hospital and given 2L intravenous 0.9% sodium chloride. She stopped breastfeeding for 12 hours during her admission. By the next day, she was feeling better, was tolerating a normal diet, and her pH, anion gap, and blood ketone levels had returned to normal.

A diagnosis of lactation ketoacidosis was made. The patient was discharged with advice to ensure sufficient energy intake and to avoid prolonged fasts while breastfeeding. She was seen at a follow-up visit two weeks later and again two months after her presentation. She remained well, with no further presentations of acidosis during the ensuing five months.

DISCUSSION
Metabolic acidosis is a common finding in patients presenting to the Emergency Department. It is classically divided into two categories: those with and those without an elevated anion gap. The causes of acidosis are legion, and indeed in many teaching arenas, mnemonics are often used to facilitate recall of the most common causes of metabolic acidosis. For example,
Diabetic ketoacidosis (DKA) is the most commonly described and most commonly encountered form of ketoacidosis. There are, however, other important causes of ketoacidosis. The two most common are alcohol intoxication and starvation. Our patient did not have diabetes, nor had she consumed any alcohol preceding this or her two prior hospital admissions. A negative toxicology screen and normal osmolar gap ruled out several other possible (ingestion-related) causes of ketoacidosis. Because none of these entities appeared to be causing our patient’s illness, we investigated other possibilities. To understand why our patient had ketoacidosis, a review of ketone body production is essential.

Ketone Body Production
Ketone body production takes place in the mitochondria. There are three major ketone bodies: acetoacetate, β-hydroxybutyrate, and acetone. Ketone bodies are used as fuels by many body tissues, especially the brain, when there is decreased glucose availability. Ketogenesis is tightly regulated by a series of biochemical reactions and regulatory hormones. Lipoprotein lipase is activated by low insulin levels, releasing long-chain fatty acids and glycerol from triglycerides in peripheral fat stores. The fatty acids are transported to hepatocytes mitochondria, where they undergo hepatic β-oxidation, forming acetyl-CoA. Acetyl-CoA is then diverted from entering the Krebs cycle and instead enters the ketogenic pathway.

Starvation Ketosis
Starvation ketosis is usually benign and not life threatening. Short-term (eg, overnight) fasting causes mild acidosis. Following an overnight fast, fatty acids are released from fat stores and used for ketone production. Initially, glucose levels are maintained by glycolysis and gluconeogenesis. As fasting becomes prolonged (days), liver glycogen stores become depleted and the body becomes more dependent on ketone bodies as a source of energy. Stimulated by low insulin levels and high counterregulatory hormones (eg, glucagon), fatty acid release increases further to fuel ketone body production. Serum levels of ketone bodies continue to increase for three to four weeks, although ketogenesis and lipolysis are maximal by three days. Under these conditions, a superimposed stressor such as pregnancy, infection, or alcohol intake may precipitate life-threatening ketoacidosis. Fasting ketosis develops more quickly in women.

Alcoholic Ketoacidosis
The pathogenesis of alcoholic ketoacidosis is complex. There are commonly three initiating events: 1) poor nutritional intake, 2) metabolism of ethanol, and 3) metabolic stress. Long-term alcohol use often coexists with malnutrition. The resulting depletion of protein and glycogen stores results in a functionally starving state, which promotes ketosis. The metabolism of ethanol causes a rise in the ratio of nicotinamide adenine dinucleotide hydride to nicotinamide adenine dinucleotide (NADH/NAD), impairing hepatic gluconeogenesis, which leads to further ketogenesis. Superimposed metabolic stressors can be caused by dehydration secondary to vomiting from acute alcohol intake or from impaired hepatic gluconeogenesis causing hypoglycemia. This stress causes a release of counterregulatory hormones (catecholamines, glucagon), which further favors ketogenesis.

Salicylate Poisoning
Salicylate intoxication causes metabolic acidosis via a variety of mechanisms. First, through its uncoupling of mitochondrial oxidative phosphorylation, it promotes anaerobic metabolism, thus increasing lactate production and lactic acidosis. Second, salicylates increase fatty acid breakdown and can promote hypoglycemia, both of which lead to a ketotic state. Last, the salicylic acid itself contributes to acidemia.

Inborn Errors of Metabolism
In the pediatric population, a number of rare, usually recessively inherited inborn errors of metabolism predispose to ketosis and ketoacidosis. These include deficiencies in succinyl CoA:3 ketoacid CoA transferase, mitochondrial 2-methylacetoacetyl-CoA thiolase deficiency and methylmalonyl-CoA mutase deficiency. These conditions usually present in infancy or early childhood with recurrent episodes of severe ketoacidosis. An extensive discussion of these conditions is beyond the scope of this article. Bovine Ketosis/Lactation Ketosis
Bovine ketosis is well described in veterinary literature. First described in 1929, it occurs in postpartum cows and is characterized by ketonemia, ketonuria, low levels of hepatic glycogen, and hypoglycemia. Bovine ketosis is thought to occur because during lactation the animal is often unable to maintain sufficient energy intake and hepatic gluconeogenesis to match the increased substrate demands of lactation. Milk
production during lactation is an energy-intensive process, resulting in high glucose utilization. Ruminants rely on hepatic gluconeogenesis as a glucose source for milk production. If sufficient energy intake and hepatic gluconeogenesis cannot be maintained, a hypoglycemic, a hypoinsulinemic state results. Just as in humans, this stimulates adipose tissue breakdown, increasing substrate availability and ketone formation. Restoration of sufficient glucose by administration of 50% dextrose solution reverses the process.

“Bovine” or lactation ketosis in humans is rare, but there have been five previously reported cases. In all these cases, as in our case, a young, non-diabetic, lactating woman experienced raised anion gap acidosis with ketosis. In our patient, as in the other cases cited, rehydration and energy replacement resulted in complete resolution of the symptoms and the ketoacidosis.

CONCLUSION
In the previously reported cases of lactation ketoacidosis, there were specific events cited as precipitating the ketoacidosis. These events included a urinary tract infection, twin lactation, a self-imposed high-protein carbohydrate-free diet, and self-imposed fasting. To our knowledge, our case is the first reported case in which no specific illness or event was identified other than the lactation itself. Ours is also the first reported case of a woman with recurrent presentations of lactation-induced ketoacidosis.

Our case highlights the importance of lactation ketoacidosis as a cause of raised anion gap metabolic acidosis in lactating women. Awareness of the condition can help early recognition and treatment. Clinician awareness will also encourage prevention, including instructions to lactating women to ensure maintaining a balanced diet. Additionally, when lactating women are fasting for medical reasons (eg, preoperatively) or when they are admitted to the hospital for other reasons, it is important to ensure adequate and proper nutrition.

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

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

References

Science and Art

Medicine is the science of uncertainty and an art of probability.

— Interns: From Students to Physicians, Emily Mumford, PhD, 1921-1987, Professor of Clinical Sociomedical Sciences
PEITC in End-Stage B-Cell Prolymphocytic Leukemia: Case Report of Possible Sensitization to Salvage R-CHOP

Arian Nachat, MD; Sam Turoff-Ortmeyer; Chunnan Liu, MD; Michael McCulloch, LAc, MPH, PhD

ABSTRACT

Introduction: B-cell prolymphocytic leukemia (B-PLL) is a rare, aggressive leukemia distinct from chronic lymphocytic leukemia, with median survival of only 3 years. B-PLL is resistant to most chemotherapy and newer targeted therapies such as alemtuzumab and thalidomide. Phenylethyl isothiocyanate (PEITC) is a natural compound from horseradish with evidence for therapeutic potential in multiple leukemia types. Case Presentation: Here we present a case report of a 53-year-old man whose chronic lymphocytic leukemia transformed to end-stage B-PLL, disqualifying him for allogenic stem cell transplantation. He was treated with PEITC followed by salvage R-CHOP (Rituximab, Cyclophosphamide, Hydroxydaunorubicin [doxorubicin hydrochloride], Oncovin [vincristine sulfate], Prednisone or Prednisolone) chemotherapy, which led to normalized white blood cell count and disease stabilization that requalified him for allogenic peripheral stem-cell transplant therapy. We conducted a systematic review to analyze and interpret the potential contribution of PEITC to his unexpectedly favorable R-CHOP response. Following sequential 8 weeks of PEITC/pentostatin and 6 cycles of R-CHOP, the patient received allogenic peripheral blood stem cell transplant on an outpatient basis and remains well at the time of this publication, with no evidence of CD20+ small B-cells.

Discussion: Given the limited data for R-CHOP in B-PLL, this patient’s recovery suggests presensitization of B-PLL cells toward R-CHOP, potentially justifying further investigation.

BACKGROUND

B-cell prolymphocytic leukemia (B-PLL) is a rare, aggressive lymphoid leukemia with gene expression distinct from that of chronic lymphocytic leukemia. B-PLL is often refractory to chemotherapy, resulting in median survival of only three years. Reports have been published of improved response rates with intravenous alemtuzumab, partial remission with thalidomide, and cure with allogeneic peripheral stem-cell transplantation. In refractory patients, R-CHOP (Rituximab, Cyclophosphamide, Hydroxydaunorubicin [doxorubicin hydrochloride], Oncovin [vincristine sulfate], Prednisone or Prednisolone) is sometimes used as salvage therapy but is seldom successful and prognosis remains poor, with little evidence supporting its clinical use.

Phenylethyl isothiocyanate (PEITC) is a natural compound obtained from horseradish and watercress, with mechanistic and therapeutic evidence for multiple types of leukemia. The antileukemic effect is dose- and time-dependent, acting through multiple tumor suppression signaling pathways: inactivation of protein kinase B (PKB/Akt) and activation of c-Jun N-terminal kinase (JNK) pathways, caspase activation, poly [ADP-ribose] polymerase (PARP) cleavage/depolymerization, and promotion of apoptosis. PEITC is a biological response modifier, acting as a strong inflammation reducer. Notably, PEITC exhibits tumor cell inhibition properties in fludarabine-resistant chronic lymphocytic leukemia cells obtained from patients, by elevation of reactive oxygen species, and by promoting immune response (increasing monocyte macrophage phagocytosis, and increasing natural killer cell cytotoxic activity). A cytotoxic effect on chronic myeloid leukemia cells is achieved through induction of reactive oxygen species (ROS) stress and oxidative damage.

Dietary chemopreventive effects have been identified for PEITC, which works through multiple signaling pathways, at typical human nutritional doses. PEITC is one of numerous dietary compounds that work at the epigenetic level: anacardic acid, curcumin, diallyldisulfide, dihydrocoumarin, diindolylmethane, folate, garcinol, genistein and soy isoflavones, indol-3-carbinol, lycopene, nordihydroguaiaretic acid, phenethyl isothiocyanate, polyphenols (present in green tea, apples, coffee, chocolate, and raspberries), resveratrol, retinoic acid, selenium, and sulforaphane or PEITC (both of which are from the cruciferous family of vegetables). Metabolic pathways influencing tumor initiation and promotion are also affected by PEITC, through inhibition in human glioma cells of hypoxia-induced HIF-1alpha accumulation and vascular endothelial growth factor expression.

PEITC reverses platinum resistance in lung cancer by inhibiting glutathione-mediated drug efflux, in cisplatin-resistant gastric cancer by suppressing PI3K-PKB/Akt, and in Adriamycin-resistant bladder cancer by blocking PKB/Akt and activating mitogen-activated protein kinase (MAPK) pathways. Additionally, there is synergy of PEITC with...
Table 1. Tumor cell growth inhibition data

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Cancer type</th>
<th>Cell type (biopsy/animal/cell culture)</th>
<th>Study type</th>
<th>PEITC Dose</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemoprevention</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sakao et al, 2013</td>
<td>Breast</td>
<td>MDA-MB-231, PC-3, and DU145 cells</td>
<td>Cell culture and animal</td>
<td>PEITC induced apoptosis and inhibited cell migration and viability, via RNA interference of vimentin</td>
<td></td>
</tr>
<tr>
<td>Tusskorn et al, 2013</td>
<td>Cholangio-carcinoma</td>
<td></td>
<td>Cell culture</td>
<td>PEITC induced mitochondrial injury and cell death via apoptosis, inhibiting mitochondria and glutathione, but action could be blocked by N-acetylcysteine</td>
<td></td>
</tr>
<tr>
<td>Liu et al, 2013</td>
<td>Colon</td>
<td>SW480 epithelial cells</td>
<td>Cell culture</td>
<td>PEITC reduced cell proliferation by upregulating apoptotic signaling</td>
<td></td>
</tr>
<tr>
<td>Roy et al, 2013</td>
<td>Colon</td>
<td>Damaged DDB2-deficient colon cancer cells</td>
<td>Cell culture</td>
<td>PEITC demonstrated chemoprevention by inducing apoptosis and senescence, through p38MAPK/JNK pathway and DDB2 activation</td>
<td></td>
</tr>
<tr>
<td>Abdull Razis et al, 2014</td>
<td>Mechanistic study</td>
<td>Carcinogenic-metabolizing enzymes, in Albino rat</td>
<td>Animal</td>
<td>0.06-6.0 µmol/g for 2 weeks</td>
<td>Modulation of carcinogenic-metabolizing enzyme systems: SULT, NAT, UDP, and EH, oral doses reflecting human intake</td>
</tr>
<tr>
<td>Palenski et al, 2013</td>
<td>Mechanistic study</td>
<td>Vascular cells</td>
<td>Cell culture</td>
<td>Restored cell phenotype and inhibited angiogenesis, with antioxidant effect and suppression of NF-κB activation</td>
<td></td>
</tr>
<tr>
<td>Chen et al, 2013</td>
<td>Oral Cancer</td>
<td>SAS cells</td>
<td>Cell culture</td>
<td>Inhibition of metastatic invasion, via EGFR and related signaling molecules, inhibition of MMP-2 and MMP-9</td>
<td></td>
</tr>
<tr>
<td>Direct tumor inhibition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al, 2014</td>
<td>Brain</td>
<td>Gioma</td>
<td>Cell culture</td>
<td>(Dose not specified)</td>
<td>Subtoxic levels of PEITC activated TRAIL</td>
</tr>
<tr>
<td>Gupta et al, 2013</td>
<td>Brain</td>
<td>Human glioma</td>
<td>Cell culture</td>
<td>Tumor inhibition by suppressing hypoxia-induced accumulation of HIF-1α and VEGF expression</td>
<td></td>
</tr>
<tr>
<td>Sarkars et al, 2013</td>
<td>Breast</td>
<td>MCF-7 and MDA-MB-231</td>
<td>Cell culture</td>
<td>PEITC activated apoptosis and suppressed tumor cell growth, by targeting heat shock proteins</td>
<td></td>
</tr>
<tr>
<td>Wang et al, 2014</td>
<td>Cervical</td>
<td>Human Cervical HeLa Stem Cells</td>
<td>Cell culture</td>
<td>PEITC induced apoptosis and cell death through the induction of DR4 and DR5 death receptors with Human Cervical HeLa cells along with up regulation of cPARP</td>
<td></td>
</tr>
<tr>
<td>Tsou et al, 2013</td>
<td>Leukemia</td>
<td>WEHI-3 Leukemia BALB/c mice in vivo</td>
<td>Animal (Mice)</td>
<td>IP injection</td>
<td>In both normal and leukemic mice, PEITC stimulated immune response, promoting phagocytosis by PBMC, increasing CD11b, Mac-3, and NK cell cytotoxic activity, and decreasing CD19</td>
</tr>
<tr>
<td>Wang et al, 2014</td>
<td>Leukemia, CML</td>
<td>K562</td>
<td>Cell culture</td>
<td>PEITC is cytotoxic, by inducing ROS stress and oxidative damage</td>
<td></td>
</tr>
<tr>
<td>Huang et al, 2014</td>
<td>Melanoma</td>
<td>A375.S2 cells</td>
<td>Cell culture</td>
<td>PEITC caused apoptosis of A375.S2 cells, via ROS-mediated mitochondria-dependent pathways</td>
<td></td>
</tr>
<tr>
<td>Jutooru et al, 2014</td>
<td>Pancreatic</td>
<td>(miR-27a)/miR-20a/miR-17-5p</td>
<td>Cell culture</td>
<td>PEITC triggered apoptosis and lessened the growth and spread of pancreatic cancer cells by activation of ROS stress</td>
<td></td>
</tr>
<tr>
<td>Stan et al, 2014</td>
<td>Pancreatic</td>
<td>Vitro and MiaPaca2 xenograft animal model</td>
<td>Cell culture</td>
<td>7 µmol/L</td>
<td>PEITC inhibited cell proliferation in-vitro and in-vivo, through down regulation of anti-apoptotic protein, up regulation of proapoptotic protein, and G2/M phase cycle arrest</td>
</tr>
<tr>
<td>Inhibition of metastasis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gupta et al, 2013</td>
<td>Breast</td>
<td>MDA-MB-231-BR</td>
<td>Animal (Mice)</td>
<td>10 µmol</td>
<td>Reduction in metastasis of breast cancer cells to the brain, and 21% increase in median survival</td>
</tr>
<tr>
<td>Li et al, 2013</td>
<td>Prostate</td>
<td>Cell LNCaP tumor</td>
<td>Laboratory - Animal (Mice)</td>
<td>3 µmol/L, oral</td>
<td>PEITC fed to mice slowed tumor growth rates by changing gene expression (up regulation of insulin-like growth factor binding protein 3, fibronectin, thyroxine degradation enzyme, and down regulation of integrin beta 6)</td>
</tr>
</tbody>
</table>

CML = chronic myeloid leukemia; cPARP = poly (ADP-ribose) polymerase cleavage; DBB2 = DNA damage-specific binding protein 2; DNA = deoxyribonucleic acid; DR = death receptor; EGFR = epidermal growth factor receptor; EH = epoxide hydrolase; HIF-1α = hypoxia-inducible factor 1-alpha; IP = intraperitoneal; JNK = c-Jun N-terminal kinase; Mac = macrophage; MAPK = mitogen-activated protein kinase; MMP = matrix metalloproteinase; NAT = N-acetyltransferase; NF-κB = nuclear factor kappa-light-chain-enhancer of activated B cells; NK = natural killer; NMU = N-methyl nitrosourea; PEITC = phenethyl isothiocyanate; PBMC = peripheral blood mononuclear cells; RNA = ribonucleic acid; ROS = reactive oxygen species; SULT = sulfotransferase; TRAIL = tumor necrosis factor-related apoptosis-inducing ligand; UDP = glucuronosyl transferase; VEGF = vascular endothelial growth factor.
chemotherapy drugs: with paclitaxel to enhance apoptosis in MCF-7 breast cancer,\textsuperscript{18} and with taxol in drug-resistant MCF7 and MDA-MB-231 breast cancer cells by growth inhibition, cell cycle arrest, and apoptosis.\textsuperscript{19} In Tables 1 and 2, we concisely summarize the evidence for PEITC: synergism with chemotherapy drugs, direct tumor inhibition, inhibition of metastases, reversal of chemoresistance, and chemoprevention.

However, PEITC has not been reported in mechanistic studies of B-PLL cells or treatment of B-PLL patients. The current case report documents possible pre-sensitization of the patient's B-PLL cells to salvage therapy with R-CHOP, a treatment that typically has poor response in B-PLL patients. This report was prepared in accordance with the CARE (CAse REPort) guidelines.\textsuperscript{20}

CASE PRESENTATION

Our patient was a 53-year-old man, who was in his usual state of health and good spirits until slow onset of fatigue, dyspnea on exertion, abdominal bloating, night sweats, joint pain, and a 15-lb weight loss from 180 lbs to 165 lbs (Figure 1). Chest radiograph found pneumonia, and palpation revealed no lymph node enlargement but marked splenomegaly. Hematology showed elevated white blood cells (WBC; 157.1 K/μL), low red blood cells (2.94 M/μL), polychromasia 1+, ovalocytes 1+, smudge cells 1+, CD20+ small B-cells with diffuse nodular infiltrate, and CD5+ cells (Figures 2-5; Table 3).

Table 2. Reversal of chemoresistance by PEITC and synergism with chemotherapy drugs

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Cancer type</th>
<th>Cell type (biopsy/animal/cell culture)</th>
<th>Study type</th>
<th>PEITC dose</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reversal of chemoresistance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang et al, 45 2013</td>
<td>Bladder/ adriamycine</td>
<td>Adriamycin-resistant human bladder carcinoma T24/ADM cells</td>
<td>Cell culture</td>
<td>PEITC</td>
<td>Reduced doxorubicin resistance by activating MAPK, blocking PKB/Akt, and decreasing expression of multidrug resistant genes and proteins</td>
</tr>
<tr>
<td>Gupta et al, 46 2013</td>
<td>Breast/ taxol</td>
<td>Drug-resistant MCF7 and MDA-MB-231 breast cancer cell lines</td>
<td>Cell culture</td>
<td>PEITC</td>
<td>Synergism with taxol in growth inhibition, cell cycle arrest, and apoptosis, in drug-resistant MCF7 and MDA-MB-231 breast cancer cells</td>
</tr>
<tr>
<td>Tang et al, 47 2014</td>
<td>Gastric/ cisplatin</td>
<td>SGC7901/DDP cell line</td>
<td>Cell culture</td>
<td>PEITC</td>
<td>Reduced cell growth and multidrug-resistant genes, via increase in ROS generation and Rhodamine-123, and depletion of glutathione</td>
</tr>
<tr>
<td>Yang et al, 48 2014</td>
<td>Lung/ cisplatin</td>
<td>Non-small cell lung cancer line</td>
<td>Cell culture</td>
<td>PEITC</td>
<td>Reversal of platinum resistance by inhibiting glutathione-mediated drug efflux</td>
</tr>
</tbody>
</table>

| Synergism with chemotherapy drugs |
| Halasi et al, 49 2013 | Breast/ bortezomib | Mouse xenograft | Animal | PEITC | Inhibition of tumor cell growth through combining the FOXM1 inhibitor bortezomib with ROS inducer PEITC |
| Cang et al, 50 2014 | Breast/ paclitaxel | MCF7 and MDA-MB-231 (MB) | Cell culture | PEITC | Synergism of PEITC and paclitaxel in apoptotic mechanisms: 1) 6-fold increase in acetylation of alpha-tubulin vs taxol alone; 2) inhibition of cell-cycle regulator Cdk1 and anti-apoptotic protein bcl-2; 3) increase in Bax and PARP protein cleavage |
| Yang et al, 48 2014 | Lung/ doxorubicin | NCI-H596 NSCLC cell line | Cell culture | PEITC | 40% greater tumor cell growth inhibition by 1:2 molar ratio of CDDP/PEITC in liposomal form, compared with the same combination in free form |

CDDP = cis-diamminedichloroplatinum; FOXM1 = forkhead box M1; MAPK = mitogen-activated protein kinase; PARP = poly (ADP-ribose) polymerase; PEITC = phenethyl isothiocyanate; PKB/Akt = protein kinase B; ROS = reactive oxygen species.
Planned frontline therapy was 6 cycles of fludarabine-cyclophosphamide-rituximab (FCR) chemotherapy (fludarabine 25 mg/m², cyclophosphamide 250 mg/m²/d, and rituximab 125 mg/m² intravenous) and supportive medication (Neupogen, Allopurinol, Bactrim DS, acyclovir, prochlorperazine, and dexamethasone). Disease progression occurred following 2 cycles of FCR, with fever, lower but still elevated WBC (110.7 K/μL), low red blood cells (3.74 M/μL), and increased anisocytosis (2+). On pathology review, the diagnosis was updated to B-PLL, stage IV, with Eastern Cooperative Oncology Group performance score of 2.

