4 Weight Loss and the Prevention of Weight Regain: Evaluation of a Treatment Model of Exercise Self-Regulation Generalizing to Controlled Eating

18 A Pharmacist-Staffed, Virtual Gout Management Clinic for Achieving Target Serum Uric Acid Levels: A Randomized Clinical Trial

24 Exploring the Reality of Using Patient Experience Data to Provide Resident Feedback: A Qualitative Study of Attending Physician Perspectives

31 Physicians Experiencing Intense Emotions While Seeing Their Patients: What Happens?

38 Difference in Effectiveness of Medication Adherence Intervention by Health Literacy Level

45 Lifestyle and Self-Management by Those Who Live It: Patients Engaging Patients in a Chronic Disease Model

Special Reports

51 Improving Care in Older Patients with Diabetes: A Focus on Glycemic Control

57 Evidence-Based Workflows for Thyroid and Parathyroid Surgery

74 The Truth about Truth-Telling in American Medicine: A Brief History

Review Articles

78 Hyperparathyroidism of Renal Disease

84 Recurrence of Epithelioid Hemangioendothelioma during Pregnancy: Case Report and Systematic Review

Narrative Medicine

102 The Use of Narrative as a Treatment Approach for Obesity: A Storied Educational Program Description

107 You Are Not Alone: Ten Strategies for Surviving a Malpractice Lawsuit

See inside for additional content as well as articles found only online www.thepermanentejournal.org
A Roman stonemason works to repair the vulnerable corner of a 1500-year-old structure. He stands sweaty in his tattered buckskin coat, blue jeans with plaster-clouded holes, and traditional blue work coat with leathers. Knee pads wait to support his work on this ground, hammering additional bits of marble, variously sized, to fit into holes that he has bored during the transition from wood to stone.

Some hours into mixing mud, his dextrous hands with learned during the transition from wood to stone. Done just like this in just this way, in a process first practiced and mastered by Roman traffic. He looks back to view with pleasure and a sure sense of contribution his master work of art. Dr. Janisse is the Editor-in-Chief of The Permanente Journal and Publisher of The Permanente Press.

112 CME EVALUATION FORM

Pick up the Pieces: What Everyone Needs to Know When a Child Dies
Adrienne L. Burnet, RN, MS, PhD, George Milburn
ISBN 10: 1931885405
Bruce Balkan, MD; Uda Wahn, MD
ISBN 10: 1855065804

Circulation: 25,000 print readers per quarter. 600,000 e-TOC readers, and in 2015, 1.4 million page views on 779 articles. Published from a broad international readership.

ORIGINAL RESEARCH & CONTRIBUTIONS

James J. Amos, PhD, FAABIM, FTOA, FAMP, PGH H Jonson, PhD, Casie A. Trammell, PhD, Kandice J. Porter, PhD, Kristen L. McHenry

Objectives: To determine the effect of a comprehensive treatment program for weight loss and weight maintenance on selected behavioral, psychological, and biological factors. Methods: Two hundred and sixty-three participants were randomized to one of two prevention groups: one that received a traditional maintenance group and one that received a comprehensive program. Results: Participants in the comprehensive program had significantly lower body weight, body mass index, and percent body fat than those in the traditional maintenance group. Conclusions: The comprehensive program is effective in preventing weight regain.

5. A Dermatologic-Facilitated Virtual Group Clinic Management System for Achieving Target Outcomes: A Randomized Clinical Trial
Robert Gelbstein, MD; Alice Peserman, PhD; MS; John Jackson, MS; Michelle di Galizia, MD

Objectives: To evaluate the efficacy of a virtual group clinic management system for achieving target outcomes. Methods: The system was evaluated in a randomized clinical trial of 200 participants divided into two groups: a control group and a treatment group. Results: Participants in the treatment group achieved significantly higher outcomes than those in the control group. Conclusions: The virtual group clinic management system is effective in achieving target outcomes.

Melanie Campbell, MD; Heather Honneth Gold, PhD; LMWW, MSW; Sarah Nguyen, MPH; Rich Nguyen-Dang, MD

Objectives: To explore the perspectives of attending physicians on the use of patient experience data to provide resident feedback. Methods: A qualitative study was conducted with 10 attending physicians. Results: Attending physicians had mixed views on the use of patient experience data to provide resident feedback. They felt that this data could be useful in identifying areas for improvement, but they also expressed concerns about its accuracy and reliability. Conclusions: There is a need for more research on the use of patient experience data to provide resident feedback.

7. The Effect of a Self-Regulation Intervention on Weight Loss and Physical Activity: A Randomized Clinical Trial
Robert Gelbstein, MD; Alice Peserman, PhD; MS; John Jackson, MS; Michelle di Galizia, MD

Objectives: To evaluate the efficacy of a self-regulation intervention on weight loss and physical activity. Methods: The intervention was delivered to 150 participants divided into two groups: a control group and an experimental group. Results: Participants in the experimental group achieved significantly greater weight loss and increased physical activity compared to those in the control group. Conclusions: The self-regulation intervention is effective in promoting weight loss and increasing physical activity.

8. The Impact of a Telephone-Based Intervention on Medication Adherence: A Randomized Controlled Trial
Honoré Goltz, PhD, LMSW, MEd; Sarah Steffanie Campbell, MD; Heather Diamond, PhD; Alice Jacobson, MS; Michele Ng, PhD; William M Vollmer, PhD

Objectives: To evaluate the efficacy of a telephone-based intervention on medication adherence. Methods: The intervention was delivered to 200 participants divided into two groups: a control group and an experimental group. Results: Participants in the experimental group achieved significantly greater medication adherence compared to those in the control group. Conclusions: The telephone-based intervention is effective in improving medication adherence.

9. The Effect of a Self-Regulation Intervention on Exercise Self-Regulation: A Randomized Clinical Trial
Robert Gelbstein, MD; Alice Peserman, PhD; MS; John Jackson, MS; Michelle di Galizia, MD

Objectives: To evaluate the efficacy of a self-regulation intervention on exercise self-regulation. Methods: The intervention was delivered to 150 participants divided into two groups: a control group and an experimental group. Results: Participants in the experimental group achieved significantly greater exercise self-regulation compared to those in the control group. Conclusions: The self-regulation intervention is effective in improving exercise self-regulation.
Evidence-Based Workflows for Thyroid Special Report

Bryan Sisk, MD; American Medicine: A Brief History. Matthew Lando, MD; Joyce Leary, MD; Shanthaiah, MD; Andrew Klonecke, MD; Annette Chavez, MD; Richard Dlott, Palmer-Toy, MD, PhD Jennifer K Polzin, PharmD; Darryl Eric A Lee, MD; Nancy E Gibbs, MD; Diabetes: A Focus on Glycemic Control.

that influenced physician behavior during centuries and outline the many pressures cornerstone of American medicine. For Permanente conducted in collaboration Southern California Regions of Kaiser of surgical practices in the Northern and based on American Thyroid Association a year, a task force developed algorithms standardizing the practice of thyroid and other interventions are suggested that should make diabetes care safer in older patients receiving hypoglycemic medications.

Evidence-Based Workflows for Thyroid and Parathyroid Surgery. Charles Meltzer, MD; Amer Burday, MD; Annette Chavez, MD; Richard Diott, MD; William Gent, MD; Deepak Gurushanthaiah, MD; Andrew Kloncke, MD; Matthew Lando, MD; Joyce Leary, MD; Sundeep Nayak, MD; Ryan Niederkoht, MD; Judith Park, MD; Alison Savitz, MBA; MD; Henry Schwartz, MD

A need exists to reduce care variations by standardizing the practice of thyroid and parathyroid surgery. During the course of a year, a task force developed algorithms representing decision points and workflows based on American Thyroid Association guidelines and on three internal studies of surgical practices in the Northern and Southern California Regions of Kaiser Permanente conducted in collaboration with Health Information Technology Transformation & Analytics (HITTA).

The Truth about Truth-Telling in American Medicine: A Brief History. Bryan Sisk, MD; Richard Frankel, PhD; Eric Kodish, MD; J Harry Isaacson, MD

Transparency has become an ethical cornerstone of American medicine. For most of American history, the intentional withholding of information was the accepted norm in medical practice. The authors trace the ethics and associated practices of truth-telling during the past two centuries and outline the many pressures that influenced physician behavior during that time period. They conclude that the history of disclosure is not yet finished, as physicians still struggle to find the best way to share difficult information without causing undue harm to their patients.

Improving Care in Older Patients with Diabetes: A Focus on Glycemic Control. Eric A Lee, MD; Nancy E Gibbs, MD; John Martin, MD; Fred Ziel, MD; Jennifer K Polzin, PharmD; Darryl Palmer-Toy, MD, PhD

Diabetes affects more than 25% of Americans older than age 65 years. This article discusses the seminal research findings that strongly suggest that hemoglobin A1c goals should be relaxed in older patients. The authors then recommend an age-specific and functionally appropriate hemoglobin A1c reference range for patients receiving medications to improve glycemic control. Other interventions are suggested that should make diabetes care safer in older patients receiving hypoglycemic medications.

Special Report

57 Evidence-Based Workflows for Thyroid and Parathyroid Surgery.

54 The Truth about Truth-Telling in American Medicine: A Brief History.

51 Improving Care in Older Patients with Diabetes: A Focus on Glycemic Control.

REVIEW ARTICLES

78 Hyperparathyroidism of Renal Disease. Noah K. Yue, MD; Shubha Ananthakrishnan, MD; Michael J Campbell, MD

Patients with renal hyperparathyroidism (rHPT) experience increased rates of cardiovascular problems and bone disease. Guidelines recommend that screening and management be initiated for all patients with chronic kidney disease stage III (estimated glomerular filtration rate, < 60 mL/min/1.73 m²). Improving medical management with vitamin D analogs, phosphate binders, and calcimimetic drugs has expanded the treatment options for patients with rHPT, but some patients still require a parathyroidectomy to mitigate the sequelae of this challenging disease.

84 Recurrence of Epithelioid Hemangioendothelioma during Pregnancy: Case Report and Systematic Review. Michael McCulloch, LAc, MPH; PhD; Michael Russin, MD; Arián Nachat, MD

The authors present a case of a 28-year-old woman whose epithelioid hemangioendothelioma (EHE) recurred during pregnancy, suggesting hormonal involvement. They conducted a systematic review to provide analysis and interpretation of the potential significance of her disease recurring, with fatal outcome, during pregnancy. Very little research has explored the use of individual hormonal markers. Strongly positive expression of 17-beta estradiol receptors have been reported. Expression of placenta growth factor (PIGF) is noteworthy in our case, in that our patient’s disease quickly and dramatically flared in the 25th week of pregnancy, near the peak in maternal PIGF production.

COMMENTARY

90 Quality Over Quantity: Integrating Mental Health Assessment Tools into Primary Care Practice. Darrell L Hudson, PhD, MPH

Depression is one of the most common, costly, and debilitating psychiatric disorders in the US. Yet, mental health services are underutilized throughout the US. Recent policy changes have encouraged depression screening in primary care settings. However, there is not much guidance about how depression screeners are administered. There are people suffering from depression who are not getting the treatment they need. It is important to consider whether enough care is being taken when administering depression screeners in primary care settings.

93 Plant-Based Diets: A Physician’s Guide. Julieanna Hever, MS, RD, CPT

This article provides physicians and other health care practitioners with an overview of the dietary benefits of a plant-based diet as well as details on how best to achieve a well-balanced, nutrient-dense meal plan. It also defines notable nutrient sources, describes how to get started, and offers suggestions on how health care practitioners can encourage their patients to achieve goals, adhere to the plan, and experience success.

NARRATIVE MEDICINE

102 The Use of Narrative as a Treatment Approach for Obesity: A Storied Educational Program Description. Marcus Griffith, MD; Jean Griffith, PhD; Mellanese Cobb, MPH; Vladimir Oge, MPH

The authors wrote an interventional children’s book and workbook (The Tale of Two Athletes: The Story of Jumper and The Thumper) and developed a three-step intervention based on the narrative. The intervention’s purpose is to increase self-awareness, reduce stigma, and help members of underserved communities become more comfortable discussing obesity. Interactive storytelling is the first step. The second step is reading. Practicing positive behaviors and decision making through games and exercises from the companion workbook is the final step.

107 You Are Not Alone: Ten Strategies for Surviving a Malpractice Lawsuit. Audrey Sheridan, MD

I wasn’t even scheduled to work that morning. I had just gone into the office for a meeting. Most physicians, about 60%, will sue at some point in their careers. Physicians typically do feel intense strain when faced with a lawsuit. We are more likely to suffer depression and burnout. Ten techniques are offered for coping that really work: resist isolation, use your strengths, retrain your brain, take care of yourself, give yourself a break, set priorities, approach law as a foreign culture, regain perspective, use distraction, and focus on what you can control.

109 The Handshake Layer Cake: Meeting and Regretting Difficulties for a Non-French Surgeon in France. Colin G Murphy, MCh, FRCSE

As always, the first work-greeting of the day, be it a handshake or les bises, is complicated by context: age, seniority, work status, employer/employee status, family, familiarity, the other people present at that interaction, whether it is break/coffee time. All of this has to be balanced against the unthinkable, not greeting someone at all, or thinking (like an idiot) that the wave or nod from a distance that you gave earlier in the day constituted a greeting.

111 Disconnection. Ahmed Obeidat, MD, PhD

It was a very familiar object that I asked her to identify. She started to look, feel, think, and she said, “It has buttons, numbers, and glass, but I can’t put them together. I am unsure!” The last task I asked her to perform was to write a sentence, which thrilled me to tears. But it was not a sentence I was looking for. “Doctor, I want to know what is wrong with me.” This was alexia (word blindness) without agraphia. She was a creative writer in her third decade.

Contents continued on next page.
The authors propose that monsters in popular culture might be studied with the hope of learning about situations and relationships that generate empathic capacities in their monstrous existences. The aim of the article is to introduce the theoretical framework and assumptions behind this idea. Both robots and monsters are posthuman creations. The knowledge we present here gives ideas about how nursing science can address the postmodern, technologic, and global world to come.

Future Challenges of Robotics and Artificial Intelligence in Nursing: What Can We Learn from Monsters in Popular Culture?
Henrik Erikson, RNT, PhD; Martin Salzmann-Erikson, RN, MHN, PhD

The authors describe an atypical presentation of active pulmonary tuberculosis with monoaortoccur oncotic disease of the right knee in a 24-year-old woman. The diagnosis of Poncet disease is mainly clinical with exclusion of other causes. It generally presents as an acute or subacute form; however, chronic forms have been described in the literature.

Monoarticular Poncet Disease after Pulmonary Tuberculosis: A Rare Case Report and Review of Literature
Paritosh Garg, MD; Nikhil Gupta, MD, MBBS; Mohit Arora, MS

The authors propose that monsters in popular culture might be studied with the hope of learning about situations and relationships that generate empathic capacities in their monstrous existences. The aim of the article is to introduce the theoretical framework and assumptions behind this idea. Both robots and monsters are posthuman creations. The knowledge we present here gives ideas about how nursing science can address the postmodern, technologic, and global world to come.

Refining Reporting Mechanisms in Oregon’s Patient-Centered Primary Care Home Program to Improve Performance.
Sherril Gelmon, DrPH; Billie Sandberg, PhD; Nicole Merrithew, MPH; Rebekah Bally, MPH

To achieve the Triple Aim, the Oregon Health Authority implemented the Patient-Centered Primary Care Home (PCPCH) Program in 2009. To assist in evaluating 500 primary care practices’ achievement along its 6 core attributes the research team developed an innovative scoring method. Initial results demonstrate that the scores enable stakeholders to compare results across similar practices and across the model’s core attributes, and to identify opportunities for improvement and technical assistance. This strategy could be replicated in other states. The article offers insights on implementation strategies, efficacy of the PCPCH model, and lessons learned.

Metastatic Renal Cell Carcinoma Presenting as Painful Chewing Successfully Treated with Combined Nivolumab and Sunitinib.
Fade Mahmoud, MD, FACP; Al-Ola Abdallah, MD; Konstantinos Arnaoutakis, MD; Issam Makhoul, MD

Metastatic renal cell carcinoma to the head and neck is the third-most common cause of distant metastasis to the head and neck, after breast cancer and lung cancer. A 71-year-old man with a single complaint of a one-year history of pain while chewing food, but without painless hematuria, weight loss, anorexia, fatigue, or anemia. An almost complete response of the metastatic disease occurred with the combination of nivolumab and sunitinib.

Treatment of Tracheoinnominate Fistula with Ligation of the Innominate Artery: A Case Report.
Rihana S Menen, MD; Jimmy J Pak, MD; Matthew A Dowell, PA; Ashish R Patel, MD; Simon K Ashiku, MD; Jeffrey B Velotta, MD

A 76-year-old man who underwent emergent tracheostomy placement presented on postoperative day 10 with massive hemorrhage concerning for tracheoinnominate fistula and was treated with median sternotomy and ligation of the innominate artery. The key to good outcomes is quick diagnosis and urgent surgical intervention.

Image Diagnosis: Pott Puffy Tumor.
Diane Apostolakos, MD, MS; Ian Tang, MD

A 20-year-old man was admitted to our hospital with complaints of frontal headache, sinusitis, and fever for one week. Sir Percivall Pott (1714-1788), a surgeon at St. Bartholomew’s Hospital in London, first described it as Pott Puffy tumor, referring to one of the four historic manifestations of inflammation noted by Aulus Cornelius Celsus (c 25 BC-c 50 AD): rubor (redness), tumor (swelling), calor (warmth), and dolor (pain).

Image Diagnosis: Tubo-ovarian Abscess with Hydrosalphinx.
Kiersten L Carter, MD; Gus M Carmel, MD, FACEP, FAAEM

Risk factors of tubo-ovarian Abscess include younger age, multiple sexual partners, nonuse of barrier contraception, and a history of pelvic inflammatory disease. Compared with ultrasound, computed tomography has increased sensitivity to detect thick-walled, rim-enhancing adnexal masses. The aim of therapeutic management is to be as noninvasive as possible. However, if this approach fails to yield clinical improvement within 3 days, reassessment of the antibiotic regimen, with consideration for laparoscopy, laparotomy, adnexectomy, hysterectomy, or image-guided abscess drainage is necessary.

Image Diagnosis: Gastric Migration of Hookworms in a Patient with Anemia.
Chalapathi Rao Achanta, MD

A 65-year-old man presented to our hospital with 4 months of fatigue and weakness. He denied any bleeding manifestations and had pallor on examination. The patients’ esophagus was normal, but there were motile hookworms in the duodenum.

Image Diagnosis: Encephalopathy Resulting from Dural Arteriovenous Fistula.
Ana Filipa Santos, MD; Célia Machado, MD; Sara Varanda, MD; João Pinho, MD; Manuel Ribeiro, MD; Jaime Rocha, MD; Ricardo Maré, MD

A 69-year-old woman presented to the Neurology Department with 2 months of progressive psychomotor slowing, inability to concentrate, and periods of disorientation. Her past medical history was unremarkable, and she was taking no medications. There was no history of trauma. The initiating events that led to the development of these symptoms are not clear, but the literature reports association with trauma, infection, recent surgery, and dural sinus thrombosis.
Weight Loss and the Prevention of Weight Regain: Evaluation of a Treatment Model of Exercise Self-Regulation Generalizing to Controlled Eating

James J Annesi, PhD, FAAHB, FTOS, FAPA; Ping H Johnson, PhD; Gisèle A Tennant, PhD; Kandice J Porter, PhD; Kristin L McEwen

ABSTRACT

Context: For decades, behavioral weight-loss treatments have been unsuccessful beyond the short term. Development and testing of innovative, theoretically based methods that depart from current failed practices is a priority for behavioral medicine.

Objective: To evaluate a new, theory-based protocol in which exercise support methods are employed to facilitate improvements in psychosocial predictors of controlled eating and sustained weight loss.

Methods: Women with obesity were randomized into either a comparison treatment that incorporated a print manual plus telephone follow-ups (n = 55) or an experimental treatment of The Coach Approach exercise-support protocol followed after 2 months by group nutrition sessions focused on generalizing self-regulatory skills from an exercise support to a controlled eating context (n = 55). Repeated-measures analysis of variance contrasted group changes in weight, physical activity, fruit and vegetable intake, mood, and exercise- and eating-related self-regulation and self-efficacy over 24 months. Regression analyses determined salient interrelations of change scores over both the weight-loss phase (baseline-month 6) and weight-loss maintenance phase (month 6-month 24).

Results: Improvements in all psychological measures, physical activity, and fruit and vegetable intake were significantly greater in the experimental group where a mean weight loss of 5.7 kg (6.1% of initial body weight) occurred at month 6, and was largely maintained at a loss of 5.1 kg (5.4%) through the full 24 months of the study. After establishing temporal intervals for changes in self-regulation, self-efficacy, and mood that best predicted improvements in physical activity and eating, a consolidated multiple mediation model suggested that change in self-regulation best predicted weight loss, whereas change in self-efficacy best predicted maintenance of lost weight.

Conclusions: Because for most participants loss of weight remained greater than that required for health benefits, and costs for treatment administration were comparatively low, the experimental protocol was considered successful. After sufficient replication, physician referral and applications within health promotion and wellness settings should be considered.

INTRODUCTION

Approximately 69% of US adults are at a weight high enough to be considered unhealthy (body mass index [BMI], calculated as weight in kilograms divided by height in meters squared, ≥ 25 kg/m²).1 Approximately 36% of US women are obese (BMI ≥ 30 kg/m²).2 As degree of overweight increases, so do health risks such as diabetes mellitus, hypertension, heart disease, and certain cancers.2 Although improving one’s dietary behaviors (eg, increasing intake of fruits and vegetables; reducing the consumption of fats and sweets) and increasing physical activity will reliably reduce weight by at least the 5% required to obtain clinically important health benefits,3 maintenance of those behaviors has been very difficult for almost all individuals.4,5 It can reliably be predicted that weight lost over the first approximately 6 months will mostly (if not all) be regained within 1 to 3 years.6,7

Even a more modest weight loss of at least 3% of original body weight sustained for 2 years, sometimes considered to be a marker of both weight-loss maintenance and some health-risk reductions,6 has been difficult to attain.7 Repeating the pattern of weight loss and regain may have adverse effects on both health risks and subsequent attempts at weight loss.8,9

Previous Behavioral Treatments

Interventions based on educating individuals on the need to lose weight by eating more healthfully and by being more physically active are the most common but have been ineffective.1 Their absence of foundation in established behavior-change theories and research is a proposed reason for this lack of success.10 Cognitive-behavioral methods consistent with Bandura’s social cognitive11 and self-efficacy12 theories (eg, goal setting, cognitive restructuring) have occasionally had more favorable effects3,13 and are presently considered to be state-of-the-art by many researchers. Several reviews, however, suggest that even those types of interventions simply defer weight regain,4,5,13 Summaries of research also suggest that longer treatments (eg, 6 to 12 months, or longer) have had somewhat better effects than shorter treatments; but initial weight loss, energy-intake requirements, financial incentives, and focusing on fat vs kilocalories (kcal) do not affect the rate of weight regain after approximately 6 months.7 Research has rarely sought to determine the psychosocial factors that predict weight-loss outcomes.14

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A group of behavioral researchers from Oxford University recently incorporated the extant theory and research to develop a highly structured Cognitive Behavioural Therapy protocol (Oxford CBT) in which maintenance of lost weight was targeted from the start. Their intervention model is instructive because it embodies much of the current thinking on both obtaining and sustaining weight loss through evidence-based behavioral methods such as self-monitoring the time, location, kcal, and type of foods and drinks consumed; regular self-weighing; and actively countering lifestyle barriers. Components of the Oxford CBT, which were administered by mostly clinical psychologists during individual 30-minute consultations, included “the role of body image in weight loss,” “addressing barriers to weight loss,” “encouraging acceptance,” “common primary goals,” and “developing long-term weight maintenance skills.” Tracking of foods, initially limiting to a 1500 kcal intake per day, and weighing and graphing weight changes were key elements of the modular protocol. The 24 sessions over 44 weeks designated the initial 24 to 30 weeks as a weight-loss phase, with the remainder devoted to weight maintenance. More in common with the available treatments, though, was that exercise was not emphasized. The treatment developers suggested that its minor impact on kcal totals render physical activity as being of minor concern for weight loss, and could possibly interfere with dietary compliance. Thus, initiating physical activity could be deferred by up to 6 months. Although the Oxford CBT was expensive at an estimated professional cost of between US$3000 and US$4500 per participant, it proved to be no more effective than standard behavioral treatment. With its sample of 49 women with obesity (ie, BMI of 30-40 kg/m²) who were tested, approximately 68% of lost weight was regained at the 2-year point, and 91% was regained 3 years past treatment initiation. Possibly because even this evidence-based and well-administered approach was judged by its developers to be ineffective at sustaining weight loss, they stated that it might be “ethically questionable to claim that psychological [behavioral] treatments for obesity ‘work’ in the absence of [favorable] data on their longer-term outcome.”

In further consideration of their findings and the entire body of research on intervention outcomes, they pessimistically yet possibly realistically, concluded their report by questioning whether continuing behavioral research in the area of weight management is even warranted any longer.

**Suggested Treatment Improvements**

Other researchers disagreed with the above conclusions, but it was acknowledged that many of the presently held assumptions and methods around behavioral weight-loss treatments are ineffective and “fresh ideas are needed for attacking the problem.” Following from this suggestion, the National Institutes of Health commissioned a multidisciplinary working group on “Innovative Research to Improve Maintenance of Weight Loss” in 2014. Its final report summarized that 1) although adherence issues need to be addressed first, exercise has promising implications for maintaining weight loss that go well beyond its obvious expenditure of energy; and 2) learning behavioral skills before starting on weight loss might be beneficial for weight-loss maintenance.

In an unrelated review of treatment results, Mann and her colleagues also recommended further research on exercise as possibly being the “potent factor” (for long-term weight loss), in lieu of any additional work on dietary or composition of the diet.

Although a program of regular exercise has been shown to be the strongest predictor of success with maintaining weight loss for some time, it remains difficult to maintain with an expected dropout rate of 50% to 65% within 3 to 6 months of its initiation. On the basis of accelerometer data from both the 2003-2004 and 2005-2006 National Health and Nutritional Examination Surveys, less than 4% of US women complete the equivalent of at least 5 moderate-intensity walks per week, which is considered to be the minimum threshold for health benefits. Pilot research indicates that even when dropout from exercise is successfully countered, typical frequencies for formerly sedentary participants with obesity are only 2 to 3 sessions per week, with an estimated energy expenditure of less than 150 kcal per session (which amounts to only approximately 0.5 kg of weight loss every 9 to 10 weeks). Although there have been advances in improving adherence to exercise through standardized cognitive-behavioral methods (eg, The Coach Approach protocol), it was proposed that the relationship of exercise with maintained weight loss is more because of its association with improvements in psychological predictors of controlled eating than associated energy expenditures.

For example, if self-regulatory skills (eg, thought-stopping) could first be internalized within an intervention component designed to facilitate regular exercise, possibly treatment elements could be constructed to promote generalization of such behavioral skills to controlled eating. This, however, runs in opposition to treatments such as the Oxford CBT and some basic research that suggests that self-regulation used for one behavior (here exercise) might deplete an individual’s limited capacity of self-regulation for success with a second behavior (here reduced kcal eating). It was also proposed that self-efficacy, or one’s feelings of ability and mastery, could be increased by demonstrating to one’s self a better control of exercise behaviors through the use of newly learned self-regulatory skills to counter barriers.

Improved self-efficacy to control exercise might, in turn, also generalize to controlled eating, the other critical weight-loss behavior of interest. Improvements in mood, a well-established by-product of initiating even manageable amounts of exercise, might serve to counter the common problem (especially for women) of emotional eating, and “… lead to a healthier psychological climate in which individuals have more cognitive and emotional resources, as well as motivation and energy, to sustain a long-term commitment to a weight-loss program.” Adherence to just 2 to 3 sessions per week of behaviorally supported exercise has been associated with significant improvements in self-regulation, self-efficacy, and mood, which were found to be the most critical psychological predictors of improvements in eating and weight over 6 months, even when previously suggested factors such as self-concept and body image were considered. Additional studies are, however, required to determine psychological predictors of longer-term weight-loss maintenance that might inform both theory and the architecture of improved behavioral treatments. Although exercise is frequently incorporated into weight-loss interventions, we have found no longer-term research where its primary focus
was on improving psychological predictors of controlled healthy eating. Thus, as an extension to earlier research on short-term psychological, behavioral, and weight-loss effects, the present study was conducted. It incorporated 1) an experimental treatment that initiated supported exercise 2 months before any changes in nutrition in attempts to improve targeted psychological and behavioral correlates of improved eating and weight loss, and 2) a comparison treatment of participants’ use of a manual that simultaneously encouraged healthy eating, physical activity, and reasonable expectations, which was supplemented by telephone follow-ups. Both treatments were based on accepted behavioral theory, yet there were substantial differences. On the basis of research consensus indicating that the initial approximately 6 months after treatment start is a time of weight loss, whereas beyond 6 months weight regain (often complete regain) can be reliably predicted, the present study investigated 1) treatment-associated weight change, 2) behavioral predictors of weight change (ie, changes in healthy eating and physical activity), and 3) hypothesized psychological predictors of the behavioral changes (ie, self-regulation, self-efficacy, mood) during those 2 time frames. Data were measured at baseline and months 3, 6, 12, and 24. This allowed contrasts of dynamic changes in targeted variables by group, and analyses of which of the possible temporal intervals best predicted weight change and weight change-related behavioral improvements. Such findings could be instrumental for determining when, and to what degree, corresponding treatment processes should be emphasized. To enhance clarity, this report is expressed in 3 parts corresponding to the aforementioned 3 areas. Hypotheses and research questions are as follows.

Hypotheses

1. Reduction in weight from baseline-month 6 (weight-loss phase) will be greater, and regain in weight from month 6-month 24 (weight-loss maintenance phase) will be less, in the experimental group when contrasted with the comparison group.

2. Improvements in the targeted behaviors of physical activity and fruit and vegetable intake will be greater during both the weight-loss and weight-loss maintenance phases in the experimental group when contrasted with the comparison group.

3. Improvements in the targeted psychological variables of mood, self-regulation, and self-efficacy—related to both exercise and eating—will be greater during both the weight-loss and weight-loss maintenance phases in the experimental group when contrasted with the comparison group.

Research Questions

1. Was change in physical activity and fruit and vegetable intake from baseline-month 3, baseline-month 6, or month 3-month 6 the better predictor of weight change during the weight-loss phase? What temporal interval of change in physical activity and fruit and vegetable intake best predicted weight change during the weight-loss maintenance phase?

2. Was change in each psychological variable from baseline-month 3, baseline-month 6, or month 3-month 6 the better predictor of physical activity and fruit and vegetable intake during the weight-loss phase? What temporal interval of change in each psychological variable best-predicted behavioral changes during the weight-loss maintenance phase?

3. Did changes in mood and/or aggregated (exercise- and eating-related) measures of self-regulation and self-efficacy significantly mediate relationships between treatment type (comparison and experimental) and changes in weight during the weight-loss and weight-loss maintenance phases?

Because participant characteristics, initial weight, cognitive-behavioral treatment orientation, and focus on weight-loss maintenance were designed to be similar to those of the previously published Oxford CBT study, the present weight-change data were also contrasted with the Oxford CBT findings.

METHODS

Participants

Participant recruitment was through local print and electronic media. Inclusion criteria were 1) women of at least 21 years of age, 2) BMI ≥ 30 and < 40 kg/m², and 3) a self-reported goal of weight loss. Exclusion criteria based on self-report were 1) present or soon-planned pregnancy; 2) present use of medications for weight loss or a psychological/psychiatric condition; 3) current participation in a medical, commercial, or self-help weight-loss program; and 4) participation in a program of regular physical activity/exercise that averaged at least 20 minutes per week during the year before the start of the study. Treatments were administered at small, community-based wellness/fitness centers in the Eastern US. Because the chance of cross-contamination of participants through intergroup interactions within the same facility would have been high, randomization to either the comparison (COM) treatment (n = 55) or the experimental (EXP) treatment (n = 55) was by site (3 sites each). Institutional review board approval and written informed consent from each participant were received. The research was conducted in accordance with requirements of the Helsinki Declaration.

Independent t- and χ² tests indicated no significant group difference in age (mean = standard deviation (SD) = 48.2 ± 7.8 years), BMI (35.3 ± 3.2 kg/m²), or racial/ethnic make-up (overall 83% white, 11% African American, and 6% of other racial/ethnic groups). On the basis of self-reported family income, most participants were middle class (overall 11% below $24,999, 21% = $25,000-$49,999, 41% = $50,000-$99,999, and 27% = $100,000 or greater). Attrition from initial study acceptance to actual treatment participation was minimal at 7% and also did not significantly differ by group. This attrition was associated with either a reported illness, a newly arisen orthopedic issue, transportation issues, or an inability of study staff to make further contact after 3 attempts. There was no cost or financial compensation for participation.

Abbreviations Keys

FV = Fruit and vegetable intake
Mood = Overall negative mood
PA = Physical activity
SE-eating = Self-efficacy for controlling eating
SE-exercise = Self-efficacy for exercise
SR-eating = Self-regulation for controlled eating
SR-exercise = Self-regulation for exercise
Measures

The self-report measures used in this study were 1) physical activity (PA) through weekly energy expenditure, 2) healthy eating through daily fruit and vegetable intake (FV), 3) self-regulation for exercise (SR-exercise), 4) self-regulation for controlled eating (SR-eating), 5) self-efficacy for exercise (SE-exercise), 6) overall negative mood (Mood), and 7) self-efficacy for controlling eating (SE-eating). Descriptions of each of these measures, along with data on their reliability and validity, are presented below (Table 1). Body weight was measured in kilograms through the use of a recently calibrated scale (800KL; Healthometer, Buffalo Grove, IL).

Procedure

Participants initially received a group orientation to their assigned EXP or COM protocol. Wellness counselors administering treatments were trained in only one of the protocols and masked to the treatment differences and the study’s research goals. Both the EXP and COM treatments were based on the social cognitive11 and self-efficacy12 theories of behavior where individuals are viewed as 1) directing their own actions through self-organization, 2) being able to manage their environments, and 3) possessing capabilities to be self-reflective of their internal abilities. Both the EXP and COM curricula incorporated cognitive-behavioral methods designed to empower participants with self-regulatory skills and abilities to deal with barriers to managing their weight effectively, while increasing their feelings of mastery and competence (ie, self-efficacy). Both treatment protocols informed participants of the recommended volume of weekly exercise to gain health benefits,10 but also suggested that any amount was also likely to be beneficial. However, the administration formats and the proposed role of physical activity (PA) varied between EXP and COM users. Both treatment protocols informed participants of the recommended volume of weekly exercise to gain health benefits,10 but also suggested that any amount was also likely to be beneficial. However, the administration formats and the proposed role of physical activity (PA) varied between EXP and COM users.

Table 1. Description of study measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Measurement instrument</th>
<th>Instrument description</th>
<th>Reliability and validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity (PA)</td>
<td>Godin-Shephard Leisure-Time Physical Activity Questionnaire</td>
<td>Requires entry of number of weekly sessions of strenuous (~ 9 METs; eg, running), moderate (~ 5 METs; eg, fast walking), and light (~ 3 METs; eg, easy walking) physical exertion for “more than 15 minutes.” Incorporates METs, or the energy costs associated with specific physical activity intensities (1 MET approximates the use of 3.5 ml of O₂/kg/minute).44</td>
<td>Test-retest reliability (2 weeks) was 0.74.46 Construct validity was indicated through strong correlations with both accelerometer and peak oxygen uptake measurements.46,47</td>
</tr>
<tr>
<td>Healthy eating measured by fruit and vegetable intake (FV)</td>
<td>Self-report survey of FV48</td>
<td>Foods and beverages consumed “in a typical day over the past week” are based on examples and serving sizes of fruits (eg, apple, banana, peach [1 small or 118 mL or 4 ounces canned]; raisins, dates [0.59 mL or 2 ounces]; 100% fruit juice [118 mL or 4 ounces]); vegetables (eg, broccoli, carrots, tomatoes, green beans [118 mL or 4 ounces]; raw spinach [236 mL or 8 ounces]) that correspond to both the US Department of Agriculture’s current MyPlate and former Food Guide Pyramid. Increases in FV were strongly associated with both weight loss and weight-loss maintenance,36 and an increase in FV was a stronger predictor of weight loss than reduction in fat intake.37 Previous research indicates that FV alone is a strong predictor of overall energy consumption and healthfulness of the diet.32,33</td>
<td>Test-retest reliability (3 weeks) was 0.77-0.83 for women.31 Validated against comprehensive food frequency questionnaires,36 in which pilot research indicated strong correlations (r-values = 0.70-0.85) with the full-length Block Food Frequency Questionnaire.34,35</td>
</tr>
<tr>
<td>Self-regulation for exercise (SR-exercise) and self-regulation for controlled eating (SR-eating)</td>
<td>Adaptation of a previously validated scale46,47</td>
<td>The 10 items for SR-exercise (eg, “I say positive things to myself about being physically active”) and SR-eating (eg, “I make formal agreements with myself regarding my eating”) assess the degree that barriers to those behaviors are addressed through the use of self-regulatory skills. Responses range from 1 (never) to 5 (often), and are summed. A higher score indicates a greater use of self-regulation.</td>
<td>Cronbach α-values for internal consistency were 0.75,46 0.83, and 0.80 for the present versions and sample, respectively. Test-retest reliability (2 weeks) was 0.77.46</td>
</tr>
<tr>
<td>Self-efficacy for exercise (SE-exercise)</td>
<td>Exercise Self-Efficacy Scale48</td>
<td>After beginning with the stem, “I am confident I can participate in regular exercise when...,” each of the scale’s 5 items end with a possible barrier to overcome (eg, “I am tired.” “I have more enjoyable things to do”). Responses range from 1 (not at all confident) to 7 (very confident), and are summed. A higher score indicates greater self-efficacy.</td>
<td>Cronbach α-values for internal consistency were 0.70-0.82. Test-retest reliability (2 weeks) was 0.90.48 Cronbach α-value for internal consistency for the present sample was 0.80.</td>
</tr>
<tr>
<td>Overall negative mood (Mood)</td>
<td>Profile of Mood States Short Form scale of Total Mood Disturbance49</td>
<td>The 30 items (5 items per factor) assess feelings during the past week on depression (eg, “sad”), tension/anxiety (eg, “tense”), vigor (eg, “energetic”), fatigue (eg, “weary”), anger (eg, “angry”), and confusion (eg, “forgetful”). Responses range from 0 (not at all) to 4 (extremely) and are summed after reversing the scores of the vigor factor. A lower score indicates better mood.</td>
<td>Cronbach α-values for internal consistency were 0.84-0.95 across factors,46 and 0.79-0.89 for the present sample. Test-retest reliability (3 weeks) averaged 0.69.46</td>
</tr>
<tr>
<td>Self-efficacy for controlling eating (SE-eating)</td>
<td>Weight Efficacy Lifestyle Scale51</td>
<td>The 20 items (4 per factor) assess feelings of ability to control eating when the following situations are present: negative emotions (eg, “I can resist eating when I am anxious [nervous]”), food availability (eg, “I can resist eating even when I am at a party”), physical discomfort (eg, “I can resist eating when I am uncomfortable”), positive activities (eg, “I can resist eating when I am watching TV”), and social pressure (eg, “I can resist eating even when I have to say ‘no’ to others”). Responses range from 0 (not confident) to 9 (very confident), and are summed. A higher score indicates greater self-efficacy.</td>
<td>Cronbach α-values for internal consistency were 0.70-0.90 across its factors,51 and 0.74-0.81 for the present sample.</td>
</tr>
</tbody>
</table>
activity/exercise in facilitating changes in eating behaviors differed substantially between the EXP and COM treatments.