Five months after diagnosis of PLL, following 12 cycles of weekly alemtuzumab, there was stabilization of WBC (5.2 K/μL) and red blood cells (4.31 M/μL), but persistent polychromasia (1+) and ovalocytes (1+). Because the patient had 2 siblings, planning and evaluation for allogenic bone marrow transplant was initiated.

Ten months after diagnosis, the patient reported profound fatigue, blurred vision, pressure behind his eyes, spontaneous unprovoked perspiration, and abdominal distention with early satiety. Palpation revealed extensive splenomegaly across the midline to the right midclavicular line, confirmed by computed

Table 3. Serology data by clinical treatment event

<table>
<thead>
<tr>
<th>Clinical events timeline</th>
<th>2 months</th>
<th>5 months</th>
<th>11 months</th>
<th>12 months</th>
<th>13 months</th>
<th>19 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (K/μL)</td>
<td>Baseline</td>
<td>After 2 cycles of FCR, stopped due to progression</td>
<td>After 12 cycles of weekly alemtuzumab</td>
<td>After splenectomy, because of progression after 2 doses of alemtuzumab, started PEITC</td>
<td>Continued disease progression, before R-CHOP</td>
<td>After first cycle of R-CHOP</td>
</tr>
<tr>
<td>RBC (M/μL)</td>
<td>157.1</td>
<td>110.7</td>
<td>5.2</td>
<td>73.4</td>
<td>207.7</td>
<td>9.8</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>2.94</td>
<td>3.74</td>
<td>4.31</td>
<td>2.72</td>
<td>2.67</td>
<td>2.60</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>8.0</td>
<td>11.2</td>
<td>13.5</td>
<td>8.2</td>
<td>8.3</td>
<td>7.9</td>
</tr>
<tr>
<td>RDW (%)</td>
<td>24.8</td>
<td>34.0</td>
<td>39.3</td>
<td>25.3</td>
<td>24.4</td>
<td>22.9</td>
</tr>
<tr>
<td>Platelet (K/μL)</td>
<td>17.1</td>
<td>22.7</td>
<td>14.5</td>
<td>16.3</td>
<td>21.4</td>
<td>20.9</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>2 months</td>
<td>5 months</td>
<td>11 months</td>
<td>12 months</td>
<td>13 months</td>
<td>19 months</td>
</tr>
<tr>
<td>Anisocytosis</td>
<td>91</td>
<td>95</td>
<td>11</td>
<td>92</td>
<td>79</td>
<td>3</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>1+</td>
<td>2+</td>
<td></td>
<td></td>
<td>1+</td>
<td>1+</td>
</tr>
<tr>
<td>Target Cells</td>
<td>1</td>
<td>11</td>
<td>2</td>
<td>1</td>
<td>0.7</td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td>5</td>
<td>4</td>
<td>77</td>
<td>32</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Polychromasia</td>
<td>3 months</td>
<td>5 months</td>
<td>11 months</td>
<td>12 months</td>
<td>13 months</td>
<td>19 months</td>
</tr>
<tr>
<td>Ovalocytes</td>
<td>1+</td>
<td>1+</td>
<td>1+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smudge Cells</td>
<td>1+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD20+ small B-cells</td>
<td>Present</td>
<td>Diffuse nodular infiltrate</td>
<td>No evidence</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMT = bone marrow transplantation; CLL = chronic lymphocytic leukemia; FCR = chemotherapy with fludarabine, cyclophosphamide, and rituximab; K = thousand; LDH = lactate dehydrogenase; M = million; PEITC = phenethyl isothiocyanate; PLL = prolymphocytic leukemia; RBC = red blood cells; R-CHOP = chemotherapy with rituximab, cyclophosphamide, hydroxydaunorubicin (doxorubicin hydrochloride), Oncovin (vincristine sulfate), prednisone or prednisolone; RDW = red blood cell distribution width; WBC = white blood cells.
PEITC in End-Stage B-Cell Prolymphocytic Leukemia: Case Report of Possible Sensitization to Salvage R-CHOP

Tomography (Figure 6). Three treatments of palliative radiation therapy were unsuccessful, therefore splenectomy was performed. Following surgery, the patient developed protein energy malnutrition, sinus tachycardia, bilateral pleural effusion, cholelithiasis, dyspnea, and portal vein thrombosis. For treatment of his significant pain, the patient was referred to the integrative pain management service for acupuncture (daily during this and following hospital admissions).

Eleven months after diagnosis, despite 2 cycles of alemtuzumab with palliative intent, there was further disease progression. The patient was readmitted for sepsis with fever, lactic acidosis (4.9 mmol/L), worsening serology, and atypical lymph at 92% (Table 1). Because of significant pleural effusion, the patient underwent transpleural thoracoscopy, exploratory thoracotomy, and lung decortication. Given the patient's deteriorating status, bone marrow transplantation was canceled and a palliative care team was assigned to his case.

Adjunctive oral PEITC was introduced, with the patient being eligible on the basis of published evidence for disease-modifying potential, and lack of evidence for herb-drug interactions. PEITC was provided to the patient on a compassionate use basis because there were no treatment options left available to him. Two weeks after PEITC was initiated, the patient's oncologist added pentostatin to his alemtuzumab, given the alemtuzumab's poor potential for success.

PEITC was provided by KW Botanicals (San Anselmo, CA) as a 1:1 watercress fluid extract of the fresh leaf, prepared from cloned Nasturtium officinale using corn alcohol, with plant identity verified by a botanist, using organoleptic methodology and microscopy. Daily oral dose of the extract was 2 mL, corresponding to an approximate daily dose of PEITC of 1 mg, for a duration of 3 weeks. Following introduction of PEITC, the patient's symptoms continued to improve, but WBC remained abnormal.

Twelve months after diagnosis, there was continued disease progression, with a new left neck mass, night sweats, chills without fever, and elevation of WBC to 207.7 K/μL. Examination revealed a 5 cm, tender mass. Computed tomography showed extensive left cervical adenopathy. Treatment was changed to salvage R-CHOP (3 cycles, every 3 weeks), and PEITC discontinued one week before starting R-CHOP. The patient's response to sequential 8 weeks of PEITC/pentostatin, followed by 6 cycles of R-CHOP, was substantial, with normalization of WBC within 2 days (from 150K/μL to 9.8 K/μL). R-CHOP was continued for 6 cycles, leading to discharge from the palliative care team.

Fifteen months after initial diagnosis, and following this course of sequential 8 weeks of PEITC/pentostatin and then 6 cycles of R-CHOP, the patient received allogenic peripheral blood stem cell transplant on an outpatient basis at Stanford University Hospital in Stanford, CA, and was followed up for 90 days after the transplant. Posttreatment bone marrow biopsy was normal; neck lesions and chest and left pelvic lymphadenopathy resolved, with only mild residual fluorodeoxyglucose (FDG) uptake. Other previously noted lesions in both lung bases appeared stable in size and FDG uptake. The patient was declared to be in remission.

Forty-three months after initial diagnosis, the patient's remission continues. Other than one episode of neutropenic fever and chronic mild to moderate graft-versus-host disease, the patient remains well to this day, with no evidence of CD20+ small B-cells.

**DISCUSSION**

PEITC exhibits synergism with numerous chemotherapy drugs, including doxorubicin, which is a component of R-CHOP. We were not able to identify published evidence for synergism of PEITC with pentostatin. Researchers have
also shown that PEITC has direct and significant oxidative cytotoxic activity against other leukemia cells—with low toxicity to normal lymphocytes—such as chronic lymphocytic leukemia cells obtained from patients whose disease was resistant to fludarabine chemotherapy. Cells from those patients were eliminated by PEITC.

At present, it is known that one way in which PEITC accomplishes this sensitization of cancer cells to chemotherapy is by depleting the cancer cells of tubulin, a normally stable cell structure protein required in the process of cell cycle progression. It has also been found that this degradation of tubulin by PEITC is an irreversible process, suggesting there is biological plausibility for this patient’s PLL tumor cells to continue to exhibit enhanced vulnerability for some time after PEITC exposure. Taken together, these data support our hypothesis that this patient’s chemoreistant B-PLL cells were sensitized to favorable response to R-CHOP, a drug not expected to have been so successful in his end-stage condition. This favorable response enabled him to qualify for life-saving allogenic peripheral blood stem cell transplant.

PEITC exhibits chemopreventive effects in the following cancer cell lines and animal models: breast, colon, oral (squamous), brain, cervical, leukemia, melanoma, and pancreatic. Two recent studies also suggest PEITC has metastasis inhibition capabilities in breast and prostate cancers (Table 1). Promising chemotherapy-specific effects have been described for PEITC: reversal of chemoresistance data exist for bladder cancer and adriamycin, breast cancer and taxol, gastric cancer and multidrug resistance gene, lung cancer and cisplatin (Table 2). Synergism with specific chemotherapy agents in defined cancers has been reported for bortezomib and paclitaxel, cisplatin and NF-κB suppression. In the animal model studies, these effects were seen at oral doses reflecting human dietary intake of PEITC-containing foods. PEITC additionally accomplishes direct tumor cell inhibition, in the following cell lines and animal models: brain (glioma), breast, cervical, leukemia, melanoma, and pancreatic. Two recent studies also suggest PEITC has metastasis inhibition capabilities in breast and prostate cancers (Table 1).

This case report provides justification of in vitro PEITC-drug synergy testing, which if successful would be a step toward in vivo and phase I combination therapy trials.

Disclosure Statement

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

Acknowledgments

We thank Greg Rumore, MD, Chief of Staff, Pathology, Kaiser Permanente Walnut Creek Medical Center in Walnut Creek CA, for providing hematoxylin and eosin stain and immunohistochemical stain photographs. Mary Corrado, ELS, provided editorial assistance.

References

21. Halasi M, Pandit B, Wang M, Nogueira V, Hay N, Gartel AL. Combination of oxidative stress and FOXM1 inhibitors induces apoptosis in cancer cells and
All Things to All Tissues

We, therefore, worked on the principle that blood is all things to all tissues, being meat to the hungry, blood to the malicious, and life-giving fluid to the collapsed and to those losing protein by the discharge of albinous exudates.

— Jacob Markowitz, MBE, MD, PhD, MS, 1901-1969, Canadian physician, pioneer in experimental surgery, and war hero
Flower Merchant
photograph
Bridget Bourgon, PA-C

Using an upside down bucket for a stool, she sits in the heat of the day, hoping to make a sale. This photograph was taken during street wanderings in Havana, Cuba in 2015.

Ms Bourgon is a recently retired Physician Assistant from Urgent Care at Kaiser Permanente Orange County in Santa Ana, CA. More of Ms Bourgon’s images may be seen at: bridgetbourgon.com/heartofhavana.
CASE REPORT
A 57-year-old woman born in the Philippines presented to the Emergency Department with 6 hours of epigastric and right upper quadrant abdominal pain radiating to her back. She denied fever, nausea, and vomiting. She described her pain as similar to pain before her cholecystectomy 46 years previously, at age 11. An ultrasound demonstrated a hypoechoic linear structure in the common bile duct and diffuse biliary duct dilation (Figure 1) that were initially read as consistent with a nonfunctioning stent, which the patient denied having. The computed tomography scan of the abdomen and pelvis that was ordered to better characterize the “stent” demonstrated only biliary dilation in the common bile duct without a radiopaque structure (Figure 2). Laboratory test results for the patient’s complete blood count, comprehensive metabolic panel, and lipase were normal.

Because biliary stents were not available in 1958 when the patient underwent her cholecystectomy, and because the ultrasound abnormality was hypoechoic without radiopaque characteristics, we considered the possibility of a biliary worm. An endoscopic retrograde cholangiopancreatography (ERCP) showed the presence of a worm, extending from the ampulla into the bowel lumen. During attempted retrieval of the worm, it retracted into the bile duct, and only a large, transected portion was removed. Our patient tolerated the procedure well and was later released from the hospital.

DISCUSSION
Biliary helminthiasis results from liver flukes, which are parasitic worms endemic in Southeast Asia. Some flukes, such as Clonorchis sinensis, Opisthorchis viverrini, Opisthorchis felineus, and Fasciola hepatica, reside primarily in the biliary tree. In contrast, Ascaris lumbricoides resides in the intestines and occasionally migrates into the bile ducts. Prevalence worldwide of the most common biliary helminth, Ascaris lumbricoides, is high, at approximately 1.2 billion.

Biliary helminthiasis can present as biliary obstruction, pyogenic cholangitis, acute pancreatitis, liver cysts, and abscesses. Patients typically have abdominal pain and may have jaundice or fever. Diagnosis is made by imaging (ultrasound or magnetic retrograde cholangiopancreatography), with antigen serum tests, or by direct visualization during ERCP. Computed tomography scans tend to only demonstrate biliary dilation, and are therefore less helpful in securing the diagnosis. Urgency of diagnosis and hospitalization are determined by severity of symptoms, findings...
of biliary obstruction, or infection, including sepsis. Drug treatment choice depends on the type of parasite.

Our patient was started empirically on mebendazole as an outpatient. The Pathology Department was unable to identify the worm from the pieces obtained during ERCP retrieval. Our patient passed the remainder of the worm five days later in her stool, which is common after a worm dies. She reported that the worm appeared “like a tiny spaghetti without its head.” Analysis of this portion of the worm was not performed because the patient discarded it. Repeat ERCP one month later showed neither retained worm nor gallstones.

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

References

Invisible Living Corpuscula
That this living effluvia is composed of invisible living corpuscula, is obvious from the innumerable worms which abound in such bodies, some of which grow large enough to be visible, while others remain of a size which is invisible. … Clothing and household goods infected … when carried somewhere else, in a short time produce tragic catastrophes; indeed not only whole cities are attacked by the sudden and unexpected contagion but also provinces and entire kingdoms.

— Athanasius Kircher, SJ, 1602-1680, 17th century German Jesuit scholar and polymath
Image Diagnosis: Capitellar Fracture

Ganesh Nagaraj, MD; Justin P Mitchelson, MD; Cameron M McFarland, MD; Matthew A Silver, MD
Perm J 2016 Spring;20(2):84
http://dx.doi.org/10.7812/TPP/15-150

CASE REPORT
A healthy 35-year-old man presented to the Emergency Department with left elbow pain and swelling after a ground-level fall onto his outstretched left hand while jogging. Physical examination revealed diffuse swelling and tenderness of the left elbow, most prominently over the distal humerus. Range of motion was markedly limited by pain. The patient’s left upper extremity was neurovascularly intact.

X-rays of the patient’s left elbow (Figures 1 and 2) revealed a displaced capitellar fracture. In Figure 2, the black arrow indicates disruption of the radiocapitellar joint, which is the articulation between the distal humerus and the radial head. The white arrow indicates a raised anterior fat pad and the resulting sail sign.

The patient underwent surgical pinning and had regained good function of the joint at four-month follow-up.

DISCUSSION
Capitellar fractures account for less than 1% of elbow fractures and are most often caused by a fall onto an outstretched hand. Associated elbow injuries include radial head fractures, posterior elbow dislocations, and medial and lateral collateral ligament injuries. Thorough evaluation of the wrist and shoulder for accompanying injuries is necessary. Neurovascular injury is uncommon in isolated fractures of the capitellum.

Diagnosis of capitellar fracture can be made most readily by examining lateral elbow images for alignment of the radiocapitellar line, which is drawn along the radial neck and should bisect the capitellum in all views, and the anterior humeral line, which is drawn along the anterior edge of the humerus and should transect the middle third of the capitellum. An oblique or radial head-capitellum view may assist in detecting a subtle fracture line. Elevated fat pads, such as a convex anterior fat pad producing a sail sign or any elevation of the posterior fat pad, suggest an underlying fracture. A computed tomography scan may be indicated in the appropriate clinical setting.

Displaced capitellar fractures frequently require prompt operative intervention in the form of open reduction and internal fixation to preserve the function of the joint. Fragment excision is often performed in comminuted fractures or for bone fragments that are too small for fixation. Isolated nondisplaced fractures, or those that have undergone successful closed reduction, may be managed nonoperatively with immobilization.

Disclosure Statement
The authors have no conflicts of interest to disclose.

References
Learning to “Swim” with the Experts: Experiences of Two Patient Co-Investigators for a Project Funded by the Patient-Centered Outcomes Research Institute

Michele Robbins; Janice Tufte; Clarissa Hsu, PhD

ABSTRACT
The Patient-Centered Outcomes Research Institute (PCORI), established in 2010, launched a new model of incorporating stakeholder perspectives into health care research. To ensure that PCORI-funded studies address issues important to health care consumers, all projects must fully involve patients and other stakeholders in every step of the research process: from planning and design to implementation and dissemination of results.

As members of the first cohort of PCORI-funded researchers, our team was on the forefront of developing new approaches to engaging patients in research. One innovation we pioneered was the creation of a “patient co-investigator” role for two nonscientists who were recruited to be active members of the research team throughout the project. This commentary, based on our experiences, aims to help other research teams to 1) understand how to effectively collaborate with stakeholder team members such as patients; 2) anticipate possible challenges; and 3) offer tools for the orientation, training, and integration of patients into a scientific team. Written from the perspective of two PCORI patient co-investigators, our commentary provides lessons learned and recommendations about incorporating nonscientists into research teams.

Specifically, we suggest recruiting people with a record of relevant volunteer experience and commitment; establishing a formal application process that provides candidates with details about expectations and responsibilities; and providing comprehensive orientation with ongoing training, encouragement, and support. We hope the points in this commentary help research teams that are incorporating patient co-investigators move toward a positive and productive experience.

INTRODUCTION: CONTEXT FROM THE PRINCIPAL INVESTIGATOR

“Because engagement of this depth is new to many researchers and patients alike, we’re developing methods to improve our ability to incorporate patients’ perspectives in research. Patient-centered research methods that are transparent and scientifically sound will enhance the credibility and usefulness of the studies we fund.” —Joe V Selby MD, MPH, Executive Director of the Patient-Centered Outcomes Research Institute (PCORI).

During the last 10 to 15 years, health care systems have increasingly included patients in the design, implementation, and evaluation of projects to improve health care.2-6 Now, with the creation of PCORI in Washington, DC, patients are even more involved in health services research. Created as part of the Affordable Care Act, PCORI is charged with providing patients, their families, and clinicians with trustworthy information to help them make better-informed health care choices.7 The goal of PCORI is to “close the gaps in evidence needed to improve key health outcomes.” To do this, PCORI states, “we identify critical research questions, fund patient-centered comparative clinical effectiveness research, or CER, and disseminate the results in ways that the end-users of our work will find useful and valuable.”8 A key feature of all PCORI-funded projects is that patients and other stakeholders provide input throughout the project. One reason this model is novel is that PCORI requires patients on research teams to make important and ongoing contributions into the research design and implementation, and it allows for financial compensation of these patient partners. This goes well beyond previous methods for encouraging inclusion of patients in research.9

As the leader of one of the first PCORI-funded projects, I (CH) had the honor of collaborating with two stakeholder co-investigators, recruited for their knowledge, experience, and dedication to the community health issues addressed in our study. In the rest of this commentary, they describe their experience and give recommendations for successfully integrating patient partners into a scientific team.

REPORT FROM PATIENT CO-INVESTIGATORS
We (MR, JT) are patient co-investigators on a Group Health Research Institute (GHRI) team that received 1 of the first 25 PCORI awards in May

Michele Robbins is a Patient Co-Investigator at the Group Health Research Institute in Seattle, WA. E-mail: michele.robbins321@gmail.com. Janice Tufte is a Patient Co-Investigator at the Group Health Research Institute in Seattle, WA. E-mail: janicetufte@yahoo.com. Clarissa Hsu, PhD, is an Assistant Investigator at the Center for Community Health and Evaluation at the Group Health Research Institute in Seattle, WA. E-mail: hsu.c@ghc.org
2012. Our project, Learning to Integrate Neighborhoods and Clinical Care (LINCC), has 2 major components. The first is piloting and evaluating an innovative approach to involving patients in care redesign. The second is designing, implementing, and evaluating, in collaboration with clinical staff and other stakeholders, a new role in primary care teams: the community resources specialist. We were recruited to be active members of the LINCC research team, and here we share our experience, starting with being invited to join.

**Becoming Patient Co-investigators**

When developing the LINCC proposal for PCORI, the team asked Group Health Cooperative (Group Health), the parent organization of GHRI, to recommend patients with experience and a high level of engagement in collaborative projects with the health care system. Group Health patients are involved in ongoing work such as standing advisory committees and shorter-term projects such as redesigning clinics. The research team wanted people with skills in collaboration and leadership as well as knowledge and experience in the following areas: community engagement/organizing, community resources, health care system design, and group facilitation.

One of us (JT) has knowledge of and is active within the Muslim and interfaith communities in the Puget Sound region of Washington State, and serves on nonprofit and governmental committees. She founded six community-building projects that address socioeconomic disparities through poverty awareness and resource-based solutions. The other of us (MR) brings professional experience in community engagement and facilitation. She also has extensive experience volunteering at Group Health and being the primary caretaker for her husband during a serious illness while at the same time being the caregiver for her aging mother-in-law.

We were both excited to participate in this unique opportunity. We thought the aims of the proposal—adding patient input to all levels of research and developing a new primary care role to help patients access community resources—were much needed in health services and would improve patient experiences. Our participation as active research team members began with reviewing proposal drafts and providing input on topics in which we had expertise. We heard that funding was very competitive and our chances were slim, so we were pleased when we learned that the project was funded. We went from being short-term volunteers to members of a research team conducting a three-year study.

**Swimming Lessons: Becoming Part of the Team**

Then the real work began. The first few meetings were challenging. This is apparent from the following comment from one of our quarterly surveys, in which the researchers asked our impressions: "I must remind myself that we are all learning as we build and create a patient integration model into all levels of medical research, most particularly [because] the implementation of patient co-investigators into the science team is a new concept. It reminds me of throwing a person into a not-too-deep pool to learn to swim; then throwing the whole team into a pool to learn at the same time. Some team members know the basic swimming methods and some do not." —Patient Co-investigator, quarterly survey response

Receiving adequate compensation for our time, travel, and related expenses has been important in facilitating our participation. We appreciate that our schedules, along with those of all the other team members, were considered when establishing meeting days and times. As the team worked out these logistical details, we began to realize that we were equal players in this project and not just two patients sitting on the sidelines observing. We were introduced to the day-to-day workings of GHRI and given office space, computers, and identification cards. We did paperwork for our monthly stipends and, in general, were treated like employees. Our first-year education and training was extensive, including:

- a self-study program on the Lean quality-improvement process used at Group Health
- human subjects training through the Collaborative Institutional Training Initiative of the University of Miami (CITI; Miami, FL), a national, Web-based, research education program
- education about patient privacy and data protection through Group Health's employee training system.

Everything was new. We were not prepared for this “job”—which did not have an application process or formal description. In the traditional employment field, all jobs have an explicit description, so not having one made us uncomfortable in the beginning. Without a clear definition of our function and duties, we questioned whether we were qualified and did not know what to expect or what was expected of us. It was hard to get our heads around the fact that our task was to bring our individual patient perspectives to this project. We also wanted an organizational chart that would show our patient co-investigator role in relationship to the team and the entire GHRI staff.

The team members understood our frustrations but, at first, they could answer our questions only with “we don’t know.” They explained that we were all learning about this role together because there were few models of full patient engagement in research on which to draw. With time, we saw that we were part of a national experiment to learn how best to incorporate patients into research teams. This realization opened the door to a deeper understanding of how we could contribute. A tool that helped us better understand our roles and the overall project was a logic model—a visual representation of the project steps, similar to a flowchart—that the research team developed. The LINCC logic model gave us and the team a sense of the big-picture goals of the project and helped clarify timelines and team member responsibilities.

Once regular team meetings began, we were overwhelmed by the language of research and health care, which is filled with acronyms and unfamiliar terms and concepts. Trying to understand the role of each new colleague at the table was frustrating and confusing.
because we were still just trying to remember their names. To address this challenge, we began holding half-hour “premeetings” with the project manager before regular research meetings. During premeetings, which are ongoing, we review the upcoming research team meeting agenda; ask and answer questions; and talk about our observations, frustrations, and any assumptions we have drawn about the project. With only the three of us in the room, we feel more comfortable voicing our questions and ideas. Our premeetings allow us to be more prepared to engage productively with the full research team and are invaluable for putting information into context. They have been the most important tool for effectively integrating us with the research team.

Making up a New Stroke as We Go

From project onset, we were told the research team was piloting the patient co-investigator as an innovation in the research world. Our research team had the advantage of being a part of Group Health, which was founded as a consumer-governed health care cooperative and encourages patients to be active in their own care by partnering with their care team. Group Health offers its members opportunities to contribute through patient caucuses, advisory panels, and focus groups. Additionally, GHRI has a strong record of working with patient participants on clinical studies, but like most research institutions, has limited experience in integrating patients into research teams. Our research team knew they were breaking new ground with our PCORI project.

To capture our experiences and recommendations, the research team implemented two data collection methods. First, a GHRI staff member who was not a part of the LINCC team conducted qualitative interviews with all project team members (including stakeholders in the delivery system). That same staff member plans to do interviews at the end of the project to see how experiences and perspectives changed. Second, we fill out quarterly, online, open-ended patient co-investigator surveys (see Sidebar: Quarterly Survey Questions). The responses are reviewed by the project manager, who writes a summary that we approve before sharing it with the rest of the team. This process gives us a safe way to share our experiences, concerns, and suggestions and to ensure team leaders receive feedback that helps improve our experience on the team. The answers to the seven questions asked in each quarterly survey inform the remainder of this article.

The first year, our survey answers reflected substantial frustration because we did not know how we could best contribute to the project or whether our knowledge base was a help or hindrance. ... over time, we came to understand how valued we were ... and the reasons why patient involvement was critical to the project.

Although PCORI funding for the LINCC project will finish in 2016, we have found that our views will continue to be valued and sought. We can still shed new light on the research. The LINCC community resource specialists are now in clinics. As members of the research team, we actively participated in selecting the clinics where they would work, determining the scope of the advisory committees and agendas that would guide them, and designing workshops to train patient advisors who participated in co-designing the new community liaison role. In addition, we helped select and/or develop the patient survey questions used to evaluate the program.
Lessons Learned

We hope that sharing our experiences and insights will make the process of learning to “swim” easier and more efficient for other research teams interested in incorporating patient co-investigators. Success begins with recruitment. Think broadly about whom you want to recruit and find innovative ways to spread the word. Use interviews to find skills that may not be on the candidates’ resumes, such as an eagerness to learn. Make sure all candidates understand that they are making a commitment to a long-term project. Being part of a team means showing up and contributing. If candidates cannot consistently do this for the entire project, the patient-centeredness is diluted. Other lessons learned are included in the Sidebar: Key Lessons Learned.

CONCLUSION

We believe our participation and involvement in one of the first PCORI-funded research projects has been worth our time and worth the time and financial commitment of our research institution. Foundational elements of this success have been that we feel fully respected and part of the LINCC team. Our contributions as patients, laypeople, and nonscientists have been given value equal to the perspectives of the other members of the research team. We feel that our experience in this early PCORI project has given us an opportunity to be agents of positive change. We hope that the lessons learned that we provide in this article make it easier for other research teams to integrate patients as partners in research and to help them maximize their input as colleagues who have unique and valuable perspectives.

Disclosure Statement

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

Acknowledgments

Research reported in this article was funded through a Patient-Centered Outcomes Research Institute (PCORI) Award (1011). The views and opinions in this article are solely the responsibility of the authors and do not necessarily represent the views of the Patient-Centered Outcomes Research Institute (PCORI), or its Board of Governors or Methodology Committee.

We would like to thank the other members of the science team who helped shape this commentary, particularly Paul Fishman, PhD, and June BlueSpruce, MPH, who reviewed and provided feedback on this commentary. We also thank Chris Tachibana, PhD, for her help framing and editing this commentary.

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

References


Key Lessons Learned

1. Have an application with a cover letter explaining the scope of the project, the time expected, reimbursements, and requirements
2. Conduct formal interviews with prospective patient co-investigators
3. Be prepared to orient patient co-investigators with resources such as:
   - a general job description (knowing the role might change over time)
   - names and roles of each team member
   - an organizational chart with each team member and co-investigator
   - a project logic model, flowchart, and/or timeline
   - background material (such as this article) about how a research team works
   - required tax and business forms (W2, 1099, travel forms, etc)
   - initial meetings to welcome patient co-investigators and provide them with office resources such as a desk, computer, and phone
   - remote e-mail access with the ability to download attachments
   - handouts with definitions of relevant research and health care terms
   - human subjects training that is available in a variety of languages and that is at a literacy level accessible to lay people (the Collaborative Institutional Training Initiative of the University of Miami system we used was too specialized)
   - support for completing organizational compliance and training requirements
   - premeetings to help prepare and integrate patient co-investigators into larger research team meetings
   - clear explanations of acronyms and unfamiliar terms and concepts
4. Be patient, encouraging, and supportive with the patient co-investigators as they learn and throughout the project

Learning to “Swim” with the Experts: Experiences of Two Patient Co-Investigators for a Project Funded by the Patient-Centered Outcomes Research Institute
The Language of Engagement: “Aha!” Moments from Engaging Patients and Community Partners in Two Pilot Projects of the Patient-Centered Outcomes Research Institute

Ming Tai-Seale, PhD, MPH; Greer Sullivan, MD, MSPH; Ann Cheney, PhD; Kathleen Thomas, PhD; Dominick Frosch, PhD

ABSTRACT

Compared with people living in the community, researchers often have different frameworks or paradigms for thinking about health and wellness. These differing frameworks are often accompanied by differences in terminology or language. The purpose of this commentary is to describe some of our “Aha!” moments from conducting two pilot studies funded by the Patient-Centered Outcomes Research Institute. Over time, we came to understand how our language and word choices may have been acting as a wedge between ourselves and our community research partners. We learned that fruitful collaborative work must attend to the creation of a common language, which we refer to as the language of engagement. Such patient-centered language can effectively build a bridge between researchers and community partners. We encourage other researchers to think critically about their cultural competency, to be mindful of the social power dynamics between patient and physician, to reflect on how their understanding might differ from those of their patient partners, and to find ways to use a common language that engages patients and other community partners.

INTRODUCTION

Community-based participatory research involves collaboration. All partners (such as researchers, administrators, health care providers, patients, elected officials, community leaders, and ordinary citizens) are equally involved in the research process, and everyone has a unique strength and contribution to a research project. Both of the pilot studies discussed in this commentary are examples of participatory research, and both are examples of the importance of finding a language of engagement for working with patients and community partners. In a study of mental health needs in the Mississippi River Delta Region, funded by the Patient-Centered Outcomes Research Institute (PCORI), our team of researchers learned the importance of word choice in building relationships with community partners, often referred to as stakeholders. The purpose of this pilot project was to compare and to contrast the use of focus groups and community forums to gather information from community leaders and ordinary citizens on their perspective of the mental health needs in their community. It was clear that differences in language signaled substantial differences in knowledge, attitudes, and underlying beliefs. For example, when we asked about their opinions on mental health, one of the community stakeholders replied:

“No one is going to talk to you about mental health. When people hear mental health they think of crazy… . I don’t know how to help you help crazy people … . If you want my expertise, you have to ask me about things I know about.”

In another PCORI project, aimed at creating a zone of openness to increase patient-centered communication between patients and primary care physicians, we engaged with patients and clinicians in the San Francisco Bay Area to co-create an intervention with us. On the basis of our previous research that found patients to be uncomfortable about disagreeing with their physicians, we invited patient stakeholders to react to our plan to help patients and clinicians get better at disagreeing with each other. One patient stakeholder told us, “You wouldn’t want to encourage patients to disagree with their doctors,” and a physician stakeholder said, “I am uncomfortable about encouraging patients to disagree with their doctors.”

The Patient Protection and Affordable Care Act established PCORI to fund comparative clinical effectiveness research to assist patients, clinicians, and other health care decision makers in making informed health decisions. As of August 2015, PCORI had approved more than one billion dollars in research funding since its inception, starting with 50 pilot projects to support the collection of preliminary data on methods that can be used to advance the field of patient-centered clinical effectiveness research. “Research done differently” has been PCORI’s approach in its first 3 years. PCORI requires significant engagement with stakeholders, patient and community stakeholders in particular, in all stages of the research effort. Some investigators have questioned the value of engagement or the need for such an explicit requirement. Typically, the

Ming Tai-Seale, PhD, MPH, is Senior Scientist at the Palo Alto Medical Foundation’s Research Institute and a Consulting Professor at Stanford School of Medicine Department of Health Research and Policy in CA. E-mail: tai-sealeem@pamfri.org. Greer Sullivan, MD, MSPH, is the Associate Dean for Population Based Research and Professor of Psychiatry at the University of California, Riverside. E-mail: greer.sullivan@ucr.edu. Ann Cheney, PhD, is a Medical Anthropologist and Assistant Professor in Residence at the University of California, Riverside School of Medicine. E-mail: ann.cheney@ucr.edu. Kathleen Thomas, PhD, is a Health Economist, a Research Fellow at the Sheps Center for Health Services Research, and Adjunct Associate Professor of Health Policy and Management at the University of North Carolina at Chapel Hill. E-mail: kathleen.thomas@unc.edu. Dominick Frosch, PhD, is a Fellow in the Gordon and Betty Moore Foundation’s Patient Care Program and Associate Professor of Medicine at the University of California, Los Angeles. He is a Consulting Investigator for the Palo Alto Medical Foundation Research Institute in CA. E-mail: froschd@pamfri.org.
response to such questioning offers points related to the big picture; for example, interventions or treatment approaches developed in partnership may increase the chance of producing culturally appropriate, effective, and sustainable interventions.\(^7\)

Our engagements with diverse stakeholder groups supported by PCORI and other funders have prompted us to critically analyze how our enculturation into biomedical theory and practice has shaped the language we use. As we have come to realize, we learn what Putsch and Joyce\(^5\) refer to as “the language of biologically based and somatically focused health care.” This language is rooted in the scientific tradition, which is characterized by objectivity and rational thought. Biomedical language, similar to other languages, is complex, has its own jargon and specialized terminology, and conveys authority and power. Our work has taught us that patient and community members use diverse language to describe their health and ascribe meaning to their experience of illness. This language is shaped by cultural beliefs about illness and healing, by philosophies of self-actualization, and, in varying ways, by biomedical understandings of disease and curing.\(^6\) For those health conditions that are stigmatized, such as mental illness, the language can be shaped by stigma, which has long been known to be pervasive and powerful.\(^9-12\) Thus, the language we learn through our academic and medical training can limit our understanding of patients’ subjective experiences of health, which extend beyond the absence of disease and encompass a broader, more holistic sense of well-being.

In our effort to activate patients and physicians to fully engage in shared medical decision making, we recognized that our mindset and the language we use can act as a wedge between ourselves and the patient populations we serve. It is critical that researchers be sensitive and make the effort to understand whether a language gap exists and, if so, to agree upon a language that is acceptable to community members, patients or other partners, and researchers.

The cases presented above, each from PCORI pilot projects conducted in different institutions, emerged from the engagement experiences of investigators and can be seen as “Aha!” moments related to language for each of the research teams. We aim to describe the observations that illustrate the need for a more fine-grained understanding of the advantages of partnering with the patient populations we serve. We wish to share the importance of creating a language of engagement across stakeholder groups and heightened mindfulness among ourselves as researchers.

**METHODS AND RESULTS**

**Assessing Mental Health Needs among Rural African Americans**

The PCORI project Assessing Mental Health Needs compared two methods for obtaining community perspectives on the mental health needs of rural African Americans in the Arkansas Delta Region. The researchers on our team engaged the community stakeholders through focus groups, a common method researchers use to collect qualitative data from preselected participants of a specific group—for example, with clergy and with members of faith communities. At the same time, our community partner conducted deliberative democracy forums, a method used to obtain informed public opinion and input from “ordinary citizens.” As a grassroots organization, they have used this method to better understand community perspectives and mobilize the community for social change. Whereas one objective of the study was to compare the process and outcomes of the two methods of engaging stakeholders in the research process, the other was to generate ideas for interventions to address the mental health needs in the community.

In developing the interview guide for the focus groups and the issue book for the forums, we sought input from our Community Advisory Board (CAB), a 12-member group consisting of community advocates, members of the clergy, community-based clinicians, local college students, and persons living with mental illness. We asked the CAB to help us write a definition of mental illness that would be understood by community members. CAB members told us we needed to step back and consider the term mental illness itself. CAB members considered mental illness a negative term and preferred the more positive term emotional wellness. CAB members pointed out that mental carries a negative, stigmatizing connotation, even when used to refer to good mental health. The CAB felt that emotional wellness implied a more holistic state of health that could speak to the community’s view of physical, spiritual, and mental health as interconnected. After engaging in this discussion and agreeing on a common terminology, we then were able to move on to define the term emotional un-wellness. Had we not understood and been sensitive to the language of the community, we would have risked alienating rather than engaging community members. From this pilot study, we learned that community members and leaders 1) understand that stress from poverty and racism are directly related to mental health, 2) are concerned about widespread stigma with mental illness, and 3) feel that community members do not effectively identify mental health problems requiring treatment.

**Creating a Zone of Openness to Increase Patient-Centered Communication (Open Communication)**

Our other PCORI-funded study, the Open Communication study, was designed to address several key gaps in patient-physician communication initially gleaned from patient focus groups and subsequently confirmed in a large survey.\(^4,5\) The findings from these studies suggested that although patients reported feeling generally comfortable about raising questions and expressing their preferences, they were much less comfortable about disagreeing with their physicians, indicating a substantial barrier to shared medical decision making.\(^4,5\)

The Open Communication study engaged 12 research partners with equal representation of patients, physicians, and clinical staff, including a nurse, two medical assistants, and a clinical department manager. Following user-centered design principles,\(^13\) we engaged in extensive discussions with the patient and physician partners about communication challenges in real-life clinical practice to design intervention tools.
The Language of Engagement: “Aha!” Moments from Engaging Patients and Community Partners
in Two Pilot Projects of the Patient-Centered Outcomes Research Institute

that would be acceptable to all stakeholders. We also leveraged insights from the scientific literature on patient-physician communication to guide our efforts to create an environment that could enable patients to feel comfortable asking questions and expressing their preferences even when they were contrary to the clinician’s recommendation. Adopting the “deep-dive” technique used to rapidly immerse a group into a situation for problem solving or idea creation, we engaged our research partners in a series of 2-hour workshops. It was in these workshops that we learned that the language we had intended to use to encourage patients to speak up when they disagree with their physicians—for example, “I respectfully disagree”—could be counterproductive. Upon hearing several patients and clinicians advising against the use of the word disagree, we decided to invite our patient and physician partners to brainstorm with us on how we might best support patients in expressing their views that can be different from those held by their physicians. After multiple iterations, we were able to develop a 1-page Visit Companion Booklet, a communication tool that enables patients to state what is important to them and jointly set an agenda with their physicians. We also designed a short (2.5 minutes) animated video. Rather than encouraging patients to disagree with their physicians when their opinions differ, the narrator in the video reassured: “We want to know when you are uncomfortable about a treatment. It’s okay to interrupt. If something makes you feel uncomfortable, there are often other options we can try.” The video then portrayed a conversation between a patient and a physician in which the patient asked, “Is there something else I can try?” Engagement with physician stakeholders enabled us to design a communication coaching program delivered by standardized patient instructors. The standardized patient instructor portrayed a patient who resisted an approach that her physician had prescribed and asked about other options. The standardized patient instructor also provides a safe space for the physician to practice communicating with empathy and patience when a patient wants something different from what the clinician would prescribe—that is, other options. This multidimensional approach addresses disagreement without using language that could introduce friction in the patient-physician relationship. By discussing options, we focus on the choices available from which the patient and physician can choose collaboratively.

DISCUSSION
These two research projects illustrate how important language is to building relationships between various stakeholder groups. In some ways, each stakeholder group is embedded in its own culture that is reflected in the language and terminology commonly used by that group. We did not initiate either of our pilot projects with an intention to address language per se, but we learned that agreement on specific words or terms was an important first step in engaging patients and community stakeholders.

Many of us had been speaking in the community for years and using the term mental illness without recognizing that we may have been, at the very best, having little impact, and at the very worst, alienating our audiences and acting as a wedge between ourselves and our community research partners. Had we not had this input from our community advisors, the Assessing Mental Health Needs study would have proceeded to use the term mental illness in the study. Likewise, had the Open Communication study not solicited the insights from patients and clinicians, it could have given the impression that the project encourages patients to disagree with their physicians. Using these terms (mental illness and disagree) could have placed a wedge between us and our community partners, therefore decreasing the likelihood of our being able to engage with community members and groups and producing meaningful study findings. When agreement on terminology is reached in a mutual way, this can effectively build a bridge between researchers and stakeholder groups.

CONCLUSION
The goal of this commentary is to encourage researchers to carefully consider the language and terminology used in their work with communities. We encourage researchers to think critically about their own mindset and how their understanding of health and wellness might differ from that of their patients, to incorporate patients’ subjective understanding of illness and disability into treatment programs, and to find ways to build bridges that lead to improved patient-physician interactions and to enhance patient well-being.

By allowing patients, physicians, and community partners to be equal participants in the design of our projects and the language of our projects, we were reminded of the obvious: that patient and community stakeholders and researchers often have different frameworks or paradigms for thinking about health, wellness, and their relationship with health care providers. These differing frameworks are often accompanied by different terminology or language. Fruitful collaborative work needs to attend to the creation of a common language, which we refer to as the language of engagement. More importantly, through engagement with our patient and community stakeholders, changes were made in our research approach that enhanced our ability to work in partnership with our respective communities or stakeholders.

Implications for Policy or Practice
Health care services are undergoing fundamental transformations. Engaging stakeholders in all phases of research has led to patient-centered design processes that have the potential to develop interventions that could empower both patients and clinicians to communicate more openly and more effectively.

It is time to transform our mindset from “the researcher knows a lot” to “the research partners know a lot.” We must be open to adaptive learning; we must be curious and courageous...
The Language of Engagement: “Aha!” Moments from Engaging Patients and Community Partners in Two Pilot Projects of the Patient-Centered Outcomes Research Institute

The Pale Shadows

Words are the pale shadows of forgotten names. As names have power, words have power. Words can light fires in the minds of men.

Words can wring tears from the hardest hearts.

— Patrick Rothfuss, b 1973, American writer of epic fantasy
Boudhanath, pictured in the background, is a Buddhist stupa, which is a resting place for reliquary and a place of meditation. Built roughly 1500 years ago, Boudhanath is one of the largest stupas in the world and a major focal point for Buddhism in the Kathmandu Valley in Nepal. This photograph was taken in 2011 during a 6-month volunteer mission at a hospital in Tansen, Nepal.

Boudhanath was heavily damaged by the magnitude 7.8 earthquake that struck Nepal in 2015. The earthquake killed and injured thousands and left hundreds of thousands homeless. Although reconstruction has begun on the ancient stupa, the country of Nepal, one of the poorest in the world, faces many challenging years ahead as its people work to recover and rebuild. Dr Sun urges readers to support humanitarian aid organizations operating in the region.

Dr Sun is a Physician in the Department of Family Medicine at the Brea Medical Offices in CA.
Integrated Strategies to Address Maternal and Child Health and Survival in Low-Income Settings: Implications for Haiti

Zulfiqar A Bhutta, MD, PhD

ABSTRACT

The Millennium Development Goals for improving maternal and child health globally were agreed on in 2000, and several monitoring and evaluation strategies were put in place, including “Countdown to 2015” for monitoring progress and intervention coverage to reach the goals. However, progress in achieving the goals has been slow, with only 13 of the 75 participating Countdown countries on track to reach the targets for reducing child mortality.

An overview of child mortality rates in low-income countries is presented, followed by a discussion of evidenced-based interventions that can bridge the equity gaps in global health. Finally, comments are included on the companion article in this issue, “Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care” (page 59), and what is needed for that new project to succeed.