The EXP treatment incorporated The Coach Approach exercise-support protocol paired with a nutrition behavior-change component developed for this research. It was based on 1) results from previous behavioral weight-management treatments, 2) exploratory studies of psychosocial predictors of weight-loss behaviors, 3) findings suggesting that behavioral mechanisms required to foster weight loss differ from those required to maintain lost weight, and 4) the suggested benefits of targeting specific and measurable behaviors for change (eg, increasing FV rather than addressing numerous and detailed elements of the diet). Beginning at baseline, The Coach Approach protocol supported adherence to newly initiated exercise through six 45-minute meetings with a trained wellness counselor possessing at least 1 national certification (eg, American College of Sports Medicine). These were conducted in a private office over 6.5 months. Each participant’s exercise plan, both initially and in revisions during subsequent meetings, was based on the participant’s preferred type of physical activity and tolerance. Most of the meeting time was, however, spent on the development of specific self-regulatory skills such as long- and short-term goal setting paired with progress monitoring, dissociation from discomfort, cognitive restructuring, stimulus control, behavioral contracting, controlling behavioral prompts and triggers, and relapse prevention. Exercise-induced changes in mood (eg, anxiety, energy level) were assessed both in response to a single bout of physical activity and for 1 to 2 months, and displayed through responses to items embedded in the supporting computer application.

After 8 weeks of concentration exclusively on maintaining regular exercise, the components for eating behavior change were sequentially added. First, guidance and practice on methods for kcal tracking was individually provided in two 30-minute meetings over 2 weeks. Energy-intake goals were based on each participant’s weight (eg, 1500 kcal/day for a weight range of 79-99 kg), and various methods for recording food and corresponding kcal intake were made available (eg, through an approved Web site, an approved application for hand-held devices, or a provided paper form and use of an approved “calorie counter” book). Next, 10 nutrition sessions of 60 minutes each focused on weight reduction were administered by trained wellness counselors (supported by a manual) at 2-week intervals in groups of 8-15 participants. Their primary aim was to generalize, adapt, and extend self-regulatory skills developed during The

Figure 1. Timeline of the Experimental Treatment, Comparison Treatment, and Oxford Cognitive Behavioural Therapy.

B = baseline; kcal = kilocalories; LEARN = lifestyle, exercise, attitudes, relationships, nutrition.
Coach Approach exercise-support protocol, to self-regulating eating behaviors (eg, dissociating from exercise-induced discomfort was generalized to dissociating from feelings of hunger; recovering from and rescheduling a missed exercise session was generalized to recovering from a day of excess kcal intake and immediately readmitting to the appropriate limit for the next day). There was a combination of brief lectures, individual tasks, and group activities within each session. The next component, now 28 weeks after baseline, was 4 group sessions in which self-regulatory skills were addressed in the context of maintaining lost weight. The final 10 sessions of the EXP treatment covered skills of self-regulation in both weight-loss and weight-loss maintenance contexts (Figure 1). Treatment content related to the diet was primarily concentrated on increasing FV intake, although there was a limited focus on minimizing the consumption of fat and sugar. Because meeting time was primarily centered on the development of self-regulatory skills and the ability to increase self-efficacy for controlling overeating, participants were referred to the ChooseMyPlate.gov Web site for access to detailed, evidence-based information on nutrition. The COM treatment replicated methods used previously in studies and consisted of participants reviewing 1 of the 12 “lessons” of a 265-page print manual entitled The LEARN (lifestyle, exercise, attitudes, relationships, nutrition) Program for Weight Management (10th edition) every 2 weeks. Sections related to behavior change included “Dealing with Pressures to Eat,” “Preventing Lapse, Relapse, and Collapse,” “Interpreting Your Progress,” and “Making Physical Activity Count.” Sections related to diet included “Fast Foods,” “Rating Your Diet,” “Vegetables in Your Diet,” and “Breads, Cereals, Rice, and Pasta in Your Diet.” Each lesson was followed by a 15-minute phone conversation initiated by a wellness counselor to clarify chapter contents, review each participant’s plans for carrying out behavioral changes, and answer the participant’s questions. The process of participants reading chapters and obtaining telephone follow-ups started at baseline and lasted 24 weeks (Figure 1). The LEARN manual suggested that women limit their energy intake to 1200 kcal per day. A paper monitoring form was provided for participants to record foods and drinks consumed, the amount consumed and their associated kcal, their corresponding food group categorization, and optional comments.

Fidelity checks were completed on approximately 15% of treatment components by study staff. Minor protocol violations were primarily related to adherence to required time frames within sessions and were easily rectified through study staff-instructor interactions. Surveys and weight measurements were completed in a private area.

Data Analyses

To avoid inappropriately inflated effect sizes such as those reported in the many studies where data from only weight-loss program “completers” were included, the conservative intention-to-treat approach was used, as suggested. Thus, data were retained from all participants who engaged in treatment processes. The expectation-maximization algorithm was used to impute data for the 14% of missing scores. The required criteria of missing at random (no systematic bias) was indicated because participants who were missing data at any assessment time did not significantly differ from the sample as a whole on demographic characteristics or any other study measure. On the basis of the planned multiple regression equations incorporating 3 predictor variables, and to detect the moderate effect of $\hat{f}^2 = 0.15$ that was indicated in pilot research at the statistical power of 0.90 ($\alpha = 0.05$), a minimum of 98 total participants was required. In tests during the weight-loss phase, tolerances (0.20-0.82) and variance inflation factors (1.23-1.67) indicated a low degree of multicollinearity. During the weight-loss maintenance phase, tolerances (0.22-0.86) and variance inflation factors (1.16-4.58) indicated a low-moderate degree of multicollinearity. Inspection of residual scatterplots indicated homogeneity of variances and linearity in the data. Both skewness and kurtosis values were < 2 standard errors. Consistent with previous suggestions for research within the present context, change scores were unadjusted for baseline values. Statistical significance was set at $\alpha = 0.05$ (2-tailed) unless otherwise noted. Statistical analyses were conducted using SPSS, version 22 (IBM, Armonk, NY).

For all study measures, general linear model mixed-model repeated measures analyses of variance (ANOVAs) were computed to determine whether there were significant score changes across the 5 measurement times (baseline; months 3, 6, 12, and 24), and whether those changes differed between the EXP and COM groups. These were followed up by planned $t$ tests to assess and contrast within-group changes during the weight-loss phase (using 1-tailed tests) and the weight-loss maintenance phase. Their associated effect sizes were computed as Cohen’s $d=(\text{mean}_\text{pre} - \text{mean}_\text{post})/\text{SD}_{\text{pre}}$. Effect sizes for ANOVA models were calculated using partial $\eta$-squared ($\eta^2_p = \text{SS}_{\text{effect}}/\text{SS}_{\text{total}}$). For $d$ and $\eta^2_p$, 0.20, 0.50, 0.80; and 0.01, 0.06, 0.14 denote small, moderate, and large effects, respectively.

Part 1: Weight Change

After completing planned ANOVAs and follow-up tests on weight, and on the basis of research suggesting that ≥ 5% weight loss...
is the threshold for health benefits, the percentage of participants attaining this criterion was reported for month 6 (end of the weight-loss phase) and month 24 (end of the study), by group. Because ≥ 3% loss has been the suggested criterion for maintained weight loss, attainment of this change was also reported at month 24. Weight-change data previously published on the Oxford CBT\(^2\) were also adapted for additional contrasting.

**Part 2: Behavioral Predictors of Weight Changes**

After completing planned ANOVAs and follow-up tests on PA and FV, data were aggregated across groups. The strengths of bivariate relationships between changes in PA and FV from baseline-month 3, baseline-month 6, and month 3-month 6, for the prediction of change in weight over the weight-loss phase, were then contrasted. Given the data collected, all possible temporal intervals of changes in PA and FV during the course of the 24-month investigation were similarly contrasted for predicting change in weight during the weight-loss maintenance phase. As was previously suggested,\(^3\) wherever possible, behavioral changes occurring during the weight-loss phase were statistically controlled for.

**Part 3: Psychological Predictors of Behavioral Changes**

After completing planned ANOVAs and follow-up tests on the five psychological variables, data were aggregated across groups. Analyses of relationships of changes in the psychological variables using temporal intervals and methods identical to Part 2 were then completed. Data from the temporal intervals found to have the strongest relationships served as the predictors of PA and FV changes in multiple regression equations.

Because 1) the EXP treatment focus was on the carry-over of exercise-related self-regulation and self-efficacy to eating-related self-regulation and self-efficacy, 2) their strong interrelations had previously been supported,\(^3\) and 3) previous theory suggested their interactions,\(^5,11\) after normalizing (centering and standardizing) scores and confirming expected interrelations, the exercise- and eating-related self-regulation and self-efficacy measures were merged for further analyses. Multiple mediation models incorporating 20,000 bootstrapped resamples\(^4\) were specified where the predictor variable was treatment...
type (0 = COM; 1 = EXP), the outcome variable was weight change during the weight-loss or weight-loss maintenance phase, and the possible mediators were changes in mood and the merged self-regulation and self-efficacy measures. In a multiple mediation model, significance of a mediator is identified when its corresponding 95% confidence interval for an indirect effect does not include 0. A graphical representation of mediation models is given in Figure 2.

If a significant mediator was found in the above analysis over the weight-loss phase, follow-up simple mediation models (eg, models with only a single mediator) were then specified to determine whether change in that psychological variable and weight demonstrated a reciprocal relationship. A reciprocal relationship is identified if, after reversing the position of the original outcome and mediator variable within a complementary mediation model, both equations demonstrate significant mediation. Because the presence of a reciprocal relationship may not be assessed directly through multiple mediation, or with covariates, these analyses were possible during only the weight-loss phase.

### RESULTS

There was no significant difference at baseline between the EXP and COM groups on any study measure. Table 2a provides descriptive statistics of data at baseline and at months 3, 6, 12, and 24. For all variables, there was a significant overall effect and a significant time × group interaction during the 24-month study (Table 2a). Results of follow-up, within-group t-tests, are given in Table 2b.

#### Part 1: Weight Change

During the weight-loss phase, although within-group reductions in weight in the EXP group (-5.73 kg) and COM group (-2.09 kg) were both significant, the EXP group had a significantly greater between-group reduction in weight, t(108) = 5.56, p < 0.001, d = 1.07. During the weight-loss maintenance phase, within-group weight regain in the EXP group (0.63 kg) was not significant, whereas it was significant in the COM group (0.84 kg). During the full 24-month duration of the study, reduction of weight was significant in the EXP group (-5.11 kg), but not significant in the COM group (-1.25 kg). Between-group reduction in weight was significantly greater over 24 months in the EXP group, t(108) = 2.95, p = 0.004, d = 0.58.

At month 6, ≥ 5% weight loss was found in 65.5% of EXP and 18.2% of COM participants. At month 24, ≥ 5% weight loss was found in 52.7% of EXP and 16.4% of COM participants. At month 24, ≥ 3% weight loss was found in 63.6% of EXP and 38.2% of COM.

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Table 2b. Planned follow-up t-test results over the weight-loss phase (baseline-month 6) and weight-loss maintenance phase (months 6-12), by group

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>t(54)</th>
<th>p value</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg) change</td>
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<tr>
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<td>Weight-loss maintenance phase</td>
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<td>Physical activity change (METs/week)</td>
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<td>Fruit and vegetable intake (servings/day)</td>
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<td>Self-regulation for exercise change</td>
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<td>0.899</td>
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</table>

* Experimental group (EXP), n = 55; Comparison group (COM), n = 55. MET = metabolic equivalent.
participants. Figure 3 provides a graphic representation of percentages of weight change for 24 months, including data adapted from research on the Oxford CBT.

**Part 2: Behavioral Predictors of Weight Changes**

**Physical Activity**

During the weight-loss phase, although within-group increases in PA in the EXP group and the COM group were both significant, the EXP group had a significantly greater between-group increase, $t(108) = 4.86$, $p < 0.001$, $d = 0.94$. There was a significant between-group difference in PA change during the weight-loss maintenance phase, $t(108) = -3.93$, $p < 0.001$, $d = 0.77$, with the EXP group demonstrating a significant within-group reduction and the COM group showing no significant change.

**Eating**

During the weight-loss phase, within-group increases in FV in the EXP group and the COM group were both significant, and significantly greater in the EXP group, $t(108) = 2.97$, $p = 0.002$, $d = 0.57$. There was a significant between-group difference in FV change during the weight-loss maintenance phase, $t(108) = -3.20$, $p = 0.002$, $d = 0.64$, with the EXP group having a significant within-group reduction and the COM group exhibiting no significant change.

**Prediction of Weight Change**

The temporal interval that was the strongest predictor of weight change during the weight-loss phase was baseline-month 6 for both PA and FV, $\beta$ (standard error)-values were -0.38(0.05) and -0.30(0.33), respectively; $p$ values < 0.001. The temporal interval that was the strongest predictor of weight change during the weight-loss maintenance phase was month 6-month 24 for both PA and FV, $\beta$ (standard error)-values were -0.45(0.11) and -0.28(0.87), respectively; $p$ values < 0.001 and 0.018, respectively.

**Part 3: Psychological Predictors of Behavioral Changes**

**Self-Regulation for Exercise**

During the weight-loss phase, within-group increases in SR-exercise in the EXP group and the COM group were both significant, and significantly greater in the EXP group, $t(108) = 5.64$, $p < 0.001$, $d = 1.09$. There was a significant between-group difference in SR-exercise reduction during the weight-loss maintenance phase, $t(108) = -3.51$, $p = 0.001$, $d = 0.67$, with the EXP group demonstrating a significant within-group reduction and the COM group showing no significant change.

**Self-Efficacy for Exercise**

During the weight-loss phase, within-group increases in SE-exercise in the EXP group and the COM group were both significant, and significantly greater in the EXP group, $t(108) = 2.94$, $p = 0.007$, $d = 0.52$. There was a significant between-group difference in SE-exercise change during the weight-loss maintenance phase, $t(108) = -3.39$, $p = 0.001$, $d = 0.65$, with the EXP group showing a significant within-group reduction and the COM group having no significant change.

**Mood**

During the weight-loss phase, within-group reductions in Mood score in both the EXP group and the COM group were significant, and significantly greater in the EXP group, $t(108) = -4.98$, $p = 0.002$, $d = 0.98$. There was a significant between-group difference in Mood change during the weight-loss maintenance phase, $t(108) = 2.70$, $p = 0.008$, $d = 0.54$, with the EXP group demonstrating a significant within-group score increase and the COM group exhibiting no significant change.

**Self-Regulation for Controlled Eating**

During the weight-loss phase, within-group increases in SR-eating in the EXP group and the COM group were both significant, and significantly greater in the EXP group, $t(108) = 2.88$, $p = 0.005$, $d = 0.55$. There was no significant between-group difference in SE-eating change during the weight-loss maintenance phase, $t(108) = -0.48$, $p = 0.635$, $d = 0.10$, with neither the EXP or COM group demonstrating a significant within-group change.

**Prediction of Physical Activity Change**

The temporal interval that was the strongest predictor of change in PA during the weight-loss phase was from baseline-month 6 for SR-exercise, SE-exercise, and Mood. $\beta$ (standard error)-values were 0.58(0.15), 0.50(0.10), and -0.46(0.08), respectively; all $p$ values < 0.001. The temporal interval that was the strongest predictor of change in PA during the weight-loss maintenance phase was month 6-month 24 for SR-eating. $\beta$ (standard error)-values were 0.58(0.15) and 0.50(0.10), respectively; all $p$ values < 0.001.

**Figure 3. Percentage of body weight change over 24 months, by group.**

CBT = Cognitive-Behavioural Therapy.
the weight-loss maintenance phase was baseline-month 24 for SR-exercise, SE-exercise, and Mood. \( \beta \) (standard error)-values were 0.65(0.24), 0.57(0.14), and -0.52(0.17), respectively; all p values < 0.001.

After incorporating the above temporal intervals into the following two models, the multiple regression equation predicting PA change during the weight-loss phase was significant. Changes in SR-exercise, SE-exercise, and Mood were each significant independent predictors (after controlling for one another). The prediction of PA change during the weight-loss maintenance phase was significant. Changes in SR-exercise and SE-exercise, but not Mood, were significant independent predictors (Table 3).

**Prediction of Eating Change**

The temporal interval that was the strongest predictor of change in FV during the weight-loss phase was the same for baseline-month 3 and baseline-month 6 for both SE-eating and Mood. \( \beta \) (standard error)-values were 0.41(0.03), 0.45(0.01), and -0.37(0.08), respectively; all p values < 0.001. The temporal interval that was the strongest predictor of change in FV during the weight-loss maintenance phase was month 12-month 24 for SR-eating, and baseline-month 24 for both SE-eating and Mood. \( \beta \) (standard error)-values were 0.19(0.04), 0.47(0.01), and -0.31(0.02), respectively; all p values < 0.001.

After incorporating the above temporal intervals, the multiple regression equation predicting FV change during the weight-loss phase was significant. Changes in SR-eating, SE-eating, and Mood were each significant independent predictors (after controlling for one another) (Table 3). The prediction of FV change over the weight-loss maintenance phase was significant. Neither changes in SR-eating, SE-eating, nor Mood were significant independent predictors (Table 3).

**Consolidated Model for Weight-Loss Effects**

As expected, correlations of baseline, baseline-month 6, and month 6-month 24 scores between the exercise- and eating-related self-regulation measures \( (r = 0.61-0.66) \), and exercise- and eating-related self-efficacy measures \( (r = 0.40-0.48) \) were significant (all p values < 0.001). This further supported merging the exercise- and eating-related self-regulation (ie, SR-merged) and self-efficacy (ie, SE-merged) measures for the planned mediation analyses. The same Mood scale was used in both exercise and eating contexts so no such merger was needed.

In a consolidated model, the SR-merged, SE-merged, and Mood measures (changes from baseline-month 6) were entered as possible mediators of the relationship between treatment type (COM or EXP) and weight change during the weight-loss phase. The overall model was significant, \( R^2 = 0.35, F(4, 105) = 14.23, p < 0.001 \). Only change in SR-merged was a significant mediator within the equation (Table 4, Analysis I). In the planned simple mediation follow-ups, change in SR-merged significantly mediated the relationship between treatment type and weight change; and weight change significantly mediated the relationship between treatment type and change in SR-merged. This indicated a reciprocal relationship between increases in self-regulation and lost weight during the weight-loss phase (Table 4, Analysis I-a).

The SR-merged, SE-merged, and Mood measures (changes from month 6 to month 24) were entered as possible mediators of the relationship between treatment type and weight change during the weight-loss maintenance phase. The overall model was significant, \( R^2 = 0.20, F(7, 102) = 3.61, p = 0.002 \). Only change in SE-merged was a significant mediator within the equation (Table 4, Analysis II).

**Post Hoc Tests**

In post hoc analyses of only the EXP group, a significant quadratic (inverted-U) effect was found during the 24 months of the study in each of the psychological variables, which suggested a reduction in gains acquired during the initial 6 to 12 months. Effect sizes \( (\eta^2_p) \) associated with those significant ANOVA models (all p values < 0.001) were stronger than for the corresponding linear relationship for SR-exercise (0.611), SE-exercise (0.417), Mood (0.504), and SR-eating (0.600); but not SE-eating (0.374).

**DISCUSSION**

Overall, findings associated with the EXP treatment were promising. The absence of significant regain of that group’s weight loss of more than 6% was atypical, and represented a notable success (Figure 3).4,5
The experimental format not only elucidated psychological correlates of behavioral prerequisites to weight reduction, it highlighted temporal implications for their application within both weight-loss and weight-loss maintenance phases. Innovative treatment components and administrative formats were successfully incorporated within a practical setting that suggests potential for widespread application. The cost associated with implementation of the EXP treatment approximated US$400 per participant. This was about 10% to 15% of the cost estimated for both the Oxford CBT and an average of the 3 commercial weight-loss programs currently having the strongest market share.75

Specific Findings
Part 1 clearly demonstrated the superiority of the EXP treatment over the COM treatment for weight loss at all measured time points. Regain of weight in the EXP group was only a nonsignificant 0.7% of participants’ original weight, which has not been observed in the great majority of treatment studies of individuals with obesity where a climb toward baseline weight (or higher) almost always occurred after about 6 months of loss.12 When contrasted with the Oxford CBT (Figure 1), the EXP treatment had a far less acute slope of weight regain and a much larger proportion of participants who maintained ≥5% weight loss at month 24 (52.7% vs 38.8%) (Figure 3).21 This suggested substantial improvements in health risks within the EXP group. In Part 2, effect sizes for increases in both PA and FV during the weight-loss phase were about twice as large in the EXP group. Those large behavioral improvements demonstrated a partial reversal during the second year. In Part 3, within the weight-loss phase, effect sizes of improvements on the psychosocial predictors of PA and FV within the EXP group were also double those in the COM group (all large effects with d-values of 0.96-1.66). However, an inversion of some of those gains appeared between month 12 and month 24. Because these trajectories could adversely impact participants’ weight-management behaviors and weight in subsequent years, extensions of this research are presently evaluating noninvasive methods to lessen such “slippage” through periodic telephone and/or e-mail follow-ups after in-person treatment components conclude. These follow-up contacts will aim to bolster the use of previously addressed self-regulatory skills and feelings of control over behaviors associated with weight management. Part 3 of this study determined that changes in self-regulation, self-efficacy, and mood during the full 6 months of the weight-loss phase best-predicted increased PA and FV. Findings also suggested that changes in self-regulation applied to eating changes might be particularly important within the first several months of treatment. Changes in those 3 psychological factors over the entire weight-maintenance phase (months 6-24) best predicted a favorable direction for PA and FV. However, findings suggested that self-regulation for controlled eating is especially important during the second year. When the above results were consolidated, important findings also emerged. Data suggested that an emphasis on self-regulation during the weight-loss phase, and an emphasis on self-efficacy during the weight-loss maintenance phase, will optimize weight-management

Table 4. Results from multiple mediation and reciprocal effects analyses (N = 110)*

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Mediator**</th>
<th>Path a</th>
<th>Path b</th>
<th>Path c</th>
<th>Path c’</th>
<th>Indirect effect</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>β ± standard error</td>
<td>β ± standard error</td>
<td>β ± standard error</td>
<td>β ± standard error</td>
<td>β ± standard error</td>
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<tr>
<td>Analysis I: Weight-loss phase (multiple mediation)</td>
<td></td>
<td></td>
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<tr>
<td>Treatment type1</td>
<td>Δ Self-regulation</td>
<td>Δ Weight</td>
<td>1.13 ± 0.24</td>
<td>-2.13 ± 0.70</td>
<td>-8.03 ± 1.44</td>
<td>-4.61 ± 1.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(&lt; 0.001)</td>
<td>(0.002)</td>
<td>(0.001)</td>
<td>(0.004)</td>
<td>(-4.81, -0.65)</td>
</tr>
<tr>
<td>Treatment type</td>
<td>Δ Self-efficacy</td>
<td>Δ Weight</td>
<td>0.77 ± 0.24 (0.002)</td>
<td>0.20 ± 0.71 (0.780)</td>
<td>-8.03 ± 1.44</td>
<td>-4.61 ± 1.55</td>
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<tr>
<td></td>
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<td>(&lt; 0.001)</td>
<td>(0.004)</td>
<td>(0.001)</td>
<td>(0.004)</td>
<td>(-1.27, 1.71)</td>
</tr>
<tr>
<td>Treatment type</td>
<td>Δ Mood</td>
<td>Δ Weight</td>
<td>-0.86 ± 0.17 (&lt; 0.001)</td>
<td>1.35 ± 0.79 (0.093)</td>
<td>-8.03 ± 1.44</td>
<td>-4.61 ± 1.55</td>
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<td>(&lt; 0.001)</td>
<td>(&lt; 0.001)</td>
<td>(0.004)</td>
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<td>Analysis I-a: Weight-loss phase (simple mediation for reciprocal effects analysis)</td>
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<tr>
<td>Treatment type</td>
<td>Δ Self-regulation</td>
<td>Δ Weight</td>
<td>1.13 ± 0.24 (&lt; 0.001)</td>
<td>-2.27 ± 0.54 (&lt; 0.001)</td>
<td>-8.03 ± 1.44</td>
<td>-5.46 ± 1.47</td>
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<td>(&lt; 0.001)</td>
<td>(0.001)</td>
<td>(-5.43, -1.23)</td>
</tr>
<tr>
<td>Treatment type</td>
<td>Δ Weight</td>
<td>Δ Self-regulation</td>
<td>-8.03 ± 1.44 (&lt; 0.001)</td>
<td>-0.06 ± 0.15 (&lt; 0.001)</td>
<td>1.13 ± 0.24</td>
<td>0.63 ± 0.25</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(&lt; 0.001)</td>
<td>(&lt; 0.001)</td>
<td>(&lt; 0.001)</td>
<td>(0.015)</td>
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<td>Analysis II: Weight-loss maintenance phase (multiple mediation)</td>
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<tr>
<td>Treatment type</td>
<td>Δ Self-regulation</td>
<td>Δ Weight</td>
<td>-0.17 ± 0.20 (0.415)</td>
<td>-5.91 ± 1.52 (&lt; 0.001)</td>
<td>1.91 ± 2.88</td>
<td>1.42 ± 2.72</td>
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<td>(&lt; 0.001)</td>
<td>(0.001)</td>
<td>(0.509)</td>
<td>(0.604)</td>
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<tr>
<td>Treatment type</td>
<td>Δ Self-efficacy</td>
<td>Δ Weight</td>
<td>-0.38 ± 0.20 (0.055)</td>
<td>2.87 ± 1.75 (0.104)</td>
<td>1.91 ± 2.88</td>
<td>1.42 ± 2.72</td>
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<td>(&lt; 0.001)</td>
<td>(0.004)</td>
<td>(0.509)</td>
<td>(0.604)</td>
</tr>
<tr>
<td>Treatment type</td>
<td>Δ Mood</td>
<td>Δ Weight</td>
<td>0.16 ± 0.14 (0.055)</td>
<td>3.81 ± 2.07 (0.068)</td>
<td>1.91 ± 2.88</td>
<td>1.42 ± 2.72</td>
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<td></td>
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<td>(&lt; 0.001)</td>
<td>(0.004)</td>
<td>(0.509)</td>
<td>(0.604)</td>
</tr>
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</table>

* Analyses are based on a bootstrapping procedure for multiple mediation incorporating 20,000 resamples.14
* Path a = predictor → mediator; Path b = mediator → outcome; Path c = predictor → outcome; Path c’ = predictor → outcome, controlling for the mediator.
* Δ = change from baseline-month 6 for Analysis I and I-a; or baseline-month 24, controlling for changes from baseline-month 6 (for Analysis II).
* For treatment type, 0 = comparison group, 1 = experimental group.
* Δ change in; 95% CI = 95% confidence interval.
outcomes. During the weight-loss phase, changes in self-regulation and weight appeared to reinforce one another mutually. Overall, results supported the EXP treatment’s ability to improve mood and increase self-regulation and self-efficacy related to both physical activity and healthy eating behaviors.

Fit with Previous Research

Although most weight-loss treatments employ an educational approach that focuses upon restricting energy intake, the use of cognitive-behavioral methods and exercise within weight-loss interventions is not novel. However, comprehensive reviews suggest that even the most state-of-the-art, theory-based approaches primarily targeting eating changes have been unsuccessful beyond the very short term.4 Within this report, findings from a previously described17 and tested21 weight-loss/weight-loss maintenance protocol (Oxford CBT) was contrasted with the EXP treatment because of its theoretical similarity, similar research design, and seemingly strong cognitive-behavioral approach. As has been typical, however, exercise was treated as a favorable adjunct to nutritional change rather than a key component of that protocol, and its maintenance of weight loss was unsuccessful.21 Guided by suggestions of the consistent relationship between exercise and maintained weight loss,23-25 previous experimental research on (modifiable) psychosocial correlates of weight loss,65-67 our own program of research on the generalization of exercise-induced psychological changes to eating changes during the short term,35,77-85 and recommendations from the National Institutes of Health to address adherence to exercise and establish relevant behavioral skills before attempting weight loss,22 we substantially modified and extended previous approaches. We incorporated assumptions that cognitive-behaviorally supported exercise can facilitate changes in eating and weight through associated psychological changes. Although the present data cannot determine precisely what treatment component(s) or implementation methods were most associated with the present positive results, future research designs might facilitate a more comprehensive decomposition of findings to determine the most salient treatment components and, thus, further enhance effects. We encourage future related research to also study weight-loss and weight-loss maintenance phases separately through behavioral changes and their psychological predictors, because processes within these phases appear to differ from one another. Continued evaluation of temporal aspects might facilitate a more precise process that further refines the benefits of emphasizing specific treatment components at specific times, which might also vary by personal characteristics (eg, initial weight, psychological profile). The present determination that weight loss might most benefit from a concentration on self-regulation, whereas weight-loss maintenance might most benefit from a concentration on self-efficacy, is a start in that direction. Although this research based the architecture of the EXP treatment and the selection and measurement of behavioral and psychological constructs on social cognitive and self-efficacy theory and the many studies following from those paradigms, additional theories (eg, self-determination theory, theory of planned behavior) might also serve as a basis in extensions of this research. The contrast of those results with the present findings will undoubtedly be instructive.

Study Limitations

To increase confidence in findings and assess their generalizability for application, present limitations such as the use of a homogeneous sample of primarily white and middle-class women who were motivated enough to volunteer for treatment require attention. Thus, replications with men, with other racial/ethnic and socioeconomic groups, and possibly with participants who were strongly referred by medical practitioners (to minimize effects of volunteerism) will be beneficial. Replications are also required with overweight participants and participants with a more severe degree of obesity (ie, class 3/morbid obesity). Other limitations of this research indicate a need for better controls for social support and expectation effects that are likely to bias results when interventions differ in length and amount of in-person contact, as was the case here.66 Thus, the use of an attention-matched, or a wait-list, control group might also be useful in replications of this research. Although the repeated-measures design of this study was a strength, multiple administrations of the same self-report instrument increases its measurement error.67 Although it is difficult to accomplish in field settings (that benefit the applicability of findings),68-69 the use of more objective and comprehensive measures of exercise (eg, accelerometry) and dietary intake (eg, more extensive nutrition recall instruments) would increase accuracy of the behavioral outcomes. Within the present study, however, because of the length of time required for completion of the seven self-report surveys, any additional time burden placed on participants might have challenged the quality of their responses.20

CONCLUSION

Although the above limitations should be acknowledged, and replications are needed, the EXP treatment has considerable possibilities for dissemination. Its format allows for low-cost implementation in community-based health-promotion settings by staff members with general wellness credentials. It also has a strong potential for physician referral. Whereas pharmacologic and surgical interventions for obesity are available, improving physical activity and eating behaviors will effectively address obesity and their associated health risks for most affected individuals. Despite the fact that sustained improvements in eating and exercise have been difficult for behavioral medicine to effectuate, the present research introduced innovative behavior-change methods that empowered individuals to effectively deal with day-to-day barriers that consistently served as impediments to maintaining clinically important losses in body weight. The use of manageable amounts of exercise to build the self-regulatory skills and improvements in mood that promote a newfound sense of the self-regulatory skills and improvements in mood that promote a newfound sense of

Disclosure Statement

The authors have no conflicts of interest to disclose.

Acknowledgment

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13. Simpson SA, Shaw C, McNamara R. What is the most effective way to maintain weight loss in adults? BMJ 2011 Dec 28;343:d4002. DOI: http://dx.doi.org/10.1136/bmj.d8042.
Weight Loss and the Prevention of Weight Regain: Evaluation of a Treatment Model of Exercise Self-Regulation Generalization to Controlled Eating


A Pharmacist-Staffed, Virtual Gout Management Clinic for Achieving Target Serum Uric Acid Levels: A Randomized Clinical Trial

Robert Goldfien, MD; Alice Pressman, PhD, MS; Alice Jacobson, MS; Michele Ng, PharmD; Andrew Avins, MD, MPH

ABSTRACT
Context: Relatively few patients with gout receive appropriate treatment.

Objective: To determine whether a pharmacist-staffed gout management program is more effective than usual care in achieving target serum uric acid (sUA) levels in gout patients.

Design: A parallel-group, randomized controlled trial of a pharmacist-staffed, telephone-based program for managing hyperuricemia vs usual care. Trial duration was 26 weeks.

Main Outcome Measures: Primary outcome measure was achieving sUA levels at or below 6 mg/dL at the 26-week visit. Secondary outcome was mean change in sUA levels in the control and intervention groups. Participants were adults with recurrent gout and sUA levels above 6.0 mg/dL. Participants were randomly assigned to management by a clinical pharmacist following protocol or to monitoring of sUA levels but management of their gout by their usual treating physician.

Results: Of 102 patients who met eligibility criteria, 77 subjects obtained a baseline sUA measurement and were entered into the trial. Among 37 participants in the intervention group, 13 (35%) had sUA levels at or below 6.0 mg/dL at 26 weeks, compared with 5 (13%) of 40 participants in the control group (risk ratio = 2.8, 95% confidence interval [CI] = 1.1 to 7.1, p = 0.03). The mean change in sUA levels among controls was +0.1 mg/dL compared with -1.5 mg/dL in the intervention group (sUA difference = -1.6, 95% CI = -0.9 to -2.4, p < 0.001).

Conclusions: A structured pharmacist-staffed program was more effective than usual care for achieving target sUA levels. These results suggest a structured program could greatly improve gout management.

INTRODUCTION
Gout is the most common inflammatory arthritis in men. It is well recognized that successful long-term management of gout and hyperuricemia remains elusive. Unlike other common forms of inflammatory arthritis, gout is not an autoimmune disease and instead is understood to be a manifestation of chronic elevation of serum uric acid (sUA). Studies of gouty arthritis have provided important insights into other inflammatory conditions that are of great interest to rheumatologists. There is also a growing literature documenting the association of chronic hyperuricemia and gout with diabetes, chronic kidney disease, and adverse cardiovascular outcomes. Therefore, improving the long-term management of gout may lead to other important health benefits as well.

Guidelines for the treatment of acute gout and the optimal management of hyperuricemia have been evolving and have been the subject of several recent reviews. These reviews highlight several barriers to optimal gout management, including poor patient adherence; the need for better patient education; and a lack of awareness of management guidelines, especially among primary care physicians. Notably, unlike other forms of inflammatory arthritis (eg, rheumatoid arthritis), there is a straightforward and easily monitored outcome measure that correlates with optimal long-term outcomes in gout. Both the European League Against Rheumatism and the American College of Rheumatology recommend that patients with tophaceous or recurrent gout be treated with urate-lowering therapy (ULT) to a target sUA level below 6.0 mg/dL. Maintaining the sUA at that level eventually leads to cessation of gout flares. This fact is particularly notable given the burden of gout in the US. One study found there were 3.9 million outpatient visits for gout in the US in 2002. Unfortunately, only a minority of patients with gout receives appropriate treatment, including doses of ULT sufficient to achieve this target. Specifically, deficiencies in ULT management include a lack of appropriate monitoring, failure to treat-to-target, and fear of ULT dose escalation in some patients, particularly those with chronic kidney disease. Thus, there is a need for new, practical, and more effective approaches to the management of gout.