INTRODUCTION

Most of the world’s sovereign countries signed the United Nations Millennium Declaration in the Year 2000 to address some of the greatest moral dilemmas of our times: unequal global health, especially maternal and child health; widespread poverty; and barriers to education and development. The Millennium Development Goals (MDGs) were established as a set of interrelated goals and targets to be met by 2015 including “Countdown to 2015” for monitoring progress and intervention coverage to reach the goals; MDG 4 and 5 set targets for all countries to reduce maternal mortality and mortality of children under age 5 years by 75% and 66%, respectively, from what they were in 1990.1

Despite major progress in reducing the burden of maternal and child mortality globally, progress has been uneven and slow. A mere 10 countries have almost two-thirds of the global burden of maternal and newborn deaths as well as stillbirths. It is estimated that 6.2 million children (uncertainty range [UR] = 5.7-6.9 million) younger than age 5 years died in 2013, a 63% reduction from 16.9 million (UR = 16.3-17.4 million) in 1970.2 However, there are still wide disparities, and in 2013, child mortality rates ranged from a high of 151.4 per 1000 population (UR = 129.3-176.2/1000) in Guinea-Bissau to 2.2 (UR = 1.7-2.8) per 1000 in Singapore. Of the 75 Countdown countries that have almost 98% of all maternal deaths and deaths of children younger than age 5 years, only 13 countries are on track to reach MDG targets for child mortality. Other global estimates from the Institute of Health Metrics and Evaluation indicate that only 31 developing countries will reach MDG 4 targets by 2015.

Of the 6.2 million children who died before age 5 years in 2013, 51.8% (3.26 million) died of infectious causes and approximately 44% (2.76 million) died in the neonatal period.3 The 3 leading causes of newborn deaths are perinatal complications (0.97 million [15.4%], UR = 0.615-1.537 million [9.8%-24.5%]), pneumonia (0.94 million [14.9%], UR = 0.82-1.06 million [13.0%-16.8%]), and intrapartum-related complications (0.66 million [10.5%], UR = 0.42-1.05 million [6.7%-16.8%]). Reductions in pneumonia, diarrhea, and measles collectively were responsible for half of the 3.6 million fewer deaths recorded in 2013 vs 2000. Causes with the slowest progress were congenital, prematurity-related deaths, neonatal sepsis, injury, and other causes. It is also clear that mere secular trends will not lead to global gains, and at present trends, the world would still lose 4.4 million children younger than 5 years in 2030 due to preventable causes.

An unrecognized and unaddressed burden of stillbirths exists globally and is not included in the current global burden of disease estimates.4 Unfortunately, 76.2% of an estimated 2.64 million stillbirths (UR = 2.14-3.82 million) in 2009 worldwide occurred in South Asia and sub-Saharan Africa, mostly among rural populations. An estimated 45% (1.19 million, UR = 0.82-1.97 million) of these stillbirths occurred in the intrapartum period, reflecting a clear extension of the neonatal deaths related to intrapartum events, previously labeled as birth asphyxia deaths. The highest risk time is around birth, when more than 40% of maternal deaths (around 125,000) and combined stillbirths during labor and neonatal deaths (a staggering 2.2 million) occur. These deaths occur rapidly, requiring urgent response by health care workers.

EVIDENCE-BASED INTERVENTIONS AND INNOVATIONS TO ADDRESS INEQUITIES

A series of rigorous research studies since 2003 have underscored the fact that we have a host of evidence-based interventions that can potentially reduce...
child mortality. Multiple recent evidence syntheses indicate that we have a range of preventive, promotive, and therapeutic interventions that can affect newborn and child survival.3

Despite the knowledge and availability of information and guidelines, major gaps remain in implementation. This is reflected in vast inequities in coverage of key interventions between countries and, importantly, within countries. These differences are sometimes systematic between subpopulations with varying attributes such as poverty, sex, ethnicity, or geographic region. Understanding the social determinants that relate to the excess burden of child mortality and morbidity is critical to action. Poverty is a huge barrier and affects all levels of care. Much of the burden of maternal and child mortality and ill health is concentrated among the poorest countries of sub-Saharan Africa and South Asia. In many of these countries, the bulk of the mortality is clustered among the poor people, frequently residing in remote and rural populations with limited access to health care services. However, a sizeable proportion of deaths also occurs among urban poor individuals living in slums with limited social support networks and abysmal living conditions.

A major advancement in our understanding of intervention strategies is also the ability to bridge these equity gaps. In addition to the selection of evidence-based interventions, this has been made possible through a range of delivery platforms such as deployment of community health workers to reach populations in need, addressing financial barriers through global and local strategies, integrated delivery platforms, and innovations involving technology solutions for diseases of poor populations. However, mere supply-side factors are insufficient on their own without creating community demand. The latter has been essential to affecting newborn health and household behaviors, including improved care seeking by families through community support strategies, especially women's groups.6

Additional innovations such as mobile health technologies, or “m-health,” have huge potential to reach populations at risk and also improve health worker performance. Indeed, m-health can be used for a wide range of purposes, including health promotion and illness prevention, health care delivery, training and supervision, electronic payments, and information systems. An additional key element critical to achieving equitable health care is the availability of high-quality health care at all levels of the health system.

POTENTIAL OF THE PLANS FOR MATERNAL AND CHILD HEALTH CARE IN HAITI

In the article, “Addressing the Child and Maternal Mortality Crisis in Haiti through a Central Referral Hospital Providing Countrywide Care,” on page 59 of this issue, we present an ambitious plan to fast-track improvements in child and maternal health in Haiti, including building a central referral hospital. The foray of a private, not-for-profit organization into areas of public health and one of the poorest countries of the world is a welcome move, and the planned set of interventions and services in Haiti is especially laudable. The development of integrated primary care and community mobilization strategies, coupled with the provision of tiered services for both secondary and tertiary care, affords a unique opportunity to provide high-quality health services at affordable costs in this poor country.

Although the genesis of the project may lie in philanthropy and humanitarian assistance, its long-term sustainability will depend on the development of financing programs that can be linked to social safety nets, cash transfers, and insurance plans. Given the emphasis on the forthcoming sustainable development goals for universal health care, this project offers a unique opportunity to “walk the talk.” Its success lies not only in implementation and reach but also in robust monitoring/evaluation and accountability, the cornerstone of global health governance.

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

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

References
The Jigsaw Puzzle in the Lunchroom

John F Steiner, MD, MPH

Over a year ago, members of our Research Department began to bring jigsaw puzzles into the office. Someone would select a puzzle and spread out the pieces on a table in our lunchroom. I watched with interest as our staff began to organize the puzzle. Border pieces were sorted, then assembled. Shapes and colors were aggregated. Some days, nothing changed. Some days, whole images emerged. Sometimes there was progress between Friday night and Monday morning. Each puzzle seemed like a multi-authored scientific paper with unknown contributors—no first author, no senior author, no titles or degrees.

Most researchers are introverts. We sit in offices with closed doors or in cubicles with powerful computers and little other equipment. A good day is one with plenty of uninterrupted time to think, to write, or to analyze data. We emerge for nutrients, caffeine, hydration, and (reluctantly) for meetings. Although we’re not averse to working on puzzles with others, we’re also content to work alone. As a result, our strategies for solving jigsaw puzzles emerge rarely from direct discussion, but rather from tacit, sequential effort.

As the director of our department, I feel an obligation to lead by example. When I am stuck on a research problem or need a break from meetings, I’ll go to the lunchroom and fit in a few pieces. To my surprise, I find that I like assembling boundaries and big splotches of color with few defining images. Some of my colleagues start with borders as I do, creating form but delaying realization. Others start with a striking feature—a mountain, a boat, a face. Some of us cluster similar pieces even if we don’t connect them. Others fit a random piece when passing by.

I particularly enjoy the times when I’m staring at the puzzle and someone walks in to heat up their lunch or get a cup of coffee, and begins a conversation. We may talk about research projects, but we also talk about family, home repairs, current events, or movies. Great ideas have emerged from such conversation, and many of them have nothing to do with research.

A puzzle can be a mirror. When all the pieces resemble each other, I get stubborn. I’ll stop by for a few minutes after work to fit more pieces before I leave. On the way home, I reflect that this stubbornness is a legacy of my clinical training. When patient after patient was admitted to my care, I would examine each person and their clinical puzzle. If I couldn’t solve it in the middle of the night, at least I could group the pieces and then wait for daylight and other eyes.

Some hard puzzles have pieces that almost fit. This problem only becomes evident when the puzzle is almost complete and we have the right number of pieces but no place to put them. At such times of “crisis,” it helps to see the problem from a new perspective. For example, if we squat and look at a puzzle along the top of the table, the image disappears but a subtle bulge may reveal where someone has jammed in a piece. One time I found a misfit piece by closing my eyes and running my fingers over the surface of the puzzle.

Puzzle-building is nonlinear, unlike the assumptions of our statistical models. At the beginning, not much changes as we turn all the pieces right side up, group colors, and find edges. If the puzzle is easy or near completion, the jumble of pieces diminishes rapidly. At this point, someone is always hovering over the puzzle, and the lunchroom conversation is enthusiastic. At other times a puzzle starts quickly, but it bogs down when nothing is left but an expanse of blue sky and hazy clouds. People passing through the lunchroom then start questioning whether we will ever finish the puzzle. The leader in me begins to wonder: what, if anything, should I do to help? Thus far we’ve never quit on a puzzle, although I suspect we would have much to learn from doing so.

One puzzle in the lunchroom is stored in a plastic bag because the box with the picture was lost. I’m curious to see if we’ll ever unpack it. In bleak moments, I worry that this puzzle is a metaphor for the health care system: a jumble of pieces with no coherent image. I worry that all of us inside that system—clinicians, staff, administrators, researchers, and policy makers—are working on entirely different puzzles. I worry that we continually mistake our part for the whole.

Thinking about the jigsaw puzzles in our lunchroom restores my optimism. In health services research, we work on hard problems. We try to understand how people deliver health care, and how people use that care. We try to identify ways to help systems serve their members and patients, improve quality, and contain costs. We have learned that to do our job, even introverts must band together—clinicians, economists, epidemiologists, social scientists, programmers, project managers, statisticians, and administrative staff. When we agree on a question and a strategy for addressing it, answers emerge like the images on a jigsaw puzzle.

John F Steiner, MD, MPH, is the Senior Director of the Institute for Health Research in Denver, CO. E-mail: john.f.steiner@kp.org.
The Jigsaw Puzzle in the Lunchroom

gradually, anonymously, without claims of ownership but with shared satisfaction in the final product.

We have plenty of good, hard problems in health care, but we may not have enough lunchrooms. If we can build learning communities where people with disparate perspectives can bring their puzzles, who knows what new methods we may develop and what new images we may discover? It may not matter which puzzle we start with as long as we work together to develop new strategies for puzzle-solving.

Watching our Research Department solve jigsaw puzzles increases my confidence that there is a big picture in health care, and that all the pieces will fit. If we create the right work space, we will gravitate to shared puzzles. If our instincts are sharp, we will choose the most promising puzzles to solve. If we are patient and persistent, we will solve them.

Disclosure Statement
The author has no conflicts of interest to disclose.

Acknowledgement
I gratefully acknowledge my colleagues at the Institute for Health Research. An earlier version of this commentary was published in August 2015 in the online newsletter of the Institute for Health Research.

Labors

A witty friend of mine once remarked that the world thinks of the man of science as one who pulls out his watch and exclaims, “Ha! half an hour to spare before dinner: I will just step down to my laboratory and make a discovery.” Who but men of science themselves are to blame for such a misconception? Out of the many memoirs which fill our libraries few recount the labors of investigators, even of those who seek to solve the secrets of the great maladies which annually destroy millions of us—surely a matter of interest to everyone. Our books of science are records of results rather than that sacred passion for discovery which leads to them. Yet many discoveries have really been the climax of an intense drama, full of hopes and despairs, visions seen in darkness, many failures, and a final triumph: in which the protagonists are man and nature, and the issue a decision for all the ages.

— Memoirs, Sir Ronald Ross, KCB, KCMG, FRS, FRCS, 1857-1932, British physician and 1902 Nobel Prize recipient for Physiology or Medicine
ABSTRACT
This case study is an example of narrative medicine applied to promote self-awareness and develop humanistic contents in medical education. The impact and the human appeal of the narrative lie in the maturity and empathy shown by a student when reporting his dramatic experience during the care given to a newborn (with Patau syndrome and multiple malformations diagnosed at birth) and to her mother. The narrative approach helped the student to be successful in bringing out the meaning behind the story and to position himself from the mother's and newborn's perspective. The student's introspection changed a seemingly scary interaction into a positive experience, overcoming many initial negative emotions, such as fear, disappointment, horror, hopelessness, and insecurity in the face of the unexpected. It is uplifting how the student was strengthened by the power of maternal love to the point of overcoming any remaining feelings of eugenics or rejection. Other important lessons emerging from the case study were the art of listening and the value of silence. This narrative shows how the development of narrative competence can help establish a good physician-patient relationship, because the physician or the student with such competence usually confirms the patient's value and demonstrates concern for them, focusing on what they say and allowing genuine contact to be established, which is necessary for effective therapeutic alliance. The student's interpretations of the meaning of love and value of life inspired him on his reframing process of a medical practice marked by vicarious suffering.

CASE REPORT
It should have been a normal day—an interview with a patient at the hospital in my third-year neonatology elective module. However, before entering the ward, I was anxious because my teachers had alerted me that the case was complex and the patient's general condition was critical. Besides, I knew the first contact is always decisive in establishing a good physician-patient relationship. Inside the ward, I (JAMP) met a shy and sad woman, Mrs F. I introduced myself and soon realized that she was very friendly and open to dialogue. She was 19 years old, married, and unemployed. She reported she had abandoned her studies after discovering she was pregnant. Now, she had just given birth to her first child, G.

Baby G was a 14-day-old newborn with an intrauterine diagnosis of holoprosencephaly (characterized by incomplete midline cleavage of the prosencephalon and associated with neurologic impairment and dismorphism of the brain and face), with multiple malformations diagnosed at birth. The diagnostic hypothesis was Patau syndrome, or trisomy 13. The prognosis of this syndrome is extremely poor: 55% to 65% of affected patients die in the first week after birth and 70% to 90% by the sixth month; only 5% to 10% survive beyond the first year of life.²,³

During the history taking, Mrs F told me very sadly that she wanted very much to have a child and that the baby had generated high expectations in her family. So I asked whether her expectations had been met. She answered, “No, they were not met. I had expectations of a beautiful and healthy baby, but my first contact was with an ugly and sick child.” I still had not looked upon baby G, and this statement by Mrs F reinforced my fears. When I turned my head, I saw a baby with multiple malformations on her face and an orogastric tube. She seemed to be looking at me too.

Frightened by the physical aspect of baby G (presenting multiple malformations in the face), I returned to the history taking with her mother. Then I asked Mrs F, “How was your first contact with your daughter soon after the birth?” She replied that she had been terrified because G was an ugly baby, contrary to all expectations that she had during pregnancy. Moreover, she reported that she did not have the courage to hold the baby in her arms during the first day of life. At that moment I put myself in the place of that mother, and then I realized that I would have had a similar reaction in this situation because I also would have had aspirations of having a beautiful and healthy child.

Continuing the history taking, I asked her about her relationship with baby G after the initial contact, and whether
was unhappy with the hospital environment because the other (which would take another three weeks). Furthermore, she information only when the karyotype analysis was ready medical staff would be capable of giving her more accurate me that she was anxious about baby G’s prognosis, and the F had gone through, with similar reactions.

is, whether I was able to go through all those stages that Mrs noticed that I had the answer to one of my questions—that warmth, love, and affection for baby G. At this moment, I

what I expected, it was one of the most beautiful scenes I had

directly into the existing slot in her upper lip. Contrary to

curious because I had never seen a child with cleft lip and

can be applied to promote self-awareness and develop human-istic content in medical education. JAMP wrote this narrative during the neonatology elective module in his third year at medical school. The reflective writing allowed the student's introspection to change a seemingly scary interaction into a positive experience, overcoming many negative initial emotions, such as fear, disappointment, horror, hopelessness, and insecurity in the face of the unexpected. This transformative experience led to increased sensitivity and empathy of the student to the conditions and feelings of the mother and the baby, promoting a humanizing effect especially in relation to

DISCUSSION

This case report is an example of how narrative medicine

women were asking questions about baby G’s disease and she was afraid about whether she was prepared to devote the rest of her life exclusively to the care of her daughter.

In one of our meetings, an important fact reported by Mrs F was that she had the unconditional support of her entire family, especially baby G’s father, who was very fond of his daughter and wife.

My encounters with Mrs F had been marked by several moments of silence, primarily because of my lack of knowl-edge about how to handle the situation. So I sought out the psychologist who gave support to the students. She suggested that we have a conversation with Mrs F away from other people in a quiet and private place. The psychologist was the one who conducted the interview and this was marked by long moments of silence interspersed with short dialogues and crying spells. Moreover, she performed the interview passively, by allowing Mrs F to reflect on her thoughts and sentences.

After this consultation I felt relieved because the moments of silence that marked my conversations with Mrs F were actu-ally the best way to handle the situation, which was allowing the mother to express her feelings.

Two days later, when I came back to talk to Mrs F, she and baby G had received medical permission to stay home for a week. I remained with several questions and only one certainty: my encounter with baby G and her mother was essential for my professional growth, and even more for my personal growth, because I had the opportunity to learn a little more about the meaning of the word life.

life.
The physician must understand not only the disease but also the patient, and the physician-patient relationship gains therapeutic significance. This model seeks a holistic view, in which psychological and social aspects are intrinsically linked to the biological ones, which requires the use of pedagogic strategies that promote the development and the preservation of the students’ self-awareness and empathy.

At the Medical and Nursing Schools of Escola Superior de Ciências da Saúde (ESCS), Brasília, Federal District, Brazil, the students complete six-year and four-year courses, respectively, that integrate basic science and clinical teaching from the first year of the medical and the nursing school. There is no separation into preclinical and clinical components. Students take part in small-group problem-solving sessions and clinical practical activities in the Universal Health System of the Federal District from primary to tertiary care in a Systems Based Curriculum. The students are gradually exposed to practice and contact with many stressors, such as dealing with a congenitally deformed baby girl and a young mother, as in this case report. These stressors, which cause repulsion and suffering in most people, are sources for introspection and reflection in order to have a less traumatic and more productive habituation process. To achieve this goal, many resources have been used in our medical school, such as psychodrama, Balint groups, and arts-related activities.

Before contact with real-world situations, simulation training is carried out. For many of the difficulties faced by our students in these scenarios, our school also has the support of psychologist professors (as narrated in this case report) and a psychoeducational advice service.

Among the major arts-related activities, the narrative medicine exercise plays an important role in enhancing empathy and clinical skills in the curriculum of the Medical School of ESCS. In a broader view, literature plays a critical role in sensitizing writers and readers. We make sense of the world and things that happen to us by constructing narratives to explain and to interpret events, both to ourselves and to other people. In this sense, Rita Charon, MD, coined the term narrative medicine to describe medicine practiced with narrative skills and marked by an understanding of complex narrative situations among physicians, patients, colleagues, and the public. Physicians are in a privileged position to become writers. Conceptually, medicine and storytelling go together because multiple narrative possibilities are generated by illness and healing: autobiographic descriptions of the patients, the physicians’ reports, and the course of the illness, exposing associations between language, subjects, and time. Physicians are in constant contact with the frailty and strength of life. They have the opportunity to observe an extremely fragile side of life: parents with malformed children, children with cancer, infertile women, young individuals deformed by burns, and all types of human misfortune. On the other hand, they can witness the miracle of life when a child is born, during the successful resuscitation of a patient with cardiac arrest, and in the happiness of surviving a malignant disease. These
situations allow a unique learning opportunity concerning the nature of human relationships.20,37

There is strong academic support regarding the importance of the study of narratives in medical education.21,24-26,38,41 Every patient has a personal story and wishes more than the treatment of his/her symptoms.20,25,42 The education focused only on the interpretation of increasingly complex diagnostic examinations and the prescription of drugs does not meet the desires of patients, who want to understand and give meaning to their own expectations at levels beyond the biological one.25,16,19,24,25

In narrative medicine, the student is invited to produce a narrative marked by the interaction with illness and healing from a self-reflective practice, in an integrated way, providing to the students not only a descriptive skill but also the ability to perceive the humanity of patients, individuals who have a history, values, knowledge, and feelings, and who developed their illness in the context of their lives.18,19,21,22,24-26,37,43 This ability to understand the meaning and significance of stories, considering the patients’ perspectives and desires, becomes a key component of clinical practice in narrative medicine. It is an invitation to the development of empathic skills, such as insight, listening, analysis, and interpretation of subjective experiences with humanization and professionalism.18,19,21,22,24-26,37,41 This practice opens up new possibilities for clinical experiences and relationships that bring the benefit of pursuing a more humanistic medical approach, by which it strengthens the therapeutic relationship.16,18,22,24-26,37,42-44

Narratives provide access to knowledge not just about patients and their conditions but also about the students themselves, as narratives allow the free expression of students’ subjectivity. This expression can speed up the maturing process of their personal and professional identities, providing not only a better understanding of the patient and his/her illness but also a chance to dive into the students’ experiences, generating greater confidence, the development of values and virtues, and the capacity to recognize and prevent errors.18,21,24-26.38 On the other hand, if the student has an impersonal or cold demeanor, without qualified listening skills, his/her narrative ends up reflecting emotional impoverishment or directly expressing natural difficulties. Then, the teacher is more likely to perceive this trivialization and the disappearance of the human dimension by reading the student’s narratives.44

CONCLUSION

Narrative medicine is a model of humanized and effective medical practice, consistent with a formation that aims to enrich medical practice, favoring the exercise of qualified and humanized medicine. This case report shows how narrative medicine can be applied to promote self-awareness and develop humanistic content in medical education. The impact and the human appeal of the narrative lie in the maturity and empathy shown by a student when reporting his dramatic experience during the care given to Mrs F and baby G, in which JAMP successfully reached the depth of his being and positioned himself from the perspective of the mother and the newborn. Reflective writing allowed the student’s introspection to change a seemingly scary interaction into a positive experience. This successful case illustrates how important narrative medicine is for building new generations of clinicians who are capable of meeting the challenges of medical practice and pursuing a more humanistic medical approach.

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

Acknowledgment
Mary Corrado, ELS, provided editorial assistance.

References
Love and the Value of Life in Health Care: A Narrative Medicine Case Study in Medical Education


Something More

Medicine alone takes as its province the whole man. … With man in all the complexity of his body and mind from his conception to his last breath; and its concern extends increasingly beyond his sicknesses, to the conditions which make it possible for him to lead a healthy and a happy life. We speak of medicine as both a science and an art, and surely these two aspects are complementary. Science is analytic, … art is intuitive, and sees in the whole something more than can be explained as the sum of its parts.

— Russell Brain, DM, FRCR, FRS, 1st Baron Brain 1895-1966, British neurologist
The Role of Clinical Records in Narrative Medicine: A Discourse of Message

John W Murphy, PhD; Jung Min Choi, PhD; Martin Cadeiras, MD

ABSTRACT
This article is designed to unite theory and practice. The focus of attention is the impact of narrative medicine on clinical records. Specifically important is that records are created through dialogue, whereby patients are able to grow the record through their ability to offer critiques and alternative explanations. Merely allowing patients to peruse their records, through advances in technology, is not sufficient to facilitate this aim. Various theoretical and practical considerations are discussed that may facilitate patient involvement and the creation of more accurate and relevant patient records.

INTRODUCTION
Narrative medicine has become a recognizable theme in the medical literature nowadays. In the most general terms, this development represents a critique of the medical model. But this trend does more than simply raise the issue that standard medical practice is reductionistic. The point, however, is not to become merely more holistic and to consult increasing amounts of data when making clinical decisions. Within the framework of narrative medicine, additional data do not necessarily result in interventions that are more attuned to the histories and daily lives of patients.

Rather than asking for more data, the nature of knowledge is called into question. In this regard, those who promote narrative medicine advance an epistemology that is not pursued regularly by those who critique reductionism. Specifically, owing to the emphasis placed on language use, a serious question is posed about the nature of both physical and social reality. A desire for more data, accordingly, does not require reflection on how knowledge is generated and used.

At the core of narrative medicine is a new perspective on how knowledge gains legitimacy. What constitutes valid knowledge is related to human action, specifically how language is employed. The basic idea is that the reality of patients is never directly encountered by a clinician, or anyone else, but is revealed gradually through the stories they tell about their lives and social conditions. Any so-called markers of illness, therefore, should not be treated as objective signs but codes because their identity is snared in layers of culture and the accompanying interpretations.

The accumulation of information about a patient is thus a hermeneutic exercise. Instead of trying to unearth facts, those who practice narrative medicine attempt to unravel the meaning of those facts. Symptoms, accordingly, should be not merely documented but situated within the stories patients weave to make sense of their lives. How these patients interpret and organize their lives, including their illnesses, is the focus of attention.

Although critics of narrative medicine view this theory to be dense, they also cite the paucity of concrete examples of how this linguistic philosophy changes clinical practice. Additionally, at times, the theory and practice seem to be worlds apart. Hence, the thrust of this article is to apply narrative medicine to a particular practice, specifically clinical record keeping, to make clear the impact of this epistemology.

THE LINGUISTIC TURN
Narrative medicine is tied intimately to the so-called linguistic turn, that is, the theoretical maneuver that identifies language as instrumental to how behavior or events are perceived. Those who accept this philosophical maneuver want to change the way in which language is often described. In traditional parlance, language is identified as a tool. Accompanying this outlook is the assumption that the influence of language can be overcome, thereby revealing an objective reality. According to Roland Barthes, a French literary critic, there is thought to be an outside to language that can be reached with the proper methodology.

This description supports a principle that pervades Western philosophy. That is, truth can be discovered only if human contingency is transcended, so that external principles can be grasped. In this particular case, language is envisioned to be a pointer that can note crucial distinctions and highlight various aspects of the world. All the while, however, the objects of these activities are not influenced by language. Their objective features are simply put on display. This perspective is called the indexical thesis.

Beginning with Wittgenstein, but enhanced by a host of writers such as Merleau-Ponty and Lyotard, many philosophers began to reject this theory. Their contention is that language is not neutral, like a pointer, but mediates...
everything that is known. Persons live through language. And owing to the ubiquity of speech, including the accompanying interpretations, no facet of social existence is directly encountered. There is nothing outside of language that eludes interpretation, including the body or any other facet of illness. In this regard, interpretation is foundational.

For this reason, Wittgenstein inaugurated the trend of referring to language as a game. The idea behind this new metaphor is that persons are immersed in language, and their speech acts shape reality. How they play the game, in other words, provides their lives with organization and meaning. Language does not merely represent reality but is creative and inventive. As a result, what phenomenologists say, now facts must be understood to have a “biography” that physicians must consult, if they are going to understand accurately a patient’s condition.

Arthur Kleinman, an aficionado of patient stories, argues that a moral world is the product of language use. Physicians must learn how to enter this domain to make a sound diagnosis and outline a sensible course of treatment. What is often acknowledged at this juncture, given the importance of these narratives, is that physicians should learn how to listen to their patients. Although that is a valuable lesson, narrative medicine moves beyond simple listening.

Listening is linked typically to exhibiting empathy or care, or extending comfort. In the end, the aim is to become more patient-centered. The problem with these traits, from the perspective of narrative medicine, is that they do not necessarily involve the co-creation of knowledge. All that may occur is that the physician is attentive to more details.

So what is important about co-creation? As opposed to monitoring details, co-creation entails recognizing that patients interpret these features, and accuracy is achieved only by infiltrating these interpretations. Rather than comprised of empirical traits, a patient’s world is an ongoing construction, undertaken with a variety of persons, including physicians, and may not be easy to enter. After all, empirical markers are neat, whereas interpretations are murky, ambiguous, and difficult to pin down. The question that becomes important is: how can the medical record facilitate entry into this elusive domain?

What is important to note is that patients always present an illness; this condition is revealed gradually and, often, circuitously by a patient. When judged by narrative medicine, however, this process is not disinterested but includes perspectives, values, and commitments. A presentation is always motivated and expresses an angle or disposition. Nothing can remove symptoms from these entanglements, even the most sophisticated laboratory tests. Furthermore, how a presentation will progress or be received is difficult to predict.

A physician, consequently, must learn how to read these scripts in a relevant manner. To fulfill this task, the standard approach to medicine must be rethought, whereby clinicians focus primarily on the empirical features of a case. To make this shift successfully, how persons construct their worlds must be elevated in importance and incorporated into a clinical record. A key principle at this juncture is that data have specific significance for patients.

BEYOND DOCUMENTATION: AN ARCHAEOLOGIST’S TOOL

The traditional purpose of the medical record is to document a patient’s condition. These data that are gathered are thought to enhance the decision making of physicians and other clinical staff. The problem with this scenario is that patients present their situation. As a result, data are not easily observed but enmeshed in perspectives, conflicting interests, and habits. Owing to these influences, some critics argue that symptoms are negotiated.

Through a process of give and take, certain ailments emerge as paramount and are given meaning. And if the physician is skilled at this dialogue, a proper assessment is made of these complaints. Within the common purpose of record keeping, a problem list is established. Care must be taken to ensure that this catalogue corresponds to what is expressed by patients, rather than cultural stereotypes or other commonly held or clinical expectations.

But in principle, documentation is expected to be dispassionate and outside of this exchange. Documentation, accordingly, is focused, attentive, and precise. Those who document properly, in fact, are taught to reflect or mimic the condition presented by a patient, in the most detailed manner possible. If undertaken properly, documentation is hardly an inspired activity. Regularity and standardization are anathema to the active engagement of a patient.

As should be noted, documentation is inconsistent with narrative medicine. For example, classifying and categorizing are presumed to be precise, and therefore are outside of the exchanges that are a part of any negotiation. But the thrust of narrative medicine is not to piece together tidy bits of data to solve a puzzle. In other words, physicians should not strive to be data processors who covet clean input to make decisions that mimic a logic-tree.

Rather, to borrow from Foucault, physicians should be “archaeologists.” According to this writer, what does an archaeologist do? As the term suggests, they get to the base or root of behavior or events. What Foucault elevates in importance, however, is the discursive or linguistic practices that are obscured by empirical traits but hold the key to their meaning or significance. Archaeologists explore this vital domain that remains hidden when empirical data are pursued. They delve into recesses that are interpretive and thought traditionally to impede sound clinical decision making and thus dismissed as risky.

The challenge that remains is how to transform the medical record into the archaeologists’ tool. How can this device be rethought, so that classification is eclipsed by entry into a realm that is often eschewed? In the next section, some themes will be addressed that can provide a new slant on record keeping that stresses the meaning of physical traits. The hope...
is that by recognizing some important distinctions, the hermeneutic task emphasized by narrative medicine can be incorporated into record keeping.

**RELEVANT INFORMATION: MESSAGE**

The term *hermeneutic* is derived from the name Hermes, the messenger god.5 The basic idea is that in every physician-patient exchange a message is at stake. Without a story, in short, data are useless. Like Hermes, those who practice hermeneutics are attuned to messages. What is required, to paraphrase Barthes, is a culturally or socially appropriate reading of texts.20 Physicians, in this regard, must learn how to read in the manner intended by authors (who, in this discussion, are their patients). The point of making the following distinctions is to prompt an awareness that messages hang in the balance of every interaction between a physician and patient.

**Körper vs Leib**

Owing to the pervasiveness of language, and thus interpretation, the practitioners of narrative medicine recognize that patients do not have bodies. In this sense, they borrow a differentiation made by phenomenologists between the *Körper* and *Leib*.21

The term *Körper* is adopted to characterize the usual view of the body. That is, a bodily existence is primarily physiologic. Even in more holistic approaches, where the body and mind are thought to interact, primacy is still given to physiology, although this connection may make an intervention complicated. Still, in the end, physiology is not understood to convey a message, other than those linked to nature.

A *Leib*, on the other hand, is never treated as such an objective entity. According to this rendition of the body, the dualism that sustains a *Körper* is illegitimate; interpretation, as Stanley Fish suggests, goes all the way down, even to physiology.17 As a result, even the body is inundated by cultural messages. Anthropologists have coined the phrase “local biology” to capture this association.22

Those who pay attention to physiology will likely miss this interpretive dimension. For example, clinicians who use the body mass index to calculate a person’s appropriate weight can fall into this trap. Whether a person is considered to be overweight is based on various physical dimensions. Although critics have noted the reductionism that is operative, the validity of interpretation is often downplayed or ignored.23 Specifically, a person’s body image may be inconsistent with these measurements, and thus s/he may engage in a range of activities, including sports, that is indicative of a healthy lifestyle. The label overweight, accordingly, may be inappropriate and encourage behavioral changes that are harmful.

In narrative medicine, persons do not have bodies, as noted originally by Gabriel Marcel, because they are not things.24 Bodies are not objects that are possessed and that physicians probe, but are lived and closely tied to images, myths, and logics about bodily functions and care that may contradict the focus of traditional medicine. Accordingly, a message may be written by the body that physicians are unprepared to read correctly.25

**From Context to the Life-World**

A key facet of a medical record is to provide background information on a patient. Given the significance of messages, even those conveyed by physiology, this function is especially important in narrative medicine. This history can offer insight into the daily lives of patients, related, for example, to their environment and relationships. A somewhat holistic, and thus relevant, picture of a patient’s life can be made available.

But true holism will be forthcoming only if a difference is recognized between context and life-world (*lebenswelt*). Typically, a comprehensive medical record supplies a social or psychological context for a patient’s ailments. In narrative medicine, however, a context may not be the framework that should be sought. What is wrong with context? Most often, context takes the form of additional data. A psychological or psychosocial report is often introduced at this juncture, so that an array of information is available about a patient’s job, educational level, or family situation. The problem, however, is that these data may simply describe surrounding conditions. The context that is supplied, in other words, may be treated as supplementary input, derived from the objective features of the environment. No messages may be involved in this collateral data.

As a result, those who adhere to narrative medicine make a startling maneuver and ignore context! Nonetheless, the holism that they desire requires that illness behavior be existentially situated, or a patient’s presenting problem will not be correctly understood. As a result, again related to phenomenology, context is now treated as the *lebenswelt*.16

A patient’s life-world is replete with interpretation and alive with meaning, instead of filled with dead or lifeless empirical indicators. The aim of the medical record, accordingly, is not to document the presence or absence of specific objective traits but to read the messages that emanate from this realm.

Take high blood pressure as an example. Clearly, stress can lead to this condition. But research shows that stress is not necessarily related to obvious social conditions.26 Identical empirical events may be interpreted very differently, thereby resulting in unique responses. The message that is present, and must be read appropriately, pertains to the meaning of stress and the personal and interpersonal interpretations of this situation. In terms of the life-world, the usual portrayal that stress leads to anything, including high blood pressure, omits a crucial factor. Specifically, the factors that spawn stress are joined together through experience, rather than by a natural, empirical link.

Messages have story lines that connect events to each other.27 This relationship may not be causal in the traditional sense—with “A” and “B” identified clearly and structurally joined—but this interpretive bond is sufficient to supply a rationale for outcomes. A storyline must be read properly, however, before the link can be understood properly between events, social or natural, and a physical condition. How patients envision this association can help to unravel the responses that lead to many physical problems.
No Message to "Markers"

The use of the term markers gained prominence during the early 1980s. These markers, sometimes known as biomarkers, are often defined as objective, measurable characteristics that are indicative of normal or pathologic conditions. Prostate-specific antigen and matrix metalloproteinases, for example, have been used to make judgments about the prospects of experiencing the onset of cancer. Furthermore, owing to their empiric character, in addition to monitoring physiologic states, biomarkers are thought to improve the assessment of health risks.

At this time, and consistent with the emerging conservative politics, the cultural side of medicine began to be rolled back. Within this historical period, the discovery of markers was celebrated. A range of disciplines adopted this nomenclature with pride that progress may finally be witnessed in terms of identifying and remedying problems. The discovery of these markers, for example, may lead to the early detection of health issues and more effective interventions. Clear insights would be in the offering because of the availability of these reliable clues.

This elevation of markers, however, is connected to an epistemology that is antithetical to narrative medicine. Specifically, markers bypass the usual cultural ambiguities and extend to the root of a problem. In view of these visible indicators, probabilities are reduced and desired outcomes improved; direct measurements are improved and causal pathways illuminated. What these objective signs provide is a sound shortcut to determining the presence of a problem and a successful course of preventive or remedial action. In this way, connections are made that might otherwise be mediated and diluted by various situational contingencies.

Nonetheless, a sort of tunnel vision might be encouraged by a reliance on markers. Specifically, markers can easily begin to overshadow experience; after all, these signs represent a direct, natural link to a deeper realm. With readily identifiable indicators available that promise the quick determination of a health issue, the lure of markers is difficult to resist.

This attraction to markers is another area that depends on dualism—an index is embraced that is not confounded by cultural and other situational influences. Accordingly, there is no message to markers, but only a clear logic and the accompanying implications. Such precision would be hard to ignore. But, here again, narrative medicine encourages a bold move on the part of medical practitioners. That is, the messages of patients should not be marginalized by markers. After all, markers are codes and thus never objective.

What happens to markers in narrative medicine is that they are recognized to be codes that are inundated by experience and in need of proper deciphering. Accordingly, their message may indicate a biological condition, along with other stories that are equally noteworthy. A marker for Down syndrome, for example, may say more about a society, family members, or a school system than a future medical disability.

The point is that markers do not stand alone, like an objective referent. These codes, instead, are part of a broader social or cultural text that hermeneutics would always incorporate. The message of markers is thus unduly truncated if their interpretive character is equated with empiric regularities. When this tactic is followed, only the story of biomedical science is told. The shortcoming is that this specific script may have limited relevance to the problem at hand.

Often these distinctions are highlighted to draw attention to the difference anthropologists note between illness and sickness. Illness relates to physiology, whereas sickness is something existential. But as should be noted, this differentiation is not stressed in narrative medicine because nothing escapes the influence of interpretation; every facet of a person’s life is existential. This distinction is simply another rendition of dualism.

So, in the end, what is accomplished by a medical record? Within the frame of narrative medicine, the aim is not to simply localize a problem and streamline decision making. Such a static image is no longer acceptable. What is required, instead, is that a problem be situated in a patient’s life-world. Such a project extends beyond documentation and demands a hermeneutic project that is dynamic and engaging, and thus requires time and sensitivity.

A Patient’s Elusive Identity

As suggested earlier in this article, the critique given thus far is thought to lead to a patient-centered orientation. Indeed, the point seems to be that patients matter, specifically their experiential accounts. The approach encouraged by narrative medicine, in this regard, may seem quite startling. Specifically, narrative medicine is not necessarily patient centered. The reason for this decision is quite simple: There is no patient!

Although this conclusion may be fairly blunt, the rationale employed has a complex theoretical heritage. Consistent with the work of both Barthes and Foucault, persons do not have an essential identity. Their identity is elusive because interpretation leaves no aspect of social existence, personal or collective, unscathed. The various facets of an identity, therefore, are shaped by narratives and must be closely read.

Again, in line with Marcel’s philosophy, persons do not have an existence but make their identity through personal decisions and initiatives and the actions of others. The end result is that identities are not discovered, observed, or encountered but revealed through dialogue. Persons define themselves, construct traits, and make choices, all of which suggest that a patient is an ongoing construction.

The term patient centered, however, suggests that a patient’s identity has a stable foundation. Properly understanding a person, accordingly, is dependent on discovering this base and the accompanying values and principles that guide this individual. For example, Biehl, Good, and Kleinman try to elevate subjectivity, a central storehouse of data, in importance, so that patients might be treated sensitively. But in terms of narrative medicine, such a core does not exist; looking for such a base, in fact, is a distraction. All that is available,
instead, is a myriad of stories that move
an identity in one direction or another.
In a manner of speaking, a patient is a
moving signifier that should be sought,
rather than a composite of basic traits.

**RATHER THAN GATHER,**
**INTERPRET KNOWLEDGE**

Instead of patient centered, narrative
medicine should be thought of as dia-
logue centered. In actual practice, this
difference is critical: knowledge about
a patient must be interpreted rather
than gathered. This change is neces-
sary because a patient is a message that
must be deciphered. Through rapport,
and the connections that are made, the
story or stories that constitute a patient
can be appreciated.

A medical record can facilitate dia-
logue, for example, by establishing a
proper framework for relevance, using
appropriate probes, situating answers,
and making sure that correct language
use is specified. Furthermore, an appre-
ciation can be established for the line of
reasoning a patient is constructing, so
that the logic of an action or response
becomes clear. A medical record can
facilitate dialogue, in sum, by no longer
directing interaction but by growing
through the discourse that is enacted.

In this way, patients participate in
the clinical record. And like any true
dialogue, language use is modified and
assumptions corrected until real un-
derstanding is achieved. Rather than
guiding the discourse, the medical
record is a product of this activity and
always vulnerable to reassessment. As a
result, relevant knowledge can become
accessible.

This process of growing the clinical
record is significantly different from
what Charon refers to as patients be-
coming curators of this document.²
Becoming a curator may mean that
patients are merely allowed to peruse
their records. In many care centers this
activity is already encouraged. Grow-
ing the record, however, requires that
patients be able to recreate the record, if
necessary, to reflect their constructions
of behavior or events. In the broadest
sense, the record is open for challenge
and revision.

The following question may arise,
however, from those who work in large
and busy medical centers: How can this
depth be acquired in a 20-minute visit?

In emergency situations a rapid re-
response is expected. But in many other
cases narrative medicine can be prac-
ticed. Nonetheless, the patient-physi-
ian experience must be reassessed. If
the focus is the life-world, a patient will
be viewed differently than in the past
from the first encounter, thereby alter-
ing the entire relationship. Completing
a health history, for example, will be
less routine and mechanical. And over
time, following the adoption of this
new perspective, a rich body of patient
information will be accumulated.

**CONCLUSION**
The goal of this article is to initiate a
critical discussion about the character
of medical records. Perhaps a fitting
conclusion is to suggest that a new
image of record keeping is needed, es-
specially from the perspective of narra-
tive medicine. The field of technology
design might have something to add at
this juncture. Specifically, patient care
may be improved if record keeping
were guided by the principle of inter-
face. In short, records must interface
with patients.

But interface can have many mean-
ings. Alignment and integration are
two examples. Both of these tactics,
however, suggest that asymmetry is
present, and the process is mechanical;
parts of an activity are simply thought
to fit together neatly.

The interface that is needed, and
consistent with narrative medicine, is
much more dynamic. In this sense, the
work of Lévinas is helpful.³⁰ What he
adds to this discussion is that persons
can meet, face-to-face, in a respectful
and dignified way. Most important,
persons can become integrated into
one another’s world. Charon, for
example, calls this sort of interface
“affiliation,” which encompasses the
“interepenetration of self and other.”³¹
This sort of adjustment represents
the interface required by narrative
medicine, so that messages are prop-
erly read.

The aim of projects such as Open-
Notes and, perhaps in the future,
OurNotes, is to facilitate the proper
reading of case notes. OurNotes, es-
pecially, attempts to promote the par-
ticipation of patients in the creation of their records.

Simply making records available, however, will not
achieve this aim.³² Most important is that patients
are able to shape a record through their insights,
challenge a physician’s assess-
ment, and propose al-
ternational explanations and
courses of action. In other
words, improved technol-
ology, along with the ability
to disseminate informa-
tion, is not necessarily the
answer to increasing the
participation of clients in
their own care.

This new mode of in-
terface, as is indicated
throughout this discus-
sion, is dialogical. The
clinical record, accordingly, grows
out of a discourse that reveals worlds,
rather than a range of evidence, and
is truly inclusive. Combined with the
other points raised in this article, the
introduction of this new imagery may
elevate in importance a patient’s life-
world. After all, true interface embod-
ies this intimacy and requires dialogue.

But as is suggested through this
article, dialogue does not occur automatic-
ly by simply talking about this
activity. And in the case of these two
computer programs (OpenNotes and
OurNotes), the introduction of such
technology may not produce this result.
After all, dialogue is a human rather
than a technical process. Patients, who
may be afraid of interacting with physi-
cians, will have to be encouraged to
make suggestions and voice opinions,
whereas physicians will have to adopt a
new image of their patients. Nonethe-
less, dialogue is rarely impossible but
must be viewed as worthwhile, and
truly pursued, if important changes
required by narrative medicine are go-
ing to occur.
Disclosure Statement  
The author(s) have no conflicts of interest to disclose.

Acknowledgment  
Mary Corrado, ELS, provided editorial assistance.

References  

Different

Taking care of patients is different from taking care of disease.

— Eugene A Stead, Jr, MD, 1908-2005, medical educator, researcher, and founder of the Physician Assistant profession
Melyssa’s Story

My name is Melyssa, and this is my story.

It had been a long day. As I walked up the hill I had walked a million times going home from my mother’s house, I couldn't help but notice that I was much more tired than usual. I’m even having a little trouble breathing, probably because of my condition.

Oh yes, my condition. How could I forget that, especially since it was the reason my day started so poorly with the terrible argument with Jean Paul. After five years of marriage you would think we would know how to listen to each other, that he would try to understand how I’m feeling. He seemed to just want to blame me. I had to start having meetings and are planning things we can do if we all work together. For the first time, I believe pregnant mothers can have hope.