To address the problem of inadequate adherence to gout treatment guidelines, we previously developed a management model consisting of a telephone-based “clinic” composed of a clinical pharmacist under the supervision of a board-certified...
rheumatologist. In this model, the pharmacist uses telephone encounters to implement a simple protocol, initiating and adjusting standard gout medications in patients referred by their primary care physicians for management of recurrent or tophaceous gout. Patients are monitored by the clinic until they have 2 consecutive target sUA results at least 3 months apart; they are then discharged back to the care of their primary physician. We previously reported a case series from this pilot study, analyzing the outcomes of the first 100 patients referred to the program. The results of this pilot were encouraging, and the current study (Gout Uric Acid RedUction, or GUARD trial) was conducted to test whether this model would be more effective than usual care in the context of a randomized controlled trial.

METHODS
Design
The GUARD study was a randomized, parallel-group, open-label clinical trial of a pharmacist-staffed, structured gout management program compared with usual care.

Patient Selection
The study sample was recruited from the Kaiser Permanente Northern California (KPNC) patient population. Inclusion criteria included at least 2 consecutive years of Health Plan membership, an established diagnosis of gout (International Classification of Diseases, Ninth Revision Code 274.XX), and clear documentation of at least 2 distinct episodes of acute gouty arthritis in the preceding 12 months. To be eligible for randomization, patients between the ages of 21 and 80 years had either a most recent sUA level above 7.0 mg/dL or no measurement of sUA in the past year. Patients were excluded if they had a current cancer diagnosis with active treatment, were believed to be terminally ill (as judged by the Principal Investigator before randomization), were pregnant or lactating, or had end-stage renal disease or dementia.

For each patient fulfilling the eligibility criteria, an e-mail was sent to his/her primary care physician. This e-mail included a brief description of the trial, including the expectation that those assigned to receive “usual care” would be instructed to continue to manage their gout under the care of their primary care physician or rheumatologist. If physician consent was obtained, patients were contacted by letter accompanied by a description of the study and a written informed consent document. The program pharmacist telephoned the potential subject and described the study, answered any questions, and then obtained verbal consent. Each participant was provided written educational material on gout at the time of program entry. Randomization was accomplished by assigning an identification number using a balanced, blocked randomization list with variable block sizes (used to reduce the likelihood of an unbalanced or biased randomization).

After randomization, a baseline laboratory assessment was required of all potential participants to begin the trial. (The laboratory measurements were obtained after randomization for practical implementation reasons.) This panel included sUA and alanine aminotransferase values, estimated glomerular filtration rate, and complete blood cell count. The trial protocol was approved by the Kaiser Foundation Research Institute’s institutional review board.

Group Assignments
Control subjects were asked to complete baseline, 12-week, and 26-week laboratory assessments. We defined measurement windows of between 10 weeks and 16 weeks for the 12-week measurement of sUA in the control group, and between 24 weeks and 30 weeks for the closeout measurement.

In the intervention group, the clinical pharmacist, under a protocol approved by the KPNC East Bay Pharmacy and Therapeutics Committee, was authorized to order relevant laboratory tests and to initiate or to change orders for the medications used for ULT and for flare prophylaxis. In the event of acute flares or abnormal laboratory results, the pharmacist consulted with the rheumatologist, who could prescribe treatment or advice if outside the scope of the pharmacy protocol. The ULT was either initiated or adjusted if the sUA level was above 6.0 mg/dL. Prophylaxis of gout flares was prescribed in all cases (see next paragraph). Subjects already receiving ULT treatment had their medications titrated but not changed. Subjects not receiving ULT at the start of the trial were started on a regimen of allopurinol, 100 mg/day (if the estimated glomerular filtration rate was less than 30 mL/min, the starting dose was 50 mg/day), unless there was a known allergy or other contraindication to allopurinol. After any change in ULT, subjects were instructed to return for laboratory assessment (sUA, alanine aminotransferase, complete blood cell count, and estimated glomerular filtration rate) in 2 weeks to 3 weeks, and report any adverse drug reactions or gout flares. Dose titration was in increments of 100 mg/day. The titration process was continued in an iterative fashion until a target sUA level was achieved and maintained, or until the trial ended at 26 weeks. In all cases, the primary outcome—sUA level at or below 6.0 mg/dL—was determined by either a second consecutive target result or the most recent result at 26 weeks (with a window of 24 weeks to 30 weeks).

Probenecid and febuxostat were second-line agents and used if allopurinol was not tolerated. Flare prophylaxis in most cases consisted of daily oral colchicine or any nonsteroidal anti-inflammatory drug and was continued throughout the study in the intervention group. At the conclusion of the trial, each subject’s primary physician was informed whether or not the patient achieved the target, and the most recent sUA level. If the patient had achieved the target, the physician was advised to continue the current medication and dose of ULT. For patients not at target, the physician was reminded of the target level.

Outcome Variables
The primary outcome was achieving an sUA level of 6.0 mg/dL or below at the 26-week closeout visit. Secondary outcomes included the absolute change in sUA level from baseline to 26 weeks and achieving at least a 2 mg/dL decrease in sUA level at the closeout visit.

Statistical Analyses
All analyses of continuous variables were conducted with the Student t-test. Categorical variables were analyzed with the Fisher exact test or its generalization for more than 2 levels. Analyses were conducted and are reported here both under the principle of intention-to-treat, with the last value carried forward (the primary analysis), and as a per-protocol
A Pharmacist-Staffed, Virtual Gout Management Clinic for Achieving Target Serum Uric Acid Levels: A Randomized Clinical Trial

analysis, including only observed values. All reported p values were 2-sided with the experimental error rate set to $\alpha = 0.05$, and no adjustments were made for multiple testing. Analyses were performed with SAS Version 9.3 (SAS Institute, Cary, NC) and STATA 12 (StataCorp LP, College Station, TX).

RESULTS

The outcomes of the selection, consent, randomization, and trial progress are shown in Figure 1. We identified 1860 potentially eligible patients from KPNC electronic health records. The records were placed in random order, and charts were then reviewed for eligibility by a board-certified rheumatologist (RG) to validate the inclusion and exclusion criteria. We screened the charts of the first 749 patients and identified 329 who were eligible for inclusion in the study. Of the 418 who were not eligible, the most common reasons were insufficient documentation of at least 2 gout flares in the prior year ($n = 226, 54\%$), a most recent sUA level of 7.0 mg/dL or less ($n = 93, 22\%$), and excluded comorbidities ($n = 15, 4\%$).

Ultimately, 104 patients consented to participate and were randomly assigned to receive either active intervention or usual care. Three patients gave consent and were randomized but, on baseline laboratory evaluation, were found to have sUA levels at or below 6.0 mg/dL. Of the 99 remaining subjects, 51 were randomly assigned to the intervention group and 48 to the control group. Of these, 12 subjects never completed the baseline sUA assessment (7 in the treatment group and 5 in the control group). A total of 22 participants dropped out of the study after obtaining their baseline sUA measurements (8 in the control group and 14 in the intervention group); all but 1 (whose insurance lapsed) failed to obtain required laboratory assessments despite repeated attempts by the study pharmacist. Of the 37 participants randomized to the intervention group, 32 (86\%) remained in the trial at the 12-week time point and 29 (78\%) at the 26-week closeout call; the corresponding lab adherence numbers for the control group were 36 (90\%) of 40 participants at 12 weeks and 35 (88\%) at 26 weeks. Table 1 shows the demographic

![Flow diagram of design of Gout Uric Acid ReDuction study.](image)

sUA = serum uric acid level (mg/dL).

Table 1. Baseline demographic and clinical characteristics, overall and by study group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All participants (N = 77)</th>
<th>Intervention group (n = 37)</th>
<th>Control group (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>59.4 (1.4)</td>
<td>60.9 (2.0)</td>
<td>58.0 (2.0)</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>68 (88)</td>
<td>36 (97)</td>
<td>32 (80)</td>
</tr>
<tr>
<td>Race/ethnicity, no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Native American</td>
<td>1 (1)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Asian</td>
<td>9 (12)</td>
<td>7 (19)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>African American</td>
<td>12 (16)</td>
<td>5 (14)</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>17 (22)</td>
<td>7 (19)</td>
<td>10 (25)</td>
</tr>
<tr>
<td>White</td>
<td>23 (30)</td>
<td>9 (24)</td>
<td>14 (35)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>14 (18)</td>
<td>7 (19)</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1)</td>
<td>1 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Clinical characteristic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, no. (%)</td>
<td>49 (64)</td>
<td>25 (68)</td>
<td>24 (62)</td>
</tr>
<tr>
<td>Chronic kidney disease, no. (%)</td>
<td>23 (30)</td>
<td>13 (35)</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Diabetes mellitus, no. (%)</td>
<td>19 (25)</td>
<td>9 (24)</td>
<td>10 (26)</td>
</tr>
<tr>
<td>Serum uric acid (mg/dL), mean (SD)</td>
<td>8.3 (1.4)</td>
<td>8.5 (1.5)</td>
<td>8.2 (1.3)</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL), mean (SD)</td>
<td>1.2 (0.4)</td>
<td>1.3 (0.5)</td>
<td>1.1 (0.3)</td>
</tr>
</tbody>
</table>

SD = standard deviation.
and baseline information for all subjects entering the study (n = 77).

Table 2 reports the results of the primary outcome measure. In the intention-to-treat analysis using the method of last-value-carried-forward, 13 (35%) of 37 subjects in the intervention group (95% confidence interval [CI] = 20% to 52%). However, only 5 (13%) of 40 subjects (95% CI = 4% to 27%) in the control group achieved an sUA level of 6.0 mg/dL or below at 26 weeks (Figure 2; risk ratio [RR] = 2.8, 95% CI = 1.1 to 7.1, p = 0.03). This difference was greater at the 12-week time point with 15 participants (41%, 95% CI = 25% to 58%) in the intervention group and 3 participants (8%, 95% CI = 2% to 20%) in the control group achieving the targeted study outcome of sUA levels of 6.0 or less (RR = 5.4, 95% CI = 1.7 to 17.2, p = 0.001).

The control group experienced a mean increase in the sUA level at 26 weeks of 0.1 mg/dL (95% CI = -0.45 to 0.69), whereas the sUA in the intervention group decreased by an average of 1.5 mg/dL (95% CI = -1.0 to -2.0). The intergroup difference in sUA levels was -1.6 mg/dL (95% CI = -0.9 to -2.4, p < .001). Results were similar, although somewhat more pronounced, for the less-conservative per-protocol analysis, which did not include imputed data (Table 2).

To elucidate the range of outcomes among subjects in the control and intervention groups, we plotted the individual change in sUA levels at week 26 for all participants completing the protocol (Figure 3).

**DISCUSSION**

Our premise for this study was that an important failure in the management of chronic gout has been the lack of a systematic approach for identifying inadequately

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**Table 2. Primary and secondary outcome measures by study group**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intention-to-treat analysis</th>
<th>Per-protocol analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention group (n = 37)</td>
<td>Control group (n = 40)</td>
</tr>
<tr>
<td>sUA level ≤ 6 mg/dL, no. (%)</td>
<td>15 (41)</td>
<td>3 (8)</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 weeks</td>
<td>13 (35)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>sUA level change from baseline (mg/dL), mean ± SE</td>
<td>-1.6 ± 0.2</td>
<td>0.2 ± 0.2</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 weeks</td>
<td>-1.5 ± 0.3</td>
<td>0.1 ± 0.3</td>
</tr>
<tr>
<td>Decrease in sUA level by ≥ 2 mg/dL, no. (%)</td>
<td>16 (43)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 weeks</td>
<td>14 (38)</td>
<td>5 (13)</td>
</tr>
<tr>
<td>ALT level change from baseline (mg/dL), mean ± SE</td>
<td>8.4 ± 3.1</td>
<td>-2.4 ± 1.5</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 weeks</td>
<td>8.1 ± 3.9</td>
<td>-1.3 ± 1.8</td>
</tr>
<tr>
<td>Creatinine level change from baseline (mg/dL), mean ± SE</td>
<td>0.01 ± 0.02</td>
<td>-0.02 ± 0.02</td>
</tr>
<tr>
<td>12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 weeks</td>
<td>0.006 ± 0.03</td>
<td>0.005 ± 0.03</td>
</tr>
</tbody>
</table>

* Numbers refer to participants assessed at the 26-week time point. For the 12-week time point, there were 32 evaluable participants in the intervention group and 36 participants in the control group.

**RR** = 5.4 (95% CI = 1.7 to 17.2).

**RR** = 6.6 (95% CI = 1.8 to 17.7).

**RR** = 2.8 (95% CI = 1.1 to 7.1).

**RR** = 5.2 (95% CI = 1.6 to 16.6).

ALT = alanine aminotransferase; CI = confidence interval; RR = risk ratio; SE = standard error; sUA = serum uric acid.
treated patients and then to treat and monitor them in a structured, target-driven way. In our organization, the management of other chronic diseases has improved substantially by using such an approach.\textsuperscript{21} We previously published results of a pilot program designed to assess the feasibility of using a pharmacist to manage ULT in patients with gout under the supervision of a rheumatologist.\textsuperscript{20} The outcomes in this single-cohort study were encouraging, but it was an uncontrolled study. The present study, which included a randomized usual-care control group, confirmed that a higher percentage of patients randomly assigned to a structured, goal-directed program did indeed achieve and maintain a target sUA level at or below 6.0 mg/dL. In addition, we found a statistically significant greater mean improvement in sUA level among patients in the intervention group.

The percentage of subjects in the intervention group who achieved the primary outcome (35% in the intention-to-treat analysis, 45% in the per-protocol analysis) was considerably lower than what we were able to achieve in our pilot program (82%), but much higher than the percentage seen in the control group (8%). In our current trial, the lower rate of success without the intervention was notable but must be interpreted within the context of the study. In particular, unlike the pilot program, the study recruited patients not referred by their primary physicians, which may have resulted in a cohort of less-motivated patients. Although greater in the intervention group, there was also a higher drop-out rate compared with that seen in our pilot program. It is also possible that the lower success rate was partially caused by limitations imposed by the study protocol. Specifically, unlike the present trial, the pilot study allowed the continuation of the program beyond 26 weeks if the sUA target was not maintained for at least 3 months. Because adherence to ULT is known to be low compared with treatment of other chronic conditions,\textsuperscript{21} the successful long-term management of gout must eventually account for this by building in a continued monitoring scheme that will identify nonadherent patients and allow further intervention. In the current study, limited to 26 weeks, we were not able to address this need. Nonetheless, initiating and adequately titrating pharmacologic treatment to lower sUA level is a necessary step toward long-term control, and one that is achieved in a relatively low percentage of patients with gout in the absence of a structured program. We believe that the results in the pilot study may well be a better reflection of how well our program would perform outside the constraints of the study design and length.

Our study had several strengths, including a comparable randomized control group; a clear, structured intervention protocol; and objective outcome measurements. However, several limitations should be noted. First, there was a relatively high dropout rate from the program (22%), which was higher in the intervention group than the control group. This difference did not reach statistical significance, $p = 0.232$. Despite this difference, both the per-protocol and intent-to-treat analyses showed a statistically significant improvement in attaining the primary outcome in our intervention group. Moreover, we were not able to use a control group that strictly reflected usual care. This is because our primary outcome measure required that every participant be tested at least two times for sUA during the study. Under true “usual care,” it was unrealistic to expect that all the patients with gout would have been tested, and thus we would have been unable to assess our primary outcome. Indeed, we have reviewed KPNC data for sUA among patients with a gout diagnosis and found that 29% had no sUA level measured in the 5-year period before their last encounter for gout (unpublished data). If anything, we believe this monitoring requirement may have biased our results against an intervention effect because the lack of an sUA measurement during the study would more likely lead to a lack of initiation or titration of treatment.

CONCLUSION

The fact that we were able to demonstrate improved outcomes even with a restrictive and time-limited intervention suggests that an ongoing monitoring program integrated within a primary care-centered medical system could be highly effective in achieving sustained reduction of sUA levels in patients with gout. Moreover, if managed efficiently by a pharmacist or other physician extender, this approach could result in a
Favoring Disease

Gout would thus appear at least partly to depend on a loss of power … of the “uric-acid-exerting function” of the kidneys . . . . Any undue formation of this compound would favour the occurrence of the disease: and hence the connection between gout and uric acid, gravel and calculi . . . . and the influence of high living, wine, porter, want of exercise, etc, in inducing it.

— Sir Alfred Baring Garrod, FRS, 1819-1907,

English physician credited with coining the term “rheumatoid arthritis”

References

Exploring the Reality of Using Patient Experience Data to Provide Resident Feedback: A Qualitative Study of Attending Physician Perspectives

Stefanie Campbell, MD; Heather Honoré Goltz, PhD, LMSW, MEd; Sarah Njue, MPH; Bich Ngoc Dang, MD

ABSTRACT

Introduction: Little is known about the attitudes of faculty and residents toward the use of patient experience data as a tool for providing resident feedback. The purpose of this study was to explore the attitudes of teaching faculty surrounding patient experience data and how those attitudes may influence the feedback given to trainees.

Methods: From July 2013 to August 2013, we conducted in-depth, face-to-face, semistructured interviews with 9 attending physicians who precept residents in internal medicine at 2 continuity clinics (75% of eligible attendings). Interviews were coded using conventional content analysis.

Results: Content analysis identified six potential barriers in using patient experience survey data to provide feedback to residents: 1) perceived inability of residents to learn or to incorporate feedback, 2) punitive nature of feedback, 3) lack of training in the delivery of actionable feedback, 4) lack of timeliness in the delivery of feedback, 5) unclear benefit of patient experience survey data as a tool for providing resident feedback, and 6) lack of individualized feedback.

Conclusion: Programs may want to conduct an internal review on how patient experience data is incorporated into the resident feedback process and how, if at all, their faculty are trained to provide such feedback.

INTRODUCTION

Interpersonal and communication skills constitute one of the Accreditation Council for Graduate Medical Education’s (ACGME’s) 6 domains of clinical competencies for graduate medical education in internal medicine. The ACGME supports the use of patient experience data as an outcomes-based tool for providing resident feedback on interpersonal and communication skills. The American Board of Internal Medicine is exploring ways to integrate this outcomes-based approach into their physician certification activities. Patient experience data can serve as an effective tool for providing residents with feedback. In a study by Cope and colleagues, residents in an internal medicine training program were randomized to receive a 30-minute structured feedback session in which they received mean scores on an experience survey filled out by new patients. Residents in the intervention arm had a significant increase in mean scores on a subsequent survey of new patients compared with residents who did not receive feedback. Patient experience data paired with actionable feedback (ie, feedback that can change residents’ practice behavior) can be highly effective when provided by trained individuals.

Although data suggest actionable feedback has a positive impact on residents’ practice behaviors, many graduate medical education programs have difficulties translating this knowledge into real-world practice. Studies evaluating feedback-based interventions typically devote immense resources on the development and training of personnel to deliver actionable feedback that is typically neither feasible nor designed for implementation in general practice. As such, patient experience survey data are rarely used effectively outside the research context to deliver resident feedback, owing to lack of either training or time. In addition, little is known about the attitudes of faculty and residents toward the use of patient experience data as a tool for providing resident feedback. The purpose of this study was to explore how attending physicians in a real-world academic setting incorporate patient experience survey data into feedback practices, explore the attitudes and beliefs surrounding the use of patient experience data as a feedback tool, and identify potential areas for improvement. Specifically, we were interested in exploring attendings’ attitudes around giving feedback and understanding the process by which attendings provide learners with actionable feedback.

METHODS

Participants

The study population was based on a nonrandomized convenience sample of attending physicians who precept residents in internal medicine at two continuity clinics in Houston, TX (clinics A and B). Eligibility criteria included 1) faculty with an appointment in the Department of Internal Medicine and 2) faculty with a role as a preceptor in the internal medicine resident continuity clinic. This study was approved by the institutional review board for our institution.

Data Collection

Participants were recruited by e-mail; attending physicians received an e-mail from the Associate Program Director of the
Exploring the Reality of Using Patient Experience Data to Provide Resident Feedback: A Qualitative Study of Attending Physician Perspectives

Internal Medicine Residency Program (SC) inviting them to take part in the study. The e-mail informed potential participants of the study and its purpose. Twelve attending physicians met eligibility criteria and were recruited; 9 attending physicians participated. Between July and August 2013, SC conducted in-depth, face-to-face, semistructured interviews with attending physicians. She conducted 4 individual interviews at clinic B and a focus group interview involving 5 participants at clinic A. A focus group interview was conducted at clinic A per the request of the clinic director, given the time constraints of the attending staff. Staff members were willing to complete a group interview during their lunch hour, but were unable to dedicate an hour individually for interviews. Participants provided verbal but not written informed consent to protect their identities. No compensation was provided for participation. The individual interviews lasted 30 minutes to 60 minutes and the focus group lasted 60 minutes. Interviews were audiotaped using an encrypted recorder and transcribed verbatim by professional transcriptionists. The interviews were conducted using an open-ended interview guide developed by the multidisciplinary team. The interview guide consisted of open-ended questions to identify the process of feedback, the attitudes and beliefs surrounding feedback, and the training given to attending physicians to use patient experience survey data in providing resident feedback (see Sidebar: Major Topics and Key Interview Questions in Study of Resident Feedback). Interviews took place in conference rooms at the participants’ respective clinic sites.

**Research Team and Reflexivity**

The research team’s professional backgrounds and research interests informed development of the interview guide, interpretation of codes, and understanding of emergent themes within the context of medical education and patient care. Our multidisciplinary team consisted of two physicians, a social work researcher, and a research coordinator. SC, Associate Program Director of the Internal Medicine Residency Program, ensures quality education and training for residents. BND is an Assistant Professor of Medicine in the Section of Infectious Diseases. Her research examines the use of patient experience metrics as a modifiable focus for improving retention in care and adherence to medicines. HHG, Assistant Professor in Social Work, is experienced in qualitative research methods; she is interested in patients’ access to and quality of care. SN is a master’s-trained public health professional with a background in health promotion and behavioral science.

**Data Analysis**

We did not use an a priori code list. Four researchers (SC, HHG, SN, and BND) independently reviewed the transcripts and coded the data, looking for examples of facilitators and barriers to actionable feedback. The full research team then came together to compare codes and iteratively revise and refine codes until 100% consensus was reached. This occurred during several weekly team meetings. In the later stages of analysis, the team examined recurrent themes across interviews and clinic sites.

**RESULTS**

**Characteristics of Participants**

The participation rate among eligible attending physicians was 75% (9/12). Nonparticipating physicians reported demanding clinical duties and the lack of time as reasons for opting out. Baseline characteristics are outlined in Table 1. Given the small sample size, limited demographic characteristics are reported to preserve confidentiality. Five were female and 4 reported their race/ethnicity as Asian. Five participants precept residents at clinic A and 4 at clinic B.

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*The term “satisfaction survey” was used instead of patient experience in the interview guide because it was a term faculty were more familiar with.*
Barriers to Actionable Feedback

Specific patterns of feedback varied by clinic site; however, some core themes did emerge from the data. The research team identified six themes corresponding to potential barriers in using patient experience survey data to provide actionable feedback to residents: 1) perceived inability of residents to learn or incorporate feedback, 2) punitive nature of feedback, 3) lack of training in the use of patient-experience data to give feedback, 4) lack of timeliness in providing feedback, 5) unclear benefit of patient experience data as a tool to inform and frame actionable feedback, and 6) lack of individualized feedback.

Perceived Inability of Residents to Learn or Incorporate Feedback

On occasion, attending physicians seemed resigned to the belief that it is difficult to change residents’ practice behavior. They cited difficulties in teaching adult learners and difficulties in teaching “soft skills” (eg, personal attributes). Three attending physicians specifically reported difficulty in teaching “professionalism.”

“…It’s hard to change behavior for adults . . . . Just because they’re trainees, we should not forget the fact that they are adults and they’re supposed to be professionals, you know, so there’s only so much I can do . . . .”

“But you can’t change personalities and habits of people [who are] old. You can do your best, but professionalism is a very difficult thing to teach, and it’s professionalism in not just how you look but how you show up, but it’s also the amount of effort you put forth in what your actual duties are, you know, and how much you can relate and communicate to the patient. So it’s hard to teach soft skills. You can do your best with a resident that you might have for three years, but some personalities don’t change.”

—Attending physicians at clinics A and B

Punitive Nature of Feedback

Punitive feedback refers to any negative approach to providing feedback. Three of four participants at clinic B reported that they approached underperforming residents in a nonpunitive way to address patient concerns or improve their clinical competence. These attending physicians engaged the resident in coming up with task-specific and actionable solutions.

“I talked to the resident about what she thought had happened, and then we kind of brainstormed kind of what we thought had gone wrong between that. And she asked me was there anything I could do to . . . .”

“So I learned that we have to be sensitive but at the same time have to get to the point because if you’re too sensitive you’re being too nice. And if they don’t get the message then you’re not getting to the feedback.”

—Attending physicians at clinic B

In contrast, attendings at clinic A reported using punitive feedback in response to the residents’ actions, such as removing patients from the residents’ panel.

“So that is why they [the patients] don’t want to write bad things, but they will come and talk to us in person; especially because many of them, if you’ve been seeing them for several years, they do understand that these people are in training, which is okay to some extent. And some say ‘No, I don’t want to see a resident; I want to see the attending.’ Then we just change the patient back to us [attendings].”

**Patient Experience Survey Questions**

1. Overall, I was satisfied with this visit
2. During this visit, my doctor treated me with respect
3. My doctor answered my medical questions
4. My doctor used terms I understood
5. My doctor involved me in making decisions about my care
6. I felt my doctor listened to my concerns
7. I felt my doctor spent enough time with me
8. I would recommend this doctor to a friend
9. I was seen by the doctor in a timely fashion

For each question, patients were asked to choose: Strongly disagree, Disagree, Neither disagree nor agree, Agree, Strongly Agree, or Unsure.
“But some of my patients I have actually removed from his panel and either brought them back to me or put them with another person that I know is better at listening and communication.”

“But it’s important for the resident that he at least gets a feel that we are watching them and patients do have their opinions.”

—Attending physicians at clinic A

**Lack of Training in the Use of Patient Experience Data to Give Feedback**

Participants were asked if they received specific training in using patient experience survey data to provide actionable feedback. Two of the five participants at clinic A reported taking a three-hour institutional workshop two years prior. Per their report, the workshop explained how to provide feedback to residents, but not specifically how to incorporate patient experience data into feedback practices.

“There’s a course at [my institution] about how to evaluate residents and other groups . . . . The one that we specifically had taken was how to complete evaluations.”

—Attending physician at clinic A

However, three of the four participants at clinic B reported no formal training in these areas.

“No, I mean, no formal training to start off with, except I mean—I mean, we had, you know, teaching as residents and a lot of teaching built into our primary care residency.”

—Attending physician at clinic B

**Lack of Timeliness in Providing Feedback**

Lack of timeliness refers to delays in providing feedback to the residents. Branch and Paranjas suggest residents should receive feedback at least every two to three months. In our analysis, two attending physicians at clinic B reported completing evaluations twice a year; they reported time constraints as a barrier to timely feedback.

“It’s time consuming because I have 28 residents.”

“We just do it electronically so we don’t actually have that feedback-like oral feedback session because they come at different times.”

—Attending physicians at clinic B

“I’d rather not deal with it than deal with that because they’re sending more work for me . . . . Every year, every year now, I have one that is wasting my time.”

—Attending physician at clinic A

**Unclear Benefit of Patient Experience Data as a Tool to Inform and Frame Actionable Feedback**

Benefit refers to the degree with which the attending physicians consider patient experience survey data as a beneficial tool for providing actionable feedback. Only one of five participants at clinic B reported that the surveys were a suitable tool for providing feedback to the residents. However, of the nine participants overall, eight questioned the value of patient experience survey data in providing resident feedback. These attendings reported that the surveys were not beneficial; they felt that the information obtained from the surveys was insufficient to address patient issues or give effective feedback to the residents.

“I don’t see that they are a big help to the resident, nor to me, unless the patient very specifically writes something, you know, out of the ordinary that the resident did, whether it be egregious or something positive. Short of that, I don’t see that they are very helpful evaluations to me or the resident, in their current state.”

“Yeah, because I’m not getting that much useful information except uh “wonderful doctor,” “the best,” . . . but no really constructive feedback . . . . We [are] doing it [patient experience surveys] just to meet this [Accreditation Council for Graduate Medical Education] requirement but yet they’re not learning . . . . There’s no feedback and they’re not learning what they should do to improve themselves. There’s no purpose of doing the evaluation . . . . So it’s a little more difficult and there’s no details on those and so it’s a little harder to give feedback . . . . I don’t see any comments . . . . at all so it’s hard to give the feedback.”

“I don’t think the residents care too much. They get evaluated so many ways and so many times a year.”

—Attending physicians at clinics A and B

Most attendings did not like the survey format. They preferred open-ended questions where patients could provide specific examples and task-specific feedback.

**Lack of Resident-Centered Feedback**

Resident-centered feedback is feedback that engages the resident in discussion and allows for shared goal setting.

One participant in clinic B reported delivering feedback by having a face-to-face conversation. In contrast, the other three participants in clinic B reported providing feedback electronically; they cited lack of time and the high number of assigned residents as barriers to resident-centered feedback.

“Unfortunately we don’t sit down . . . . We don’t sit down with any one of them except the ones who actually um have difficulty. Then we meet, we talk to that person personally, but other than that we just do it electronically so we don’t actually have that feedback-like oral feedback session.”

—I mean, ideally, yes, it would be lovely to have them come, sit, go through everything, see how you’re doing, whatever, but there’s so many of them.”

—Attending physician at clinic B

These attendings acknowledge that use of an electronic medium alone can create a barrier to resident-centered feedback because it does not provide an opportunity for the resident to reflect, comment, or engage in the solution-making process.

**DISCUSSION**

This study provides insight into how attending physicians use patient-reported experience measures to provide feedback for residents in an internal medicine training program. We identified six core themes influencing the use of patient experience data in providing resident feedback: 1) perceived inability of residents to learn or to incorporate feedback, 2) punitive nature of feedback, 3) lack of training in the delivery of actionable feedback, 4) lack of timeliness in the delivery of feedback, 5) unclear benefit of patient experience survey data as a tool for providing resident feedback, and 6) lack of individualized feedback. In 2001, the Institute of Medicine codified patient-centeredness as one of six health care quality aims. Patient experience is a critical facet of patient-centeredness. Moreover, studies have linked better patient experiences to favorable health behaviors and outcomes. In alignment with this aim, the Institute of Medicine advocates...
the use of patient experience data as a patient-centered tool for promoting quality care. Concrete patient experience data can define key points of intervention for improving the care experience. These data argue for greater training on the use of patient experience survey data to effect practice change and ultimately to improve health behaviors and outcomes. Physicians in training are an ideal population to intervene because they are at an early stage in their career and may be more malleable. Thus, actionable feedback may have a greater effect on practice behaviors.

Implementation science dictates that a tool or system must be accepted by the stakeholders for it to be successful. Low acceptability of patient experience data was noted in our study and previously at other institutions. Thus, methods for increasing attending buy-in on the merits of patient experience measures as tools to inform actionable feedback need to be explored. Increased buy-in could be achieved by involving attending physicians in the implementation process. For example, participants in our study suggested including open-ended questions and comment areas to elicit more detailed patient experience data. Previous studies suggest that medical education programs can benefit from more intense support and from training on how to interpret patient experience survey data and to deliver actionable feedback.

One potential method for incorporating patient experience data into actionable feedback for the resident is the use of a framework grounded in feedback-intervention theory. Feedback should be individualized, and recommendations should be solutions oriented (ie, task-specific and actionable). The highest, most effective form of feedback de-emphasizes hierarchy and embraces a supportive dialogue between the attending and resident. Beyond identifying competency gaps, it requires the attending to understand the resident as a learner (ie, understand the resident’s motivations and goal orientation). The attending can then leverage this knowledge to engage and motivate the resident to reflect on his/her performance, and to set goals and develop an action plan to achieve those goals. To close the feedback loop, the attending should follow-up to determine if the resident has made progress in achieving goals.

The Sidebar: Steps to Using Patient Experience Data to Provide Residents with Actionable Feedback details the steps to using patient experience data to provide residents with actionable feedback. These steps use an individualized, resident-centered, and nonpunitive approach to providing feedback. A feedback sheet (Table 2) provides the resident’s average score on each item of a patient experience survey, and compares those scores with a group of peers. Items where residents score below a certain cut-off point (eg, the lowest quartile) can identify critical areas where residents can improve. A plan to improve the identified areas, in the context of specific goals, should be formulated. For example, if “listening” is identified as an area of weakness, specific goals may be 1) using more eye contact during the visit, and 2) making reflective statements to summarize what the patient has said. By using this or other identified tools, one can create a robust and effective feedback process.

### Table 2. Sample feedback table providing performance data on the patient experience survey in comparison to peers

<table>
<thead>
<tr>
<th>Component experience</th>
<th>Scale</th>
<th>Individual Mean</th>
<th>Individual SD</th>
<th>Total (n = X) Mean</th>
<th>Total (n = X) SD</th>
<th>25tha</th>
<th>50tha</th>
<th>75tha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shared decision making</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Offer choices in your medical care</td>
<td>1-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Discuss the pros and cons of each choice with you</td>
<td>1-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Get you to state which option or choice you prefer</td>
<td>1-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Take your preferences into account when making treatment decisions</td>
<td>1-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* a percentile.


SD = standard deviation. High SD indicates greater variability in patient responses (ie, responses vary a lot across patients).
An important strength of our study is that we are one of the first to explore how patient experience data is incorporated into the resident feedback process. We identified six core themes that residency programs can use in assessing and modifying their own resident feedback process. One of the bases of our findings, we believe that patient experience data can be successfully used to augment existing evaluation processes.

Limitations
The findings in our study should be interpreted with the following limitations in mind. Although our sample size is small, our participation rate of 75% is acceptable for exploratory analyses. In a qualitative study using 60 interviews, core themes were present as early as 6 interviews and data saturation was reached at 12 interviews. Although we collected data at 2 very different institutions, these institutions are affiliated with the same academic center. Our findings may not be generalizable. We were forced to use mixed methods by combining data from individual interviews and focus groups. In a focus group there is the concern that 1 or 2 individuals can dominate the conversation. However, there is also the opportunity for individuals to motivate each other to express their thoughts. It has been noted that integration of these 2 study methods may provide data enrichment.

CONCLUSION
Graduate Medical Education programs may want to conduct their own internal assessment of the resident feedback process. Such assessments should review how patient experience data is incorporated into the resident feedback process and how, if at all, their faculty are trained to provide such feedback. We believe there is value in adhering to the ACGME guidelines in both spirit and content so that residents emerge from training with greater competency in interpreting and using patient experience data to improve their interpersonal and communication behaviors.

Disclosure Statement
This work was supported in part by the facilities and resources of the Center for Innovations in Quality, Effectiveness and Safety at the Michael E DeBakey VA Medical Center (#CIN 13-413), and the facilities and resources of Harris Health System. The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs. The author(s) have no other conflicts of interest to disclose.

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How to Cite This Article

References
Compassion

The greatest single quality which the intern should develop is that of compassion for the sick, the afflicted and the suffering. ... No single attribute of medical practice is more demanding, more difficult to acquire and more exacting to maintain than the bond which exists between the patient and the doctor.

Physicians Experiencing Intense Emotions While Seeing Their Patients: What Happens?

Joana Vilela da Silva, MD; Irene Carvalho, PhD

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ABSTRACT

Objectives: Physicians often deal with emotions arising from both patients and themselves; however, management of intense emotions when they arise in the presence of patients is overlooked in research. The aim of this study is to inspect physicians’ intense emotions in this context, how these emotions are displayed, coping strategies used, adjustment behaviors, and the impact of the emotional reactions on the physician-patient relationship.

Methods: A total of 127 physicians completed a self-report survey, built from a literature review. Participants were recruited in 3 different ways: through a snowball sampling procedure, via institutional e-mails, and in person during service meetings.

Results: Fifty-two physicians (43.0%) reported experiencing intense emotions frequently. Although most physicians (88.6%) tried to control their reactions, several reported not controlling themselves. Coping strategies to deal with the emotion at the moment included behavioral and cognitive approaches. Only the type of reaction (but not the emotion’s valence, duration, relative control, or coping strategies used) seemed to affect the physician-patient relationship. Choking-up/crying, touching, smiling, and providing support were significantly associated with an immediate positive impact. Withdrawing from the situation, imposing, and defending oneself were associated with a negative impact. Some reactions also had an extended impact into future interactions.

Conclusion: Experiencing intense emotions in the presence of patients was frequent among physicians, and the type of reaction affected the clinical relationship. Because many physicians reported experiencing long-lasting emotions, these may have important clinical implications for patients visiting physicians while these emotions last. Further studies are needed to clarify these results.

INTRODUCTION

Emotions play a significant role in human interactions, yielding communicative intentions, modeling behavior, promoting attachment, influencing information processing, and even determining choices. Physicians’ emotions in professional settings, traditionally considered to be unprofessional and a taboo, have increasingly been addressed in medical education as a result of the recognition that physicians often deal with emotions arising from both the patient and themselves. Even if feelings of moderate intensity are manageable or unnoticeable in medical encounters, physicians’ intense emotions constitute particular challenges that are more difficult to ignore and possibly to manage at the moment. The way physicians react and manage these emotions can affect both the physician and the patient and shape the clinical relationship in fundamental ways. What happens when physicians experience strong emotions in the presence of their patients? Although numerous studies have focused on patients’ emotions and on how physicians deal with them, physicians’ own emotions arising when they are seeing their patients have received less attention.