As the three of us sat down around the table, the pastor was the first to speak. “Melyssa, I have good news for you. Although I don’t know all the details, the leaders in the village have started having meetings and are planning things we can do if we all work together. The pastor was the first to...”

http://dx.doi.org/10.7812/TPP/15-140

Lee Jacobs, MD, is the President and Chief Executive Officer of the Bethesda Referral & Teaching Hospital in Haiti and the Associate Editor-in-Chief of The Permanente Journal. E-mail: jacobs@securenym.net.
It all sounded very confusing to me, and I was still thinking about what it must feel like to have hope. But since I was asked a question, all I could do was nod my head. It occurred to me later that a nod of my head was kind of a weak reply.

“What does all this mean to my baby?”

Jean Paul jumped into the discussion. “Pastor, tell Melyssa what you told me earlier.” Jean Paul sounded like he wanted to make sure that what he had heard earlier he heard correctly. “I think she needs to hear it.”

“Melyssa,” replied the pastor, “the first thing they plan to do is to identify all the pregnant women in the village and then organize the nurses and midwives so that they will always be available to assist when it comes time for the babies to be born. They want to make certain that women and their husbands will never again have to have babies at home alone.”

I cried.

Jean Paul and I hugged. He was crying too! He was the first to talk. “What is our next step, Pastor?”

“I’ll take you both to meet with Marie in the morning. She will know what to do.”

It was a night of very little sleep—mostly out of excitement. For the first time in my life I prayed—well, I actually talked with God if that is what prayer is. Why didn’t I pray when I had so much fear? I guess I felt alone.

In the morning Pastor Michel took us to meet with Marie at a little clinic in the village. I had never been there before; as a matter of fact, I had never been to any clinic. The Pastor left, and Jean Paul and I sat down, having no idea what to expect.

Marie asked me about my health and my pregnancies. I told her how I was feeling now, and then I told her about the two terrible experiences I had with my first two pregnancies.

She listened to everything I had to say. When I finished her first words were: “Melyssa, I’m so sorry this happened to you. I can’t imagine the fear you both must be having with this third pregnancy. In this village and surrounding area, unfortunately the majority of women are alone when they are having their babies and many experience tragedies just as you did. It is a major problem. We want to help.

“We will run tests this morning to check on your health and the baby’s health, and then I will meet with you and Jean Paul this afternoon to give you the reports.”

Now this you won’t believe. The nurse put a metal stick on my stomach and we all could see my baby on the glass of Marie’s computer. My baby! Jean Paul was grinning ear to ear.

Oh, in case I didn’t mention it—our baby is a girl!

A nurse then took some of my blood—another first for me—gave me a shot, and then gave me some special vitamins to help my baby. Another new experience: someone caring for me.

That afternoon we sat down with Marie to hear the results of the tests. “First of all, the people down at Bethesda Hospital have reviewed the ultrasound that we did this morning, and they estimate your baby to be 28 weeks old. Although she is little, she looks healthy.”

How could anyone that far away see my baby on Marie’s computer? I could tell Jean Paul was also perplexed.

But neither of us wanted to interrupt Marie.

Marie continued, “We do need to give you some pills since your blood pressure is high, and then we will follow your blood pressure and kidney tests closely. Other than that, you and your baby should do well.”

Hope. I have hope. Thank you God for helping us!

After we left the clinic we went to Pastor Michel’s home where we all celebrated the incredible happenings of the day. Then Pastor Michel prayed a prayer of thanksgiving and also prayed how he knew God has always had a purpose for Jean Paul, and me, and my baby.

Well, two months later, Marie sent me down to the new hospital—to Bethesda—because of my blood pressure and kidney issues. At first when she said I would be going, both Jean Paul and I must have appeared a little uneasy because she quickly added, “A Bethesda Hospital van will be picking you both up tomorrow morning to take you and others on the four-hour trip.” How amazing is that!

Jean Paul looked at me and asked, “Who are these Bethesda people?” He didn’t expect an answer but I replied anyway, “I guess we’ll find out.”

In all my 25 years I have never left the area around my village, although I was a little nervous, I was excited. When we arrived at the Bethesda Hospital and when we stepped out of the van, I couldn’t help but notice, in large print above the front door, the words Hope and Health for Haiti.

Well, the rest is history. My baby was born seven days later, and she sure was tiny. What she lacked in size she sure made up for in noise. Yes, my little Hope is healthy.

The entire experience at Bethesda was like a dream. A wonderful group of doctors and nurses—a combination of North Americans and Haitians—all took great care of Hope and me.

I have to finish my story here because I have to catch a Bethesda van to go back to the hospital this morning. No, it is not because we are sick. I thank the good Lord that Hope and I are in good health. You see, I am training at the hospital so I can become a midwife in my village. I want to do everything I can to make sure no woman—or her husband—ever have to experience childbirth alone. I want them to have hope.

My name is Melyssa, and this is my story.

Rural Haiti

January 2019
“Trauma 99 activation, ETA 5 min!” As an emergency medicine resident, this type of overhead page is what gets my adrenaline pumping. Finally, I thought, I’ve been waiting for some action all night. I looked over at the call sheet: 30-year-old male, single gunshot wound to the torso, CPR in progress. Eager and excited, I ran over to the trauma bay and prepared mentally and physically to save this man’s life. I gathered intubation materials, a cricothyroidotomy tray, chest tubes, central lines, and a thoracotomy kit. This is what I went into emergency medicine for, I thought.

As the paramedics rushed the patient into the trauma bay, an unnatural hush came over the room. He didn’t even look human; his skin was gray, his eyes were fixed to the side, and blood was seeping out of a single jagged exit wound in his back. His shirt was torn, but I could still see brown burn marks on what was left of the white T-shirt that was covering a small-caliber bullet wound on his chest. Right over his heart. I felt queasy as the medics told us how the man’s family had heard the gunshot, how they found him slumped against a chair, how the medics had been doing CPR for 45 minutes already. I could envision his heart taking its last few valiant beats, his life slowly oozing out of him.

As I quickly inspected the rest of his body, I noticed a tattoo on his forearm: he had the stamp of a soldier. I heard my attending physician gasp; he knew this man. They had once worked together and had bonded over the stories and hardships of wartime. Although my attending was not consumed with grief, his eyes were wide with shock. His shirt was torn, but I could still see brown burn marks on what was left of the white T-shirt that was covering a small-caliber bullet wound on his chest. Right over his heart. I felt queasy as the medics told us how the man’s family had heard the gunshot, how they found him slumped against a chair, how the medics had been doing CPR for 45 minutes already. I could envision his heart taking its last few valiant beats, his life slowly oozing out of him.

As I quickly inspected the rest of his body, I noticed a tattoo on his forearm: he had the stamp of a soldier. I heard my attending physician gasp; he knew this man. They had once worked together and had bonded over the stories and hardships of wartime. Although my attending was not consumed by the black hole of PTSD, our patient was not so lucky. This man’s last act was a self-inflicted gunshot wound, and now he was dying in front of us in the trauma bay.

That family meeting was one of the toughest things I have ever experienced. Seeing the look on his wife’s face and listening to her describe how she found him is something I will never forget. I always told myself that I wasn’t allowed to cry, that it was not my grief to experience, that I had to be strong. I had always prided myself on being able to compartmentalize my emotions and my ability to hold my emotions close to the vest. But here, I struggled to hold back the tears. It wasn’t the fact that he was so young, or even that he had died in front of me; it was the fact that he did it on purpose. I had to excuse myself and take a walk—I had 9 hours left in this shift and I had to pull it together.

The next day, there was a similar overhead page, “Trauma 99, ETA 5.” And again, there was that same feeling of giddiness and excitement. The call sheet indicated a 30-year-old female who fell off the roof of a house. I made my way to the trauma bay, ready for action. The paramedics brought in a young woman who was moaning but was otherwise unresponsive. As they gave report, a similar queasy feeling came over me. She had jumped.

The woman’s body was oddly contorted, and the initial imaging studies showed that in addition to suffering other severe injuries, she had essentially snapped her spine in half. We all worked tirelessly to save her, intubating her, placing central lines, splinting her broken extremities, and starting her on pressors until she was stable enough to make it up to the ICU. She was still alive because of our care, yet I kept wondering if we were doing the right thing. I couldn’t imagine the amount of pain she had to be feeling, and even if she were to survive her devastating injuries, at best she would be ventilator-dependent, paralyzed, and have a severe brain injury—why would we ever condemn anyone to a life like that? For the rest of my shift, I felt so guilty and almost hated myself for hoping that she would pass.

As I drove home the next morning, I was exhausted both emotionally and physically. I couldn’t wait to curl up in bed and just sleep. I was lost in my thoughts when someone cut me off on the freeway. I slammed on the brakes, and instead of my typical tirade of curse words, I just started crying. I didn’t even really cry at my wedding, so this display of emotions surprised me. And then I realized: as residents, we work hard to become medically proficient and learn the nuances of our respected specialties; however, we do not really learn how to handle emotionally taxing situations or how to grieve. We often bottle up our emotions in an effort to protect ourselves from the pain of tragedy. We don’t like to talk about our tough cases because it makes us vulnerable. However, by not letting ourselves properly process our experiences, the emotional burden compounds, sometimes to a dangerous tipping point. I realized that it was okay to feel for our patients, that it was okay to hurt, and that it was okay to openly admit it. I was crying for the overwhelming depression and sense of despair that the former soldier experienced. I was crying for the immense sense of hopelessness that drove the young woman off the roof. I was crying for the sadness and grief that their families were experiencing or were about to experience. And, finally, I was crying for myself.

Akhila Pamula, MD, is a Resident in the Stanford/Kaiser Emergency Medicine Residency Program in CA. E-mail: akhilapamula@gmail.com.
Spring 2016
CME Evaluation Program

Section A.

Objective 1
Integrate learned knowledge and increase competence/confidence to support improvement and change in specific practices, behaviors, and performance.

Objective 2
Lead in further developing “Patient-Centered Care” activities by acquiring new skills and methods to overcome barriers, improve physician/patient relationships, better identify diagnosis and treatment of clinical conditions, as well as, efficiently stratify health needs of varying patient populations.

Objective 3
Implement changes and apply updates in services and practice/policy guidelines, incorporate systems and quality improvements, and effectively utilize evidence-based medicine to produce better patient outcomes.

Referring to the CME articles, how likely is it that you will implement this learning to improve your practice within the next 3 months?

Key
5 = highly likely
4 = likely
3 = unsure
2 = unlikely
1 = I already did this
0 = I already did this

<table>
<thead>
<tr>
<th>Objective 1</th>
<th>Objective 2</th>
<th>Objective 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Article 1</td>
<td>Article 2</td>
<td>Article 3</td>
</tr>
<tr>
<td>Article 4</td>
<td>Article 4</td>
<td>Article 4</td>
</tr>
</tbody>
</table>

Mail or fax completed form to:
The Permanente Journal
500 NE Multnomah St, Suite 100
Portland, Oregon 97232
Phone: 503-813-3286
Fax: 503-813-2348

The Kaiser Permanente National CME Program is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The Kaiser Permanente National CME Program designates this journal-based CME activity for 4 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Physicians may earn up to 1 AMA PRA Category 1 Credit™ per article for reading and analyzing the designated CME articles published in each edition of TPJ. Each edition has four articles available for review. Other clinicians for whom CME is acceptable in meeting educational requirements may report up to four hours of participation. The CME evaluation form may be completed online or via mobile Web at www.tjpce.org. The Certification of Credit will be e-mailed immediately upon successful completion. Alternatively, this paper form may be completed and returned via fax or mail to the address listed below. All Sections must be completed to receive credit. Certification of Credit will be mailed within two months of receipt of the paper form. Completed forms will be accepted until June 2017.

To earn CME for reading each article designated for AMA PRA Category 1 Credit, you must:
- Score at least 50% in the posttest
- Complete the evaluation and provide your contact information
Image Diagnosis: Bronchioloalveolar Carcinoma Presenting as Unilateral “Crazy-Paving” Pattern on High-Resolution Computed Tomography

Vikas Pilaniya, MD; Shekhar Kunal, MBBS; Sudhir Jain, MD; Ashok Shah, MD

CASE REPORT
A 70-year-old man presented to our hospital with 18 months of cough and breathlessness. He was tachypneic and had decreased breath sounds and coarse crackles over his left chest. He was human immunodeficiency virus-negative and had never smoked. The 6-minute walk test revealed blood oxygen desaturation from 94% to 86%. The patient was admitted to the hospital for further tests and monitoring to establish a diagnosis.

A radiograph of the patient's chest showed inhomogeneous opacity in left mid and left lower zones (Figure 1). A high-resolution computed tomography (HRCT) scan done one year before presentation highlighted a classic “crazy-paving” pattern, where thickened interlobular septa and intralobular lines, with distinct geographic margins on a background of ground-glass opacification, could be seen in the left upper lobe (Figure 2A). HRCT performed on presentation showed that in the intervening year the lesion had increased dramatically along with minimal left-side pleural effusion (Figure 2B). Sputum stains and cultures for Mycobacterium tuberculosis, fungi, and other aerobic organisms were negative. Fiberoptic bronchoscopy showed no gross abnormality. Bronchial aspirate was negative for all organisms, as was the GeneXpert test for M tuberculosis. Transbronchial biopsy confirmed bronchioloalveolar carcinoma (BAC) (Figures 3A and 3B).

These investigations were carried out during the patient's five-day stay in our institution. After confirmation of the diagnosis, he was referred to a tertiary oncology center for further management and was lost to follow-up.

DISCUSSION
The first-ever portrayal of crazy-paving on HRCT was recorded in a patient with pulmonary alveolar proteinosis and is still considered a hallmark of the disease. Since then, a number of clinical conditions have been associated with this radiologic pattern visible on HRCT. This pattern has also been reported in viral/opportunistic infections, Pneumocystis carinii pneumonia, exogenous lipid pneumonia, diffuse alveolar haemorrhage, and sarcoidosis. The crazy-paving pattern appears on HRCT as diffuse ground-glass opacification superimposed with interlobular septal thickening and intralobular lines in a geographic distribution resembling irregularly laid cobblestones. These areas are usually bilateral and feature distinct margins, which sharply demarcate these areas from the normal lung parenchyma. It has been postulated that the crazy-paving pattern occurs because of processes that cause alveolar filling, because of interstitial fibrosis, or because of a combination of both of these elements.

BAC, a term coined by Liebow in 1960, accounts for approximately 4% of lung cancers. It is a type of non-small cell lung cancer that arises from the bronchioloalveolar epithelium and is typically an adenocarcinoma. The diagnosis of BAC is typically made on transbronchial biopsy, but other diagnostic tools such as sputum cytology, bronchoalveolar lavage, and surgical biopsy may also be used. The treatment of BAC is typically surgical resection, and the prognosis is generally better than other types of lung cancer.
of all primary lung malignancies. It is more common in females and never-smokers. The radiologic presentations of BAC are diverse and range from solitary or multiple pulmonary nodules to cystic disease, cavitation, and consolidation. Most consolidations in BAC are peripheral in location, can persist for a long duration, and can be difficult to differentiate from consolidation of an infective origin.

The revised World Health Organization lung tumor classification recognized this infrequently seen clinical entity as a subtype of adenocarcinoma with three distinct histologic forms: mucinous, nonmucinous, and mixed or indeterminate. In 2011, the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society proposed that BAC be categorized under four new subtypes: adenocarcinoma in situ; lepidic predominant nonmucinous adenocarcinoma; and invasive mucinous adenocarcinoma. The preinvasive lesion subtypes included adenocarcinoma in situ and minimally invasive adenocarcinoma. The invasive subtypes were lepidic predominant nonmucinous adenocarcinoma and invasive mucinous adenocarcinoma. The main purpose of this newer classification was to delineate categories having distinct clinical, radiologic, and histologic characteristics. However, the term BAC is still widely used. BAC presenting radiologically as a crazy-paving pattern is a distinct rarity. BAC should always be considered in the differential diagnosis of this singularly unusual HRCT imaging pattern.

Disclosure Statement
The authors have no conflicts of interest to disclose.

References
The Permanente Journal/ Spring 2016/ Volume 20 No. 2

ONLINE ONLY

CASE REPORTS

Sclerosing Polycystic Adenosis: A Rare Tumor of the Salivary Glands

Christopher G Tang, MD; Justin B Fong; Karen L Axelson, MD; Deepak Gurushanthaiah, MD

ABSTRACT

Case Presentation: A 74-year-old woman presented to the Head and Neck Surgery clinic with a 4-year history of a slowly growing, painful, left-sided neck mass in the tail of the parotid gland. Fine-needle aspiration suggested well-differentiated adenocarcinoma.

Discussion and Results: The patient underwent a superficial parotidectomy and super-selective neck dissection (level 2). Pathology revealed a tumor consistent with sclerosing polycystic adenosis.

Conclusion: Sclerosing polycystic adenosis is a rare inflammatory process that causes fibrocystic changes in the salivary gland. Apocrine-like metaplasia and epithelial atypia are common pathologic features. To our knowledge, a total of 51 cases have been described in the English-language literature.

INTRODUCTION

Sclerosing polycystic adenosis (SPA) is a rare, reactive, inflammatory lesion of the salivary glands resulting in fibrocystic changes and adenosis, similar to what occurs in the mammary glands. Lesions present as slow-growing masses in salivary gland parenchyma. They are discrete, pale, and rubbery nodules. The tumors are not encapsulated but are well defined. Pathologically, they display dense sclerotic lobules and cystic change with hyalinized collagen separation. Apocrine-like metaplasia; epithelial atypia; and ductal, acinar hyperplasia are commonly observed. A distinguishing feature of this lesion is focal cystic spaces within the fibrotic stroma. Most observed cases occur in the parotid gland. We report a typical case of SPA occurring in the parotid gland.

CASE PRESENTATION

A 74-year-old woman presented to the Head and Neck Surgery clinic at the Kaiser Permanente Medical Center in Oakland, CA, with a 4-year history of a growing, painful, left-sided neck mass. Two years before presentation, the patient underwent fine-needle aspiration with negative results for malignancy and did not pursue further workup. The mass persisted and continued to enlarge. The patient now had a firm 3.5-cm mass in the tail of the left parotid gland without overlying erythema. Fine-needle aspiration suggested a well-differentiated adenocarcinoma. Magnetic resonance imaging showed a well-defined, peripherally enhancing 3.5-cm lobe mass (Figures 1 and 2). Surgery was scheduled, and a superficial parotidectomy and a selective neck dissection (level 2) were performed. Final pathology revealed a 3.5-cm, well-circumscribed tumor consistent with SPA (Figures 3-5).

DISCUSSION AND RESULTS

SPA is a rare, benign tumor of the salivary glands, which was first described in 1996. About 80% of SPA cases present in the major salivary glands—specifically, the parotid gland. However, cases have been observed in the minor salivary glands of the nasal septum, buccal mucosa, hard palate, floor of the mouth, and retromolar pad. SPA has also been reported in the lacrimal gland. SPA is equally common in men and women, and reported cases have a wide age of distribution.

Usually, parotid SPA comprises deep-seated, slow-growing, round, palpable masses. Pain and tenderness may be present. The masses are multinodular, with cysts 1 mm to 2 mm in diameter. SPA may be multifocal. Histologically, SPA is characterized by acinar cells with robust eosinophilic structures similar to zymogen granules. Ductal epithelial atypia is common, and epithelial cells exhibit various cells of acocrine, foamy, vacuolated, and mucinous nature. The lobular architecture usually includes atypical nests of myoepithelial cells. However, infiltrative carcinoma growth does not occur.
CASE REPORTS

Sclerosing Polycystic Adenosis: A Rare Tumor of the Salivary Glands

SPA is considered benign. However, one case of ductal carcinoma in situ has been reported. Most cases of SPA are treated with localized surgical resection with clear margins. Recurrence has been reported in up to one-third of cases. Recurrence generally occurs because of inadequate surgical resection and because of the multifocality of the SPA. We found no cases of death or of metastasis attributed to SPA in a MEDLINE literature search.

There is a high chance of misdiagnosis because of the rarity of the disease and because clinicians and pathologists may be unfamiliar with it; for example, the present case was initially diagnosed as a well-differentiated adenocarcinoma. Differential diagnosis included pleomorphic adenoma; benign polycystic disease; sclerosing sialadenitis; and malignant glandular neoplasias, such as mucoepidermoid carcinoma, acinic cell carcinoma, adenocarcinoma NOS (not otherwise specified), and salivary duct carcinoma.

Our case was a 3.5-cm mass in the tail of the parotid gland. Presentation in the parotid gland and histologic findings of cysts and lobular architecture with collagen separation are characteristic of SPA.

CONCLUSION

SPA is a rare inflammatory process that causes fibrocystic changes in the salivary gland. Apocrine-like metaplasia and epithelial atypia are common features. To our knowledge, only 51 cases have been described in the English literature.

Disclosure Statement

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

Acknowledgment

Leslie Parker, ELS, provided editorial assistance.

References

Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

Mitsuro Chiba, MD, PhD; Tsurufuji Tsuji, MD, PhD; Kenichi Takahashi, MD; Masafumi Komatsu, MD, PhD; Takeshi Sugawara, MD; Iwao Ono, MD, PhD

ABSTRACT

In Japan, Helicobacter pylori eradication has been approved since 2013 for treatment of H pylori-induced chronic gastritis, in an attempt to reduce the prevalence of gastric cancer, a leading cancer in Japan. H pylori infection affects more than 50% of the world’s population. H pylori eradication therapy is generally safe. To our knowledge, no case of newly diagnosed ulcerative colitis occurring immediately after H pylori eradication therapy has previously been reported.

A 63-year-old man received a diagnosis of chronic gastritis and H pylori infection. In early March 2014, primary H pylori eradication therapy was initiated; lansoprazole, amoxicillin, and clarithromycin were administered for 1 week. On the fourth day, he had watery diarrhea twice a day. From the 11th day, bloody stools and watery diarrhea increased to 6 times a day. Colonoscopy, performed on the 40th day after termination of drug therapy, revealed diffuse inflammation in the distal aspect of the colon, with histologic findings consistent with ulcerative colitis. He was admitted to the hospital and was provided with a semivegetarian diet and metronidazole. He noticed a gradual decrease in the amount of blood in his feces then a disappearance of the blood. A fecal occult blood test on the 11th hospital day recorded 337 ng/ml. Fecal occult blood test is not indicated during macroscopic bloody stool but is indicated after disappearance of bloody stool. Therefore, he achieved clinical remission by the 11th hospital day. He was in remission on discharge.