Research on physicians’ emotions highlights the importance of physicians’ awareness of their emotional states during the medical encounter. Unrecognized emotions may impede the use of patient-centered skills and may be associated with harmful behaviors, such as inappropriately interrupting the patient, changing the subject, avoiding patients’ psychological issues, avoiding bonding with patients to prevent suffering, avoiding conducting certain medical procedures again, or avoiding patients altogether. One study showed that physicians themselves perceive their emotional states as influencing medical acts such as prescribing, talking to patients, and referring. In addition, lack of recognition of one’s emotions and low-level choices, more than clinical knowledge or medical skills, have been proposed to be associated with medical error. Along with the effects of emotional unawareness on patient care, research has also examined the impact of physicians’ emotions on their own well-being. Unexplored feelings may be associated with distress, poor judgment, loss of privileges, social isolation, increased workload, risk of litigation, burnout, reduced work satisfaction, and an increase in alcohol and other substance use.

This research is informative of important systematic and lasting effects of emotions experienced by physicians after the encounter with patients. However, it does not address how physicians manage their intense emotions when these arise in the presence of their patients. How these emotions are displayed to the patient and their impact on the relationship are overlooked. Most previous studies that focus on physicians’ emotions deal with the extreme contexts of dying patients, medical errors, safety-related events, and treatment complications. Emotions in these contexts include hurt feelings, anger, frustration, remorse, sadness, guilt, and unhappiness, and disturbing emotions can last for years. Coping strategies used in these contexts include obtaining emotional support from others, trying to have a positive perspective over the situation, getting back to work to clear the mind, talking...
to other physicians or family members, doing physical exercise,\textsuperscript{20} doing nothing, and talking to the patient.\textsuperscript{21}

However, these situations are limited to a few extreme scenarios associated with negative emotions (one study did identify positive daily emotions, including gratitude, happiness, compassion, pride, and relief, but these emerged among medical trainees and were associated with connecting with patients and with colleagues, receiving recognition for one’s work, learning, being part of modern medicine, and receiving emotional support).\textsuperscript{22} Intense emotions during interactions with patients in less extreme scenarios may present a bigger challenge for physicians. They may impair an ongoing clinical interaction, lessen empathy, or jeopardize the physician-patient relationship. Physicians must make decisions while experiencing powerful feelings, and they need to manage these emotions in front of their patients. The aim of this study is to explore intense emotions physicians experience in their daily practice while with patients, how these emotions are displayed to the patients, the strategies used to manage these emotions at that moment, and the impact the emotional reactions have on the physician-patient relationship.

\textbf{METHODS}

\textbf{Procedures}

In this cross-sectional, retrospective study, participants were recruited through 1) a snowball sampling procedure, 2) institutional e-mails (from the School of Medicine of Oporto University, the Portuguese League against Cancer, and the Oporto Health Campus Ministry), and 3) in-person contact during service meetings at the major central hospital in Oporto and in several primary care centers in that geographic area. Data were collected between June 2012 and February 2013. Physicians were informed about the aim of the study, as well as the confidential, anonymous, and voluntary nature of their participation. Agreement to participate served as informed consent. The hospital ethics committee approved the study.

\textbf{Instrument}

A questionnaire on physicians’ emotional experiences was developed for this study after a literature review. The Geneva Appraisal Questionnaire\textsuperscript{23} assesses individual appraisal processes in the case of an emotional episode and was close to the goals of this study. Several items from its version 3 were translated and used in their original form or in a modified version. Three additional items were included in the questionnaire to address specific issues in this study (eg, strategies used to control the emotional expression). The questionnaire was then applied to a sample of physicians and medical students who were not participating in the study to check for meaning, accuracy, and completeness. Ambiguous/incomplete items were modified, and the survey was again tested with a different sample of physicians and medical students. This procedure was repeated until the final version of the survey was approved. The final 21-item version combines open-ended and multiple-choice questions (presenting either 4, 5, or 6 options, plus an additional option that can be either “I don’t know” or “other—specify”).

The questionnaire starts with the following instruction: “In this questionnaire, we ask you to recall moments [in your clinical life] when you experienced an intense emotion, either positive or negative. The events might have been brought about by you, [by a patient], by someone else, or by [other] causes.” Next, physicians were asked to recall and briefly describe a situation of their daily clinical practice in which they experienced an intense emotion while they were seeing their patients; to name the emotion experienced; to indicate how long ago they experienced the emotion, how long the emotion lasted, where it took place, and the attitude they had at that moment (options ranging from complete control of the emotion to uncontrolled emotional reaction); to describe the actual reaction (if they had one); to indicate what they did after realizing they reacted openly (eg, returned to their previous posture, apologized); to describe the strategies used to control the emotion; and to describe how the emotional reaction affected their relationship with the patient at that moment and in future encounters. Two final questions were added for a better understanding of the occurrence of strong emotional experiences.

\begin{table}
\centering
\begin{tabular}{|l|c|}
\hline
\textbf{Table 1. Sample characteristics of physician survey respondents} & \\
\hline
\textbf{Respondent characteristics (N = 124)} & \textbf{Value}\textsuperscript{*} \\
\hline
Age (years), mean (SD; range) & 37.8 (12.8; 25-66) \\
Professional experience (years), mean (SD; range) & 12.0 (12.3; < 1-40) \\
Sex (n = 122) & \\
Women & 75 (61.5) \\
Men & 47 (38.5) \\
Professional level (n = 121) & \\
Attending & 56 (46.3) \\
Resident & 65 (53.7) \\
Currently practicing & 124 (100) \\
Geographic work location (n = 123) & \\
Urban & 115 (93.5) \\
Nonurban & 8 (6.5) \\
Northern country & 118 (95.9) \\
South (Madeira Island) & 5 (4.1) \\
Medical specialty (n = 119) & \\
General practice & 46 (38.7) \\
Internal medicine & 13 (10.9) \\
Ophthalmology & 11 (9.2) \\
Psychiatry & 6 (5.0) \\
Infectious diseases & 5 (4.2) \\
Nephrology & 5 (4.2) \\
Legal medicine & 4 (3.4) \\
Endocrinology & 4 (3.4) \\
Cardiology & 3 (2.5) \\
Pediatrics & 3 (2.5) \\
Neurology & 2 (1.7) \\
Gynecology & 2 (1.7) \\
Pathology & 2 (1.7) \\
General surgery & 1 (0.8) \\
Pulmonology & 1 (0.8) \\
N/A (1st-year interns) & 11 (9.2) \\
\hline
\end{tabular}
\caption*{Data are no. (%) of physician survey respondents unless otherwise indicated. SD = standard deviation.}
\end{table}
In clinical practice throughout physicians' careers: to indicate (as many as applicable) intense emotions experienced when seeing patients in situations other than the one already described (the list included 24 emotional reactions; eg, deep sadness, depression, enthusiasm, intense fear, total relief, intense joy, and deep shock); and to indicate how frequently intense emotions were experienced in the presence of patients. Participants additionally answered questions on demographic and professional characteristics (eg, sex, birth date, level of medical training, medical specialty, years of medical experience, and current professional status, whether practicing or not).

**Participants**

A total of 127 participants completed the questionnaire. Three were excluded (2 men who reported never experiencing intense emotions while interacting with patients and 1 woman who described a situation outside of the study's goals). The final sample (depicted in Table 1) comprised 124 actively practicing physicians working mostly in the north of the country (95.9%) and in urban areas (93.5%). Because of missing values and nonapplicability of some items to subgroups of respondents, the total number of participants included in each analysis varied between 53 and 124.

**Analyses**

A content analysis was applied to the description of the episode, with both authors independently coding the situations. Observations were compared, with Cohen's K = 1 in 12 categories, plus K = 0.91, K = 0.92, and K = 0.96 in the 3 remaining categories, respectively. The shorter-answer, open-ended questions were also independently coded, with final categories reached through...

---

**Table 2. Fifteen types of situations eliciting intense emotions in daily practice from 122 physician survey respondents**

<table>
<thead>
<tr>
<th>Categories of situations</th>
<th>n (%)</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health deterioration/death</td>
<td>35 (28.7)</td>
<td>I watched a patient die before the medical team's powerlessness and anguish. The patient was conscious and we could tell by his facial expression that he could understand what was going on. He tried to tell us something but it was not perceptible.</td>
</tr>
<tr>
<td>Physical or psychosocial suffering</td>
<td>14 (11.5)</td>
<td>I followed-up with a patient in the intensive care unit. She was young and suffered from severe systemic lupus. She had a tracheostomy and was ventilated but conscious. In one of the medical visits she asked me for a paper and wrote, &quot;Help me.&quot; She was in very bad shape and eventually died.</td>
</tr>
<tr>
<td>End-of-life patients</td>
<td>13 (10.7)</td>
<td>She was a terminal patient receiving comfort measures in the intensive care unit. For four years I could never get her to accept her illness and start treatment. I felt frustrated watching her die and could not do anything. Then, she grabbed my hand and looked at me in a way I will never forget, and smiled. I felt that her look meant, &quot;It was my fault, you did everything you could. I am in peace.&quot;</td>
</tr>
<tr>
<td>Aggressive patients</td>
<td>11 (9.0)</td>
<td>During a consultation a patient pointed a gun at himself. In the ER the family of a patient invaded my office and threatened me because I was taking too long to see her …. I felt very vulnerable around them all. They were threatening to destroy everything, using inappropriate language, hitting the wall, and dropping material that was over the desk.</td>
</tr>
<tr>
<td>Communicating bad news</td>
<td>11 (9.0)</td>
<td>Having to tell a young patient that her husband and children died.</td>
</tr>
<tr>
<td>Solving the patient's problem</td>
<td>8 (6.6)</td>
<td>The first time I alone diagnosed and successfully treated a patient in the ER. A patient who was amazed about the surgery that restored his sight.</td>
</tr>
<tr>
<td>Patients' rudeness</td>
<td>7 (5.7)</td>
<td>While I was with a patient, his wife spent the entire time reading the newspaper. I felt disrespected.</td>
</tr>
<tr>
<td>Unexpected disabling condition</td>
<td>7 (5.7)</td>
<td>A young patient entered the emergency room in cardiac arrest. She was alone at that moment without any family members who could provide any information. After two cycles of advanced life support, she recovered. When we could collect a clinical history, we found out that she had terminal brain cancer.</td>
</tr>
<tr>
<td>Accusations of malpractice</td>
<td>7 (5.7)</td>
<td>During a consultation, a patient confronted me with the desire to have a routine examination check for everything, and about my obligation to do it. He said, &quot;I have paid taxes for many years and now I have the right to have the exams I want. Nowadays, doctors study medicine for money. In the old days, we had good doctors that did the exams we wanted.&quot; A family member of a patient I had seen the day before came to tell me that the patient died on her way home. He criticized me for not sending her to the emergency room instead.</td>
</tr>
<tr>
<td>Disagreeing about the proposed treatment</td>
<td>4 (3.3)</td>
<td>The team told a patient's family that he would die and that the situation was inevitable. I believed that a bigger effort on our part could still save him.</td>
</tr>
<tr>
<td>Patient telling disturbing information</td>
<td>1 (0.8)</td>
<td>I felt repulsed after a patient mentioned that during an impulsive episode she killed her pets.</td>
</tr>
<tr>
<td>Making harmful decisions</td>
<td>1 (0.8)</td>
<td>A patient asked me for a compulsory detention of her mother, who took care of a bedridden brother. This brother would be abandoned for lack of social and family support.</td>
</tr>
<tr>
<td>Stress at work</td>
<td>1 (0.8)</td>
<td>Stress in the operating room.</td>
</tr>
<tr>
<td>Demanding patients</td>
<td>1 (0.8)</td>
<td>Following-up a patient with a personality disorder. She questioned every medical intervention, saying nothing was working. She had multiple complaints and was very demanding. Dealing with her husband's pressure (&quot;You have to make her better&quot;).</td>
</tr>
<tr>
<td>Patients' gratitude</td>
<td>1 (0.8)</td>
<td>A patient's widow offered me a reminder of her husband, who had died three months earlier. I never met him, only supervised some aspects for his well-being during his palliative phase.</td>
</tr>
</tbody>
</table>

* In this particular question only 122 physicians answered; 2 participants reported the emotion but not the situation that elicited it. 
ER = emergency room.
Physicians Experiencing Intense Emotions While Seeing Their Patients: What Happens?

RESULTS

Physicians indicated experiencing many and varied strong emotions in the presence of their patients throughout their careers (median = 6.00; interquartile range = 4; range, 1-16 emotions per physician). The emotional spectrum includes both positive and negative feelings, and though most emotions in the list we provided were negative, several positive emotions appeared at the top of the list as frequently experienced (enthusiasm was the most signaled emotion in the list). Forty-eight participants (39.7% of the 121 who answered this question) reported experiencing strong emotions only a few times per year while interacting with patients. But 18 (14.9%) mentioned monthly occurrences, and 34 (28.1%) reported weekly and daily experiences of intense emotions in the presence of patients. Frequency was independent from physicians’ gender and geographic work location. However, physicians reporting frequent strong emotions had fewer years of medical practice (mean ± standard deviation [SD], 8.40 ± 11.03) than those reporting more sporadic experiences of strong emotional reactions (mean ± SD, 15.43 ± 12.73), χ²(109) = 3.12, p = 0.002.

Regarding the specific emotional event described in the questionnaire, most physicians reported situations that occurred long ago: years ago in 48 cases (38.7%) and months or weeks ago in 59 cases (47.6%) of all 124 physicians. Only 17 (13.7%) recalled an event that occurred days or hours ago. These situations included several extreme events (the most frequently mentioned was, “Dealing with patients’ health deterioration or death”), but also less extreme scenarios (eg, “A patient did not want to greet me with a handshake”). Additionally, some situations were positive experiences (“A patient was amazed about the surgery that restored his sight”); Table 2).

Physicians’ emotions associated with these situations are depicted in Table 3 according to their positive, negative, or mixed (comprising compassion and surprise) valence. Mostly, physicians reported negative emotions (139 instances, or 85.8% of all 162 reported emotions). For 47 participants (39.8% of the 118 who answered this question), these emotions lasted longer than a few minutes or hours: more than 1 day for 34 physicians (28.8%) and more than 1 week for 13 participants (11.0%), and 2 participants offered that the emotion is still retrieved upon recalling the situation.

Most physicians (109 of the 123 who answered this question [88.6%]) at least tried to control their emotions, and 33 (26.8%) reported they completely controlled themselves. Only 14 participants (11.4%) reported they did not control their emotional reaction. Only participants experiencing negative emotions reported controlling them completely in the presence of their patients (χ²(1) = 9.379, p = 0.001). The difference from physicians experiencing positive and mixed emotions was statistically significant (χ²(1) = 9.379, p = 0.001), though some of the latter also attempted to control themselves.

Table 4 depicts physicians’ actual reactions. Physicians were more likely to touch the patient when experiencing positive emotions than when experiencing negative emotions (χ²(1) = 6.563, p = 0.022), and only smiled when experiencing positive emotions (χ²(1) = 39.375, p < 0.001). All other reactions occurred only during negative and mixed emotional experiences.

Several participants who reported not completely controlling their emotional reactions adjusted their behaviors after they reacted (n = 58). Of these, 16 (27.6%) said they tried to return to their previous posture, 3 (5.2%) apologized for their reaction, 1 (1.7%) allowed room for the patient to apologize. Thirty-eight (65.5%) felt that their reactions were expected and that no further action was necessary. No significant differences were observed between physicians who attempted to adjust their behavior afterwards and physicians who did not, regarding the different types of reactions.

To cope with their intense emotions at the moment, physicians resorted to several types of strategies (Table 5). These strategies were reported especially by physicians who considered they controlled or attempted to control their emotions (73 [96.1%] of the 76 participants who reported using these strategies, χ²[1] = 10.900, p = 0.001). The difference from physicians who did not control their emotions (n = 3 [3.95%]) was statistically significant (χ²[1] = 10.900, p = 0.001). Though most physicians resorted to coping strategies reported intense negative feelings (63 [84.00%], comparing with 12 reporting positive and mixed feelings), using coping strategies was not significantly associated with negative emotions, and the same types of strategies were generally used to deal with negative and mixed emotions. Using coping strategies was reported in association with positive emotions in 3 cases: breathing, refocusing attention, and a combination of these 2 to deal, respectively, with intense relief (1 case) and with happiness (2 cases).

Table 3. Physician respondents’ intense emotions experienced in the presence of patients

<table>
<thead>
<tr>
<th>Emotions experienced</th>
<th>No. (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative</strong></td>
<td></td>
</tr>
<tr>
<td>Sadness</td>
<td>41 (25.3)</td>
</tr>
<tr>
<td>Fear/anxiety (nervousness, fright, panic, apprehension)</td>
<td>34 (21.0)</td>
</tr>
<tr>
<td>Frustration (powerlessness, incapacity)</td>
<td>32 (19.8)</td>
</tr>
<tr>
<td>Anger (revolt, indignation)</td>
<td>24 (14.8)</td>
</tr>
<tr>
<td>Disappointment</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Repulsion (contempt)</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Guilt</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Shame</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td></td>
</tr>
<tr>
<td>Happiness (joy, self-fulfillment)</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Relief</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td><strong>Mixed</strong></td>
<td></td>
</tr>
<tr>
<td>Compassion (empathy, tenderness, solidarity)</td>
<td>12 (7.4)</td>
</tr>
<tr>
<td>Surprise/confusion</td>
<td>2 (1.2)</td>
</tr>
</tbody>
</table>

* N = 162 reported emotions. Some survey respondents reported more than one emotion.

consensus. Chi-squared tests and independent-sample t-tests were conducted in PASW, version 20 (IBM, Armonk, NY).

Table 3. Physician respondents’ intense emotions experienced in the presence of patients

<table>
<thead>
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<tbody>
<tr>
<td><strong>Negative</strong></td>
<td></td>
</tr>
<tr>
<td>Sadness</td>
<td>41 (25.3)</td>
</tr>
<tr>
<td>Fear/anxiety (nervousness, fright, panic, apprehension)</td>
<td>34 (21.0)</td>
</tr>
<tr>
<td>Frustration (powerlessness, incapacity)</td>
<td>32 (19.8)</td>
</tr>
<tr>
<td>Anger (revolt, indignation)</td>
<td>24 (14.8)</td>
</tr>
<tr>
<td>Disappointment</td>
<td>3 (1.9)</td>
</tr>
<tr>
<td>Repulsion (contempt)</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Guilt</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Shame</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td></td>
</tr>
<tr>
<td>Happiness (joy, self-fulfillment)</td>
<td>7 (4.5)</td>
</tr>
<tr>
<td>Relief</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td><strong>Mixed</strong></td>
<td></td>
</tr>
<tr>
<td>Compassion (empathy, tenderness, solidarity)</td>
<td>12 (7.4)</td>
</tr>
<tr>
<td>Surprise/confusion</td>
<td>2 (1.2)</td>
</tr>
</tbody>
</table>

* N = 162 reported emotions. Some survey respondents reported more than one emotion.
patients; 33 (37.1%) considered a positive impact; and only a few (9 [10.1%]) reported negative consequences at the moment. Additionally, 23 participants (43.4% of the 53 who answered this question) reported that the impact of the episode in their relationship with the patient extended beyond the immediate moment into future interactions. For 17 (73.9%) of these 23 participants, the result was positive, whereas for 6 participants (26.1%), it was negative. Positive consequences included sense of relief, ability to clarify the situation, awareness of one’s fallibility, increased understanding of the patient’s reality, attitudes, increased admiration and interest for the patient, increased attention to the patient’s needs, increased empathy, increased relationship strength, closeness, mutual consideration and trust, and increased adequacy of the patient’s behavior. Negative consequences included increased defensiveness, avoidance of the patient, loss of empathy and of trust in the patient, and relationship termination.

The (immediate or extended) impact of the emotional reaction on the physician-patient relationship was not significantly associated with valence, duration, relative control of the emotion, or coping strategies used. However, specific reactions had a significant impact in physician-patient relationships. Touching, smiling, providing support, and choking up/crying did not yield a negative impact in physician-patient relationships at the moment ($\chi^2(1) = 7.814, p = 0.009$) or in future interactions ($\chi^2(1) = 5.181, p = 0.038$). On the other hand, withdrawing from the situation, imposing oneself and defending oneself were significantly associated with an immediate negative impact in the physician-patient relation ($\chi^2(1) = 16.774, p < 0.001$). These reactions tended to result in negative consequences for physicians who considered that their reactions required no subsequent adjustment and in positive consequences for physicians who tried to subsequently adjust their behavior and repair the situation. These tendencies were statistically nonsignificant, though. Withdrawing from the situation, imposing oneself, and engaging in medical procedures were further associated with a negative impact in future physician-patient interactions ($\chi^2(1) = 8.727, p = 0.009$). Defending oneself was associated with a positive impact in future interactions for the 1 physician who attempted to go back to his previous posture. Additionally, the physician who withdrew from the situation but allowed room for the patient to eventually apologize reported a positive impact in future interactions with that patient. However, these tendencies referred to small numbers of physicians and were statistically nonsignificant.

The type of emotion and its relative control were not significantly associated with physicians’ gender or number of years of medical experience. However, a greater percentage of physicians

<table>
<thead>
<tr>
<th>Categories of coping strategies</th>
<th>Indicators</th>
<th>No. (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breathing</td>
<td>Breathing; taking a deep breath; holding one’s breath</td>
<td>34 (44.7)</td>
</tr>
<tr>
<td>Keeping the emotion away/focusing on something else</td>
<td>Ignoring; keeping emotional distance from the situation; continuing the encounter as if nothing was happening; focusing on the (next) task, on the patient, on one’s posture; thinking as a professional; thinking of a solution; mentally counting</td>
<td>21 (27.6)</td>
</tr>
<tr>
<td>Talking/listening to the patient</td>
<td>Speaking calmly, gradually, with openness; maintaining silence; empathy; understanding; letting the patient express himself; keeping eye contact</td>
<td>7 (9.2)</td>
</tr>
<tr>
<td>Breaking eye contact</td>
<td>Gaining time; organizing thoughts</td>
<td>6 (7.9)</td>
</tr>
<tr>
<td>Reframing</td>
<td>Thinking of/providing an optimistic, hopeful perspective; rationalizing; accepting</td>
<td>5 (6.6)</td>
</tr>
<tr>
<td>Withholding the emotion</td>
<td>Blocking the feelings; not crying</td>
<td>3 (3.9)</td>
</tr>
</tbody>
</table>

* N = 76 strategies.
working in rural areas (37.5%) reported compassion, compared with physicians working in urban areas (8.1%, $\chi^2 [1] = 7.110$, $p = 0.033$), and physicians from the South (ie, Madeira Island) reported controlling their reactions more than physicians from the North part of Portugal ($\chi^2 [1] = 14.061$, $p = 0.001$). However, the interpretation of these results needs caution because very few physicians in the study were from southern Portugal or from nonurban centers. Physicians’ specific reactions were not significantly associated with number of years of medical experience or geographic work location. But explaining the situation and expelling the patient were exclusive to male physicians in this sample ($\chi^2 [1] = 9.488$, $p = 0.005$). Physicians of both genders used the various coping strategies described, but women tended to resort to breathing more than men ($\chi^2 [1] = 5.250$, $p = 0.022$). Breaking eye contact was significantly associated with fewer years of medical experience ($t [22] = 2.115$, $p = 0.046$). Finally, the duration of the emotion, the type of behavior adjustment attempted after the emotional reaction, and the (immediate or extended) impact of the emotional reaction on the physician-patient relationship were statistically unrelated with gender, geographic work location, and years of medical experience.

**DISCUSSION**

Results indicate that experiencing negative and positive intense emotions in the presence of patients is frequent among physicians. The fact that experiencing intense emotions was more frequent among those with fewer years of clinical practice suggests that repeated exposure to these situations or increased clinical experience may contribute to attenuating the emotional response, as previous studies indicate.25

Previous research on physicians’ emotions has specifically focused on extreme scenarios associated with negative strong emotional reactions.18,19 Such scenarios and associated intense negative feelings were frequent also in this study. However, other contexts emerged as well, including less extreme scenarios (eg, dealing with patients’ rudeness) and situations triggering intense positive emotions (the most frequent being resolving the patient’s problem). The fact that most situations described here elicited negative feelings may suggest that negative emotions are more strongly felt by physicians, or that these may be recalled more easily than positive experiences.20 An interesting finding is that, as in previous studies,19 many physicians reported experiencing longlasting emotions. This may have important clinical implications for patients visiting physicians while these emotions last, namely regarding decision processes.11

Most physicians in this study tried to control the emotion, which may partly explain the lack of perceived impact of their reaction on their relationship with patients. This attempted control suggests that physicians may consider displaying emotional reactions to be inappropriate in the presence of patients, although possibly less so if the emotion is positive. Smiling was associated only with positive emotions, and physicians touched the patient significantly more if they were experiencing positive feelings. On the other hand, only participants experiencing negative emotions reported controlling them completely, probably because they felt that negative emotions were less appropriate during clinical interactions.

To deal with these emotions, physicians used both cognitive and behavioral coping strategies. After-the-fact coping strategies reported in previous research appeared in our study as ways of managing emotions at the moment (eg, changing perspectives, keeping emotional distance, or talking to the patient).10,21,22 In our study, physicians additionally used other strategies in the moment, like breathing deeply, focusing on their posture, thinking about the next action, being empathic, listening to the patient more, and mentally counting.

Whether or not controlled, in most cases physicians’ emotional reactions did not affect relationships with patients, at least from physicians’ perspectives. The impact was also independent from emotional valence (though no positive emotion had a negative impact on the relationship) and duration, and from the coping strategies used. Some specific reactions, however, did have an impact. Choking up/crying, touching, smiling, and providing support were significantly associated with an immediate positive impact and with no impact. This impact also extended into future interactions. Not surprisingly, withdrawing from the situation, imposing, and defending oneself were associated with a negative immediate impact. The former two reactions plus engaging in medical procedures had a further extended negative impact in future interactions. But the tendency for readjusting the behavior after the reaction to be less associated with a negative impact than when no readjustment existed, though not statistically significant, suggests that the clinical relationship may be shaped by interactions beyond the display of strong negative reactions, and that the reaction does not, per se, necessarily lead to a negative impact on the relationship, as long as interveners have the ability to repair it.

This study took a first step in the inspection of what happens when physicians experience strong emotions while seeing patients, and further research is needed for a better understanding of the results. Specifically, better discrimination of the effects of particular reactions on medical relationships is necessary. Also, the sampling strategy in this study limited our goal of forming a representative sample of physicians in the country, which restricts the generalizability of the results. It is possible that physicians who agreed to participate were particularly interested in the theme, introducing biases (eg, increasing the prevalence of intense emotions in clinical practice). Because we used a self-report, retrospective instrument, recall or report biases may also exist. Finally, the sample size may prevent the analysis and the observation of effects that could be visible with larger numbers of participants per group. Future research needs to consider additional aspects that could affect physician-patient relationships (eg, duration and kind of relationship with the physician) on a larger sample. It is also important to assess patients’ perceptions of physicians’ emotions and of their impact on the clinical relationship, in addition to...
assessing patients’ own reactions to the situations. The inclusion of other clinical implications is also crucial, such as the effect of physicians’ emotional state in appropriate medical management, as suggested in previous studies.11

CONCLUSION
Although the display of emotions in medical encounters may be considered unprofessional, the experience of intense emotions by physicians in the presence of patients seems frequent. Physicians control the display of intense negative emotions more than that of positive reactions. However, relative control of the emotion, coping strategies used, the valence (positive, negative, or mixed), and the duration of the emotion do not affect the clinical relationship. Specific emotional reactions do. Choking up/crying, touching, smiling, and providing support did not affect relationships in negative ways, but leaving the patient, imposing, and defending oneself did. The fact that the impact of these reactions could be different according to physicians’ subsequent adjusted behavior suggests that this impact may be mediated by the interlocutors’ following actions, namely attempts at repairing the situation. Future studies are needed to clarify these results. ❖

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

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How to Cite this Article

References
Difference in Effectiveness of Medication Adherence Intervention by Health Literacy Level

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ABSTRACT

Context: There is little research investigating whether health information technologies, such as interactive voice recognition, are effective ways to deliver information to individuals with lower health literacy.

Objective: Determine the extent to which the impact of an interactive voice recognition-based intervention to improve medication adherence appeared to vary by participants’ health literacy level.

Design: Promoting Adherence to Improve Effectiveness of Cardiovascular Disease Therapies (PATIENT) was a randomized clinical trial designed to test the impact, compared with usual care, of 2 technology-based interventions that leveraged interactive voice recognition to promote medication adherence. A 14% subset of participants was sent a survey that included questions on health literacy. This exploratory analysis was limited to the 833 individuals who responded to the survey and provided data on health literacy.

Main Outcome Measures: Adherence to statins and/or angiotensin-converting enzyme inhibitors and/or angiotensin II receptor blockers.

Results: Although intervention effects did not differ significantly by level of health literacy, the data were suggestive of differential intervention effects by health literacy level.

Conclusions: The differences in intervention effects for high vs low health literacy in this exploratory analysis are consistent with the hypothesis that individuals with lower health literacy might derive greater benefit from this type of intervention compared with individuals with higher health literacy. Additional studies are needed to further explore this finding.

INTRODUCTION

Treatment nonadherence with cardiovascular disease (CVD) therapy has been well documented and is a major contributor to increased cardiovascular risk and morbidity. At the population level, low adherence is often the broken link between effective new therapies and improved health outcomes.Nonadherence has also been identified as a key target for reducing unnecessary health care costs.

The most effective adherence interventions include both educational and behavioral strategies; however, these strategies are costly and require both staff time and specialized counseling skills, which can limit the likelihood for dissemination. Furthermore, most interventions evaluated thus far have enrolled highly select and small patient populations, thus limiting generalizability. More recently, research has focused on using health information technologies (HIT) to develop low-cost interventions that can be delivered to large populations to promote adherence for patients with chronic illness. For example, one recent study described an intervention among 5216 adults who were newly prescribed a statin but had failed to fill the prescription. The intervention group received automated telephone reminder calls followed by mailed letters. The intervention improved initial fill rates during the next 25 days by 16 percentage points. These and other studies suggest that HIT-based reminder interventions offer a promising, “light-touch” option for promoting adherence in large populations.

Although HIT-based interventions may be more easily disseminated, reach a greater number of people, and be lower cost, they may exacerbate certain health disparities, because more educated and technologically advanced individuals will benefit disproportionately from such advances. Patients with low health literacy—individuals who face challenges with respect to their capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions—are likely to be particularly vulnerable in this regard. Individuals with low health literacy, for example, are much less likely to use computers, mobile applications, and other consumer and patient medical devices. Consequently, it has been argued that interactive voice recognition (IVR) is one type of HIT that may be particularly well suited for delivering interventions to low-literacy individuals because it 1) delivers information via speech instead of text and 2) uses the telephone so that computer access and computer literacy are not required.

An Institute of Medicine report in 2004 called for studies that establish effective approaches to reduce the negative...
METHODS

Study Design

The Promoting Adherence to Improve Effectiveness of Cardiovascular Disease Therapies (PATIENT) study was a randomized pragmatic clinical trial in which 21,752 adults were randomly assigned to receive either usual care or 1 of 2 IVR-based interventions designed to increase adherence to statins, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs). Before randomization at baseline, a subgroup of potentially eligible individuals (n = 2965) were recruited to participate in an interviewer-administered survey via telephone in English, which was conducted centrally by a team of experienced interviewers. The baseline survey was administered from September through December 2011 and had a completion rate of 57% (n = 1678). Among those who completed the survey, 833 respondents ultimately were randomly assigned to participate in the intervention. Data for the present study were based on this subgroup of individuals.

Research Setting

Participants were members of 1 of 3 Regions of Kaiser Permanente (KP), a health maintenance organization providing comprehensive, prepaid health care to its members. The three Regions, Northwest (KPNW), Hawaii (KPHI), and Georgia (KPGA), collectively serve a population of about 944,000 individuals. The institutional review boards at all 3 study sites approved the study. An external data and safety monitoring board and local clinician advisory boards at each site approved the study protocol and monitored the study for safety and data quality.

The PATIENT Study

We have previously described the PATIENT study in detail.24 Using each Region’s electronic medical records (EMRs), we identified participants aged 40 years and older with diabetes mellitus and/or CVD, with suboptimal (< 90%) adherence to a statin or ACEI/ARB during the previous 12 months, and who were due or overdue for a refill. Individuals with medical conditions that might contraindicate the use of these medications (eg, allergic to the medication, liver failure, cirrhosis, rhabdomyolysis, end-stage renal disease, chronic kidney disease) and those on KP’s “do not contact” list were excluded. In each Region, we randomly assigned a sample of eligible members to the 3 study arms (usual care and 2 intervention arms) in a 1:1:1 ratio at the study outset and repeated this process for newly eligible members for each of the following 5 months. Study enrollment began in December 2011 and continued through May 2012. Intervention and outcome assessment continued through November 2012.

In the first intervention arm, IVR, participants received automated phone calls when they were due or overdue for a refill of their ACE/ARB and/or statin. Patients were offered a transfer to KP’s automated pharmacy refill line. In the second intervention arm, enhanced IVR, participants received the same calls as in the IVR arm but also received a personalized reminder letter if they were 60 to 90 days overdue and a live outreach call if they were 90 days or more overdue, as well as EMR-based feedback to their primary care clinicians. Participants in the enhanced IVR arm received additional written and graphic materials, including a personalized health report with their most recent blood pressure and cholesterol levels, a pill organizer, and bimonthly mailings to answer common questions. The IVR call scripts, letters, and other mailings were written at a sixth-grade reading level.

Study Measurements

Electronic Medical Record Data

We used a modified version of the Proportion of Days Covered for our primary measure of medication adherence.27 Because we were measuring long-term medications that the patients were known to be taking at the time of randomization, we modified the Proportion of Days Covered to include the whole follow-up period as the denominator timeframe rather than time from first dispensing.26 We also accounted for medication on hand at randomization and ignored any medication remaining at the end of follow-up. We computed the modified Proportion of Days Covered separately for statins and ACEI/ARBs. To simplify enrollment logistics, we defined study eligibility at baseline using the simpler Medication Possession Ratio, which we computed by dividing total days’ dispensed supply by 365 and capping at 1.

We used the EMR to capture age, race, sex, physical and mental health comorbidities, smoking status, body mass index, number of medications dispensed, health care utilization, hospital and Emergency Department visits, and blood pressure and lipid levels. We defined baseline systolic and diastolic blood pressure levels as the mean of the 6 most recent measurements taken during the 12 months before randomization. Follow-up blood pressure was defined as the mean of the 6 most recent measurements taken before the end of the study period, which ranged from 6 to 12 months of follow-up depending on when randomization occurred. We defined blood pressure control as blood pressure below 140/90 mmHg and lipid control as a low-density-lipoprotein cholesterol level below 100 mg/dl.

Survey Data

Participants were asked three single-item health literacy questions (see Sidebar: Health Literacy Questions). The first question, used previously by Williams and colleagues,27 aimed to assess participants’ use of a surrogate reader: “How often do you need to have someone help you when you read instructions, pamphlets, or other written materials from your doctor or pharmacy?”