New onset of ulcerative colitis should be added to a list of adverse events of H pylori eradication therapy.

INTRODUCTION

With the growing knowledge of the etiopathogenetic role of Helicobacter pylori in gastrointestinal and systemic diseases, attempts to eradicate H pylori have been expanding in the treatment of peptic (gastroduodenal) ulcers, gastric mucosa-associated lymphoid tissue lymphoma, iron-deficiency anemia, idiopathic thrombocytopenic purpura, and vitamin B12 deficiency. In Japan, H pylori eradication therapy was approved for peptic ulcer treatment in 2000, and for mucosa-associated lymphoid tissue lymphoma and idiopathic thrombocytopenic purpura in 2010. With regard to gastric cancer, one of the leading cancers not only in the Asia-Pacific region including Japan but also in the world, the critical role of H pylori in the development of gastric cancer has been established. Consequently, in Japan in 2010, H pylori eradication was approved for patients after endoscopic resection of early-stage gastric cancer. Three years later, eradication of H pylori was drastically expanded to include H pylori-induced chronic gastritis. Namely, in February 2013, H pylori eradication was approved for H pylori-induced chronic gastritis in an attempt to reduce gastric cancer. This means that more than half of the adult population of Japan are identified as possible candidates for H pylori eradication. Along with the development of evaluating cancer risk by combined assay for H pylori infection and serum pepsinogen levels, namely the ABC method, H pylori eradication therapy will prevail more than ever.

H pylori eradication therapy is generally safe. For the primary triple therapy, lansoprazole-amoxicillin-clarithromycin, the main adverse effects reported are diarrhea and soft stools, with frequencies of 7% and 12%, respectively. Only 1 of 271 patients was withdrawn from eradication treatment because of adverse effect (skin eruption). However, there are reports of Clostridium difficile colitis or pseudomembranous colitis associated with H pylori eradication therapy. There is also a report of relapse of ulcerative colitis during the therapy, which eventually required subtotal colectomy. To our knowledge, no case of newly diagnosed ulcerative colitis occurring immediately after H pylori eradication therapy has been reported.

CASE PRESENTATION

A 63-year-old man, 165 cm in height and 55 kg in body weight, was referred to our division in May 2014. He was previously admitted because of vertigo in 2012. Since that time, he received medications for treatment of vertigo and hypertension: betahistine mesylate, meclobamalin, adenosine triphosphate disodium hydrate, clotiazepam, and amlodipine besilate. His family history...
Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

CASE REPORTS

Did not include inflammatory bowel disease (IBD). He reported that he had a daily bowel movement. In early January 2014, he was screened for gastric cancer: a blood test for pepsinogen and esophagastroduodenoscopy. Chronic gastritis and \textit{H} \textit{pylori} infection were diagnosed (Figure 1).

The following month he participated in the 2014 Tokyo Marathon. In early March, primary \textit{H} \textit{pylori} eradication therapy was initiated: lansoprazole, 30 mg; amoxicillin, 750 mg; and clarithromycin, 200 mg, twice daily for 1 week. From Day 4 of treatment, he had watery diarrhea twice a day. The symptoms were not so severe as to halt administration of the medication. From the 11th day, 3 days after termination of the eradication therapy, bloody stools and watery diarrhea increased to 6 times a day. Antibiotic-associated colitis or hemorrhagic colitis was suspected, and he was expected to recover quickly because administration of the eradication therapy drugs had already been terminated. However, bloody stool persisted.

Colonoscopy, performed on the 40th day after the termination of the drugs, revealed diffuse inflammation in the distal aspect of the colon (Figure 2A). The histologic findings from the rectum were consistent with ulcerative colitis: crypt abscess, goblet cell depletion, and marked infiltration by inflammatory cells (Figure 3). The urea breath test was positive for \textit{H} \textit{pylori} infection.

The patient was referred to Akita City Hospital in Akita, Japan, for treatment of ulcerative colitis. His chief complaint was bloody, soft stool twice a day. His appetite was good, and he reported no abdominal pain. Results of physical examination, including the abdomen, were normal. He was admitted to the hospital, where he stayed for 24 days, a typical period of time for a patient with these symptoms of this severity in our hospital. Routine laboratory data, including hematologic studies, liver and kidney function tests, and C-reactive protein, were normal. \textit{C difficile} antigen and toxin were not detected by TECHLAB \textit{C Diff Quik Chek Complete} (TECHLAB Inc, Blacksburg, VA). Stool culture did not reveal any pathogen, including enterohemorrhagic \textit{Escherichia coli}, \textit{Campylobacter jejuni}, \textit{Salmonella} species, \textit{Staphylococcus aureus}, and \textit{Klebsiella oxytoca}. A double-contrast barium enema study showed micropicula and fine barium flakes in the sigmoid colon.

![Figure 1. Timeline of case.](image1)

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>Diagnosis of \textit{HP}-induced chronic gastritis</td>
</tr>
<tr>
<td></td>
<td>Participation in Tokyo Marathon</td>
</tr>
<tr>
<td>2014</td>
<td>\textit{HP} eradication therapy</td>
</tr>
<tr>
<td></td>
<td>Diagnosis of UC</td>
</tr>
<tr>
<td></td>
<td>\textit{UBT} for \textit{HP}, positive</td>
</tr>
<tr>
<td>May</td>
<td>Hospitalization (SVD &amp; metronidazole)</td>
</tr>
<tr>
<td>Jun</td>
<td>\textit{UBT} for \textit{HP}, negative</td>
</tr>
<tr>
<td>2015</td>
<td>Participation in Tokyo Marathon</td>
</tr>
</tbody>
</table>

![Figure 2. Photographs of the distal colon during colonoscopy before (A) and after (B) treatment. Diffuse inflammation was markedly improved after treatment.](image2)

![Figure 3. Photomicrograph of biopsy specimen of the rectum. Crypt abscess (center), goblet cell depletion, and marked inflammatory cell infiltration are observed (hematoxylin and eosin stain, 20x magnification).](image3)
In this case, metronidazole that Westernized Metronidazole, in this case, symptoms lasted for 24 hours. A semivegetarian diet was prescribed to treat ulcerative colitis of mild severity was diagnosed. The patient was provided with a semivegetarian diet designed for patients with IBD. Metronidazole, 750 mg/day, was administered orally during the hospitalization. He noticed a gradual decrease of blood in his feces, then a disappearance of the blood. A fecal occult blood test on the 11th hospital day recorded 337 ng/mL, and this test result became negative (<50 ng/mL) on the 18th hospital day. Colonoscopy on the 23rd day showed a marked improvement (Figure 2B).

The patient and his wife were provided a dietary guidance for a semivegetarian diet from a registered dietitian before discharge. The urea breath test yielded normal results one month after discharge. The patient has remained in remission without medication until time of this publication (Figure 1). In 2015, he again participated in the Tokyo Marathon.

**DISCUSSION**

Because antibiotics are prescribed for *H pylori* eradication, various adverse events of antibiotics can occur in patients undergoing eradication of *H pylori*. Patients are informed of the possible adverse events of the medication, including rash, diarrhea, and bloody diarrhea. In this case, diarrhea appeared on the fourth day of treatment, but it was mild enough to allow continued administration of the medication. After termination of treatment with the medication, diarrhea increased to six times a day and was mixed with blood. Generally, antibiotic-associated diarrhea or colitis subsides spontaneously within a few days after withdrawal of antibiotics. In this case, symptoms lasted for more than a month. *C difficile* toxin, *Klebsiella oxytoca*, or other pathogen was not identified. Pseudomembrane was not observed by endoscopy. Diffuse inflammation in the distal aspect of the colon and the histologic findings of crypt abscess and goblet cell depletion were consistent with ulcerative colitis. The association between antibiotic use and subsequent diagnosis of IBD two to five years later is well documented. The mechanism of this association is not known. Long-term effects of antibiotics on gut microflora might be related to a subsequent onset of IBD. Alternatively, a genetically altered inflammatory response to pathogens may lead to both IBD and infections that require antibiotics, without the former being etiologically related to the latter. In the present case, ulcerative colitis developed immediately after *H pylori* eradication therapy. This indicates an immediate effect of antibiotics on gut microflora, resulting in imbalance (dysbiosis) leading to IBD.

Gut microflora is a critical environmental factor in IBD. Westernized diet-induced dysbiosis of gut microflora can explain the high frequency of IBD in developed countries. A semivegetarian diet has been designed to combat dietary westernization. We recommend that all IBD-diagnosed patients are prescribed a semivegetarian diet, with counseling and education to support the patient’s compliance. In our hospital, this recommendation includes admission to the hospital for treatment to experience and familiarize patients with a semivegetarian diet to ensure compliance at least initially. We treat moderate or severe cases of ulcerative colitis with drugs specific for IBD including 5-aminosalicylic acid, steroid hormones, and biologics together with a semivegetarian diet, but we treat mild cases initially only with a semivegetarian diet. This case is an example showing the induction and maintenance of remission without medication specific for IBD such as 5-aminosalicylic acid. In our practice, oral metronidazole is initially used for about 1 month in treatment of active IBD, with the expectation of eliminating any potentially pathogenic bacteria. Metronidazole is the second-line drug for *H pylori* eradication in Japan. In this case, metronidazole that was prescribed to treat ulcerative colitis seemed to induce *H pylori* eradication.

*H pylori* affects more than 50% of the world’s population. Cases of IBD similar to the present case are
Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

anticipated to appear more frequently along with an expanding requirement for *H. pylori* eradication. It is recommended that practitioners keep in mind that IBD might develop immediately after *H. pylori* eradication therapy.

**CONCLUSION**

We encountered a case in which ulcerative colitis developed immediately after *H. pylori* eradication therapy. Therapy was indicated for the prevention of gastric cancer. More than half of the world's population is affected with *H. pylori*. Th...
CASE PRESENTATION

We report a case of a 24-year-old woman who was incidentally found to have a 2-cm left kidney mass during an evaluation after a motor vehicle accident in 2010. Fine-needle aspiration performed at a local tertiary hospital revealed metanephric adenofibroma, which is one of the rarest benign renal tumors. She has had recurrent urinary tract infections since 2013. A routine ultrasound during her pregnancy in 2012 showed a slight progression in the left kidney mass. In April 2014, a follow-up contrast computed tomography scan of the abdomen and pelvis revealed a 6.4 × 4.8 cm left upper pole kidney mass. She underwent left laparoscopic radical nephrectomy and adrenalectomy with para-aortic lymph node resection.

Sections of tumor show a multinodular neoplasm (Figure 1). Histologic patterns range from sheets of small round blue cells to areas with tubule formation (Figure 2). The tumor is predominantly composed of epithelial and blastemal elements, with scant stromal elements present (Figure 3). Areas of necrosis and frequent mitotic figures are present, but no areas of anaplasia are seen (favorable histology). Immunohistochemical stains show patchy nuclear staining for Wilms tumor 1 (WT1) protein, patchy areas positive for cytokeratin 7, and diffusely strong positive nuclear staining for PAX-8 and CD56. Staining for CD57 and CD99 are negative. Cytogenetic testing revealed normal female chromosome analysis 46, XX [20]. The immunohistochemical profile and the morphology support the diagnosis of Wilms tumor.

We presented this case at a multidisciplinary pediatric oncology tumor board. Adjuvant chemotherapy is the standard of care for patients with favorable histology in the early stage of Wilms disease. The patient completed a full course of adjuvant chemotherapy per the National Wilms Tumor Study Roadmaps pediatric protocols to treat Wilms disease. Her chemotherapy regimen included dactinomycin, vincristine, and doxorubicin per protocol.1

A follow-up computed tomography scan of the chest, abdomen, and pelvis every three months starting at the end of adjuvant chemotherapy did not show evidence of recurrence. The patient is free of disease two years later.

DISCUSSION

Wilms tumor is the most common kidney tumor in children, whereas renal cell carcinoma is most common in adults.2 Only 3% of Wilms tumors are reported in adults.
Wilms Tumor: An Uncommon Entity in the Adult Patient

Wilms tumor is primarily a sporadic disease. Only 1% to 2% of patients have a family history of Wilms tumor. Loss-of-function mutations of a number of tumor suppressor genes, including the WT1 gene located on chromosome 11p13, p53, familial WT1 and 2 (FWT1 and FWT2) genes, and at the 11p15.5 locus, are detected in patients with Wilms tumor. More often than children, adults present with pain, weight loss, decrease in performance status, or fever; but sometimes, as with most children, they present with indolent growing renal mass.

Wilms tumor is frequently misdiagnosed, as was our patient 4 years earlier, as metanephric adenofibroma, one of the rarest benign renal tumors. Pathologic features of metanephric adenofibroma (6 cases) and Wilms tumor (7 cases) were reported in a case series. Six cases of metanephric adenofibroma were strongly and diffusely positive with antibodies to Wilms tumor (WT1) protein and CD57 and focally positive with antibodies to cytokeratin. Seven cases of Wilms tumor were strongly and diffusely positive with WT1 in the blastema and epithelium but showed only weak focal positivity in stromal cells. Moreover, 6 cases of Wilms tumor were diffusely positive and 1 case showed focal positivity for CD56.

There are 2 major systems in use to stage Wilms tumor, namely the National Wilms Tumor Study adopted in Canada and the US and the International Society of Pediatric Oncology adopted in Europe. The National Wilms Tumor Study was established in 1969 and was 1 of the first multidisciplinary cooperative groups that included oncologists, surgeons, pathologists, radiation oncologists, radiologists, and statisticians with the ultimate goal of finding a cure for children with kidney cancer, with emphasis on Wilms tumor. During the course of 5 clinical trials, with the last patient enrolled in 2002, tumor mortality rates were cut in half, so that today nearly 90% of children with Wilms and other kidney tumors can expect to survive at least until their teenage years, with excellent prospects thereafter.

Staging is based upon the anatomic extent of the tumor without consideration for genetic, histologic, or biologic markers. The prognosis of the disease in adults was reported to be dismal in the 1980s, with an event-free survival of 20% to 30%. Dramatic improvement in overall survival has occurred during the past decade because of improved surgical techniques, effective chemotherapeutic agents, advances in radiation oncology, and improved supportive care. Adults with Wilms tumor are treated with the same risk-based protocols used in children. These risk-based protocols incorporate multimodal therapy including surgery, chemotherapy, and radiation. This approach resulted in a dramatic improvement in outcomes with 5-year overall survival approaching 90%. The histopathology of Wilms tumor in adults seems to be identical to that in children and tends to respond to the same protocols used in children. However, the rate of treatment-related toxicity, such as fatigue, nausea, vomiting, fever, pneumonitis, neuropathy, liver function test abnormalities, skin rash, allergic reaction, pneumonitis, and congestive heart failure, appears to be higher in adult patients.

CONCLUSION

Wilms tumor, the most common kidney tumor in children, is rarely seen in adults. More often than children, adults present with pain, weight loss, drop in performance status, or fever; but sometimes, as with most children, they present with indolent growing renal mass. Staging is based upon the anatomic extent of the tumor and currently there are two staging systems: the National Wilms Tumor Study and the International Society of Pediatric Oncology. Wilms tumor in adults is a curable disease if managed with the multimodal therapy according to pediatric protocols, including surgery and chemotherapy with or without radiation therapy.
Wilms Tumor: An Uncommon Entity in the Adult Patient

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

Acknowledgment
Mary Corrado, ELS, provided editorial assistance.

References
Lunar Love was painted in 2009, with mixed media on a 20" x 20" wood panel. It is a depiction of moonlight’s grace and beauty. Dr. Nikravan has enjoyed and practiced meditation for many years, and this has influenced his practice of medicine and life in general in a very substantial way. His art, whether landscape or abstract, is a byproduct of this influence. His usual mediums are oil and acrylic paints on canvas or wood panels. You can find more of his work at: www.nikravan.com. Dr. Nikravan is an Urologist at the West Los Angeles Medical Center in CA.
A 70-year-old man presented to our hospital with 18 months of cough and breathlessness. He was tachypneic and had decreased breath sounds and coarse crackles over his left chest. He was human immunodeficiency virus-negative and had never smoked. The 6-minute walk test revealed blood oxygen desaturation from 94% to 86%. The patient was admitted to the hospital for further tests and monitoring to establish a diagnosis.

A radiograph of the patient’s chest showed inhomogeneous opacity in left mid and left lower zones (Figure 1). A high-resolution computed tomography (HRCT) scan done one year before presentation highlighted a classic “crazy-paving” pattern, where thickened interlobular septa and intralobular lines, with distinct geographic margins on a background of ground-glass opacification, could be seen in the left upper lobe (Figure 2A). HRCT performed on presentation showed that in the intervening year the lesion had increased dramatically along with minimal left-side pleural effusion (Figure 2B). Sputum stains and cultures for Mycobacterium tuberculosis, fungi, and other aerobic organisms were negative. Fiberoptic bronchoscopy showed no gross abnormality. Bronchial aspirate was negative for all organisms, as was the GeneXpert test for M tuberculosis. Transbronchial biopsy confirmed bronchioloalveolar carcinoma (BAC) (Figures 3A and 3B).

These investigations were carried out during the patient’s five-day stay in our institution. After confirmation of the diagnosis, he was referred to a tertiary oncology center for further management and was lost to follow-up.

**DISCUSSION**

The first-ever portrayal of crazy-paving on HRCT was recorded in a patient with pulmonary alveolar proteinosis and is still considered a hallmark of the disease. Since then, a number of clinical conditions have been associated with this radiologic pattern visible on HRCT. This pattern has also been reported in viral/opportunistic infections, Pneumocystis carinii pneumonia, exogenous lipoid pneumonia, diffuse alveolar haemorrhage, and sarcoidosis. The crazy-paving pattern appears on HRCT as diffuse ground-glass opacification superimposed with interlobular septal thickening and intralobular lines in a geographic distribution resembling irregularly laid cobblestones. These areas are usually bilateral and feature distinct margins, which sharply demarcate these areas from the normal lung parenchyma. It has been postulated that the crazy-paving pattern occurs because of processes that cause alveolar filling, because of interstitial fibrosis, or because of a combination of both of these elements.

BAC, a term coined by Liebow in 1960, accounts for approximately 4%...
of all primary lung malignancies. It is more common in females and never-smokers. The radiologic presentations of BAC are diverse and range from solitary or multiple pulmonary nodules to cystic disease, caviation, and consolidation. Most consolidations in BAC are peripheral in location, can persist for a long duration, and can be difficult to differentiate from consolidation of an infective origin.

The revised World Health Organization lung tumor classification recognized this infrequently seen clinical entity as a subtype of adenocarcinoma with three distinct histologic forms: mucinous, nonmucinous, and mixed or indeterminate. In 2011, the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society proposed that BAC be categorized under four new subtypes: adenocarcinoma in situ; minimally invasive adenocarcinoma; lepidic predominant nonmucinous adenocarcinoma; and invasive mucinous adenocarcinoma. The preinvasive lesion subtypes included adenocarcinoma in situ and minimally invasive adenocarcinoma. The invasive subtypes were lepidic predominant nonmucinous adenocarcinoma and invasive mucinous adenocarcinoma. The main purpose of this newer classification was to delineate categories having distinct clinical, radiologic, and histologic characteristics. However, the term BAC is still widely used.

BAC presenting radiologically as a crazy-paving pattern is a distinct rarity. BAC should always be considered in the differential diagnosis of this singularly unusual HRCT imaging pattern.

Disclosure Statement
The authors have no conflicts of interest to disclose.

References
Sclerosing Polycystic Adenosis: A Rare Tumor of the Salivary Glands

Christopher G Tang, MD; Justin B Fong; Karen L Axelsson, MD; Deepak Gurushanthaiah, MD

ABSTRACT

Case Presentation: A 74-year-old woman presented to the Head and Neck Surgery clinic with a 4-year history of a slowly growing, painful, left-sided neck mass in the tail of the parotid gland. Fine-needle aspiration suggested well-differentiated adenocarcinoma.

Discussion and Results: The patient underwent a superficial parotidectomy and super-selective neck dissection (level 2). Pathology revealed a tumor consistent with sclerosing polycystic adenosis.

Conclusion: Sclerosing polycystic adenosis is a rare inflammatory process that causes fibrocystic changes in the salivary gland. Apocrine-like metaplasia and epithelial atypia are common pathologic features. To our knowledge, a total of 51 cases have been described in the English-language literature.

INTRODUCTION

Sclerosing polycystic adenosis (SPA) is a rare, reactive, inflammatory lesion of the salivary glands resulting in fibrocystic changes and adenosis, similar to what occurs in the mammary glands.1 Lesions present as slow-growing masses in salivary gland parenchyma. They are discrete, pale, and rubbery nodules. The tumors are not encapsulated but are well defined. Pathologically, they display dense sclerotic lobules and cystic change with hyalinized collagen separation. Apocrine-like metaplasia; epithelial atypia; and ductal, acinar hyperplasia are commonly observed. A distinguishing feature of this lesion is focal cystic spaces within the fibrotic stroma. Most observed cases occur in the parotid gland.1–4 We report a typical case of SPA occurring in the parotid gland.

CASE PRESENTATION

A 74-year-old woman presented to the Head and Neck Surgery clinic at the Kaiser Permanente Medical Center in Oakland, CA, with a 4-year history of a growing, painful, left-sided neck mass. Two years before presentation, the patient underwent fine-needle aspiration with negative results for malignancy and did not pursue further workup. The mass persisted and continued to enlarge. The patient now had a firm 3.5-cm mass in the tail of the left parotid gland without overlying erythema. Fine-needle aspiration suggested a well-differentiated adenocarcinoma. Magnetic resonance imaging showed a well-defined, peripherally enhancing 3.5-cm lobe mass (Figures 1 and 2). Surgery was scheduled, and a superficial parotidectomy and a selective neck dissection (level 2) were performed. Final pathology revealed a 3.5-cm, well-circumscribed tumor consistent with SPA (Figures 3–5).

DISCUSSION AND RESULTS

SPA is a rare, benign tumor of the salivary glands, which was first described in 1996.1 About 80% of SPA cases present in the major salivary glands—specifically, the parotid gland.1 However, cases have been observed in the minor salivary glands of the nasal septum,2 buccal mucosa,3 hard palate, floor of the mouth, and retromolar pad.4 SPA has also been reported in the lacrimal gland.3 SPA is equally common in men and women, and reported cases have a wide age of distribution.1

Usually, parotid SPA comprises deep-seated, slow-growing, round, palpable masses. Pain and tenderness may be present. The masses are multinodular, with cysts 1 mm to 2 mm in diameter. SPA may be multifocal.1,4,5

Histologically, SPA is characterized by acinar cells with robust eosinophilic structures similar to zymogen granules. Ductal epithelial atypia is common, and epithelial cells exhibit various cells of apocrine, foamy, vacuolated, and mucinous nature.1,4 The lobular architecture usually includes atypical nests of myoepithelial cells.1,4 However, infiltrative carcinoma growth does not occur.6

Christopher G Tang, MD, is a Head and Neck Surgeon at the San Francisco Medical Center in CA. E-mail: christopher.g.tang@kp.org.