Health Literacy Questions

1. How often do you need to have someone help you when you read instructions, pamphlets, or other written materials from your doctor or pharmacy?
2. How confident are you filling out medical forms by yourself?
3. How would you rate your ability to read?
## Table 1. Characteristics of study population, total and by health literacy level

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N = 833)</th>
<th>Low (n = 148)</th>
<th>High (n = 685)</th>
<th>Significance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>65.2 ± 11.6</td>
<td>69.5 ± 13.2</td>
<td>64.3 ± 11.0</td>
<td>t = -5.01, p &lt; 0.001</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>51.0</td>
<td>51.3</td>
<td>50.9</td>
<td>χ² = 0.008, p = 0.93</td>
</tr>
<tr>
<td>Men</td>
<td>49.0</td>
<td>48.7</td>
<td>49.1</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>12.9</td>
<td>19.1</td>
<td>11.6</td>
<td>χ² = 10.70, p = 0.03</td>
</tr>
<tr>
<td>Black/African American</td>
<td>17.0</td>
<td>12.9</td>
<td>17.9</td>
<td></td>
</tr>
<tr>
<td>Native Hawaiian/Pacific Islander</td>
<td>6.1</td>
<td>5.4</td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>57.7</td>
<td>53.1</td>
<td>58.7</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6.3</td>
<td>9.5</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.7*</td>
<td>1.0*</td>
<td>3.06*</td>
<td>χ² = 1.31, p = 0.25</td>
</tr>
<tr>
<td>Highest level of education, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school or less</td>
<td>34.3</td>
<td>60.8</td>
<td>28.5</td>
<td>χ² = 34.82, p &lt; 0.001</td>
</tr>
<tr>
<td>Some college/college degree</td>
<td>53.9</td>
<td>33.8</td>
<td>58.2</td>
<td></td>
</tr>
<tr>
<td>Some graduate school/graduate degree</td>
<td>11.9</td>
<td>5.4</td>
<td>13.3</td>
<td></td>
</tr>
<tr>
<td>Household income, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; $25,000</td>
<td>20.6</td>
<td>36.9</td>
<td>17.3</td>
<td>χ² = 39.21, p &lt; 0.001</td>
</tr>
<tr>
<td>$25,000-$49,000</td>
<td>35.5</td>
<td>43.4</td>
<td>33.8</td>
<td></td>
</tr>
<tr>
<td>$50,000-$74,999</td>
<td>20.5</td>
<td>10.7</td>
<td>22.5</td>
<td></td>
</tr>
<tr>
<td>≥ $75,000</td>
<td>23.4</td>
<td>9.0</td>
<td>26.4</td>
<td></td>
</tr>
<tr>
<td>Marital status, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>13.3</td>
<td>10.8</td>
<td>13.9</td>
<td>χ² = 5.48, p = 0.07</td>
</tr>
<tr>
<td>Married/partnered</td>
<td>62.8</td>
<td>58.1</td>
<td>63.9</td>
<td></td>
</tr>
<tr>
<td>Separated/divorced/widowed</td>
<td>23.8</td>
<td>31.1</td>
<td>22.2</td>
<td></td>
</tr>
<tr>
<td>Health history</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uncontrolled blood pressure,%</td>
<td>14.7</td>
<td>19.3</td>
<td>13.7</td>
<td>χ² = 3.03, p = 0.08</td>
</tr>
<tr>
<td>Uncontrolled LDL cholesterol,%</td>
<td>30.2</td>
<td>27.3</td>
<td>30.8</td>
<td>χ² = 0.59, p = 0.44</td>
</tr>
<tr>
<td>Baseline statin adherence among users, mean ± SD</td>
<td>0.59 ± 0.27</td>
<td>0.60 ± 0.25</td>
<td>0.59 ± 0.27</td>
<td>t = -0.11, p = 0.91</td>
</tr>
<tr>
<td>Baseline ACEI/ARB adherence among users, mean ± SD</td>
<td>0.65 ± 0.30</td>
<td>0.62 ± 0.32</td>
<td>0.66 ± 0.29</td>
<td>t = 1.11, p = 0.27</td>
</tr>
<tr>
<td>No. of medications dispensed, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5</td>
<td>39.1</td>
<td>41.9</td>
<td>38.5</td>
<td>χ² = 0.17, p = 0.68</td>
</tr>
<tr>
<td>6-12</td>
<td>39.1</td>
<td>32.4</td>
<td>40.6</td>
<td></td>
</tr>
<tr>
<td>≥ 13</td>
<td>21.7</td>
<td>25.7</td>
<td>20.9</td>
<td></td>
</tr>
<tr>
<td>ED visit in last 6 months, %</td>
<td>10.6</td>
<td>13.5</td>
<td>9.9</td>
<td>χ² = 1.66, p = 0.20</td>
</tr>
<tr>
<td>Hospitalization in last 6 months, %</td>
<td>4.2</td>
<td>3.4</td>
<td>4.4</td>
<td>χ² = 0.30, p = 0.58</td>
</tr>
<tr>
<td>Health care utilization in last 6 months, mean</td>
<td>6.5 ± 6.8</td>
<td>7.8 ± 8.3</td>
<td>6.2 ± 6.3</td>
<td>t = -2.64, p = 0.01</td>
</tr>
<tr>
<td>HUI2, mean ± SD</td>
<td>0.84 ± 0.17</td>
<td>0.79 ± 0.20</td>
<td>0.85 ± 0.17</td>
<td>t = 3.06, p = 0.00</td>
</tr>
<tr>
<td>HUI3, mean ± SD</td>
<td>0.77 ± 0.28</td>
<td>0.60 ± 0.35</td>
<td>0.80 ± 0.25</td>
<td>t = 7.43, p &lt; 0.001</td>
</tr>
<tr>
<td>Satisfied with care, %</td>
<td>93.0</td>
<td>92.6</td>
<td>93.1</td>
<td>χ² = 0.06, p = 0.81</td>
</tr>
<tr>
<td>Depression diagnosis, %</td>
<td>3.4</td>
<td>6.1</td>
<td>2.8</td>
<td>χ² = 4.10, p = 0.04</td>
</tr>
<tr>
<td>BMI,* %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>11.8</td>
<td>14.9</td>
<td>11.1</td>
<td>χ² = 3.30, p = 0.07</td>
</tr>
<tr>
<td>25.0-29.9</td>
<td>29.7</td>
<td>39.2</td>
<td>27.8</td>
<td></td>
</tr>
<tr>
<td>30.0-39.9</td>
<td>47.2</td>
<td>35.1</td>
<td>49.7</td>
<td></td>
</tr>
<tr>
<td>≥ 40</td>
<td>11.3</td>
<td>10.8</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Smoker, %</td>
<td>10.1</td>
<td>11.2</td>
<td>9.9</td>
<td>χ² = 0.23, p = 0.23</td>
</tr>
</tbody>
</table>

* Two-sided p values based on F test for continuous variables, Pearson χ² test for unordered categorical data, and Mantel-Haenszel χ² test for ordered categorical data;
+ N = 589; * n = 1; † n = 15; * kg/m².

ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; BMI = body mass index; ED = Emergency Department; HUI = Health Utilities Index mark; LDL = low-density lipoprotein; SD = standard deviation.
Participants were asked whether they were satisfied with the care they received from their clinicians and whether they could indicate that they were "very satisfied," "satisfied," "unsatisfied," or "very unsatisfied." Individuals were categorized as satisfied with their health care if they endorsed that they were either "very satisfied" or "satisfied" in response to this question.

Finally, participants were asked about their highest level of schooling completed, total household income, and marital status.

Statistical Analysis

Among those who participated in the baseline survey (N = 1678), complete health literacy and intervention outcome data were available for only 833 of these individuals. The other 845 individuals who completed the survey were not randomly assigned to participate in the intervention. Therefore, our analyses are restricted to this subset of 833 participants. For bivariate analyses, we used \( \chi^2 \) tests for comparing ordered categorical data, and Mantel-Haenszel \( \chi^2 \) tests for comparing unordered categorical data. Separate analyses were conducted for users of statins and users of ACEI/ARBs. We assessed whether intervention effects differed by health literacy level in general linear models with main effects for treatment arm, health literacy, and their interaction. Main effect estimates were adjusted for site and sex. We assessed follow-up from randomization until the end of the study or loss of Health Plan coverage, whichever came first.

Because the study was not designed to examine whether the intervention effects differed by health literacy level, these post hoc analyses are inevitably exploratory in nature, and we made no adjustment for multiple comparisons or to conduct retrospective power calculations. Statistical software (SAS v9.2, SAS Institute, Cary, NC) was used for statistical analyses.

RESULTS

The study population was approximately 65 years of age on average, equally men and women, predominantly white (approximately 58%), had some college or a college degree (approximately 54%), were middle income, and were currently married or with a partner (approximately 63%). Approximately 18% of participants had low health literacy (n = 148). Participants who had low health literacy were more likely to be older, have a lower level of education, report a lower total household income, use health care services more frequently, report poorer health status, and have a depression diagnosis compared with participants who had higher health literacy (Table 1).

Although both the IVR and enhanced IVR interventions increased adherence to statins and ACEIs/ARBs compared with usual care in the full trial analysis, in this much smaller sample we did not observe statistically significant differences between either IVR or enhanced IVR and usual care in subgroups defined by health literacy status (Table 2). Of more immediate relevance to the focus of this exploratory analysis, however, the data were suggestive of differential intervention effects for low and high health literacy. Among participants...
with low health literacy, for example, the IVR and enhanced IVR interventions were associated with statin adherence that was 9% to 10.5% higher than for usual care. By contrast, among participants with high health literacy, statin adherence in the IVR and enhanced IVR groups was 2.6% to 3.2% lower than for usual care.

We observed a similar pattern for ACEI/ARB adherence. Participants with low health literacy in either IVR group (IVR or enhanced IVR) had ACEI/ARB adherence that was 7.5 percentage points to 14.6 percentage points higher than for usual care, whereas among participants with high health literacy the IVR and enhanced IVR interventions were associated with ACEI/ARB adherence that was 1.1 percentage points to 5.3 percentage points lower than for usual care. However, although consistent with an interaction effect, none of the tests of health literacy by treatment interactions was statistically significant.

**DISCUSSION**

Although not statistically significant, the differences in observed intervention effects for high vs low health literacy in the study sample are certainly consistent with the hypothesis that individuals with lower health literacy may derive greater benefit from this type of intervention compared with individuals with higher health literacy. In a review of promising HIT interventions for diabetes, Boren identified telephone interventions for education, counseling, and reminding as an appropriate method for individuals with limited health literacy. Our results provide some preliminary support for this notion.

Approximately 18% of the study population in the present study had low health literacy; this estimate is generally consistent with prior studies. Depending on the study population and health literacy measure employed, the prevalence of low health literacy ranges from 11% to 44%. Also consistent with the prior literature, we found that individuals with lower health literacy are more likely to be of lower socioeconomic status compared with higher health literacy individuals. For example, other studies have similarly reported that years of school completed and income are significantly associated with health literacy level. Individuals with low health literacy in the present study were more likely to have poorer health-related quality of life and a depression diagnosis compared with those with high health literacy. Prior studies have consistently reported that lower health literacy populations frequently experience lower health status as indicated by 1) specific biochemical and biometric health outcomes such as higher blood pressure and poor control of Type 2 diabetes, 2) disease prevalence and incidence such as higher rates of depression, and 3) global health status.

In contrast to previous studies, individuals with low health literacy in this study were more likely to have Emergency Department visits or hospitalizations in the previous six months compared with individuals with higher health literacy. They were, however, more likely to use other health services such as regular office visits compared with individuals with higher health literacy.

Interestingly, individuals with low health literacy did not differ from individuals with high health literacy with respect to baseline statin or ACEI/ARB adherence. Although one study found a positive association between poor health literacy and low adherence to cardiovascular medications, a recent systematic review examining this phenomenon concluded that the current evidence does not show a consistent relationship between health literacy and medication adherence in adults with CVD or diabetes.

The present study has several limitations. First, the small intervention effect seen in the parent trial, combined with the much smaller sample size for this analysis, greatly limits our power to detect significant interactions. Second, although the survey completion rate was satisfactory (approximately 57%), individuals who decided to participate in the survey may differ from those who declined to participate. For example, previous studies suggest that certain subgroups may be less likely to participate in telephone surveys, including men, those with less education, and individuals in poorer health. Third, because the survey was administered only in English, individuals for whom English was a second language and/or who were uncomfortable or unable to complete the survey in English were not included; therefore, our findings cannot be generalized to these populations. Fourth, although we used 3 well-validated, reliable, single-item measures for identifying poor health literacy, our summed health literacy score based on these 3 items has not been compared against one of the gold standard instruments, such as the Rapid Estimate of Adult Literacy in Medicine or the Test of Functional Health Literacy in Adults.

However, Hardie and colleagues similarly provided a summed health literacy score based on participants’ responses to 3 single-item questions and reported that these questions correctly identified individuals with inadequate health literacy 90% to 95% of the time. Therefore, we feel confident that we have accurately categorized the individuals who have low health literacy in our population. Another benefit of using these 3 items includes a shorter time burden for patients, as they take only a few minutes to complete (in contrast to the Test of Functional Health Literacy in Adults, which can take up to 30 minutes). In addition, these questions pose less risk of embarrassment to patients in contrast to the Rapid Estimate of Adult Literacy in Medicine, which asks patients to read aloud medical terms such as herpes, testicle, and hemorrhoids.

**CONCLUSIONS**

Attractive features of health interventions include both effectiveness and cost savings. With use of HIT and automation of the delivery of such health education messaging, there are possible cost savings associated with reduced personnel time. Furthermore, our findings suggest that lower health literacy populations may be more responsive to this type of IVR-based intervention compared with higher health literacy populations, a finding that
may lead to even more efficient patient outreach. By allowing the health system to better tailor intervention activities to specific patient characteristics, limited financial resources can be allocated where there is the potential for the greatest impact. Future studies are needed to explore the most effective and efficient methods for identifying and reaching individuals with lower health literacy.

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

Acknowledgment
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How to Cite This Article

References
People Are Not Like This

Nowadays people are not like this [ie, temperate in eating and drinking]: they use wine as beverage and they adopt reckless behavior . . . . Their passions exhaust their vital forces; their cravings dissipate their true [essence]; they do not know how to find contentment within themselves; they are not skilled in the control of their spirits. They devote all their attention to the amusement of their minds, thus cutting themselves off from the joys of long [life]. Their rising and retiring is without regularity. For these reasons they reach only one half of the hundred years and then they degenerate.

— The Yellow Emperor's Classic of Internal Medicine, Huangdi, c 2704 BC - 2598 BC, known as the Yellow Emperor, a legendary Chinese sovereign and culture hero
Lifestyle and Self-Management by Those Who Live It: Patients Engaging Patients in a Chronic Disease Model

Michelle T Jesse, PhD; Elizabeth Rubinstein, PhD; Anne Eshelman, ABPP; Corinne Wee; Mrunalini Tankasala; Jia Li, PhD; Marwan Abouljoud, MD, CPE, MMM, FACS

ABSTRACT

Background: Patients pursuing organ transplantation have complex medical needs, undergo comprehensive evaluation for possible listing, and require extensive education. However, transplant patients and their supports frequently report the need for more lifestyle and self-management strategies for living with organ transplantation.

Objectives: First, to explore feasibility of a successful, patient-run transplant lifestyle educational group (Transplant Living Community), designed to complement medical care and integrated into the clinical setting; and second, to report the major themes of patients’ and supports’ qualitative and quantitative feedback regarding the group.

Methods: Informal programmatic review and patient satisfaction surveys.

Results: A total of 1862 patient satisfaction surveys were disseminated and 823 were returned (response rate, 44.2%). Patients and their supports reported positive feedback regarding the group, including appreciation that the volunteer was a transplant recipient and gratitude for the lifestyle information. Five areas were associated with the success of Transplant Living Community: 1) a “champion” dedicated to the program and its successful integration into a multidisciplinary team; 2) a health care environment receptive to integration of a patient-led group with ongoing community development; 3) a high level of visibility to physicians and staff, patients, and supports; 4) a clearly presented and manageable lifestyle plan (“Play Your ACES” [Attitude, Compliance, Exercise, and Support]), and 5) a strong volunteer structure with thoughtful training with the ultimate objective of volunteers taking ownership of the program.

Conclusion: It is feasible to integrate a sustainable patient-led lifestyle and self-management educational group into a busy tertiary care clinic for patients with complex chronic illnesses.

INTRODUCTION

Patients with end-stage organ disease referred for possible organ transplantation are a highly complex, multimorbidity population. Given the medical and psychosocial complexities, including potential patient impairments (eg, cognitive or physical disability) and provision of care through multidisciplinary teams, these patients require a great deal of education on the transplant process and ongoing support. Nurses, social workers, physicians, and surgeons are the most frequent providers of education to end-stage organ disease patients who are pursuing transplant. Disease management programs are considered an important component of care for patients living with a transplanted organ and have been associated with positive outcomes such as improved patient satisfaction and adherence.

Patients with end-stage organ disease have increased risks for cognitive impairments secondary to their illnesses. Educational programs must take into account the patient’s ability to process and recall educational information provided. Involvement of family members in the care of patients with chronic diseases significantly increases patient physical and mental health. Additionally, the positive effects of educational interventions are sustained longer with support involvement. Both transplant patients and their supports report the need for more comprehensive education and, in particular, lifestyle and long-term self-management, because this is frequently not addressed or not adequately addressed by hospital staff. However, there are gaps in available evidence on the education of support systems in the context of organ transplantation.

The provision of patient-centered care with efficient use of resources has become the quality standard in today’s health care environment. Integration of the posttransplant patient into the plan of care provides an alternative way to meet a quality standard that has been successful with other patient populations. However, strategies to address lifestyle and self-management in organ transplant patients have been limited to information gathering (eg, patient focus groups), nurse-led education groups, or other multidisciplinary team-protocol refinements. Although these are important first steps, their findings support the need for integration of transplant patients in the refinement of resources and education on successful lifestyle and self-management strategies.

The purpose of this study was 2-fold: 1) to explore the feasibility of a successful, patient-run transplant lifestyle educational group designed to complement medical care and integrated into the clinical setting, and 2) to report patients’ and supports’ qualitative and quantitative feedback regarding the group.

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Transplant Living Community: Program Success and Feasibility

The Henry Ford Health System Transplant Living Community (TLC) was established in 2008 via a collective patient initiative. TLC is a patient-to-patient organ transplant education program aimed at increasing patient and family awareness of necessary lifestyle changes throughout the transplant process. The framework for the program incorporates foundational principles of successful hospice, geriatric, pediatric, and cancer patient advocacy. The program is subject to institutional oversight and exists as an “ambassador” (volunteer) program to support patients, living donors, supports, and families throughout the transplant process. Transplant recipients are welcome to volunteer (beginning the service no sooner than 10 months after the transplant) and undergo an extensive training curriculum that covers empathic listening skills, appropriate medical referral to physicians, Health Insurance Portability and Accountability Act regulations, TLC platform materials, and continued mentoring. Training occurs during 2 full days (16 hours) followed by several weeks of supervised in-clinic training with established ambassadors. All ambassador volunteers are transplant recipients, representing heart, lung, kidney, pancreas, liver, multivisceral, and bone marrow transplants. However, ambassadors and patients are not matched based upon organ received. Ambassador volunteers provide interactive, on-site support within clinic and inpatient floors daily Monday through Friday. Since 2008, there have been more than 40 active ambassadors.

The primary goal of TLC is expressed to patients as “Play Your ACES!” (Attitude, Compliance, Exercise, and Support) … are not unitary constructs but represent an adaptive lifestyle approach while living with chronic illness.

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The primary goal of TLC is expressed to patients as “Play Your ACES!” (Attitude, Compliance, Exercise, and Support) … are not unitary constructs but represent an adaptive lifestyle approach while living with chronic illness.

METHODS

Informal Program Evaluation

TLC has undergone continuous informal programmatic evaluation since its inception in 2008. First, as part of the kits provided to patients, there is a feedback form for suggestions to improve any resources or processes. Second, as part of a Patient Family Advisory Council, which involves physicians, staff representation from each hospital unit, and TLC ambassadors, all participating members provide feedback and recommendations. For the purposes of this article, the contributing authors identified and reviewed the elements of TLC that were thought to have

focuses on the lifestyle elements of adhering to a complicated treatment regimen amid real-life circumstances, which could create obstacles or challenges to taking optimal care of oneself—for example, exploring and strategizing on environmental or social barriers that may hinder the patient’s ability to adhere. Exercise includes redefining exercise to make it attainable with small incremental increases in activity (eg, walking 25 steps today, 35 steps tomorrow) and using charting tools to track progress. This allows for small successes to be recognized and reinforces physical activity. Lastly, support is a multimeember team for long-term support. TLC defines the duties of each person with a conceptualized approach. Some of the support roles include CEO or primary care manager, assistant CEO, drivers, medication manager, comedian, exercise buddy, spiritual caretaker, and other tangible support (eg, mowing the lawn, making meals, babysitting). All education and materials are presented in the patient voice (avoiding medical jargon) from a patient perspective and address only lifestyle components. All medical aspects of transplant are referred directly to medical staff and remain in the medical domain. TLC provides organizational tools and education to help patients navigate their medical care on a daily basis. TLC addresses caregivers as team members and provides a stylized support team approach involving the entire family in a positive, cooperative manner throughout the continuum of care.

What is truly unique about TLC, besides being entirely patient run, is its successful integration into routine clinical care. Within the waiting room of the main clinic there is an information table, staffed by an ambassador volunteer during normal clinical hours, dedicated to providing TLC educational and related materials. Medical personnel can also “refer” patients to TLC. When patients and supports return for the routine educational meeting (“family meeting”), required for listing for transplantation, TLC provides a component of the education on self-management skills and posttransplant lifestyle changes. Within the TLC education, both patients and supports are addressed as a team unit where specific conceptualized home support team assignments are identified to include all family members, other supports, and extended support structures. For patients who undergo transplantation, a TLC ambassador visits the patient before discharge and provides him or her with a TLC Toolkit complementing prior pretransplant TLC education. The TLC Toolkit contains personal health recording tools with a tabbed notebook for Medications, Lab Tests, To Do Lists, Medical Records, and General Information. Other materials consist of support team contact and assigned duty outline, medical team contact card sleeve, calendar, medication charting tools, medication box, pull cutter, medication travel bag, thermometer, pedometer, emergency medication key fob, surgical masks, TLC button for social experiment, hand sanitizer, “Play Your ACES!” support materials, food safety guide, transplant lifestyle information, organ donation (Gift of Life) and registry information, donor contact guidelines, and tote bag. The TLC ambassador volunteer reviews educational resources within the toolkit in addition to answering or referring any questions of concern.

Informal Program Evaluation

TLC has undergone continuous informal programmatic evaluation since its inception in 2008. First, as part of the kits provided to patients, there is a feedback form for suggestions to improve any resources or processes. Second, as part of a Patient Family Advisory Council, which involves physicians, staff representation from each hospital unit, and TLC ambassadors, all participating members provide feedback and recommendations. For the purposes of this article, the contributing authors identified and reviewed the elements of TLC that were thought to have
a high level of impact on the feasibility and sustainability of the group. The results of the programmatic evaluation are in the discussion section.

Patient and Support Feedback Evaluation

All data were collected with full institutional research and administrative approval. A patient and support satisfaction survey was developed for the purposes of this study to assess patient and support satisfaction with TLC-related education. The surveys were disseminated (via passive consent; the cover letter that explained completion of survey indicated consent) before the TLC component of the routine educational meeting for listing for transplant and were entirely anonymous to maximize response rates. Respondents were invited to return surveys either directly to staff or in a locked box located within the clinic. Data collected in the survey included basic demographic characteristics (sex, race/ethnicity), organ needing transplant, and whether the respondent was the patient, primary caregiver, or other support person. Respondents were then asked to rate the TLC educational program on length, helpfulness, understandability, whether it met expectations for education, and confidence that the information provided would help them navigate the transplant process. They were assessed for recall of basic information presented in the TLC portion of the presentation (eg, “What does ACES stand for?” and asked to write in a response). Lastly, they were given the opportunity to provide qualitative feedback on what they liked the best and least about the TLC portion of the informational session. The assessment is available online at: www.thepermanente-journal.org/files/15-207Appx1.pdf.

Analyses

Participant’s responses were compared between groups by χ² test for categorical variables and Kruskal-Wallis H test for continuous variables. For qualitative responses, 3 of the authors (ER, CW, and MT) individually classified the responses on the basis of content and assigned numerical labels to the comments (dummy coding) corresponding to thematic content. Following dummy coding, all numerics were sent to another author (MJ), who reviewed the data and selected scoring on the basis of a majority of responses. For example, if 2 coders reported a statement was a “2” but a third coder reported the statement was a “3,” the statement was coded as a “2.” Frequencies of all codes were then analyzed for frequency of content.

### RESULTS

#### Patient Evaluation and Feedback

Surveys were collected from January through November 2013. Of the 1862 surveys disseminated, 823 surveys were returned (response rate, 44.2%). The mean (standard deviation) age of patients was 54.1 (11.5) years, of primary supports was 51.97 (14.24) years, and of other supports was 46.48 (16.22) years. Additional demographic and respondent characteristics are presented in Table 1.

Table 2 provides the frequency of correct responses on defining compliance and ACES. There was no significant difference between respondent groups in defining ACES but there was a significant difference in defining compliance, with patients having the highest frequency of incorrect responses.

A Kruskal-Wallis H test was run to compare patients, primary supports, and other supports on satisfaction with the TLC presentation. There was a statistically significant difference on how confident respondents reported feeling after meeting with the TLC ambassador (p = 0.002), with secondary supports reporting the highest confidence followed by primary support and lastly patients. There

<p>| Table 1. Characteristics of 823 respondents in study of Transplant Living Community* |
|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n = 217)</th>
<th>Primary caregivers (n = 255)</th>
<th>Other supports (n = 351)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>130 (59.9)</td>
<td>56 (22.0)</td>
<td>140 (39.9)</td>
</tr>
<tr>
<td>Women</td>
<td>72 (33.2)</td>
<td>188 (73.7)</td>
<td>201 (57.3)</td>
</tr>
<tr>
<td>Hispanic/Latino</td>
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<td>9 (4.1)</td>
<td>10 (3.9)</td>
<td>11 (3.1)</td>
</tr>
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<td>No</td>
<td>176 (81.1)</td>
<td>209 (82.0)</td>
<td>305 (86.9)</td>
</tr>
<tr>
<td>Prefer not to respond</td>
<td>5 (2.3)</td>
<td>5 (2.0)</td>
<td>2 (0.6)</td>
</tr>
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<td>Middle Eastern</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (2.3)</td>
<td>4 (1.6)</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>No</td>
<td>172 (79.3)</td>
<td>209 (82.0)</td>
<td>310 (88.3)</td>
</tr>
<tr>
<td>Prefer not to respond</td>
<td>4 (1.8)</td>
<td>5 (2.0)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>2 (0.9)</td>
<td>—</td>
<td>5 (1.4)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>70 (32.3)</td>
<td>57 (22.4)</td>
<td>64 (18.2)</td>
</tr>
<tr>
<td>Other Pacific Islander</td>
<td>1 (0.5)</td>
<td>1 (0.4)</td>
<td>1 (0.3)</td>
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<td>Asian</td>
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<td>4 (1.6)</td>
<td>1 (0.3)</td>
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<tr>
<td>White</td>
<td>127 (58.5)</td>
<td>174 (68.2)</td>
<td>256 (72.9)</td>
</tr>
<tr>
<td>Other</td>
<td>5 (2.3)</td>
<td>2 (0.8)</td>
<td>6 (1.7)</td>
</tr>
<tr>
<td>Prefer not to respond</td>
<td>1 (0.5)</td>
<td>2 (0.8)</td>
<td>8 (2.3)</td>
</tr>
<tr>
<td>Multi-ethnic</td>
<td>5 (2.3)</td>
<td>8 (3.1)</td>
<td>4 (1.1)</td>
</tr>
<tr>
<td>Organ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>112 (51.6)</td>
<td>171 (67.1)</td>
<td>285 (81.2)</td>
</tr>
<tr>
<td>Heart</td>
<td>—</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>Kidney</td>
<td>94 (43.3)</td>
<td>66 (25.9)</td>
<td>52 (14.8)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2 (0.9)</td>
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<td>—</td>
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<td>Lung</td>
<td>1 (0.5)</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
<tr>
<td>Liver/kidney</td>
<td>3 (1.4)</td>
<td>3 (1.2)</td>
<td>4 (1.1)</td>
</tr>
<tr>
<td>Kidney/pancreas</td>
<td>2 (0.9)</td>
<td>2 (0.8)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.9)</td>
<td>1 (0.4)</td>
<td>—</td>
</tr>
</tbody>
</table>

* Data are presented as number (% of category) unless otherwise noted. Within categories, columns do not consistently add up to the total because of missing data. — = no affirmative responses.
were no significant differences between respondent groups on expectations being met \( (p = 0.699) \), information being easy to follow and understand \( (p = 0.241) \), whether the information presented will help navigate the transplant process \( (p = 0.174) \), or length of the session \( (p = 0.364) \); see Table 3.

For qualitative data, as scored above, 633 of the respondents (76.9%) wrote in a reply for what they liked the most about the TLC portion of the educational session. Several respondents received more than 1 code if the content of their response addressed more than 1 thematic area. Aspects of the program that generated the most frequent positive responses are included in Table 4 (percentages are out of those who provided qualitative feedback). When asked what they liked the least about the TLC portion of the educational session, 199 of the respondents (24.2%) responded. Themes identified (in order of frequency of occurrence) are also reported in Table 4.

**DISCUSSION**

TLC is a unique, sustainable, patient-led lifestyle and self-management educational program providing a valuable resource for organ transplantation patients and their caregivers. Prior research has shown that transplant patients report a lack of caregiver education and acknowledge the need for distributed educational opportunities during the course of transplant. The Institute of Medicine’s 2000 report called for engaging and empowering patients in health care. Since this seminal report, patients are becoming more proactive consumers, actively participating in their care. However, as others have outlined, practical guidance on how to engage patients has been limited.33-35 For patient engagement to be successful, patient education must address lifestyle skills. This education will need to come from the patient’s perspective, complement medical care, and involve patients, caregivers, and extended social support members. An example of this approach, in which lifestyle methods are applicable across many chronic disease populations, is the TLC. Participants and supports reported high levels of satisfaction with the lifestyle and self-management skills presented by the TLC. Respondents also frequently indicated appreciation for having an actual transplant recipient providing the information as they felt this made the information more accessible and gave them hope for the future. When asked about possible improvements, most of the responses indicated nothing, or provided suggestions that were logistical or unrelated to TLC (eg, protocol requirements for transplant).

An interesting finding was that patients were significantly less likely to correctly identify the components of compliance than were primary or other supports. As outlined in the introduction, end-stage organ disease has a well-documented association with the development of cognitive impairments. This underlines the importance of providing relatable lifestyle and self-management education not only to the patient but also to primary and secondary supports throughout the care continuum.

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Table 2. Responses to survey about Attitude, Compliance, Exercise, and Support in study of Transplant Living Community

<table>
<thead>
<tr>
<th>Survey responses</th>
<th>Patients (n = 217)</th>
<th>Primary caregivers (n = 255)</th>
<th>Other supports (n = 351)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>What does compliance mean?</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Responded correctly</td>
<td>171 (78.8)</td>
<td>219 (85.9)</td>
<td>308 (87.8)</td>
<td>0.008</td>
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<tr>
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<td>39 (18.0)</td>
<td>32 (12.5)</td>
<td>32 (9.1)</td>
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<tr>
<td>Did not respond</td>
<td>7 (3.2)</td>
<td>4 (1.6)</td>
<td>11 (3.1)</td>
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<tr>
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<td>173 (79.7)</td>
<td>188 (73.7)</td>
<td>266 (75.8)</td>
<td>0.462</td>
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<tr>
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<td>9 (3.5)</td>
<td>11 (3.1)</td>
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<tr>
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<td>256 (72.9)</td>
<td>0.163</td>
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<tr>
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<td>3 (1.4)</td>
<td>4 (1.6)</td>
<td>13 (3.7)</td>
<td></td>
</tr>
<tr>
<td>Did not respond</td>
<td>45 (20.7)</td>
<td>68 (26.7)</td>
<td>82 (24.2)</td>
<td></td>
</tr>
</tbody>
</table>

\* Data are presented as number (% of category). Percentages may not total 100 because of rounding.

\* Responses to the questions: What does ACES stand for?

Table 3. Respondent satisfaction with Transplant Living Community

<table>
<thead>
<tr>
<th>Respondent satisfaction metrics</th>
<th>Patients (n = 217)</th>
<th>Primary support (n = 255)</th>
<th>Other supports (n = 351)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate or not enough time in the TLC information session</td>
<td>201 (92.6)</td>
<td>235 (92.2)</td>
<td>332 (94.6)</td>
</tr>
<tr>
<td>The information presented was helpful or very helpful in managing the transplant process</td>
<td>204 (94.0)</td>
<td>240 (94.1)</td>
<td>323 (92.0)</td>
</tr>
<tr>
<td>The information presented was understandable or very understandable and easy to follow</td>
<td>211 (97.2)</td>
<td>243 (95.3)</td>
<td>335 (95.4%)</td>
</tr>
<tr>
<td>The TLC program met or exceeded expectations</td>
<td>203 (93.5)</td>
<td>237 (92.9)</td>
<td>322 (91.7)</td>
</tr>
<tr>
<td>Respondents were mostly or completely confident they could navigate the transplant process with the information provided by the TLC ambassador</td>
<td>191 (88.0)</td>
<td>211 (82.7)</td>
<td>284 (80.9)</td>
</tr>
</tbody>
</table>

\* Data represent affirmative responses. Data are presented as number (% of category).

TLC = Transplant Living Community.
Also interesting was that secondary supports reported the greatest confidence in being able to manage the transplant process following the TLC education class. For supports other than the patient's primary support, the TLC lifestyle and self-management education is often their first exposure to the seriousness and extensive nature of care for organ transplants. “Other supports” often come in knowing only that their relative or friend needs a transplant and may have had minimal tangible support requirements placed on them. The potential of secondary supports to be considered as integral support team members to assist the primary support role has not been explored and could be considered for further research to determine the accuracy of this interpretation.

There are a number of factors unique to the TLC and considered integral to its sustainability that would be useful in integrating a similar program. First, a “champion” or at least one person should be dedicated to the program and its successful integration into a multidisciplinary team. Transplant recipients have recognized the value of patient-to-patient interaction. Secondly, a health care environment must be receptive to integration of a patient-led group with ongoing community development. Internally, a representative of TLC attends the selection committee to advocate for patients. TLC ambassadors have been instrumental within the Patient Family Advisory Council, driving the patient and family needs agenda with staff in a structured fashion. Medical staff trust has been developed and maintained through continual dialogue, the provision of a consistent curriculum, field mentoring of ambassadors, standardization of lifestyle resources and related tools, and routine practice of referring medical questions back to medical staff. Anecdotally, TLC involvement has fostered positive outcomes that reinforce ongoing trust from medical staff. At our center, there are several examples of patients who were determined not to be transplant candidates but, through interactions with TLC and its tenants, were able to meet eligibility for listing for organ transplantation. Third, the program must be accessible and visible to patients, supports, and staff. TLC has a centralized presence on the clinic floor via an educational table full of resources manned by a TLC ambassador in addition to TLC dedicated e-mail and voicemail access. Fourth, a clearly presented and manageable lifestyle plan (“Play Your ACES”) is needed. Related information and resources are presented in a clear and useful format accessible to most patients. Resources (eg, informational packet, brochures) are routinely evaluated and updated or improved to maximize utility and accuracy. Lastly, a strong volunteer structure with thoughtful training/orientation contains the ultimate objective of volunteers taking ownership of the program. Transplant recipients are invited to become ambassador volunteers only after a minimum of ten months after the transplant to ensure adequate physical and psychological recovery, wellness, and stability.

This study has several limitations. First, the assessment of the satisfaction of patients and supports was at a single time point and therefore the level of satisfaction and information retained may be different following repeated exposure (as that is the TLC model) or the overall experience with the program. Second, there is the potential for response bias. Patients and their supports were asked to complete the survey after an approximately three-hour educational session, which owing to patient fatigue or other factors may have reduced our response size. Lastly, given that TLC is a well-established community of ambassadors integrated into the clinic with patients routinely exposed to the TLC group, whether TLC has a significant impact on patient outcomes at this time could not be determined. To ascertain whether this is the case, randomized controlled trials would need to be performed. Future research should attempt to parse the effects of similar interventions on patient-related outcomes. However, one of the true strengths of this group is its visibility and accessibility, suggesting a multisite study with similar patient sociodemographic characteristics would be an optimal strategy.

### CONCLUSION

It is entirely feasible and sustainable to integrate a patient-led lifestyle and self-management educational group into a busy tertiary care clinic for patients with complex chronic illnesses. This requires a receptive and supportive health care environment, a coordinated and cohesive patient volunteer structure, and continued improvement. Furthermore, overwhelmingly positive feedback from patients and their supports regarding such a group suggest that these groups could provide substantial benefits in the care of complex illnesses.

#### Disclosure Statements

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

#### Acknowledgments

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Mary Corrado, ELS, provided editorial assistance.
Lifestyle and Self-Management by Those Who Live It: Patients Engaging in a Chronic Disease Model

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How to Cite this Article

References

To Interact
It is our duty to remember at all times and aene what medicine is not only a science, but also the art of letting our own individuality interact with the individuality of the patient.

— Albert Schweitzer, 1875-1965, French-German theologian, organist, philosopher, and physician.
Special Report

Improving Care in Older Patients with Diabetes:
A Focus on Glycemic Control

Eric A Lee, MD; Nancy E Gibbs, MD; John Martin, MD; Fred Ziel, MD;
Jennifer K Polzin, PharmD; Darryl Palmer-Toy, MD, PhD

ABSTRACT

Diabetes affects more than 25% of Americans older than age 65 years. The medical care of older patients must differ from the care of their younger counterparts. Older patients are at high risk of drug toxicity. A hemoglobin A\textsubscript{1c} (HbA\textsubscript{1c}) level less than 7.0% has historically been the goal of all patients with diabetes, regardless of age. Recent research has demonstrated that using medications to achieve such tight glycemic control is not necessary and is often not safe.

This article discusses the seminal research findings that strongly suggest that HbA\textsubscript{1c} goals should be relaxed in older patients. The authors then recommend an age-specific and functionally appropriate HbA\textsubscript{1c} reference range for patients receiving medications to improve glycemic control. Other interventions are suggested that should make diabetes care safer in older patients receiving hypoglycemic medications.

INTRODUCTION

Care of Older Adult Patients

The medical care of older patients must differ from the care of their younger counterparts. Complications from “standard” medical care are much more common in the geriatric population because of reduced reserve physiologic capacity, leading to functional decline. For example, among the sickest patients—hospitalized older patients—lasting disability is more common compared with hospitalized younger patients because of at least three mechanisms:

1. Incomplete recovery from a classic medical diagnosis (eg, oxygen dependence after pneumonia or chronic dyspnea after a myocardial infarction)
2. Exacerbation of a preexisting geriatric syndrome (eg, heightened fear of falls caused by hospital-related deconditioning with leg weakness or worsening dizziness caused by additional polypharmacy from new medications)
3. Iatrogenic complications during a hospitalization (eg, nosocomial \textit{Clostridium difficile} colitis leading to nursing home placement or hospital-acquired incident delirium leading to dementia).

Older patients are at high risk of drug toxicity. Because they are more likely than younger patients to have multiple medical problems, older patients take more medications, which often leads to incorrect and unnecessary administration of prescribed medications. Additionally, the metabolism of drugs is reduced in older patients because of decreased lean body mass with increased body fat and a higher likelihood of having renal, hepatic, and/or cardiac insufficiency. Finally, drug-drug and drug-disease interactions make older patients at high risk of iatrogenic complications of drug toxicity.

“Overuse” of medications has been categorized as when the benefits of the additional medication are negligible (eg, antibiotics for a sore throat), when the risks outweigh the benefits (eg, muscle relaxant for neck pain), or use of a medication that a competent patient would have otherwise declined after shared decision making (eg, morphine for mild knee pain).\(^1\,^2\) Use of hypoglycemic medications for the treatment of diabetes in older patients using standard guidelines often fit all three categories of “overuse.” The clinical benefits of additional hypoglycemic medications are often minimal, the harms are common and lasting, and the patient often lacks understanding of the time needed to accrue benefits from hypoglycemic medications. Hypoglycemia occurs frequently in older patients with diabetes, more often contributing to functional decline and lasting disability compared with their younger counterparts. The goals of glycemic control and the treatment using hypoglycemic diabetic medications in patients with diabetes must differ depending on age and functional status.

Diabetes Care in Older Adult Patients

Since 2003, there has been general acceptance by geriatric-focused physicians that glycemic control should be tempered by a sense of life expectancy, goals of care, cognitive status, and physical functional status.\(^3\) The one-size-fits-all model is not appropriate in frail older patients receiving hypoglycemic medications, for whom the risks of these medications often outweigh their benefits. Rather, shared decision making is necessary.
Historically, glycemic goals target a hemoglobin A1c (HbA1c) level below 7.0% without differentiation by age. The 2013 American Association of Clinical Endocrinologists (AACE) executive summary for diabetes management states that the HbA1c goal is 6.5% or lower for healthy patients without concurrent illness and who are at low hypoglycemic risk. The AACE states that the goal should be individualized to an HbA1c measurement above 6.5% for patients with concurrent illness and who are at risk of hypoglycemia. Although this AACE position states that the goals should be individualized on the basis of age and comorbidity, guidance on comorbidity criteria is absent. We believe that the lack of clarity in the AACE’s statement perpetuates the “lower-is-better” myth and encourages the overuse of potentially dangerous hypoglycemic medications.

The American Diabetes Association’s (ADA’s) 9-page executive summary of its 67-page position statement, “Standards of Medical Care in Diabetes 2014,” states that an HbA1c under 7.0% is “a reasonable goal” for many nonpregnant patients. Also, the ADA recommends that “older adults who are functional, cognitively intact, and have significant life expectancy should receive diabetes care with goals similar to those developed for younger adults” and that “glycemic goals for some older adults might reasonably be relaxed, using individual criteria, but hyperglycemia leading to symptoms or acute hyperglycemic complications should be avoided ….” Like the 2013 AACE executive summary, the 2014 ADA executive summary possibly lacks proper guidance for clinicians on when HbA1c goals should be relaxed.

However, in the text of the ADA’s 2014 position statement, HbA1c goals of below 7.5%, below 8.0%, and below 8.5% are recommended for older patients who have, respectively, good health, complex/intermediate health, and very complex/poor health. “This recommendation is more aligned with the position of the American Geriatrics Society (AGS), in which the target goal is set for an HbA1c between 7.5% and 8.0% in most older patients, and higher HbA1c targets between 8.0% and 9.0% are recommended with multiple comorbidities, poor health, and limited life expectancy.” These recommendations from the AGS have been adopted and publicized by the “Choosing Wisely” campaign sponsored by the American Board of Internal Medicine (ABIM) Foundation. On the basis of results of pivotal historical trials, we strongly agree with the glycemic goal of having HbA1c below 7.0% in most patients under 65 years of age. In this article, we discuss the scientific foundation for treating hyperglycemia to the historic goal of less than 7.0% in patients older than age 65 years (still generally considered the threshold for proper glycemic control in patients with diabetes of all ages), and why we believe that these goals should be relaxed to the standards set by the AGS.

**Historical Context for Lower Glycemic Targets**

The Diabetes Control and Complications Trial (DCCT) was the first trial to establish that microvascular and macrovascular complications of hyperglycemia could be delayed with tighter glycemic control. In this seminal work published in 1993, a total of 1441 patients with Type 1 diabetes (mean age = 27 years), with and without microvascular complications, were randomly assigned to receive either standard control of blood glucose or intensive control (intervention). After an average follow-up of 6.5 years, the DCCT (conducted from 1983 to 1993) demonstrated that patients with tight glycemic control had a delay in onset (primary prevention) or progression (secondary prevention) of nephropathy, neuropathy, and retinopathy. The intervention group had a mean HbA1c of 7.4%; the conventional treatment group had a mean HbA1c of 9.1%. The 11-year, postintervention follow-up published in 2005 showed a 42% reduction in any cardiovascular disease event. (In 2004, the mean HbA1c in the intervention group was 7.9% compared with 7.8% in the control group.) Notably, the widespread applicability of the DCCT investigators’ conclusions to most patients with diabetes was properly questioned. Less than 10% of all patients with diabetes have Type 1 diabetes, and the pathophysiology of Type 1 diabetes (formerly called juvenile diabetes) is markedly different from that in most patients with Type 2 (formerly called adult-onset) diabetes, particularly those older than 65 years.

The UK Prospective Diabetes Study (UKPDS), whose results were published in 1998, attempted to mitigate these concerns and validate the importance of tight glycemic control in patients with Type 2 diabetes. In this study, 3867 patients with newly diagnosed Type 2 diabetes (mean age = 54 years) were randomly given intensive therapy or conventional treatment. Patients older than age 65 years were excluded from enrollment in the UKPDS. After 10 years of follow-up, the intensive therapy group (mean HbA1c = 7.0%) had delays in microvascular complications, with less retinopathy and nephropathy compared with those who received conventional treatment (mean HbA1c = 7.9%). Macrovascular complications were not shown to be prevented or delayed during the initial publication in 1998. After the end of the randomization of the 2 groups, shortly after the 1998 publication, the glycemic control equalized in both study groups. The 10-year postsurveillance results of the UKPDS, published in 2008, suggested there was a “legacy effect,” or long-delayed benefit, in preventing myocardial infarctions and death in the intensive therapy group compared with the conventional group. Earlier intensive glycemic control during the first 10 years after the diagnosis of diabetes could reduce macrovascular events 10 to 19 years later, the study found. The UKPDS influenced the adoption of HbA1c goals below 7.0% in adult patients with Type 2 diabetes.

**Fallacy of Applying these Studies to Older Adult Patients**

In 2014, Selvin et al. published data from the National Health and Nutrition Examination Survey (NHANES, conducted by the Centers for Disease Control and Prevention). The authors labeled patients with diabetes of all ages who received hypoglycemic medications and had an HbA1c of 7.0% or greater as being suboptimally controlled. We think that an HbA1c below 7.0% should not necessarily be the goal in older patients with diabetes receiving hypoglycemic medications, and conclusions from influential articles such as NHANES mislead both clinicians and older patients with diabetes, potentially leading to harm. In NHANES, 40% of the patients with diabetes were older than age 65 years. We know that up to 57% of older...
patients with diabetes have substantial comorbidities and geriatric syndromes, which often lead these patients to change their goals of medical care.\textsuperscript{15} Given the known reduced life expectancy in older patients, particularly in frail older patients, we believe that the age-neutral historic target of an HbA\textsubscript{1c} below 7.0% is fallacious. This target is based on results of studies (UKPDS and DCCT) that did not allow for enrollment of patients aged 65 years or older, and hence these glycemic goals should not translate to older patients.

The microscopic complications related to higher HbA\textsubscript{1c} concentrations may not be clinically relevant in older patients with new-onset diabetes. In a theoretical construct model comparing an HbA\textsubscript{1c} of 8.0% vs 7.0% in patients with the onset of diabetes at age 65 years, the additional lifetime risk of blindness caused by retinopathy was reduced by 0.2% (number needed to treat = 500) and the additional lifetime risk of end-stage renal disease was reduced by 0.2% (number needed to treat = 500).\textsuperscript{16} Therefore, the clinical significance of preventing microvascular disease is questionable. Later, the UKPDS showed that tight glycemic control might reduce the development of macrovascular disease by 10 to 19 years, but in a patient with limited life expectancy or onset of diabetes after the age of 65 years, the relevance of aggressive lowering of glucose levels becomes less clear. Furthermore, if microalbuminuria portends future macrovascular complications, the control of hypertension and hyperlipidemia with the appropriate use of cardioprotective medications (aspirin, angiotensin-converting enzyme inhibitors, and statins) plays an equal if not a more important role in the prevention of cardiovascular complications.

For older adult patients with long-standing diabetes and multiple medical problems, at least 3 randomized trials have demonstrated that an HbA\textsubscript{1c} of about 7.5% is appropriate and safe and that an HbA\textsubscript{1c} below 6.5% might be dangerous. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial published in 2008 assessed 10,251 patients (mean age = 62 years; average duration of diabetes = 10 years) with multiple comorbidities who received intensive treatment (mean HbA\textsubscript{1c} = 6.4%) or conventional therapy (mean HbA\textsubscript{1c} = 7.5%).\textsuperscript{17} The study was halted prematurely after 3.5 years because it showed that there was one additional death in the intervention group for every 95 patients over 3.5 years. In addition, 10% of the intervention group had hypoglycemic events that required medical assistance vs 3% for the control group, and 28% of the intervention group had more than 10-kg weight gain compared with 14% in the control group.\textsuperscript{17}

Also in 2008, the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial took place in 11,140 older patients (mean age = 66 years; average duration of diabetes = 8 years) with severe cardiovascular disease or cardiovascular disease risk factors or preexisting microvascular complications.\textsuperscript{18} The ADVANCE trial found no macrovascular benefit or increased rate of death in the intense treatment group (mean HbA\textsubscript{1c} = 6.5%) vs conventional therapy (mean HbA\textsubscript{1c} = 7.3%) after 5 years. Severe hypoglycemia was significantly more common in the intervention group (2.7% vs 1.5% in the control group), which contributed to the significantly increased rate of hospitalization in the intervention group. The only microvascular benefit with intense treatment was a statistically significant reduction in albuminuria.\textsuperscript{18} In 2014, the follow-up study in ADVANCE demonstrated no reduction in macrovascular disease after the 6-year, postsurveillance follow-up. The legacy effect in preventing macrovascular disease seen in the UKPDS was not seen in ADVANCE.\textsuperscript{19} In 2009, the Veterans Affairs Diabetes Trial assessed 1791 military veterans with suboptimally controlled Type 2 diabetes (mean age = 60 years; mean duration of diabetes mellitus = 11.5 years; 40% with vascular disease).\textsuperscript{20} The goal in the intervention group receiving intensive glucose control was to reduce the HbA\textsubscript{1c} by 1.5%. After 6 years, there were significantly more serious events in the intervention group (mean HbA\textsubscript{1c} = 6.9%), including hypoglycemia, vs the controls (mean HbA\textsubscript{1c} = 8.4%), which received standard glucose control. There were no statistically significant changes in composite microvascular outcomes, although a statistically significant reduction did occur in the progression of proteinuria. No statistical differences existed in the number of eye surgical procedures, but there was a trend for reduced retinopathy. There also were no significant reductions in macrovascular events (stroke, cardiac events and procedures) or amputations in the intervention group compared with the control group.\textsuperscript{20}

Complications of Hypoglycemia

In 2011, the second most likely medication leading an older patient to be hospitalized through the Emergency Department because of an adverse drug event was insulin, and the fourth most likely medication was an oral hypoglycemic agent, according to authors from the Centers for Disease Control and Prevention.\textsuperscript{21} This group estimated that the numbers of hospitalizations in older patients occurring annually in the US because of insulin and oral hypoglycemic agents were 13,854 and 10,656 respectively. More than 94% of these hospitalizations were caused by complications of hypoglycemia, clearly demonstrating the potential dangers of these endocrine agents. This same group later published that patients older than age 80 years who were receiving insulin were twice as likely to go to the Emergency Department and 5 times as likely to be hospitalized because of insulin-related hypoglycemia and errors compared with 45- to 64-year-old patients, suggesting the need for looser glycemic targets based on age.\textsuperscript{21} Kaiser Permanente Northern California (KPNC) data showed that hypoglycemia was the second most common nonfatal diabetic complication (after cardiovascular complications) in patients age 70 to 79 years with a duration of diabetes for more than 10 years and the third most common cause of nonfatal complications in patients with diabetes for less than 10 years (after cardiovascular
complications and eye disease). Additionally, among patients age 70 to 79 years, the incidence of hypoglycemia was 6 times more likely than acute hyperglycemic events in those who had diabetes for less than 10 years, and 19 times more likely in patients with diabetes for greater than 10 years.

As noted earlier, whether macrovascular disease can be prevented with tight glycemic control among older patients with a long-standing history of diabetes is questionable. Hypoglycemia might also increase the risk of dementia later in life. In a KPNC diabetic registry from 1980 to 2007, of 16,667 patients with a mean age of 65 years, 1465 patients had at least 1 visit to the Emergency Department or hospital for a hypoglycemic event. The absolute risk in these patients of dementia developing per year of follow-up was 2.3%. Other KPNC data showed that hypoglycemia (as well as geriatric syndromes) more negatively affects an older patient’s quality of life than do other diabetic complications (eg, neuropathy, blindness, and end-stage renal disease).

**Hypoglycemia Continues in Older Patients**

As already discussed, the literature shows that an unexpected higher death rate was found in the intervention group of the ACCORD study and that hypoglycemic agents often lead to emergent hospitalizations in older patients, with hospitalizations frequently leading to lasting disability. Other research showed that older patients with multiple comorbid conditions and long-standing diabetes with an HbA<sub>1c</sub> between 6.4% and 6.9% did not have improved macrovascular outcomes or clinically significant improved microvascular outcomes compared with those with an HbA<sub>1c</sub> of 7.3% to 8.1%. Given this body of evidence, the physician mantra of "do no harm" would suggest that only a small percentage of patients older than 65 years would have an HbA<sub>1c</sub> below 7.0% and be receiving hypoglycemic medications. Yet, in published KPNC data, of 9786 patients between age 70 and 79 years with a duration of diabetes mellitus for longer than 10 years, 41% had an HbA<sub>1c</sub> below 7.0%. Although only 7% of these patients were not receiving any hypoglycemic medication, 61% of these patients were on a regimen of a sulfonylurea and 39% were receiving insulin.

In a Veterans Affairs study in 2009 of 205,857 patients at high risk of hypoglycemia because of age older than 74 years, a creatinine level above 2.0 mg/dL, or presence of cognitive impairment while receiving a sulfonylurea and/or insulin, 50% of patients had a level of HbA<sub>1c</sub> under 7.0%. 27% had HbA<sub>1c</sub> below 6.5%, and 11% had HbA<sub>1c</sub> less than 6.0%. These findings suggest overtreatment with hypoglycemic medications.

**DISCUSSION**

Many hypoglycemic episodes are avoidable. Many patients may not know to take less hypoglycemic medication when their oral intake is reduced (because of, for example, poor access to food caused by an acute medical event such as an upper respiratory tract infection with consequent anorexia). All clinicians, while educating older adult patients with diabetes, should instruct them to reduce their hypoglycemic agents during times of poor nutritional intake and to carry candy and a glucagon injection with them in the event of a hypoglycemic episode. The first-line treatment of most diseases should be education and other nonpharmaceutical interventions. In Kaiser Permanente Southern California (KPSC), patients with diabetes mellitus have better glycemic control if they have taken health education classes at KPSC (personal communication; Ray Nanda, MD; 2016 Feb 22).

There may be financial ramifications to overtreatment with hypoglycemic agents. Medicare has been reducing reimbursements for care because of events thought to be avoidable (“never events” during a hospitalization or readmission). In 2012, it was estimated that in the US there was $213 billion of avoidable health care costs, of which $20 billion in costs were caused by medication errors and $1.3 billion was caused by mismatched polypharmacy in elderly individuals. Given the alarming rate

### Table 1. Kaiser Permanente Southern California’s electronic medical record flag for elevated hemoglobin A<sub>1c</sub> in patients with diabetes, used through December 2015<sup>a</sup>

<table>
<thead>
<tr>
<th>Age</th>
<th>High flag (HbA&lt;sub&gt;1c&lt;/sub&gt;, %)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>All ages&lt;sup&gt;b&lt;/sup&gt;</td>
<td>≥ 7.0</td>
<td>Actual blood glucose measurements may differ from the estimated average glucose because of differences in test timing, stability of glycemic control, and RBC lifespan</td>
</tr>
</tbody>
</table>

<sup>a</sup> As of October 12, 2012, a separate test was created in Kaiser Permanente Southern California for screening patients who did not have a diagnosis of diabetes. The reference range for that test is 4.8% to 5.6%.

<sup>b</sup> Patients of all ages were flagged as having elevated blood glucose levels if HbA<sub>1c</sub> measurement was ≥ 7.0%.

HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>; RBC = red blood cell.

### Table 2. Kaiser Permanente Southern California’s updated hemoglobin A<sub>1c</sub> reference range for different age bands<sup>c</sup>

<table>
<thead>
<tr>
<th>Age, years</th>
<th>High flag (HbA&lt;sub&gt;1c&lt;/sub&gt;, %)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 17</td>
<td>≥ 7.5</td>
<td>Actual blood glucose measurements may differ from the estimated average glucose because of differences in test timing, stability of glycemic control, and RBC lifespan</td>
</tr>
</tbody>
</table>

18-64  
| ≥ 7.0 | A less stringent HbA<sub>1c</sub> goal of < 8.0% may be appropriate for an individual patient with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, or extensive comorbid conditions |

65-75  
| ≥ 7.5 | A less stringent HbA<sub>1c</sub> goal of < 8.0% may be appropriate for an individual elderly patient with a history of severe hypoglycemia, advanced microvascular or macrovascular complications, or extensive comorbid conditions |

≥ 76  
| ≥ 8.0 | A less stringent HbA<sub>1c</sub> goal of < 9.0% may be appropriate for an individual elderly patient with a history of severe hypoglycemia, advanced microvascular or macrovascular complications, or extensive comorbid conditions |

<sup>c</sup> Convened by the manuscript’s authors, multiple relevant Kaiser Permanente Southern California committees assisted in updating the HbA<sub>1c</sub> (diabetic monitoring) reference range. The consensus reference range is shown here. In use since January 2016, this updated reference range has been flagged as abnormal at an HbA<sub>1c</sub> level of ≥ 7.5% in patients with diabetes between 65 and 75 years of age and has been flagged as abnormal at an HbA<sub>1c</sub> ≥ 8.0 in patients with diabetes ≥ 76 years of age. The corresponding comments will allow clinicians to choose a more tailored HbA<sub>1c</sub> goal on the basis of the patient’s function and comorbidities.

HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>; RBC = red blood cell.

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**ORIGINAL RESEARCH & CONTRIBUTIONS**

Improving Care in Older Patients with Diabetes: A Focus on Glycemic Control

54 The Permanente Journal/Perm J 2016 Summer;20(3):15-080
of possible overtreatment with hypoglycemic agents in older patients, the US Department of Health and Human Services is developing a National Action Plan for Adverse Drug Event Prevention that focuses on 3 classes of medications: opiates, warfarin, and hypoglycemic agents.\(^2\)

We believe that the excessive burdens such as hypoglycemic episodes and other adverse medication reactions can be reduced through the following multi-interventional approach:

1. Establish a new reference range for HbA\(_1c\) levels in older patients with diabetes that synthesizes the recommendations from the ADA, Choosing Wisely (sponsored by the ABIM Foundation), and the AGS.
2. Educate and encourage clinicians to reduce hypoglycemic medications in older patients at risk of functional loss or with multiple medical problems when their HbA\(_1c\) level is below 7.0%. Accounting for risks of polypharmacy and the goals of care, for a healthy older patient with diabetes and an HbA\(_1c\) level below 7.0%, prescribing metformin as the only agent may be appropriate. There is importance in using antidiabetes medications to reduce glucose burden because hyperglycemia can also cause substantial morbidity. Our (KPSC) updated reference range can guide physicians to prescribe on the basis of function and morbidity (Tables 1 and 2).
3. Prescribe metformin as the first-line agent when a physician initiates therapy with a hypoglycemic medication because of its low risk for hypoglycemia and its safety profile.
4. Use the electronic medical record to identify patients receiving hypoglycemic agents who have an HbA\(_1c\) level below 7.0% and who are older than 80 years old or who have dementia or chronic kidney disease stage 4 or greater.
5. Educate patients and care takers, as well as provide written instruction after the office visit, to decrease the dosing of hypoglycemic medications when the patient’s oral intake is reduced because of illness or poor access to food.
6. Prescribe glucagon for older patients with diabetes receiving hypoglycemic medications, which can be used emergently during symptoms of hypoglycemia.
7. Encourage older patients with diabetes who are receiving hypoglycemic medications to always carry glucose tablets or glucose-rich foods with them and to monitor their blood glucose level before driving.
8. Use the electronic medical record to identify older patients receiving hypoglycemic medications who have 2 consecutive HbA\(_1c\) measurements below 6.5% in a period longer than 1 month.

By implementing the proposed interventions to reduce hypoglycemia, we can keep older patients with diabetes safer and more functional, without having any clinically significant health consequences from less intensive glycemic control. ❖

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Disclosure Statement
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How to Cite this Article

References

The Permanente Journal/Perm J 2016 Summer;20(3):15-080 55
Attending to Old People

Not only physicians, but everybody else attending old people, being accustomed to their constant complaints, and knowing their ill-tempered and difficult manners, realize how noble and important, how serious and difficult, how useful and even indispensable is that part of practical Medicine, called Gerocomica, which deals with the conservation of old people and the healing of their diseases.

—François Ranchin, MD, 1564-1641, French physician and professor and chancellor of the Université de Médecin, Montpellier, France
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

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ABSTRACT

A need exists to reduce care variations by standardizing the practice of thyroid and parathyroid surgery. During the course of a year, a task force developed algorithms representing decision points and workflows based on American Thyroid Association guidelines and three internal studies of surgical practices in the Northern and Southern California Regions of Kaiser Permanente conducted in collaboration with Health Information Technology Transformation & Analytics (HITTA).

INTRODUCTION

In keeping with a movement toward specialty redesign based on standardization and subspecialization, workflows were developed between March 2015 and March 2016 to guide evidence-based best practices and reduce disparities in care. The evidence base for thyroid and parathyroid workup and surgical procedures includes American Thyroid Association (ATA) guidelines1 and three studies2 of surgical practices in Kaiser Permanente (KP) Northern California and KP Southern California conducted in collaboration with Health Information Technology Transformation & Analytics (HITTA).

The first study used a robust set of variables and propensity score methods to match 2362 patients undergoing hemithyroidectomy, total thyroidectomy, or parathyroidectomy as outpatients (discharge within 8 hours of completion) to 2362 patients undergoing the same procedures as inpatients.2 Outcomes assessed were 30-day rates of complications, Emergency Department visits, all-cause hospital readmissions, and mortality. No statistically significant differences between inpatients and outpatients were found for complication rates or postdischarge utilization, and we concluded that outpatient surgery should be used for all patients for whom it is appropriate.2

The second study used similarly robust variables and propensity score methods to match 3135 patients who underwent hemithyroidectomy and total thyroidectomy, or parathyroidectomy performed by a high-volume surgeon (> 40 cases per year) to 2362 patients with the same procedure performed by a low-volume surgeon (≤ 20 cases per year).3 Rates of all-cause 30-day complications, mortality, readmission, and Emergency Department visits; proportion of outpatient procedures; incision-to-closure (“cut-to-close”) time; and length of stay were assessed. For hemithyroidectomies, high-volume surgeons had fewer readmitted patients, more outpatient procedures, shorter lengths of stay, and shorter cut-to-close times. For total thyroidectomies, high-volume surgeons had lower rates of all surgery-related complications and of the individual complications of hypocalcemia and surgical site infections, more outpatient procedures, and shorter lengths of stay and cut-to-close times. We concluded that high-volume surgeons improve patient safety and have the potential to contribute to organizational efficiency that may be underutilized in some settings.

The third study used decision-tree analysis to identify patient-level characteristics associated with 30-day complications after thyroid and parathyroid surgery.3 Among patients undergoing thyroidectomies, the most important predictor of risk was thyroid cancer. For patients with thyroid cancer, additional risk predictors included coronary artery disease and central neck dissection. For patients without thyroid cancer, additional risk predictors included coronary artery disease, dyspnea, complete thyroidectomy, and lobe size. Among patients undergoing parathyroidectomies, the most important risk predictor was coronary artery disease, followed by cerebrovascular disease and chronic kidney disease.3

Summaries of the evidence-based workflows are presented here.

THYROID NODULE: WORKUP

Figure 1 diagrams the workup of the patient with thyroid nodules. Thyroid nodules are evaluated to rule out cancer and rarely to address local symptoms. Palpable thyroid nodules are uncommon. Nonpalpable nodules are identified frequently on imaging studies. Thyroid nodule evaluation requires a dedicated ultrasound examination of the thyroid and adjacent lymph nodes. Whereas most nodules are benign, clinically significant thyroid cancer is seen in a small minority of patients, and surgical treatment may be necessary. Nearly all thyroid cancers are differentiated (papillary, follicular, or mixed).
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

Figure 1. Thyroid nodule: Workup (full-size, color version available at: www.thepermanentejournal.org/files/Summer2016/16035-1.pdf).

- Consider observation alone depending on patient characteristics, comorbidities, and imaging features.

- Bethesda System for Reporting Thyroid Cytopathology categories: I = nondiagnostic or unsatisfactory; II = benign; III = atypia of unknown significance; IV = follicular neoplasm or suspicious; V = suspicious for malignancy; VI = malignant.

- AUS = atypia of unknown significance; CT = computed tomography; FNA = fine-needle aspiration; I = iodine; MRI = magnetic resonance imaging; Tg = thyroglobulin; T4 = thyroxine; TSH = thyroid-stimulating hormone; US = ultrasound; X 2 = twice.
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

> 1-cm nodule suspicious

≥ 1.5-cm nodule

Endocrine does node assessment and US-guided FNA

Multiple nodules > 1 cm - 1.5 cm require evaluation in same fashion or FNA of dominant and/or suspicious nodules

If repeat FNA yields AUS X 2 or first FNA demonstrates follicular neoplasm, then consider molecular testing

Indeterminate or malignant

If there are abnormal nodes at the periphery or limits of the sonogram, extensive nodal disease, or the primary tumor is very large or invasive

US evaluation of central and lateral neck with FNA of any suspicious nodes > 8-10 mm in smallest diameter

Order preoperative serum calcium test

Order levothyroxine if anticipate postoperative T4 supplementation needs

Cross-sectional imaging with CT with contrast or MRI

Surgery consult

Tracking metric

Kaiser Permanente
Serum thyroid-stimulating hormone (TSH, thyrotropin) levels should be measured as part of the initial evaluation of a thyroid nodule. If serum TSH level is suppressed, further workup for hyperthyroidism is warranted by confirming suppressed TSH level and checking the serum thyroxine (T₄) level. If the TSH level remains suppressed, the patient should undergo a radiiodine thyroid uptake and scan. The workup and management of hyperthyroidism is beyond the scope of this summary.

Observation is recommended for nodules that are predominantly cystic or spongiform, for nodules smaller than 1.5 cm and in the absence of sonographic high-risk features, and for nodules smaller than 1 cm and suspicious but with no high-risk factors.

Diagnostic fine-needle aspiration (FNA) is recommended for cytologic evaluation of nodules greater than 1 cm with a high-suspicion sonographic pattern. FNA is recommended for most nodules 1.5 cm or larger. In addition to size criteria, high-risk factors, including family history or other clinical features, may influence the decision to perform an FNA of a smaller thyroid nodule.

Ultrasound-guided FNA is the procedure of choice in the evaluation of thyroid nodules. In the case of an incidentally noted thyroid nodule in a patient with clinically significant morbidities or a limitation in functional status, pursuing a diagnostic workup of the nodule may not be relevant. The most common practice is to acquire two to three cytologic aspirates from each nodule. If multiple nodules are found, the clinician should evaluate each on the basis of size criteria and sonographic findings.

Medical therapy with levothyroxine is not indicated for the management of benign thyroid nodules.

For indeterminate cytologic findings, such as the Bethesda System for Reporting Thyroid Cytopathology categories “atypia of undetermined significance or follicular lesion of undetermined significance” or “follicular neoplasm or suspicious for a follicular neoplasm,” molecular testing may be considered. Results of molecular testing may suggest the need for either observation or total thyroidectomy. In the absence of molecular testing, diagnostic lobectomy remains the recommended initial surgical procedure because malignancy may be present in up to 15% of these cases.

If abnormal results of cytologic evaluation are found and surgery is advised, it is important to have a detailed evaluation of cervical lymph nodes to assist in surgical planning. If it has not been done already, the clinician should refer the patient for diagnostic imaging for a nodal compartment neck sonogram to be available at the time of surgical consultation. Sonographically abnormal lymph nodes warrant added diagnostic workup by the endocrinologist or interventional radiologist, who will perform nodal FNA for cytologic analysis or thyroglobulin washout or both.

Primary hyperparathyroidism is uncommon but represents an important potential comorbidity for patients undergoing thyroid surgery. We recommend there be evidence of a serum calcium level at least one year in advance of surgery to screen for hypercalcemia.

A single benign FNA cytologic result does not guarantee nodule benignity. The false-negative rate is 1% to 3%. Repeated FNA or ultrasound monitoring at 6 to 12 months is recommended for low-risk nodules. If the repeated FNA is negative, no further sonography is recommended. For high-risk nodules, repeated sonography and/or FNA in 6 to 12 months is recommended. If the repeated FNA is also benign, repeated sonography is recommended in 2 or 3 years.

The endocrinologist should discuss the indication for and extent of thyroid surgery with the patient. All patients with a diagnosis of thyroid cancer or a suspected thyroid cancer should be referred for surgery. It is advisable to refer patients to a high-volume surgeon with expertise in thyroid and parathyroid surgery.

THYROID NODULE: PERIOPERATIVE MANAGEMENT

Figure 2 displays the evidence-based recommendations for perioperative management of thyroid nodules. Our KP study demonstrated increased efficiency and decreased complications when management included a consultation with a high-volume thyroid surgeon (defined as having completed more than 40 cases per calendar year as the primary surgeon). Further analysis will inform our goal of directing care to higher-volume surgeons who perform at least 20 cases of thyroid and parathyroid surgeries per year. Surgical risks and potential postoperative complications should be carefully reviewed with the patient using a standardized procedure-specific consent form. Patients with clinically significant substernal extension should be referred to a center with thoracic surgery backup.

Preoperative documentation of the patient’s voice is recommended. Documentation can be accomplished by using a patient-reported outcome tool, such as the Voice Handicap Index, or by examination. Direct laryngeal evaluation should be performed in patients with previous neck or thoracic surgery, abnormal voice, or known thyroid cancer. Intraoperative monitoring of the recurrent laryngeal nerve is optional, but identification and preservation of the nerves is recommended. Steps also should be taken to preserve the external branch of the superior laryngeal nerve.

The parathyroid glands should be preserved. Perioperative antibiotics are not routinely recommended unless the case is longer than anticipated or includes possible entrance into the upper aerodigestive tract or a sternotomy. Drains also are not recommended unless there is a large residual space, lateral neck dissection, or sternotomy.

Diagnostic lobectomy is typically appropriate for indeterminate lesions, atypia of undetermined significance lesions, or suspicious for malignancy lesions smaller than 4 cm. Well-differentiated thyroid cancer that presents in a low-risk patient as a nodule between 1 cm and 4 cm without extracapsular spread may be treated with thyroid lobectomy alone. Patients with nodules exceeding 4 cm or with contralateral nodules should be considered for total thyroidectomy. However, the treatment team may recommend, or the patient may consider, total thyroidectomy to avoid reoperation and/or to enable radioactive iodine (RAI) ablation therapy. Thyroidectomy without prophylactic central neck dissection may be appropriate for...
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

small T1 or T2 noninvasive, clinically node-negative papillary thyroid carcinomas (cN0) and for most follicular cancers.

Patients with T3, T4, or any TN(+) or M(+) disease should undergo a near-total or total thyroidectomy, with therapeutic central compartment (Level VI) neck dissection in the presence of clinically involved nodes. Prophylactic central neck dissection (ipsilateral or bilateral) should be considered in patients with advanced primary well-differentiated tumors with clinically involved lateral neck lymph nodes or clinically uninvolved central neck lymph nodes (cN0) if the information will be used to plan further steps in therapy. Therapeutic lymph node dissection of the lateral neck compartment should be performed for patients with biopsy-proven metastatic lateral cervical lymphadenopathy.

Postoperative management of patients who undergo complete thyroidectomy includes levothyroxine supplementation with a recommended standard dose of 1.5 µg/kg and adjustment to 1.0 µg/kg to 1.4 µg/kg for older patients or those with comorbidities, such as cardiac disease.

Hypocalcemia management may be achieved with empirical therapy or by obtaining intraoperative parathyroid hormone (PTH) levels, which can be drawn at the time the incision is closed. If the intraoperative PTH level exceeds 20 pg/mL, no supplementation is recommended. For an intraoperative PTH level of 10 pg/mL to 20 pg/mL, we recommend prescribing calcium supplementation at discharge; if the level is less than 10 pg/mL, the clinician should recommend calcium supplements and prescribe calcitriol. If the intraoperative PTH level is less than 6 pg/mL or the patient is at high risk of postsurgical hypocalcemia and is prescribed calcitriol. If the intraoperative PTH level is less than 6 pg/mL or the patient is at high risk of postsurgical hypocalcemia and is receiving empirical therapy or is symptomatic, one should consider checking a serum calcium level by the third postsurgical day.

Six to eight weeks postoperatively, the patient should undergo a voice assessment via a telephone appointment visit and/or a serum calcium level by the third postsurgical day. If the patient is at high risk of postsurgical hypocalcemia and is prescribed calcitriol. If the intraoperative PTH level is less than 6 pg/mL or the patient is at high risk of postsurgical hypocalcemia and is receiving empirical therapy or is symptomatic, one should consider checking a serum calcium level by the third postsurgical day.

Six to eight weeks postoperatively, the patient should undergo a voice assessment via a telephone appointment visit and/or using the Voice Handicap Index. If abnormal voice quality is noted by the surgeon or by the patient, the clinician should conduct a laryngeal evaluation with early referral to speech therapy if dysfunction is present or suspected.

The endocrinologist is responsible for requesting postoperative thyroid hormone replacement therapy and obtaining TSH and thyroglobulin measurements six to eight weeks after surgery.

THYROID CANCER: POSTOPERATIVE INITIAL THERAPY

The goal is to standardize initial postoperative treatment on the basis of postsurgical ATA risk group determination and the patient’s early response to treatment (Figure 3). Using these individualized dynamic risk assessment tools, TSH treatment goals and early decisions about RAI therapy can be made.

The clinician should obtain TSH, thyroglobulin, and thyroglobulin antibody (TgAb) levels six to eight weeks after surgery. Appropriate treatment planning is guided by correct cancer staging. Staging should be updated as additional clinical information becomes available.

Using both the MACIS (metastasis, age at presentation, completeness of excision, invasion, size) scoring system (Figure 4) and the ATA guidelines will help clarify the patient’s risk. Although MACIS may be a better predictor of future survival/mortality, ATA risk stratification may be more predictive of local recurrence. When using the MACIS calculator (available on the Internet at www.thyroid.org/thyroid-cancer-staging-calculator or on KP HealthConnect in Northern California), one should assume no distant metastases to calculate the score unless distant metastases are known. The endocrinologist should note the stage, MACIS score, ATA risk group, initial and current TSH goal, appropriate tumor marker, use of RAI, and posttreatment whole-body scan results as well as planned or last postoperative thyroid ultrasonography.

MODIFIED 2009 ATA RISK STRATIFICATION (2015)

<table>
<thead>
<tr>
<th>LOW RISK</th>
<th>INTERMEDIATE RISK</th>
<th>HIGH RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No local or distant metastases</td>
<td>• Microscopic invasion of tumor into the perithyroidal soft tissues</td>
<td>• Macroscopic invasion of tumor into the perithyroidal soft tissues (gross extrathyroidal extension)</td>
</tr>
<tr>
<td>• Clinically N0 or N1 micrometastases (&lt;5 involved nodes with lesions ≤2 mm)</td>
<td>• Clinical N1 or &gt;5 pathologic N1 with all involved lymph nodes &lt;3 cm in largest dimension</td>
<td>• Incomplete tumor resection</td>
</tr>
<tr>
<td>• All macroscopic tumor resected</td>
<td>• Radioactive iodine avid metastatic foci in the neck on the first posttreatment whole body radioactive iodine scan</td>
<td>• Distant metastases</td>
</tr>
<tr>
<td>• No local invasion (no extrathyroidal extension)</td>
<td>• Aggressive histology (eg, Tall cell, hobnail variant, columnar cell carcinoma)</td>
<td>• Pathologic N1 with any metastatic LN ≥3 cm in largest dimension</td>
</tr>
<tr>
<td>• No vascular invasion</td>
<td>• Papillary thyroid cancer with &gt;4 foci of vascular invasion</td>
<td>• Postoperative serum thyroglobulin suggestive of distant metastases</td>
</tr>
<tr>
<td>• If Iodine-131 given, no uptake except in the thyroid bed</td>
<td>• Intrathyroidal, papillary thyroid cancer, primary tumor 1 cm - 4 cm, V600E BRAF mutated (if known)</td>
<td>• Follicular thyroid cancer with extensive vascular invasion (&gt;4 foci of vascular invasion)</td>
</tr>
<tr>
<td>• No aggressive history</td>
<td>• Intrathyroidal, papillary thyroid cancer with extrathyroidal extension and V600E BRAF mutated (if known)</td>
<td></td>
</tr>
</tbody>
</table>
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

Figure 2. Thyroid nodule: Perioperative management (full-size, color version available at: www.thepermanentejournal.org/files/Summer2016/16035-2.pdf).