Justin B Fong is a Student at Washington University in St Louis, MO. E-mail: justinhf56@gmail.com.

Karen L Axelsson, MD, is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: karen.axelsson57@gmail.com.

Deepak Gurushanthaiah, MD, is a Head and Neck Surgeon at the Oakland Medical Center in CA. E-mail: d.gurushanthaiah@kp.org.
Sclerosing Polycystic Adenosis: A Rare Tumor of the Salivary Glands

SPA is considered benign. However, one case of ductal carcinoma in situ has been reported. Most cases of SPA are treated with localized surgical resection with clear margins. Recurrence has been reported in up to one-third of cases. Recurrence generally occurs because of inadequate surgical resection and because of the multifocality of the SPA. We found no cases of death or of metastasis attributed to SPA in a MEDLINE literature search.

There is a high chance of misdiagnosis because of the rarity of the disease and because clinicians and pathologists may be unfamiliar with it; for example, the present case was initially diagnosed as a well-differentiated adenocarcinoma. Differential diagnosis included pleomorphic adenoma; benign polycystic disease; sclerosing sialadenitis; and malignant glandular neoplasias, such as mucoepidermoid carcinoma, acinic cell carcinoma, adenocarcinoma NOS (not otherwise specified), and salivary duct carcinoma.

Our case was a 3.5-cm mass in the tail of the parotid gland. Presentation in the parotid gland and histologic findings of cysts and lobular architecture with collagen separation are characteristic of SPA.

CONCLUSION

SPA is a rare inflammatory process that causes fibrocystic changes in the salivary gland. Apocrine-like metaplasia and epithelial atypia are common features. To our knowledge, only 51 cases have been described in the English literature.

Disclosure Statement

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

Acknowledgment

Leslie Parker, ELS, provided editorial assistance.

References

Onset of Ulcerative Colitis after *Helicobacter pylori* Eradication Therapy: A Case Report

Mitsuro Chiba, MD, PhD; Tsuyotoshi Tsuji, MD, PhD; Kenichi Takahashi, MD; Masafumi Komatsu, MD, PhD; Takeshi Sugawara, MD; Iwao Ono, MD, PhD

**ABSTRACT**

In Japan, *Helicobacter pylori* eradication has been approved since 2013 for treatment of *H pylori*-induced chronic gastritis, in an attempt to reduce the prevalence of gastric cancer, a leading cancer in Japan. *H pylori* infection affects more than 50% of the world’s population. *H pylori* eradication therapy is generally safe. To our knowledge, no case of newly diagnosed ulcerative colitis occurring immediately after *H pylori* eradication therapy has previously been reported.

A 63-year-old man received a diagnosis of chronic gastritis and *H pylori* infection. In early March 2014, primary *H pylori* eradication therapy was initiated; lansoprazole, amoxicillin, and clarithromycin were administered for 1 week. Beginning on the fourth day, he had watery diarrhea twice a day. From the 11th day, bloody stools and watery diarrhea increased to 6 times a day. Colonoscopy, performed on the 40th day after termination of drug therapy, revealed diffuse inflammation in the distal aspect of the colon, with histologic findings consistent with ulcerative colitis. He was admitted to the hospital and was provided with a semivegetarian diet and metronidazole. He noticed a gradual decrease in the amount of blood in his feces then a disappearance of the blood. A fecal occult blood test on the 11th hospital day recorded 337 ng/mL. Fecal occult blood test is not indicated during macroscopic bloody stool but is indicated after disappearance of bloody stool. Therefore, he achieved clinical remission by the 11th hospital day. He was in remission on discharge.

New onset of ulcerative colitis should be added to a list of adverse events of *H pylori* eradication therapy.

**INTRODUCTION**

With the growing knowledge of the etiopathogenetic role of *Helicobacter pylori* in gastrointestinal and systemic diseases, attempts to eradicate *H pylori* have been expanding in the treatment of peptic (gastroduodenal) ulcers, gastric mucosa-associated lymphoid tissue lymphoma, iron-deficiency anemia, idiopathic thrombocytopenic purpura, and vitamin B12 deficiency. In Japan, *H pylori* eradication therapy was approved for peptic ulcer treatment in 2000, and for mucosa-associated lymphoid tissue lymphoma and idiopathic thrombocytopenic purpura in 2010. With regard to gastric cancer, one of the leading cancers not only in the Asia-Pacific region including Japan but also in the world, the critical role of *H pylori* in the development of gastric cancer has been established. Consequently, in Japan in 2010, *H pylori* eradication was approved for patients after endoscopic resection of early-stage gastric cancer. Three years later, eradication of *H pylori* was drastically expanded to include *H pylori*-induced chronic gastritis. Namely, in February 2013, *H pylori* eradication was approved for *H pylori*-induced chronic gastritis in an attempt to reduce gastric cancer. This means that more than half of the adult population of Japan are identified as possible candidates for *H pylori* eradication. Along with the development of evaluating cancer risk by combined assay for *H pylori* infection and serum pepsinogen levels, namely the ABC method, *H pylori* eradication therapy will prevail more than ever.

*H pylori* eradication therapy is generally safe. For the primary triple therapy, lansoprazole-amoxicillin-clarithromycin, the main adverse effects reported are diarrhea and soft stools, with frequencies of 7% and 12%, respectively. Only 1 of 271 patients was withdrawn from eradication treatment because of adverse effect (skin eruption). However, there are reports of *Clostridium difficile* colitis or pseudomembranous colitis associated with *H pylori* eradication therapy. There is also a report of relapse of ulcerative colitis during the therapy, which eventually required subtotal colectomy. To our knowledge, no case of newly diagnosed ulcerative colitis occurring immediately after *H pylori* eradication therapy has been reported.

**CASE PRESENTATION**

A 63-year-old man, 165 cm in height and 55 kg in body weight, was referred to our division in May 2014. He was previously admitted because of vertigo in 2012. Since that time, he received medications for treatment of vertigo and hypertension: betahistine mesylate, mecobalamin, adenosine triphosphate disodium hydrate, clotiazepam, and amlodipine besilate. His family history...
Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

Did not include inflammatory bowel disease (IBD). He reported that he had a daily bowel movement. In early January 2014, he was screened for gastric cancer: a blood test for pepsinogen and esophagogastroduodenoscopy. Chronic gastritis and *H pylori* infection were diagnosed (Figure 1).

The following month he participated in the 2014 Tokyo Marathon. In early March, primary *H pylori* eradication therapy was initiated: lansoprazole, 30 mg; amoxicillin, 750 mg; and clarithromycin, 200 mg, twice daily for 1 week. From Day 4 of treatment, he had watery diarrhea twice a day. The symptoms were not so severe as to halt administration of the medication. From the 11th day, 3 days after termination of the eradication therapy, bloody stools and watery diarrhea increased to 6 times a day. Antibiotic-associated colitis or hemorrhagic colitis was suspected, and he was expected to recover quickly because administration of the eradication therapy drugs had already been terminated. However, bloody stool persisted.

Colonoscopy, performed on the 40th day after the termination of the drugs, revealed diffuse inflammation in the distal aspect of the colon (Figure 2A). The histologic findings from the rectum were consistent with ulcerative colitis: crypt abscess, goblet cell depletion, and marked infiltration by inflammatory cells (Figure 3). The urea breath test was positive for *H pylori* infection.

The patient was referred to Akita City Hospital in Akita, Japan, for treatment of ulcerative colitis. His chief complaint was bloody, soft stool twice a day. His appetite was good, and he reported no abdominal pain. Results of physical examination, including the abdomen, were normal. He was admitted to the hospital, where he stayed for 24 days, a typical period of time for a patient with these symptoms of this severity in our hospital. Routine laboratory data, including hematologic studies, liver and kidney function tests, and C-reactive protein, were normal. *C difficile* antigen and toxin were not detected by TECHLAB C Diff Quik Chek Complete (TECHLAB Inc, Blacksburg, VA). Stool culture did not reveal any pathogen, including enterohemorrhagic *Escherichia coli*, *Campylobacter jejuni*, *Salmonella* species, *Staphylococcus aureus*, and *Klebsiella oxytoca*. A double-contrast barium enema study showed micropicula and fine barium flakes in the sigmoid colon.

**Figure 1. Timeline of case.**

**Figure 2. Photographs of the distal colon during colonoscopy before (A) and after (B) treatment.** Diffuse inflammation was markedly improved after treatment.

**Figure 3. Photomicrograph of biopsy specimen of the rectum. Crypt abscess (center), goblet cell depletion, and marked inflammatory cell infiltration are observed (hematoxylin and eosin stain, 20x magnification).**
Finally, a proctosigmoiditis type of ulcerative colitis of mild severity was diagnosed. The patient was provided with a semivegetarian diet designed for patients with IBD. Metronidazole, 750 mg/day, was administered orally during the hospitalization. He noticed a gradual decrease of blood in his feces, then a disappearance of the blood. A fecal occult blood test on the 11th hospital day recorded 337 ng/mL, and this test result became negative (<50 ng/mL) on the 18th hospital day. Colonoscopy on the 23rd day showed a marked improvement (Figure 2B).

The patient and his wife were provided a dietary guidance for a semivegetarian diet from a registered dietitian before discharge. The urea breath test yielded normal results one month after discharge. The patient has remained in remission without medication until time of this publication (Figure 1). In 2015, he again participated in the Tokyo Marathon.

DISCUSSION

Because antibiotics are prescribed for H pylori eradication, various adverse events of antibiotics can occur in patients undergoing eradication of H pylori. Patients are informed of the possible adverse events of the medication, including rash, diarrhea, and bloody diarrhea. In this case, diarrhea appeared on the fourth day of treatment, but it was mild enough to allow continued administration of the medication. After termination of treatment with the medication, diarrhea increased to six times a day and was mixed with blood. Generally, antibiotic-associated diarrhea or colitis subsides spontaneously within a few days after withdrawal of antibiotics. In this case, symptoms lasted for more than a month. C difficile toxin, Klebsiella oxytoca, or other pathogen was not identified. Pseudomembrane was not observed by endoscopy. Diffuse inflammation in the distal aspect of the colon and the histologic findings of crypt abscess and goblet cell depletion were consistent with ulcerative colitis.

The association between antibiotic use and subsequent diagnosis of IBD two to five years later is well documented. The mechanism of this association is not known. Long-term effects of antibiotics on gut microflora might be related to a subsequent onset of IBD. Alternatively, a genetically altered inflammatory response to pathogens may lead to both IBD and infections that require antibiotics, without the former being etiologically related to the latter.

In the present case, ulcerative colitis developed immediately after H pylori eradication therapy. This indicates an immediate effect of antibiotics on gut microflora, resulting in imbalance (dysbiosis) leading to IBD. Gut microflora is a critical environmental factor in IBD. Westernized diet-induced dysbiosis of gut microflora can explain the high frequency of IBD in developed countries. A semivegetarian diet has been designed to combat dietary westernization. We recommend that all IBD-diagnosed patients are prescribed a semivegetarian diet, with counseling and education to support the patient’s compliance. In our hospital, this recommendation includes admission to the hospital for treatment to experience and familiarize patients with a semivegetarian diet to ensure compliance at least initially. We treat moderate or severe cases of ulcerative colitis with drugs specific for IBD including 5-aminosalicylic acid, steroid hormones, and biologics together with a semivegetarian diet, but we treat mild cases initially only with a semivegetarian diet. This case is an example showing the induction and maintenance of remission without medication specific for IBD such as 5-aminosalicylic acid. In our practice, oral metronidazole is initially used for about 1 month in treatment of active IBD, with the expectation of eliminating any potentially pathogenic bacteria. Metronidazole is the second-line drug for H pylori eradication in Japan. In this case, metronidazole that was prescribed to treat ulcerative colitis seemed to induce H pylori eradication. H pylori affects more than 50% of the world’s population. Cases of IBD similar to the present case are
Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

CASE REPORTS

Onset of Ulcerative Colitis after Helicobacter pylori Eradication Therapy: A Case Report

anticipated to appear more frequently along with an expanding requirement for $H$ pylori eradication. It is recommended that practitioners keep in mind that IBD might develop immediately after $H$ pylori eradication therapy.

CONCLUSION

We encountered a case in which ulcerative colitis developed immediately after $H$ pylori eradication therapy. Therapy was indicated for the prevention of gastric cancer. More than half of the world’s population is affected with $H$ pylori. The indication of $H$ pylori eradication therapy has been expanding along with the growing knowledge of the etiopathogenetic role of $H$ pylori in gastrointestinal and systemic diseases. Onset of ulcerative colitis should be added to a list of adverse events of $H$ pylori eradication therapy.

Disclosure Statement

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

Acknowledgment

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

References


CASE REPORTS

Wilms Tumor: An Uncommon Entity in the Adult Patient

Fade Mahmoud, MD, FACP; M Brandon Allen, MD; Roni Cox, MD; Rodney Davis, MD

ABSTRACT
Wilms tumor, the most common kidney tumor in children, is rarely seen in adults, making it a challenge for the adult oncologist to diagnose and treat. Unlike with renal cell carcinoma, patients with Wilms tumor should receive adjuvant chemotherapy with or without radiation therapy. Adult oncologists may not be familiar with pediatric oncology protocols, so it is important to consult with pediatric oncologists who have more experience in this disease. Multimodal therapy based on pediatric protocols improved the outcomes of adults with Wilms tumor worldwide. We report a rare case of a 24-year-old woman with a slow-growing mass of the left kidney during a 4-year period. The mass was surgically removed and final diagnosis confirmed by pathology to be Wilms tumor. The patient received adjuvant chemotherapy and has been free of disease since 2014.

CASE PRESENTATION
We report a case of a 24-year-old woman who was incidentally found to have a 2-cm left kidney mass during an evaluation after a motor vehicle accident in 2010. Fine-needle aspiration performed at a local tertiary hospital revealed metanephric adenofibroma, which is one of the rarest benign renal tumors. She has had recurrent urinary tract infections since 2013. A routine ultrasound during her pregnancy in 2012 showed a slight progression in the left kidney mass. In April 2014, a follow-up contrast computed tomography scan of the abdomen and pelvis revealed a 6.4 × 4.8 cm left upper pole kidney mass. She underwent left laparoscopic radical nephrectomy and adrenalectomy with para-aortic lymph node resection.

Sections of tumor show a multinodular neoplasm (Figure 1). Histologic patterns range from sheets of small round blue cells to areas with tubule formation (Figure 2). The tumor is predominantly composed of epithelial and blastemal elements, with scant stromal elements present (Figure 3). Areas of necrosis and frequent mitotic figures are present, but no areas of anaplasia are seen (favorable histology). Immunohistochemical stains show patchy nuclear staining for Wilms tumor 1 (WT1) protein, patchy areas positive for cytokeratin 7, and diffusely strong positive nuclear staining for PAX-8 and CD56. Staining for CD57 and CD99 are negative. Cytogenetic testing revealed normal female chromosome analysis 46, XX [20]. The immunohistochemical profile and the morphology support the diagnosis of Wilms tumor.

We presented this case at a multidisciplinary pediatric oncology tumor board. Adjuvant chemotherapy is the standard of care for patients with favorable histology in the early stage of Wilms disease. The patient completed a full course of adjuvant chemotherapy per the National Wilms Tumor Study Roadmaps pediatric protocols to treat Wilms disease.

A follow-up computed tomography scan of the chest, abdomen, and pelvis every three months starting at the end of adjuvant chemotherapy did not show evidence of recurrence. The patient is free of disease two years later.

DISCUSSION
Wilms tumor is the most common kidney tumor in children, whereas renal cell carcinoma is most common in adults. Only 3% of Wilms tumors are reported in adults.
Wilms Tumor: An Uncommon Entity in the Adult Patient

Wilms tumor is primarily a sporadic disease. Only 1% to 2% of patients have a family history of Wilms tumor. Loss-of-function mutations of a number of tumor suppressor genes, including the WT1 gene located on chromosome 11p13, p53, familial WT1 and 2 (FWT1 and FWT2) genes, and at the 11p15.5 locus, are detected in patients with Wilms tumor. More often than children, adults present with pain, weight loss, decrease in performance status, or fever; but sometimes, as with most children, they present with indolent growing renal mass. Staging is based upon the anatomic extent of the tumor and currently there are two staging systems: the National Wilms Tumor Study and the International Society of Pediatric Oncology. Wilms tumor in adults is a curable disease if managed with the multimodal therapy according to pediatric protocols, including surgery and chemotherapy with or without radiation therapy.

CONCLUSION

Wilms tumor, the most common kidney tumor in children, is rarely seen in adults. More often than children, adults present with pain, weight loss, drop in performance status, or fever; but sometimes, as with most children, they present with indolent growing renal mass. Staging is based upon the anatomic extent of the tumor and currently there are two staging systems: the National Wilms Tumor Study and the International Society of Pediatric Oncology. Wilms tumor in adults is a curable disease if managed with the multimodal therapy according to pediatric protocols, including surgery and chemotherapy with or without radiation therapy.

Figure 2. Epithelial elements within the tumor show cells with hyperchromatic nuclei and eosinophilic cytoplasm arranged in a tubular architecture (haematoxylin and eosin stain, 10x magnification).

Figure 3. Blastemal elements within the neoplasm show sheets of monomorphic, primitive-appearing cells with small, hyperchromatic nuclei and scant clear to lightly eosinophilic cytoplasm (haematoxylin and eosin stain, 10x magnification).

(> 16 years old), making it a challenging entity for diagnosis and treatment. Wilms tumor is primarily a sporadic disease. Only 1% to 2% of patients have a family history of Wilms tumor. Loss-of-function mutations of a number of tumor suppressor genes, including the WT1 gene located on chromosome 11p13, p53, familial WT1 and 2 (FWT1 and FWT2) genes, and at the 11p15.5 locus, are detected in patients with Wilms tumor. More often than children, adults present with pain, weight loss, decrease in performance status, or fever; but sometimes, as with most children, they present with indolent growing renal mass, as in this case. Wilms tumor is frequently misdiagnosed, as was our patient 4 years earlier, as metanephric adenofibroma, one of the rarest benign renal tumors. Pathologic features of metanephric adenofibroma (6 cases) and Wilms tumor (7 cases) were reported in a case series. Six cases of metanephric adenofibroma were strongly and diffusely positive with antibodies to Wilms tumor (WT1) protein and CD57 and focally positive with antibodies to cytokeratin 7. Seven cases of Wilms tumor were strongly and diffusely positive with WT1 in the blastema and epithelium but showed only weak focal positivity in stromal cells. Moreover, 6 cases of Wilms tumor were diffusely positive and 1 case showed focal positivity for CD56.

There are 2 major systems in use to stage Wilms tumor, namely the National Wilms Tumor Study adopted in Canada and the US and the International Society of Pediatric Oncology adopted in Europe. The National Wilms Tumor Study was established in 1969 and was 1 of the first multidisciplinary cooperative groups that included oncologists, surgeons, pathologists, radiation oncologists, radiologists, epidemiologists, and statisticians with the ultimate goal of finding a cure for children with kidney cancer, with emphasis on Wilms tumor. During the course of 5 clinical trials, with the last patient enrolled in 2002, tumor mortality rates were cut in half, so that today nearly 90% of children with Wilms and other kidney tumors can expect to survive at least until their teenage years, with excellent prospects thereafter.

Dramatic improvement in overall survival has occurred during the past decade because of improved surgical techniques, effective chemotherapeutic agents, advances in radiation oncology, and improved supportive care. Adults with Wilms tumor are treated with the same risk-based protocols used in children. These risk-based protocols incorporate multimodal therapy including surgery, chemotherapy, and radiation. This approach resulted in a dramatic improvement in outcomes with 5-year overall survival approaching 90%. The histopathology of Wilms tumor in adults seems to be identical to that in children and tends to respond to the same protocols used in children. However, the rate of treatment-related toxicity, such as fatigue, nausea, vomiting, fever, pancytopenia, neuropathy, liver function test abnormalities, skin rash, allergic reaction, pneumonitis, and congestive heart failure, appears to be higher in adult patients.
**Disclosure Statement**

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

**Acknowledgment**

Mary Corrado, ELS, provided editorial assistance.

**References**

OriGinal ReseArch & ContriButions

4 Association of Age to Mortality and Repeat Revascularization in End-Stage Renal Disease Patients: Implications for Clinicians and Future Health Policies.
Ashok Krishnaswami, MD, MAS; Thomas Alloggiamento, MD, Daniel E Forman, MD; Thomas K Leong, MPH; Alan S Go, MD; Charles E McCulloch, PhD

10 Emergency Care of Patients with Acute Ischemic Stroke in the Kaiser Permanente Southern California Integrated Health System.
Kori Sauser-Zachrison, MD, MSc; Ernest Shen, MD; Zahra Ajani, MD; William P Neal, MD; Nadeep Sangha, MD; Michael K Gould, MD, Adam I. Sharp, MD, MS

14 Risk of Delayed Intracerebral Hemorrhage in Anticoagulated Patients after Minor Head Trauma: The Role of Repeat Cranial Computed Tomography.
Clifford Swap, MD, MS; Margo Sidell, ScD; Raquel Ogaz; Adam Sharp, MD, MS

17 Using Principles of Complex Adaptive Systems to Implement Secondary Prevention of Coronary Heart Disease in Primary Care.
Thomas E Kottke, MD, MSPH; Jacquelyn A Huebsch, RN, PhD; Paul McGinnis, MD; Jolleen M Nichols, RN; Emily D Parker, PhD; Juliana O Tillema, MPH; Michael V Maciosek, PhD

25 Low Back Imaging When Not Indicated: A Descriptive Cross-System Analysis.
Rachel Gold, PhD, MPH; Elizabeth Esteb, MS; Celine Hollombe, MPH; Jill Arkind, MPH; Patricia Aylward; Huong Tran, MS; Tim Burdick, MD, MSc; Jennifer E DeVoe, MD, DPhil; Michael A Horberg, MD, MAS, FACP, FIDSA

35 Physician Professional Satisfaction and Area of Clinical Practice: Evidence from an Integrated Health Care Delivery System.
John P Caloyeras, MPhil; Michael Kanter, MD; Nicole Ives, MHA; Chong Y Kim, PhD; Hemal K Kanzaria, MD, MSHPM; Sandra H Berry, MA; Robert H Brook, MD, ScD