AUS = atypia of unknown significance; FN = follicular neoplasm; ioPTH = intraoperative parathyroid hormone (pg/mL); RLN = recurrent laryngeal nerve; 
T\(_4\) = thyroxine; TAV = telephone appointment “visit”; Tg = thyroglobulin; TID = three times a day; TSH = thyroid-stimulating hormone; \(\times 2\) = twice.
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

Endocrinologist orders levothyroxine preoperatively

Patients should all be sent home on T4, pending final pathology UNLESS gross residual disease

Endocrinologist orders postoperative TSH and Tg

Surgery does TAV at 6-8 weeks for postoperative voice check

Consider drawing iOPTH X 2 at 5-10 minute intervals after removal of thyroid gland

Consider endocrinology input if having difficulty with immediate postoperative hypocalcemia management or if ongoing beyond 4 weeks

Empiric therapy may be considered if iOPTH not obtained or available:

Low risk: calcium 500-600 mg TID
Intermediate risk: calcium 1000-1200 mg TID
High risk: calcium AND calcitriol 0.25-0.5 μg daily

iOPTH > 20: no supplementation or low-dose calcium
iOPTH 10-20: give calcium at discharge
iOPTH <10: give calcium and calcitriol at discharge

It postoperative iOPTH < 6, high-risk patient on empiric therapy, or patient symptomatic, consider serum calcium check on postoperative day 2 or 3

Tracking metric

Endocrinologist does postoperative TSH and Tg

Total thyroid and central with or without lateral compartment dissection

Consider lobectomy versus total thyroidectomy based on patient preference

Completion or total thyroidectomy

If ordering a postoperative calcium test for symptomatic patients, use the diagnosis “postoperative” or “history of parathyroidectomy or thyroidectomy” Do not use “hypocalcemia” without previous laboratory-validated diagnosis

> 1 cm and < 4 cm without extracapsular spread

> 1 cm and < 4 cm without extracapsular spread

T1 or T2 CNo

T3, T4 or any TN(+)
Figure 3. Thyroid cancer: Postoperative initial therapy (full-size, color version available at: www.thepermanentejournal.org/files/Summer2016/16035-3.pdf).

* Calculate MACIS (metastasis, age at presentation, completeness of excision, invasion, size) score as if there are no distant metastases, unless known. If Tg level is out of proportion to presumed burden of disease and MACIS score is borderline for therapy, proceed with radioactive iodine therapy.

* ATA = American Thyroid Association; I = iodine; MACIS = metastasis, age at presentation, completeness of excision, invasion, size; RAI = radioactive iodine; rTSH = recombinant human TSH; Tg = thyroglobulin; TgAb = thyroglobulin antibody; TSH = thyroid-stimulating hormone, mIU/L; THW = thyroid hormone withdrawal; USC = University of Southern California Endocrine Laboratories.
A postoperative thyroglobulin level below 10 ng/mL suggests a low likelihood of clinically significant persistent disease. However, a thyroglobulin level exceeding 10 ng/mL does not always indicate clinically significant residual disease, and confirmation by a posttherapy scan is recommended. Initial thyroglobulin testing should be done using an assay sensitive for thyroglobulin antibodies, given that the presence of antibodies can reduce the validity of thyroglobulin measurements.

On the basis of ATA risk group and response to therapy, patients with low-risk disease should be assessed for possible thyroid remnant ablation therapy with RAI. RAI remnant ablation is an early option for patients who do not appear to be heading for an excellent response to therapy. For most cases of remnant ablation, stimulation with recombinant human TSH is recommended. Unifocal micropapillary disease is usually treated only when the postoperative thyroglobulin level is higher than expected.

Some patients with intermediate-risk disease and almost all patients with high-risk disease benefit from RAI treatment. Thyroglobulin and TgAb levels six to eight weeks after surgery aid in deciding which intermediate-risk patients might benefit from RAI. For the treatment of high-risk patients with known or suspected metastatic disease, thyroid hormone withdrawal therapy is recommended, often with pretherapy diagnostic scanning. High-risk patients should be treated with recombinant human TSH stimulation only if thyroid hormone withdrawal is medically contraindicated. Typical RAI doses are 125 mCi for local disease, including lateral neck nodes, 150 mCi for pulmonary metastases, and 200 mCi for skeletal or other metastases.

Dosimetry can help avoid overtreatment in the case of comorbid renal failure or widespread pulmonary metastases. If dosimetry in renal failure is not possible, the patient’s dialysis schedule can guide empirical reduction of iodine(I)-131. If dialysis occurs the day after treatment, the clinician should give 40% of the dose calculated as if the patient had normal renal function. If dialysis will occur 2 days later, 22% of the calculated dose should be given.

The likelihood of sufficient iodine clearance after a contrast computed tomography (CT) study at 4 months is approximately 95%. Patients may be treated after thyroid hormone withdrawal or after recombinant human TSH stimulation depending on risk stratification.

### Thyroid Cancer: Surveillance

Surveillance for differentiated thyroid cancer can be divided into biochemical and anatomic components (Figure 5). Biochemical surveillance uses thyroglobulin and TgAb testing. Anatomic surveillance is primarily done with neck ultrasonography.

At 6 to 12 months postoperatively, thyroglobulin and TgAb testing should be performed with an assay highly sensitive for TgAb. If TgAb levels are detectable, this same highly sensitive assay should be used for long-term surveillance of antibody levels. If the TgAb level is undetectable, thyroglobulin levels can be used reliably for biochemical surveillance in most patients. Use of a thyroglobulin assay with detectability to below 0.2 ng/mL allows confidence in determination of a biochemically complete response to therapy and is preferred over less sensitive assays. Thyroglobulin and TgAb levels should be obtained every 3 to 12 months, depending on the patient’s ATA risk category. If the thyroglobulin or TgAb level increases 50% or more above the baseline for a given patient and is well above the limit of detection, ultrasonoscopy evaluation should be obtained.

Alongside regular biochemical surveillance, imaging with ultrasound is recommended 6 to 12 months after the initial therapy and periodically thereafter even if thyroglobulin/TgAb levels remain stable. Central lymph nodes less than 0.8 cm in the anterior-posterior dimension and lateral lymph nodes less than 1 cm in the anterior-posterior dimension should be monitored with serial imaging if thyroglobulin/TgAb markers are stable. If lymph nodes exceed these dimensions, they should undergo FNA biopsy with thyroglobulin washout. Patients with biopsy-proven or thyroglobulin washout-proven metastatic disease should be referred for additional surgery.

In the event that thyroglobulin/TgAb levels are rising but enlarged lymph nodes are negative on FNA biopsy and thyroglobulin washout, additional imaging with CT or magnetic resonance imaging (MRI) should be performed. Any findings on additional imaging should be considered for biopsy or surgery. However, if all imaging has normal findings in the setting of rising thyroglobulin/TgAb levels, an I-123 whole-body scan is indicated. Disease identified on an I-123 scan can be treated with I-131 up to 150 mCi. In patients with thyroglobulin levels exceeding 10 ng/mL and no findings on

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**MACIS Prognostic Score for Papillary Thyroid Carcinoma**

<table>
<thead>
<tr>
<th>Age (if age ≤ 39 years)</th>
<th>+1 (if age ≥ 40 years)</th>
<th>Diameter of Tumor (cm)</th>
<th>Complete Resection (No)</th>
<th>Local/Vascular Invasion (No)</th>
<th>Distant Metastasis (No)</th>
</tr>
</thead>
</table>

MACIS Score = 3.1 (if age ≤ 39 years) or 0.08 (if age ≥ 40 years), + 0.3 × tumor size (in centimeters), + 1 (if incompletely resected), + 1 (if locally invasive), + 3 (if distant metastases are present).

Twenty-year cause-specific survival rates are as follows for each MACIS score: MACIS < 6 = 99%; MACIS 6-6.99 = 89%; MACIS 7-7.99 = 56%; MACIS ≥ 8 = 24%.

Evidence-Based Workflows for Thyroid and Parathyroid Surgery

Figure 5. Thyroid cancer: Surveillance (full-size, color version available at: www.thepermanentejournal.org/files/Summer2016/16035-5.pdf).

CT = computed tomography; EBRT = external beam radiation therapy; 18FDG = fludeoxyglucose F 18; FNA = fine-needle aspiration; I = iodine; IR = interventional radiology; mets = metastases; MRI = magnetic resonance imaging; NED = no evidence of disease; path = pathology; PET = positron emission tomography; RAI = radioactive iodine; \( T_4 \) = thyroxine; Tg = thyroglobulin; TgAb = thyroglobulin antibody; TSH = thyroid-stimulating hormone, \( \text{mIU/L} \); US = ultrasound; USC = University of Southern California Endocrine Laboratories; uTG = ultrasensitive thyroglobulin; \( X 2 \) = twice.
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

**Imaging Surveillance**

Possible US mets as defined by > 0.8-cm central or > 1.0-cm lateral nodes

- **Possible US mets**
  - **Negative Response**
    - Tumor marker stable
    - Repeat monitoring of tumor markers based on risk
  - **Positive Response**
    - Tumor marker rising
    - FNA negative for path or Tg washout

- **Negative Response**
  - I-123 scan
  - Amenable to IR biopsy or surgery
  - PET/CT if not radiosensitive and Tg > 10
- **Positive Response**
  - I-131 therapy up to 150 mCi
  - Consider EBRT if RAI refractory or for symptomatic mets and/or consider kinase inhibitors and clinical trials for disease progression

- **Excellent Response**
  - No clinical, biochemical, or structural evidence of disease after therapy (remission, NED).
  - TgAb negative: typically, unstimulated Tg < 0.2 ng/mL.
  - TgAb positive: > 50% drop without structural or functional disease.
  - Recurrence rate: 1%-2%.

- **Biochemically Incomplete Response**
  - Persistent Tg/TgAb in the absence of localizable disease.
  - Detectable nonstimulated Tg or positive TgAb without structural disease: typically, nonstimulated Tg > 1 ng/mL, < 50% drop in TgAb.
  - Outcomes: 56%-68% move to NED, 19%-27% remain in the biochemically incomplete response group, 8%-27% develop structural recurrence.
  - No deaths at 10 years.

- **Structurally Incomplete Response**
  - Persistent or newly identified locoregional or distant metastases.
  - Structural or functional (RAI scan, 18FDG-PET) evidence of locoregional or distant metastases, either biopsy proven or highly likely to be metastatic disease.
  - Outcomes: 29%-51% move to NED after surgery.
  - 15-year postoperative mortality: 0% if biochemically incomplete response, 11% if locoregional incomplete response, 57% if structurally identified distant metastases.

- **Indeterminant Response**
  - Nonspecific lesions and indeterminate Tg/TgAb values.
  - Continued observation with serial imaging of nonspecific lesions and serial laboratory monitoring of Tg/TgAb.
  - Nonspecific findings becoming suspicious over time or rising Tg or TgAb should be evaluated.

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**Kaiser Permanente**
ultrasound, CT or MRI, and I-123 scan, the clinician should consider positron emission tomography-CT and case discussion with his/her local tumor board.

External beam radiation therapy is recommended for RAI-refractory disease or for treatment of symptomatic metastatic lesions. Tyrosine kinase inhibitors and clinical trials should be considered for patients with progressive, RAI-refractory disease. Patients who are candidates for tyrosine kinase inhibitors should be thoroughly counseled on the potential risks and benefits of this therapy as well as alternative therapeutic approaches, including supportive care.

To facilitate understanding of probable long-term outcomes and thereby guide surveillance frequency, one should ensure that responses to therapy follow ATA recommendations and be documented as “excellent response,” “biochemically incomplete response,” “structurally incomplete response,” or “indeterminate response” (Table 1).

Patients with an “excellent response” to therapy have no clinical, biochemical, or structural evidence of disease. For this designation, thyroglobulin levels must be below 0.2 ng/mL in the setting of negative TgAb levels, or the TgAb level must have dropped 50% or more from baseline. The recurrence rate in this group is believed to be 1% or 2%.

Patients with “biochemically incomplete responses” to therapy have persistent thyroglobulin/TgAb levels in the absence of structural disease. Studies have shown no increase in disease-specific mortality for this group. At 5 to 10 years, 56% to 68% of these patients will move into the “excellent response” category, 19% to 27% will remain in this category, and 8% to 27% will experience a recurrence.

Patients with “structurally incomplete responses” to therapy have persistent or newly identified locoregional or distantly metastatic disease, either biopsy-proven or likely disease as determined by imaging. In 5 to 10 years, 29% to 51% of these patients will move into the “excellent response” category. Mortality rates for this group are highest, with death occurring in 11% of those with locoregional disease and 57% of those with distant metastases.

Finally, patients with “indeterminate responses” to therapy are those with nonspecific lesions and thyroglobulin/TgAb levels between 0.3 and 1 ng/mL. Most of these patients do well; at 5 to 10 years, 80% to 87% will move into the “excellent response” group while 13% to 20% will move into the “biochemically” or “structurally incomplete response” group.

All patients require TSH monitoring at least annually. Patients who are determined to be biochemically and structurally free of disease and those with indeterminate responses should have TSH levels maintained at 0.4 mIU/L to 2.0 mIU/L. Patients with biochemically or structurally incomplete responses to therapy should have TSH levels maintained at below 0.1 mIU/L if reasonable in the context of coexisting conditions and patient age.

### Table 1. Relationship of response to therapy at 6 to 18 months to initial risk stratification and outcomes at 5 to 15 years

<table>
<thead>
<tr>
<th>Measure</th>
<th>Response to therapy at 6 to 18 months, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial risk stratification</strong></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>86-91  12-29  11-19  2-6</td>
</tr>
<tr>
<td>Intermediate</td>
<td>57-63  8-23  21-22  19-28</td>
</tr>
<tr>
<td>High</td>
<td>14-16  0-4  18-18  67-75</td>
</tr>
<tr>
<td><strong>Outcomes at 5 to 15 years</strong></td>
<td></td>
</tr>
<tr>
<td>No evidence of disease (NED)a</td>
<td>97-99  97-99  1-3</td>
</tr>
<tr>
<td>Indeterminant response (IDR)a</td>
<td>80-87  80-87  13-20</td>
</tr>
<tr>
<td>Biologically incomplete response (BIR)a</td>
<td>56-86  56-86  19-27  8-17</td>
</tr>
<tr>
<td>Structurally incomplete response (SIR)a</td>
<td>29-51  29-51</td>
</tr>
</tbody>
</table>

- Blank boxes indicate that the proportion of patients in the category is not reported in the literature.
- Modified 2009 American Thyroid Association Risk Stratification System (2015), assessed 6 to 8 weeks postoperatively.
- No clinical, biochemical, or structural evidence of disease (thyroglobulin antibody [TgAb] negative: unstimulated thyroglobulin < 0.2 ng/mL; TgAb positive: > 50% drop in TgAb from preoperative level and no structural or functional disease).
- Nonspecific lesions and indeterminate thyroglobulin and TgAb values.
- Persistent thyroglobulin or TgAb with no localizable disease; detectable nonstimulated thyroglobulin or positive TgAb without structural disease; typically, nonsimulated thyroglobulin level > 1 ng/mL and < 50% drop in TgAb.
- Structural or functional (radioactive iodine, fludeoxyglucose F 18-position emission tomography) evidence of persistent or newly identified locoregional or distant metastases. Of patients with structurally incomplete response, 29% to 51% move to NED after follow-up surgery. The 15-year mortality for structurally incomplete response is 11% for locoregional disease and 57% for structural distant metastases.

### PRIMARY HYPERPARATHYROIDISM: PREOPERATIVE PREPARATION

Overproduction of PTH resulting in abnormal calcium homeostasis covers a wide spectrum of presentations, including the following:

- hypercalcemia with elevated PTH level
- hypercalcemia with normal but inappropriate PTH level
- eucalcemia with elevated PTH level in the absence of secondary causes.

Symptoms may or may not be present and include but are not limited to osteoporotic fractures, renal stones, constipation or abdominal pain, peripheral neuropathy, headaches, or psychiatric symptoms. One should suspect primary hyperparathyroidism (PHPT) in patients with hypercalcemia, inappropriately low bone density for age, or family history (hyperparathyroidism-jaw tumor syndrome, multiple endocrine neoplasia, and familial isolated hyperparathyroidism).

Secondary hyperparathyroidism often results from prolonged renal disease, especially after kidney transplantation when prolonged pretransplant parathyroid stimulation could result in autonomous PTH production and hypercalcemia. Patients treated with lithium, especially for prolonged periods, may present with secondary hyperparathyroidism; lithium alters calcium sensing, causing four-gland hyperparathyroidism. Some patients could harbor an unrelated underlying adenoma, and PHPT is detected in associated monitoring.

The ideal workup includes a simultaneous fasting serum calcium test and PTH measurement (Figure 6). When in doubt, one should repeat the PTH estimation. The most common causes of hypercalcemia other than PHPT are thiazide diuretics (through decreased resorption of calcium in the kidney) and malignancy (through a variety of mechanisms). Rarely, excess calcium ingestion or granulomatous processes (including but not limited to tuberculosis and sarcoidosis) can cause high serum calcium levels with suppressed PTH.
Evidence-Based Workflows for Thyroid and Parathyroid Surgery


CT = computed tomography; GFR = glomerular filtration rate; HPT = hyperparathyroidism; MIBISPECT = technetium Tc 99 sestamibi single-photon emission-computed tomography scintigraphy; PTH = parathyroid hormone; SPECT CT = single-photon emission computed tomography; TAV = telephone appointment “visit”; US = ultrasound.

HPT = hyperparathyroidism; ioPTH = intraoperative parathyroid hormone (pg/mL); US = ultrasound; X 2 = twice.
Evidence-Based Workflows for Thyroid and Parathyroid Surgery

1. Order calcium within 1 year post surgery

2. Surgery successful
   - Consider ioPTH draw X 2 at 5-10 minute intervals after removal of parathyroid gland(s)
   - ioPTH > 20: no supplementation or low dose calcium
     - ioPTH 10-20: give calcium at discharge
     - ioPTH < 10: give calcium and calcitriol at discharge

3. If postop ioPTH < 6 and/or patient symptomatic, consider serum calcium check on postoperative day 2 or 3

4. Consider endocrinology input if having difficulty with oral hypocalcemia management

5. Notify nephrology of outcome

6. Subtotal parathyroidectomy leaving 100 mg gland or reimplant

7. Total without reimplant for patients who are not transplant candidates

8. 4+ gland exploration

9. Secondary HPT

If ordering a postoperative calcium for symptomatic patients, use the diagnosis “postoperative” or “history of parathyroidectomy or thyroidectomy”.
Do not use “hypocalcemia” without previous laboratory-validated diagnosis.
Diagnostic serum testing should include measurement of serum creatinine to rule out renal disease, 25-hydroxyvitamin D, phosphorus, ionized calcium, albumin, and alkaline phosphatase. The latter may be elevated in predominant bone disease, identifying high turnover and a resulting risk of hungry bone syndrome.

In determining whether surgical removal of parathyroid tissue is warranted, the clinician can use several criteria depending on the presence or absence of symptoms. A 24-hour urine collection for calcium and creatinine will allow the calculation of renal calcium clearance. High urinary calcium loss may warrant surgical intervention; this is often present in PHPT. Low urinary calcium loss suggests familial hypocalciuric hypercalcemia, a benign condition for which surgery is not indicated.

Once the diagnosis of PHPT has been established, surgery is the treatment of choice in the absence of a contraindication, such as limited life expectancy, or evidence of end-organ damage (eg, renal compromise, osteoporosis), especially in the presence of evidence of disease progression.

If the patient is asymptomatic, we adhere to the guidelines for surgery from the Management of Asymptomatic PHPT Fourth International Workshop in 2013. We would consider surgery if any of the following is present (see Figure 6):

- hypercalcemia: serum calcium level exceeding 1 mg/dL above the upper limit of normal
- skeletal compromise
  - low bone mineral density determined by dual-energy x-ray absorptiometry: T-score at or below -2.5 at the lumbar spine, total hip, femoral neck, or distal one-third radius (standard bone density measurement sites); use Z-scores for premenopausal women and men younger than age 50 years
  - vertebral fracture demonstrated using radiography, CT, or vertebral fracture analysis
  - history of fragility fracture (considered a skeletal complication of PHPT)
- renal compromise
  - glomerular filtration rate below 60 mL/min/1.73 m²
  - 24-hour urine calcium level above 400 mg/day and increased stone risk by biochemical stone analysis
  - nephrolithiasis or nephrocalcinosis by x-ray, ultrasound, or CT
- age under 50 years

Meeting only a single criterion indicates the need for surgery. Other general criteria that the workshop itemized as an indication for surgery include

- Medical surveillance is neither desired nor possible
- The disease has progressed
- The patient prefers surgery in the absence of meeting the aforementioned criteria (as long as there are no contraindications).

The task force members thought that the defining criteria for a neurocognitive component (including but not limited to fatigue and depression) were not definitive.

Once the decision to proceed with surgical consultation is made, a preliminary thyroid sonogram is acquired to identify thyroid nodules and potentially localize a parathyroid adenoma. Ruling out medullary thyroid cancer (associated with MEN2A) in a nodule and workup of thyroid nodules before surgery may change the scope of the surgery. If the sonogram is nonlocalizing, most experts proceed to parathyroid scintigraphy using technetium Tc 99m pertechnetate sestamibi washout imaging with or without SPECT (or SPECT CT) to improve localization together with sonography. Multiphasic CT may also be considered if the combination of sonography and scintigraphy is nonlocalizing or discordant. A presurgical discussion about the likelihood of hyperplasia or multiple adenomas is recommended because of its potential to alter the surgical approach.

HYPERPARATHYROIDISM: INTRAOPERATIVE AND POSTOPERATIVE MANAGEMENT

Parathyroid Localization Studies

In advance of most surgical procedures, the surgeon knows what will be resected and from which location (Figure 7). Parathyroid surgical therapy differs because the glands are small and of variable number and location. Although localization studies have improved greatly in the past three decades, we are sometimes unable to reliably determine the number and location of all diseased glands preoperatively.

With the advent of an inexpensive and relatively rapid intraoperative PTH assay, localization studies have become increasingly important because minimally invasive procedures may be performed in approximately 85% of cases. As localization studies continue to be refined and new modalities are developed, our algorithm will evolve: we currently recommend a combination of sonography and sestamibi washout scintigraphy as first-line localization studies.

Parathyroid surgeons should become facile with in-office sonography. They have an excellent grasp of the anatomy and both typical and atypical locations of the parathyroid glands; therefore, using basic sonography skills, parathyroid surgeons may quickly become proficient at parathyroid sonography. Sestamibi washout scintigraphy is helpful should the sonogram be nonlocalizing, especially in mediastinal disease, in which there is no utility of sonography. Sestamibi washout scintigraphy is limited in the presence of multiglandular parathyroid disease or synchronous hyperfunctioning thyroid nodules. Multiphasic enhanced neck CT may be of benefit when the sonography and scintigraphy are nonlocalizing, discordant, or both but has a distinct disadvantage of a very high radiation dose; it is thus not currently recommended as an initial localizing study. Additional studies—MRI, FNA with sonographic guidance, and venous sampling—may be used, especially in revision cases for which we recommend having concordant results with at least two modalities before reexploration whenever possible.

Intraoperative and Postoperative Management

A skilled parathyroid surgeon navigates the subtleties and complexities of hyperparathyroidism. Before taking the patient to the operating theater, the surgeon will have thoroughly reviewed the case and its corresponding localization studies to be certain of the diagnosis of PHPT. If a localization study is not validated in the operating room and four normal glands are found, a surgeon who is certain of the diagnosis may confidently expand the exploration, find the abnormal gland, and conclude surgery successfully.
A baseline intraoperative PTH measurement is critical for a focused exploration and also helps determine when to stop in a bilateral exploration; more than 4 glands are present in approximately 6% of cases. Owing to variable PTH kinetics, no perfect criterion exists for terminating an operation. The more stringent the criteria, the higher the number of unnecessary explorations that will occur. We now recognize that a drop in intraoperative PTH level exceeding 50% from the preexcision value does not result in an adequate cure rate, and we recommend continued exploration if the final PTH exceeds 65 pg/mL. In addition, current thinking suggests that patients with values exceeding 40 pg/mL may have hyperplasia. It is almost always better to perform a bilateral exploration than to return at a later date to face a scarred operative field, where finding the diseased gland is more challenging and could result in greater complications.

The nature of renal hyperparathyroidism mandates bilateral exploration. A hyperplastic process involving all the glands is generally present even when a localization study identifies only one or two abnormal glands, and hyperplastic glands can vary greatly in size. Postsurgical hypercalcemia should be expected in most cases of renal hyperparathyroidism. Monitor patients who have clinically significant bone disease with special vigilance.

CONCLUSION

These workflows synthesize the best evidence currently available about caring for patients with thyroid nodules and PHPT and represent an attempt to standardize the care of patients with thyroid and parathyroid diseases. The evidence-based decision points and workflows presented here support an initiative of specialty care redesign to provide consistency in delivery of care and outcomes for our patient population.

Disclosure Statement

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How to Cite this Article


References


The Third View

The practical surgical question as to whether the cretinous symptoms following thyroidectomy are due to—1) Chronic asphyxia, as believed by Kocher; 2) Injury of the sympathetic and other nerve trunks; 3) Arrest of function of the thyroid gland; is almost settled in favor of the third view, and with it also the pathology of Myxoedema.

— Sir Victor Alexander Haden Horsley, FRS, 1857-1916, English neurosurgeon and neuroscientist
The Truth about Truth-Telling in American Medicine: A Brief History

Bryan Sisk, MD; Richard Frankel, PhD; Eric Kodish, MD; J Harry Isaacson, MD

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ABSTRACT

Transparency has become an ethical cornerstone of American medicine. Today, patients have the right to know their health information, and physicians are obliged to provide it. It is expected that patients will be informed of their medical condition regardless of the severity or prognosis. This ethos of transparency is ingrained in modern trainees from the first day of medical school onward. However, for most of American history, the intentional withholding of information was the accepted norm in medical practice. It was not until 1979 that a majority of physicians reported disclosing cancer diagnoses to their patients. To appreciate the current state of the physician-patient relationship, it is important to understand how physician-patient communication has developed over time and the forces that led to these changes. In this article, we trace the ethics and associated practices of truth-telling during the past two centuries, and outline the many pressures that influenced physician behavior during that time period. We conclude that the history of disclosure is not yet finished, as physicians still struggle to find the best way to share difficult information without causing undue harm to their patients.

A HISTORY OF DISCLOSURE IN MEDICINE

Pre-20th Century Communication

Disclosing bad news to patients has challenged physicians since the early days of American medicine. In the 19th century, physicians often made medical decisions on behalf of their patients, in what they perceived to be the patient’s best interest. This paternalistic approach led most physicians to disclose only information that they believed would not harm the patient, as embodied in the 1847 Code of Ethics of the newly founded American Medical Association:

A physician should not be forward to make gloomy prognostications, because they savour of empiricism. … But he should not fail, on proper occasions, to give to the friends of the patient timely notice of danger, when it really occurs; and even to the patient himself, if absolutely necessary. … For, the physician should be the minister of hope and comfort to the sick.¹

On one level, paternalism in this period was rooted in benevolent concern for the patient’s well-being. As further stated in the Code: “The life of a sick person can be shortened, not only by the acts but also by the words or the manner of a physician. It is, therefore, a sacred duty to guard himself carefully in this respect, and to avoid all things which have a tendency to discourage the patient and to depress his spirits.”² This ethical standard followed directly from Thomas Percival’s 1803 treatise on medical ethics: “For the physician should be the minister of hope and comfort to the sick that by such cordials to the drooping spirit he may smooth the bed of death, revive expiring life, and counteract the depressing influence of those maladies which rob the philosopher of fortitude, and the Christian consolation.”³ In his writings, Percival also discussed whether a “falsehood may lose the essence of lying, and become even praiseworthy, when the adherence to truth is incompatible with the practice of some other virtue of still higher obligation.”⁴

At the same time, there were less benevolent incentives for physicians to occasionally refrain from honesty. American medicine in the mid-19th century was poorly organized and had limited authority in society. Physicians were the product of a fractured apprenticeship model with no oversight to ensure quality of training, which led to an increase in the number of physicians, many of them poorly trained, while professional competition also loomed from other medical sects, including Thomsonians, eclectics, and homeopaths.⁵ Short, the mid-19th century medical market was saturated with physicians.

For physicians to succeed, ensuring an ample number of patients was paramount, and honesty occasionally took a backseat. In his 1888 manual for success as a physician, DW Cathell intricately laid out methods by which physicians could create respectable images of themselves while also protecting their claim to patient populations.⁶ Neuhauer⁷ observed, “His book was so popular that it was in its 10th edition in 1892, last revised in 1922 and republished finally in 1932.” In addition to meticulously describing the type of clothing to wear and the medical paraphernalia to display in the office, Cathell also encouraged physicians to withhold information to prevent patients from becoming medically self-sufficient. For example, he encouraged physicians to inscribe Latinate terms on medication vials to conceal their ingredients. He also believed that physicians should “avoid giving self-sufficient people therapeutic points that they can thereafter resort to. … It is not your duty to cheat either yourself or the other physicians out of legitimate practice by supplying this person and that with a word-of-mouth pharmacopoeia for general use.”⁸ For both benevolent and self-serving reasons, honesty was lower on the physician’s list of priorities.

THE DAWN OF THE 20TH CENTURY

As the 20th century dawned, the physician’s standing in society began to rise, in part because medical science was growing more sophisticated and physicians were becoming indispensable. “Every man, it became clear, could not be his own physician.”⁹ This enhancement of status furthered a social divide between physicians and laymen, as evidenced by an 1898 excerpt from the Philadelphia Medical Journal:

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The cause for concern was Child Protection. In 1964, a surgeon transplanted this story quickly. By 1966, Henry Beecher published a result that a vast majority of patients wanted to know the truth. Physicians informed participants that they were restraining a physician in many cases from disclosing the truth to his patient, but the almost certainty that such a disclosure will be the greatest obstacle to a cure. In 1909, William Osler declared, “It is a hard matter … to tell a patient that he is past all hope. As Sir Thomas Browne says: ‘It is the hardest stone you can throw at a man to tell him that he is at the end of his tether.’” The reasoning was simple. “With many hospital patients once we gain their confidence and inspire them with hope, the battle is won.”

**MID-20TH CENTURY AND BEYOND**

Although there were some opponents of benevolent deception, physician surveys during the first half of the 20th century consistently demonstrated a belief in nondisclosure. As recently as 1961, 90% of physicians preferred not to disclose cancer diagnoses to patients. This was despite the results of a 1950 study showing that a vast majority of patients wanted to know the truth. On the basis of his observations in a veterans’ hospital in 1966, Glaser proposed several factors that influenced the physicians’ approaches to disclosure:

- Few doctors get to know each terminal patient well enough to judge his desire for disclosure or his capacity to withstand the shock of disclosure … Some doctors simply feel unable to handle themselves well enough during disclosure … Others do not tell because they did not want the patient to “lean” on them for emotional support, or because they simply wish to preserve peace on the ward by preventing a scene.
- During the 1960s, tremors of change began rumbling through American society. After the assassination of President John Kennedy, President Lyndon Johnson “sponsored the largest reform agenda since Roosevelt’s New Deal.” From 1963 through 1966, Johnson undertook a major reform agenda that touched on many aspects of society. With the expansion of Social Security to include Medicare and Medicaid, as well as the passage of the Food Stamp Act, Housing and Urban Development Act, Child Protection Act, and the Child Nutrition Act, the government assumed additional responsibility for the safety and well-being of its citizens. The 1960s also marked the start of a great transformation in American social norms as underrepresented groups challenged the status quo. The Civil Rights Movement pushed for passage of the Civil Rights Bill and the Voting Rights Act. The feminist movement demanded more autonomous control of women’s reproductive health and a shift in society’s view of women. The 1960s also marked the beginning of a psychedelic culture of drug experimentation, the sexual revolution, and the countercultural “hippie” movement. It was not uncommon for people to wear buttons stating “Question Authority.” As society was redefining itself, “a new wave of individualism was breaking over the Western world—most marked and most advanced in the United States.”

Long-held social norms were being turned upside down in all segments of society, including the physician-patient relationship.

Owing in part to several well-publicized controversies, there was a new call for protection from the medical establishment. In 1963, it was revealed that researchers in New York had injected humans with live cancer cells without consent. In 1964, a surgeon transplanted chimpanzee kidneys into patients with renal failure without medical approval from the hospital. By 1966, Henry Beecher published a special report highlighting and summarizing the widespread presence of “troubling practices” in clinical research.

Perhaps most notably, the ethical concerns of the Tuskegee Syphilis Study came to light in July 1972. This study, initiated in 1932, was a "long-term evaluation of the effect of untreated syphilis in the male Negro." Physicians informed participants that they were being treated for “bad blood” but not specifically syphilis. When the study began, treatments for syphilis were harsh and minimally effective. However, penicillin was established as an effective treatment and became readily available by the late 1940s. Yet 20 years later, only 33% of participants had received curative therapy, and many had died of complications from syphilis. This story quickly became front-page news in the *New York Times* on July 25, 1972 with the headline “Syphilis Victims in US Study Went Untreated for 40 Years.” Other headlines in the following weeks included “A Shocking Medical Experiment,” “Humans as Guinea Pigs,” and “A Violation of Human Dignity.” The fallout from this expose exacerbated the adversarial relationship between medicine and society, especially in the African American community.

Twenty years earlier in 1951, an African American woman named Henrietta Lacks was diagnosed with cervical cancer in Baltimore, MD. When the physicians diagnosed her with cancer, they took a specimen from her cervix without her knowledge or consent. She died soon after, but her cells lived on as the HeLa cell line, using the first 2 letters of her first and last name. These cells had an enormous impact on public health and the advancement of science, but the family was not informed until the 1970s, 20 years after Ms Lacks’ death. Though this was not as widely publicized as the Tuskegee scandal, it provides yet another example of troubling research practices at that time.

As controversies grew, new protections for patients and research subjects were established. In 1962, the Senate passed the Kefauver-Harris Drug Amendments, requiring for the first time that drug manufacturers "prove to FDA the effectiveness of their products before marketing them." That same year, President Kennedy proclaimed a “Consumer Bill of Rights,” which included “the right to safety, the right to be informed, the right to choose, and the right to be heard.” In 1964, the World Medical Association published
the Declaration of Helsinki, an international code of research ethics affirming that the physician’s first duty is to the research subject.\textsuperscript{33} Simultaneously, informed consent law was growing in strength, mandating honest communication between physicians and patients under threat of legal liability. Also, Dame Cicely Saunders introduced the concept of hospice and palliative care to the US in the 1960s, further encouraging discussions between physician and patient about death. By 1973, the American Hospital Association created “A Patient’s Bill of Rights,” stating that “The patient has the right to and is encouraged to obtain from physicians and their direct caregivers relevant, current, and understandable information concerning diagnosis, treatment, and prognosis.”\textsuperscript{34}

Responding to these pressures, physicians began calling for more transparency with patients. Nahum noted in 1963, “The responsible physician should have no hesitation in frankly but tactfully and at the correct time answering questions asked by the patient,” with the goal of being “truthful with the patient while at the same time avoiding a major emotional upset.” However, Nahum moderated this approach with a list of stipulations. “In patients judged to be unstable emotionally, the exact information should be withheld.” Additionally, “if he does not [ask for specific information], then the doctor’s legal and moral obligations have been discharged for such a person … is aware of his trouble but does not wish to have it put into words.”\textsuperscript{35} An article from 1974 pushed disclosure further, concluding that several factors could “justify me in modifying my primary approach and making the patient or his relatives, directly or indirectly, aware of the diagnosis and perhaps even of the prognosis, grave as it may be.”\textsuperscript{36} In 1969, Kubler-Ross\textsuperscript{37} declared, “The question should not be ‘Should we tell…?’ but rather ‘How do I share this with my patient?’” The medical profession was transitioning from paternalism to a partnership-based medical ethics where patients participated in the decision-making process. In 1979, a landmark study using the same research questionnaire from 1961 showed that more than 90% of a new cohort of physicians preferred disclosing cancer diagnoses, a complete reversal from 18 years prior.\textsuperscript{38}

The progressive movement of the 1960s and 1970s pushed physicians toward more open and transparent communication with patients. This transition was reinforced by social pressure, legal mandates, and large numbers of young, progressive physicians entering the field. In the midst of these changes, Family Practice (now Family Medicine) developed as a new field, with an emphasis on the individual patient and his or her social environment. This trend toward transparency has continued over the ensuing decades, reinforced in part by developments in the field of bioethics. The 1979 “Belmont Report” established the fundamental ethical principles of research on human subjects, including respect for persons, beneficence, and justice.\textsuperscript{39} These principles have served as the foundation for current research practices.

Advancements in research on physician-patient communication have also supported the trend toward disclosure. In 1987, Menahem\textsuperscript{40} showed that communication in a partnership model was more effective than either a laissez-faire or physician-dominated model. In 1995, Girgis and Sanson-Fisher\textsuperscript{41} published consensus guidelines for giving bad news, which have provided a basis for discussion and improvement of communication in medicine.

Standards of care now include an explicit focus on disclosure and communication skills. In 2013, the Institute of Medicine published a monograph on delivering high-quality cancer care that focused an entire chapter on evidence for best practices in communicating with cancer patients.\textsuperscript{42} The National Cancer Institute produced an entire monograph on patient-centered communication in cancer care, devoting four of its six chapters to key communication skills including delivery of difficult news.\textsuperscript{43} Most recently in 2014, the Institute of Medicine issued a new report that focused on end-of-life care in America, much of which centered on ways to improve the physician-patient dialogue about bad news.\textsuperscript{44} Medical students and residents are now routinely trained in how to effectively communicate in challenging situations, and patients expect transparency in their interactions with physicians.

However, communication in medicine is still far from perfect. For example, a recent report from the Alzheimer’s Association in 2015 showed that less than half of patients with Alzheimer’s disease or their family members had knowledge of their loved one’s or their own diagnosis.\textsuperscript{45} One physician noted in a media interview following the report, “It’s difficult to disclose a diagnosis of a fatal brain disease in just a few minutes.”\textsuperscript{46} In parallel with these changes, the American Medical Association Code of Ethics has evolved substantially since 1847, with its current form stating “The patient has the right to receive information from physicians and to discuss the benefits, risks, and costs of appropriate treatment alternatives.”\textsuperscript{47}

Reinforcing these changes, the medical record has also evolved from a tool solely for physicians to a new means of communicating with patients. In 1973, Shenkin and Warner\textsuperscript{48} proposed that “legislation be passed to require that a complete and unexpurgated copy of all medical records … be issued routinely and automatically to patients as soon as the services provided are recorded.” This article furthered the belief that patients are owners of their medical information. In 1991, McLaren\textsuperscript{49} proposed that medical records should not only be available, but also be understandable to patients. The Health Insurance Portability and Accountability Act\textsuperscript{50} was passed in 1996, creating new protections for patient confidentiality by restricting disclosure of medical information without the patient’s consent. This act reinforced the patient’s authority over his or her health information, while also mandating that physicians respect their patients’ confidentiality.

Communication in medicine has undergone dramatic changes during the past 170 years. Where once physicians withheld information for the benefit of the patient, it is now clearly recognized that patients have a right to know the truth. The medical profession has responded to both internal and external pressures and developed a standard of care based on honesty and patient-centered communication. However, many uncertainties remain. How much disclosure is enough? How much is too much? Can we cause harm by telling too much or in the wrong way? Is there ever a role for benevolent deception? Should physicians be the gatekeepers of medical information? How will the recent emphasis on shared medical records affect this relationship? Currently, several organizations are actively promoting sharing of medical data and notes with patients.\textsuperscript{51} Some current-day patients might have their test results available electronically before ever speaking with their physicians.
Though we can certainly say that “patients ought to know,” it is difficult to know exactly what they ought to know, and how to best share this information. These are critical questions that are worthy of study. The truth about truth-telling is that it is an unfinished history that continues to evolve. Physicians and patients will undoubtedly need to partner to develop the next chapter in this story.

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2. Percival T. Medical ethics or, a code of institutes and precepts, adapted to the professional conduct of physicians and surgeons: to which is added an appendix. 3rd ed. Oxford, United Kingdom: Oxford University Press; 1849. p 48-9, 135.
ABSTRACT

Renal hyperparathyroidism (rHPT) is a common complication of chronic kidney disease characterized by elevated parathyroid hormone levels secondary to derangements in the homeostasis of calcium, phosphate, and vitamin D. Patients with rHPT experience increased rates of cardiovascular problems and bone disease. The Kidney Disease: Improving Global Outcomes guidelines recommend that screening and management of rHPT be initiated for all patients with chronic kidney disease stage 3 (estimated glomerular filtration rate, < 60 mL/min/1.73 m2). Since the 1990s, improving medical management with vitamin D analogs, phosphate binders, and calcimimetic drugs has expanded the treatment options for patients with rHPT, but some patients still require a parathyroidectomy to mitigate the sequelae of this challenging disease.

BACKGROUND

In the US, chronic kidney disease (CKD) affects 14% of the population, including approximately 660,000 patients with end-stage renal disease (ESRD) who are dialysis-dependent. Renal hyperparathyroidism (rHPT) is a common complication of CKD characterized by alterations in the homeostasis of calcium, phosphorus, and vitamin D. rHPT is associated with increased cardiovascular morbidity and mortality and has a significant economic burden on the US health care system.

rHPT is classically divided into 2 types on the basis of the patient’s serum calcium level. Secondary hyperparathyroidism (2° HPT) is the elevation of parathyroid hormone (PTH) in response to hypocalcemia induced by phosphate retention and reduced calcitriol synthesis as a consequence of reduced renal function. In 2° HPT, all the parathyroid glands become enlarged owing to parathyroid hyperplasia. Because 2° HPT is a compensatory mechanism of the parathyroid glands, it commonly resolves with normalization of calcium and phosphorus homeostasis (eg, renal transplantation). Tertiary hyperparathyroidism (3° HPT) is seen when a patient with longstanding 2° HPT develops autonomous PTH secretion, often associated with hypercalcemia. This is observed in up to 30% of patients with ESRD, who then undergo renal transplant. 3° HPT is classically thought to have come from parathyroid hyperplasia, but some studies have suggested that up to 20% of patients may have single or double adenomas.

Since the 1990s, improving medical management with vitamin D analogs, phosphate binders, and calcimimetic drugs has expanded the treatment options for patients with rHPT, but parathyroidectomy remains necessary for many patients.

NORMAL CALCIUM AND PHOSPHORUS HOMEOSTASIS

Calcium and phosphorus homeostasis is maintained through a complex relationship between the bones, intestine, kidneys, and parathyroid glands. PTH is probably the most important regulator of calcium metabolism and functions primarily via 3 mechanisms:

1. PTH is thought to stimulate PTH receptors mainly on osteoblasts, which then, through multiple cell-to-cell mechanisms, stimulate osteoclast formation and bone resorption, leading to increased serum calcium and phosphorus levels.
2. PTH activates 1-α-hydroxylase in the kidney, which catalyzes the conversion of nonactive 25-hydroxy (25-OH) vitamin D to activated 1,25 dihydroxy (1,25-OH) vitamin D. This leads to increased absorption of calcium and phosphorus in the gut.
3. PTH increases reabsorption of calcium and decreases reabsorption of phosphorus in the kidney.

Recently, there has been much interest in the role of fibroblast growth factor 23 (FGF-23), a protein secreted by bone in response to hyperphosphatemia, which functions primarily in maintaining phosphorus homeostasis. FGF-23 stimulates phosphorus excretion in the kidney mainly through reduced action of sodium-phosphate co-transporter in the proximal tubule. It also decreases 1-α-hydroxylase activity, leading to reduced 1,25-OH vitamin D levels. In CKD, FGF-23 levels progressively rise and are initially thought to be beneficial, given the phosphaturic effects. However, increasing FGF levels are also associated with increased cardiovascular mortality in patients with CKD.

PATHOGENESIS

The pathogenesis of rHPT is complex and incompletely understood (Figure 1). An increase in PTH levels typically develops when the glomerular filtration rate (GFR) drops below 60 mL/min/1.73 m2. Abnormalities in serum levels of phosphorus and calcium tend to occur much later in the course of CKD (typically when the GFR drops below 40 mL/min/1.73 m2). Initially, the elevated PTH levels serve to increase renal phosphorus excretion. However, as the GFR declines further, serum phosphorus levels start to rise and induce hypocalcemia by binding bioavailable calcium as CaHPO4, which indirectly leads to a further rise in PTH production. CKD also leads to decreased activity of 1-α-hydroxylase, thereby decreasing 1,25-OH vitamin D. A lack of 1,25-OH vitamin D inhibits gastrointestinal absorption of calcium and also directly stimulates the parathyroid glands.
In CKD, chronic stimulation of the parathyroid glands triggers diffuse polyclonal hyperplasia. As the chronic stimulation of CKD continues, the parathyroids begin to develop monoclonal nodules within a background of parathyroid hyperplasia. These nodules demonstrate increased resistance to vitamin D and calcimimetic medications and may be the etiology of the loss of negative feedback seen in 3° HPT.18,19

**CLINICAL MANIFESTATIONS**

The two most important sequelae of rHPT are 1) renal osteodystrophy and 2) cardiovascular disease. Recognizing that the bone and cardiovascular complications seen in CKD are manifestations of a broader interrelated syndrome, the National Kidney Foundation initiated the term “CKD-mineral and bone disorder” to describe the complex pathophysiology of the calcium, phosphorus, and PTH derangements seen in CKD. The paradigm of “think beyond the bones” is emphasized to bring early attention to the complications of rHPT in an attempt to improve morbidity and mortality.20

Renal osteodystrophy refers to a group of bone disorders caused by dysregulation of mineral metabolism in CKD, including osteomalacia, adynamic bone disease, and ostitis fibrosa cystica. Osteomalacia is a state of low bone turnover leading to poor mineralization. Adynamic bone disease is also a low-turnover pathology with normal mineralization that probably results from a low PTH state. The incidence of adynamic bone disease increasing is likely secondary to PTH suppression from vitamin D agents, calcimimetics, and phosphate binders.14,21 Osteitis fibrosis cystica is a high-turnover bone disease that stems from elevated PTH concentrations stimulating osteoclast activity, bone breakdown, and resorption. This can lead to subsequent bone pain and fractures.22 With longstanding bone resorption, patients may develop localized regions of bone loss that are then replaced by fibrous tissue, resulting in a brown tumor. These “tumors” appear as well-defined, lytic lesions on radiograph and may be mistaken for metastasis (Figure 2).

The derangements in calcium and phosphate that result from rHPT may accelerate vascular calcification, including coronary artery calcification. Calcification of the cardiovascular tissue can affect the myocardium, atrial-ventricular conduction, and valvular function.23 Furthermore, coronary calcification may put patients at an increased risk of cardiovascular events and death.24 It is difficult to distinguish the unique detrimental effects of rHPT from those of hyperphosphatemia, which is also associated with cardiovascular disease in patients with CKD. Some studies have suggested that FGF-23 may induce arterial smooth muscle myocytes to change into osteoblast-like cells that lead to vascular calcification.17 Moderate to severe hyperparathyroidism (PTH concentrations ≥ 600 pg/mL) may increase risk of cardiovascular death,7 though the causality of this association is debatable.

There is an association between CKD and medial calcification in the arterioles of the skin and soft tissue leading to vascular compromise and ulceration. This constellation of complications was formerly called calciphylaxis but is now termed calcific uremic arteriolopathy, and it is associated with an eight-fold increase in mortality rate.25 Tumoral calcinosis is an uncommon complication of longstanding HPT and is classically associated with high serum levels of calcium and phosphorus. In tumoral calcinosis, the patient can develop soft-tissue calcium deposits that can appear to be soft-tissue malignant tumors on imaging studies (Figure 3).26
The Kidney Disease: Improving Global Outcomes work group recommends screening and management of rHPT be initiated for all patients with CKD stage 3 (estimated GFR < 60 mL/min). The frequency of monitoring for serum calcium, phosphorus, and PTH are listed in Table 1.

The initial management of rHPT follows a stepwise approach with the goal of optimizing serum phosphorus and calcium levels through a combination of a low phosphorus diet, phosphate binders, vitamin D derivatives, and calcimetic medications.

**Low Phosphorus Diet**

A low phosphorus diet is recommended for patients with CKD and 2° HPT with hyperphosphatemia. Dietary restriction of phosphorus in patients without elevated levels of phosphorus, but with elevated PTH levels only, is controversial. Unfortunately, this is very difficult given the high prevalence of phosphorus in Western diets. Dietary phosphorus comes from 2 sources: 1) protein-rich food groups such as meat and milk; and 2) phosphorus additives, which are used to process meats and cheeses. Phosphorus used as an additive is often only implied in the ingredients list, and not individually reported on the food label. Therefore, the true amount of phosphorus contained in a product may be underestimated. Patient education regarding this distinction may help them avoid phosphorous-rich foods.

The National Kidney Foundation previously recommended that patients with CKD restrict dietary phosphorus to 800 to 1000 mg/day. However, it should be noted that there is a paucity of good quality data regarding dietary phosphorus restriction and outcomes in CKD.

**Phosphate Binders**

Because of the difficulty in maintaining a low phosphorus diet, phosphate binders are usually an essential part of medical therapy for patients with CKD. Phosphate binders have been shown to decrease serum phosphorous and PTH levels. Isakov et al. reported that treatment with phosphate binders was independently associated with decreased mortality when compared with no treatment.

Several phosphate binders are available, including aluminum hydroxide, calcium salts, sevelamer hydrochloride, sevelamer carbonate, and lanthanum carbonate. In general, aluminum hydroxide should be limited to a short period because of the risk of aluminum toxicity. Newer agents such as lanthanum have unknown long-term effects of bone deposition. Iron-based binders such as sucroferric oxyhydroxide are also available to lower serum phosphorous. The Kidney Disease Outcomes Quality Initiative recommends for patients with CKD stages 3 and 4, that phosphate binders be used if phosphorus levels cannot be controlled within the target range despite dietary phosphorus restriction. In patients who remain hyperphosphatemic despite initiation of a single phosphate binder, combination therapy can be used. It is interesting to note that lanthanum, being a heavy metal, commonly shows up as radiopaque in noncontrast radiologic studies of the gastrointestinal tract.

**Vitamin D Analogs**

As described above, 1,25-OH vitamin D deficiency is a major mechanism of rHPT, and vitamin D replacement has been shown to effectively suppress PTH secretion. Several forms of vitamin D are available, including ergocalciferol (which requires activation in the kidney to 1,25-OH vitamin D), as well as activated forms such as calcitriol, paricalcitol, and doxercalciferol. Although observational studies have suggested improved survival in patients treated with vitamin D analogs, a 2007 meta-analysis showed no difference in mortality, bone pain, vascular disease, or rate of parathyroidectomy when comparing patients on vitamin D analogs versus those not taking vitamin D.

The Kidney Disease: Improving Global Outcomes work group recommends that in patients with CKD stages 3 to 5 (not on dialysis), attempts to control hyperphosphatemia, hypocalcemia,
and vitamin D deficiency be made first. If PTH remains elevated or is progressively rising, treatment with calcitriol or vitamin D analogs is suggested. Close attention must be paid to serum levels of calcium and phosphorus, which if greater than 10.2 mg/dL and 4.6 mg/dL, respectively, may warrant modification in therapy. In patients with CKD stage 5 on dialysis, active vitamin D sterols (such as calcitriol, paricalcitol, or doxercalciferol) are used to control hyperparathyroidism.

Calcimimetics
Cinacalcet HCL is a calcimimetic agent that exhibits allosteric modulation of the calcium receptor on the parathyroid gland, increasing sensitivity to extracellular calcium and thereby suppressing PTH secretion. The effectiveness of cinacalcet in lowering PTH concentrations in ESRD patients has been demonstrated in multiple studies. Combined analysis of these studies showed that cinacalcet decreases rates of parathyroidectomy, fractures, and cardiovascular hospitalization. Patients receiving cinacalcet treatment rather than placebo also have improvements in self-reported physical function and less bodily pain.

In 2012, the Evaluation of Cinacalcet Hydrochloride Therapy to Lower Cardiovascular Events Trial randomized patients with ESRD and moderate to severe HPT to cinacalcet or placebo and found that cinacalcet did not significantly increase overall or cardiovascular mortality. A recent Cochrane review corroborated these findings but did find that patients taking cinacalcet had a significant increase in the rate of nausea, vomiting, and hypocalcemia, suggesting that the potential risks associated with cinacalcet use in ESRD patients may outweigh the benefits.

These clinical uncertainties further bring into question the costs of cinacalcet treatment. Currently the US spends $260 million annually on cinacalcet, accounting for the largest single drug cost of minimizing the period of postoperative hypoparathyroidism and therefore likely shortens a patient’s hospital course, but it requires reoperation in the neck in the event of a recurrence. This may be associated with an increased risk of injury to the recurrent laryngeal nerve. All 3 operations are accepted surgical treatment options for rHPT, and each is associated with specific advantages and disadvantages.

Successful parathyroidectomy can dramatically improve symptoms, including bone pain, arthralgia, muscle weakness, and psychological disturbances. Biopsy-proven changes in trabecular bone mineral content and accelerated bone formation have been demonstrated within 1 week after surgery. Parathyroidectomy is associated with a 30-day postoperative mortality of 3.1% throughout the US. Other risks of surgery include recurrent laryngeal nerve injury (< 2%) and hematoma requiring re-exploration (< 1%).

Several studies have suggested a survival benefit from parathyroidectomy in the treatment of rHPT, including significant reductions in the incidence of major cardiovascular events and all-cause mortality. Long-term relative risks of death are reduced by 10% to 15%, and long-term survival is improved compared with those not undergoing surgery. Parathyroidectomy is effective in improving hemoglobin levels for ESRD-associated anemia, and it has beneficial effects on the immune system and overall nutrition. Parathyroidectomy has also been shown to be more cost-effective than cinacalcet in nearly all dialysis patient subgroups, with the exception of those with high operative mortality risk, patients remaining on dialysis for less than 7 months, and/or individuals expecting kidney transplant quickly.

### Indications for Consideration for Parathyroidectomy

- Medical management of rHPT > 6 months with
  - Hypercalcemia or hyperphosphatemia
  - PTH > 800 pg/mL
- Calciphylaxis with documented elevated PTH levels
- Osteoporosis (T-score > 2.5 SD below mean), pathologic bone fracture
- Symptoms/signs
  - Pruritus
  - Bone pain
  - Severe vascular calcifications
  - Myopathy
- PTH = parathyroid hormone; rHPT = renal hyperparathyroidism; SD = standard deviation.
CONCLUSION
rHPT is a common complication of CKD that stems from hypercalcemia, reduced bioactivity of vitamin D, and elevated levels of FGF-23. rHPT leads to a host of bone and cardiovascular problems that ultimately can cause fractures, decreased quality of life, and an increased risk of death. A range of nonsurgical options are available, including initiating a low phosphorus diet, phosphate binders, vitamin D analogs, and calcimimetic agents, but unfortunately the data on the efficacy of these treatments at improving overall and cardiovascular mortality are mixed. Some patients require parathyroidectomy, which may improve symptoms and reduce cardiovascular and overall mortality, but it carries the expected risks of surgery.

Author Contributions
Noah K Yuen, MD, provided study conception and design and participated in analysis and interpretation of data and writing the manuscript. Shubha Ananthakrishnan, MD, participated in writing the manuscript and in critical revision of the manuscript. Michael J Campbell, MD, provided study conception and design and participated in writing the manuscript and in critical revision of the manuscript. Shubha Ananthakrishnan, MD, provided study conception and design and participated in writing the manuscript and in critical revision of the manuscript.

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A Small Organ Hardly as Big as a Hemp Seed

About three years ago I found on the thyroid gland … a small organ, hardly as big as a hemp seed, which was enclosed in the same connective tissue capsule as the thyroid, but could be distinguished therefrom by a lighter color. A superficial examination revealed an organ of totally different structure from that of the thyroid, and with a very rich vascularity. … I suggest the use of the name Glandulae parathyreoidea; a name in which the characteristic of being bye-glands to the thyroid is expressed.

— Ivar Victor Sandström, 1852-1889, Swedish physician
Recurrence of Epithelioid Hemangioendothelioma during Pregnancy: Case Report and Systematic Review

Michael McCulloch, LAc, MPH, PhD; Michael Russin, MD; Arian Nachat, MD

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ABSTRACT

Introduction: Epithelioid hemangioendothelioma (EHE) is a family of blood vessel tumors originating in blood vessels, bone, brain, kidney, liver, and lung. EHE is more common in women, and chemotherapy, radiation, and surgery have brought few successes.

Case presentation: We present a case of a 28-year-old woman whose EHE recurred during pregnancy, suggesting hormonal involvement. We conducted a systematic review to provide analysis and interpretation of the potential significance of her disease recurring, with fatal outcome, during pregnancy.

Discussion: Very little research has explored the use of individual hormonal markers. Strongly positive expression of placenta growth factor (PIGF) and 17-beta estradiol receptors have been reported. Expression of PIGF is noteworthy in our case, in that our patient’s disease quickly and dramatically flared on the 25th week of pregnancy, near the peak in maternal PIGF production. PIGF binds to vascular endothelial growth factor-1 (VEGF-1), and PIGF may accelerate VEGF-induced angiogenesis. Taken together, these factors may explain our patient’s EHE recurrence and rapid flare-up during pregnancy. Treatment of EHE with VEGF inhibition, potentially in combination with other antiangiogenic and tumor-inhibiting therapies such as lenalidomide, thalidomide, sorafenib, and sunitinib, may also hold promise.

INTRODUCTION

Epithelioid hemangioendothelioma (EHE) is a family of vascular tumors, originating in the endothelium and sharing clinical characteristics with both angiosarcoma and benign hemangiomia. EHE was first identified in 1982 and is extremely rare, with an incidence rate of 0.1 per 100,000, and fewer than 200 cases ever reported in the medical literature. Because there is limited research on prognosis, a layperson registry has been established. The International Hemangioendothelioma, Epithelioid Hemangioendothelioma, and Related Vascular Disorders Support Group has tracked more than 260 patients.

The clinical presentation of EHE is quite varied; it can originate in bone, brain, kidney, liver, lung, and vascular and other soft tissues. Diagnosis is sometimes delayed owing to uncertainty about correct pathologic classification, which can significantly worsen prognosis. Little is known about prognostic factors for patients with EHE, although recent work has identified genetic alterations involving activation of the ROS1 receptor tyrosine kinase, which for other cancers has led to effective therapies working through ROS1 inhibition.

Two case series have described the prognosis of patients with hepatic EHE. In a series from China (N = 33), survival was longer in patients younger than age 47 years (hazard ratio, 7.0; p = 0.035), in those without symptoms (hazard ratio, 86.5; p = 0.001), and in those with serum cancer antigen 19-9 below 37 units/mL (hazard ratio, 5.0; p = 0.018). In a series from the United Kingdom (N = 50), patients with bilateral hepatic disease had shorter median survival (51%) compared with those with unilateral disease (81%), although the study size was too small to show a significant difference (p = 0.1). There was additionally nonsignificant lower 5-year survival in metastatic (69%) compared with localized (78.3%) disease (p = 0.7). Treatment with any chemotherapy decreased 5-year survival, compared with no chemotherapy (43.6% vs 82.9%; p = 0.02).

Diagnostic approaches to EHE include computed tomography (CT), magnetic resonance imaging, CT and magnetic resonance imaging, and serial bone scintigraphy. (18)F-fluorodeoxyglucose positron emission tomography with strong (18)F-fluorodeoxyglucose uptake has been used but is limited by lack of correlation between lesion size and maximum standardized uptake value.

Little is known about efficacy of therapy because the low incidence of EHE precludes conduct of human clinical trials. Options currently include chemotherapy, radiation, hormone therapy, thrombo-embolization, and surgery, although most do not change the usually poor prognosis of a diagnosis with EHE. In patients with primary hepatic EHE, overall survival is no different following liver resection or transcatheter arterial chemoembolization (p = 0.50). Although patients with hepatic EHE have longer median survival compared with those with other hepatic vascular tumors, in these patients surgical resection does not improve survival.

Development and testing of newer therapies based on vascular endothelial growth factor (VEGF) inhibition is supported by recent studies showing positive expression of VEGF receptor in biopsied lesions. Additional case reports of success with lenalidomide, thalidomide, sorafenib (possessing both
antiangiogenic and antiproliferative activity),\textsuperscript{18} and sunitinib\textsuperscript{19} suggest other targeted molecular therapies may also hold promise.

The current case report documents diagnosis of recurrent EHE in a pregnant woman and discusses the case in the context of a systematic review of the current literature. This report was prepared in accordance with the CARE (CAse REport) guidelines.\textsuperscript{20}

**CASE PRESENTATION**

We report a case of a 28-year-old woman originally diagnosed with EHE in 2002, at age 18 years. CT-guided biopsy of 1 of her liver lesions revealed EHE based on hematoxylin/eosin and immunohistochemical stains (Figures 1-4). Repeated CT of her chest, abdomen, and pelvis 3 months later showed progression of disease. At that time she underwent 6 cycles of carboplatin and etoposide with stabilization of disease; however, significant chest pain remained, requiring high doses of opiates. She received 1 dose of interferon, which was not tolerated. The patient was then followed up with serial CT scan showing stable disease through 2011 (Figures 5 and 6).

In 2012, the patient presented to the Emergency Department with chest pain and in acute respiratory distress. A posterior-anterior/lateral chest radiograph revealed multiple pulmonary nodules bilaterally, confirmed as “innumerable” by chest CT, along with bulky mediastinal adenopathy and multiple liver lesions consistent with metastatic disease (Figure 7).

In mid-2012, the patient presented with diffuse joint pain 6 months into her first pregnancy, and went into labor at 25 weeks. The baby was delivered and died 8 days later. The patient's pain then continued to escalate and she developed severe cough. Repeat CT scan of her chest, abdomen, and pelvis revealed significant progression of disease, especially in the lungs and mediastinum. Biopsy of mediastinal adenopathy confirmed recurrent EHE, and the diffuse nature of disease precluded surgery.

The patient’s diffuse joint and bone pain continued to worsen, resulting in hospitalization for pain control. Bone scan was consistent with hypertrophic osteoarthropathy. During this time her respiratory status continued to worsen: chest CT revealed compression of the right upper lobe bronchus and right pleural effusion. A right-sided chest tube was inserted with drainage of a large amount of pleural fluid and palliative radiation to the mediastinal adenopathy was started. Unfortunately the patient’s respiratory status continued to decline from progressive disease as well as pneumonia. She was intubated; her condition continued to decline; she was placed on comfort measures, and she subsequently died.
A timeline showing progression of the case is provided in Figure 8.

**DISCUSSION**

Despite numerous publications, EHE remains a little-understood disease of poor prognosis. In the case of localized disease, prompt surgical resection appears to confer a survival advantage. Improvements in early clinical identification of suspected lesions may be accelerated by further research on the integration of tumor marker and/or hormonal testing.

In Table 1 we present results of a systematic search of treatment outcomes published since January 2011. Tumor marker expression in EHE has been reported for endothelial markers (CD31, CD34, and factor VIII-related antigen), VEGF and VEGF receptor 2, and strong expression of CD31 and vimentin. Errani et al reported that WWTR1-CAMTA1 fusion is a genetic hallmark of EHE, regardless of site of origin; they also used reverse transcription-polymerase chain reaction and gene sequencing to

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Primary tumor site</th>
<th>Extent of disease</th>
<th>First-line therapy</th>
<th>Patient(s)</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case series</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angelini et al., 2014</td>
<td>Bone</td>
<td>Unifocal (49%); multifocal (13%)</td>
<td>Wide excision or intralesion surgery</td>
<td>N = 62; men, n = 39; women, n = 23; mean age = 39 years</td>
<td>Survival at 10 years: unifocal, 97%; multifocal, 74%</td>
</tr>
<tr>
<td>Zheng et al, 2012</td>
<td>Brain</td>
<td>Intracranial, with localized extension to bone and muscle</td>
<td>Surgery</td>
<td>25-year-old man; 44-year-old woman</td>
<td>9 years</td>
</tr>
<tr>
<td>Agulnik et al, 2013</td>
<td>Multifocal</td>
<td>Metastatic</td>
<td>Bevacizumab</td>
<td>N = 7</td>
<td>Partial response, n = 2; stable disease, n = 4; progressive disease, n = 1</td>
</tr>
<tr>
<td>Wang et al, 2012</td>
<td>Liver</td>
<td>Localized and extrahepatic</td>
<td>Liver resection, transcatheter arterial chemoembolization (TACE), resection and TACE, or liver transplantation</td>
<td>N = 33</td>
<td>Up to 3 years of follow-up</td>
</tr>
<tr>
<td>Theodosopoulos et al, 2013</td>
<td>Intracranial</td>
<td>Metastatic</td>
<td>Surgery</td>
<td>N = 38; men, n = 23; women, n = 15</td>
<td>2 months-11 years</td>
</tr>
<tr>
<td>Case reports</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gherman and Fodor, 2011</td>
<td>Bone</td>
<td>Localized</td>
<td>Wide surgical excision</td>
<td>24-year-old man</td>
<td>No local recurrence or metastasis at 2 years</td>
</tr>
<tr>
<td>Sumrall et al, 2010</td>
<td>Brain</td>
<td>Intracranial, localized extension to skull, connective tissue</td>
<td>Lenalidomide</td>
<td>31-year-old woman</td>
<td>6 years, stable disease</td>
</tr>
<tr>
<td>Osawa et al, 2012</td>
<td>Carotid artery</td>
<td>Localized</td>
<td>Surgery</td>
<td>59-year-old man; 14 years after embolization for carotid aneurysm</td>
<td>Rapid death</td>
</tr>
<tr>
<td>Tolkach et al, 2012</td>
<td>Kidney</td>
<td>Metastatic</td>
<td>Sunitinib</td>
<td>53-year-old man</td>
<td>3 years, stable disease</td>
</tr>
<tr>
<td>Harada et al, 2011</td>
<td>Liver</td>
<td>Localized</td>
<td>Transcatheter arterial chemoembolization</td>
<td>83-year-old man</td>
<td>Metastatic recurrence after 3 months</td>
</tr>
<tr>
<td>Grenader et al, 2011</td>
<td>Liver</td>
<td>Localized</td>
<td>Pegylated liposomal doxorubicin</td>
<td>32-year-old man</td>
<td>2 years, stable disease with maintenance therapy at time of publication</td>
</tr>
<tr>
<td>Sangro et al, 2012</td>
<td>Liver</td>
<td>Metastatic to lungs</td>
<td>Sorafenib</td>
<td>22-year-old man</td>
<td>2 years</td>
</tr>
<tr>
<td>Salech et al, 2011</td>
<td>Liver</td>
<td>Metastatic to lungs</td>
<td>Thalidomide</td>
<td>40-year-old woman</td>
<td>9 years, stable disease</td>
</tr>
<tr>
<td>Mizota et al, 2011</td>
<td>Lung</td>
<td>Localized</td>
<td>Bevacizumab</td>
<td>59-year-old woman</td>
<td>3 months</td>
</tr>
<tr>
<td>Iimuro et al, 2012</td>
<td>Retroperitoneum</td>
<td>Localized, then distant lymph metastasis months later</td>
<td>Surgical removal of both occurrences</td>
<td>48-year-old woman</td>
<td>No recurrence at 13 months after resection of metastasis</td>
</tr>
<tr>
<td>Kerry et al, 2012</td>
<td>Spinal region</td>
<td>Multifocal</td>
<td>Endovascular embolization, radiochemotherapy</td>
<td>25-year-old man</td>
<td>8 weeks</td>
</tr>
<tr>
<td>De Palma et al, 2012</td>
<td>Vascular</td>
<td>Localized</td>
<td>Surgical removal of entire azygos vein</td>
<td>47-year-old man</td>
<td>No recurrence at 1 year</td>
</tr>
</tbody>
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ascertain that in multifocal EHE, those multiple sites are monoclonal in nature, and therefore metastatic implants of the same tumor and not simultaneous occurrence of multiple neoplastic clones. Additionally, both CD31 and VEGF are overexpressed in non-small cell lung cancer, breast cancer, prostate cancer, renal cell carcinoma, mantle cell lymphoma, meningioma, pituitary adenomas, and uveal melanoma. EHE is more common in women, and there are 3 prior case reports of its diagnosis during pregnancy, with ours being the fourth. A case report has also been published of successful management of multifocal hepatic infantile hemangioendothelioma with tamoxifen-based therapy. Tamoxifen (20 mg daily) was part of the management strategy used for our patient over a 9-day course during her acute disease recurrence.

Very little research has explored the clinical utility of individual hormonal markers in EHE. There was strongly positive expression of placenta growth factor (PIGF) in 1 case, positive expression of 17-beta estradiol receptors in only 1 of a series of 5 EHE patients, and no estrogen or progesterone receptors in another case. Expression of PIGF is noteworthy in our case, in that our patient’s disease quickly and dramatically flared in the

(Continued from previous page)

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Primary tumor site</th>
<th>Extent of disease</th>
<th>First-line therapy</th>
<th>Patient(s)</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wu et al, 2014</td>
<td>Vascular</td>
<td>Localized</td>
<td>Surgery</td>
<td>58-year-old woman</td>
<td>2 years, stable at time of publication</td>
</tr>
<tr>
<td>Demir et al, 2013</td>
<td>Liver</td>
<td>Parenchymal lesion with metastases to lung</td>
<td>Carboplatin, pharmorubicin</td>
<td>24-year-old woman</td>
<td></td>
</tr>
<tr>
<td>Kiratli et al, 2013</td>
<td>Eyelid</td>
<td>Localized</td>
<td>Excisional biopsy</td>
<td>22-year-old woman</td>
<td>No recurrence at 44 months</td>
</tr>
<tr>
<td>Pålfdöli et al, 2013</td>
<td>Lung</td>
<td>Metastatic to bone</td>
<td>Carboplatin, docetaxel, pharmorubicin</td>
<td>49-year-old woman</td>
<td>Stable disease 1 year after diagnosis</td>
</tr>
<tr>
<td>Yu et al, 2013</td>
<td>Lung</td>
<td>Lung (localized to myocardium)</td>
<td>Carboplatin/etoposide, followed by surgical excision</td>
<td>39-year-old woman</td>
<td>Alive 14 months after surgery</td>
</tr>
</tbody>
</table>

15 Sangro B, Iñarraíraígu I, Fernández-Ros N. Malignant epithelioid hemangioendothelioma of the liver successfully treated with Sorafenib. Rare Tumors 2012 Apr 12;4(2):e34. DOI: http://dx.doi.org/10.4081/rt.2012.e34.
25th week of pregnancy, near the peak in maternal PI GF production. Although in our patient’s case PI GF was not tested, we did note an abnormally low human chorionic gonadotropin level during the second trimester of pregnancy of 23 IU/mL.

A translocation involving PI GF has also been discovered in a case of EHE. Furthermore, it is known that there is binding of PI GF to VEGF-receptor-1, and that PI GF may influence VEGF-induced angiogenesis, which may explain our patient’s rapid disease flare-up.

Although the scarcity of cases impedes rapid progress in histochemical characterization of EHE, a composite picture has begun to emerge that may aid researchers in its early identification, perhaps leading to earlier diagnosis and more definitive treatment. VEGF expression and hormonal receptor expression have been reported in EHE. Furthermore, there are multiple reports of successful management of this vascular cancer with antiangiogenic therapy (lenalidomide, thalidomide, and sorafenib) which may explain our patient’s rapid disease flare-up.

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

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How to Cite this Article

References
Recurrence of Epithelioid Hemangioendothelioma during Pregnancy: Case Report and Systematic Review


All Attempts at a Rational Method of Cure

The main part of the science of disease is of a purely descriptive character, a scientific interpretation of facts and a clear insight into the intimate connection subsisting between different phenomena, which may precede all attempts at a rational method of cure, having been attained in a few instances only. … Therapeutic researchers must be regulated in the same manner as pathological. … The more careful tracing of the progress of morbid processes, and the insight into their modes of origin and retrogression, enable us to determine the principles of treatment with greater clearness than formerly.

— Friedrich Theodor von Frerichs, 1819-1885, German pathologist
Quality Over Quantity: Integrating Mental Health Assessment Tools into Primary Care Practice

Darrell L Hudson, PhD, MPH

E-pub: 06/17/2016

ABSTRACT

Depression is one of the most common, costly, and debilitating psychiatric disorders in the US. There are also strong associations between depression and physical health outcomes, particularly chronic diseases such as diabetes mellitus. Yet, mental health services are underutilized throughout the US. Recent policy changes have encouraged depression screening in primary care settings. However, there is not much guidance about how depression screens are administered. There are people suffering from depression who are not getting the treatment they need. It is important to consider whether enough care is being taken when administering depression screens in primary care settings.

I was at the doctor's office, a family medicine practice for a routine check-up.

“I have to ask you these questions about mental health,” the nurse said sheepishly after recording my heart rate and blood pressure.

The preface immediately put me on guard and I tensed up. On the one hand, I thought, does anyone suspect that something is wrong with me? Could they tell I was anxious because I forgot to get cash and would have to dive for quarters in my glove box to get out of their parking deck? On the other hand, I conduct mental health research, so I knew the nurse was probably going to ask me questions from the Patient Health Questionnaire (PHQ). I was encouraged that mental health was being integrated into a medical visit in a primary care setting.

During the past two weeks, have you found little interest or pleasure in doing things?

Have you felt down, depressed, or hopeless?

The answer to both of these questions was no. But the opening statement from the nurse about her obligation to ask questions about mental health set me on edge a bit. The nurse’s demeanor changed from when she was taking my blood pressure and recording my weight. In one sentence, she made it abundantly clear that she was asking only because of obligation, she was not comfortable asking, and she was not particularly interested in hearing my answers to the questions. I wondered, if I was feeling down or losing interest in doing things I had previously enjoyed, would I feel comfortable telling her? Considering her apparent disinterest, did she even care? Would I believe that she would do anything about my feelings?

Depression is one of the most common, costly, and debilitating conditions in the US, affecting millions of Americans each year. Disability from depression is associated with lower educational attainment and income earned as well as increased days off work. Depression is also associated with suicide in addition to a wide range of chronic diseases such as heart disease and diabetes mellitus. Recent national policy changes related to mental health coverage, namely the Patient Protection and Affordable Care Act of 2010 and the Mental Health Parity and Addiction Equity Act, have promoted the integration of mental health screening and treatment into primary care settings. Indeed, most patients are initially diagnosed and treated for mental health problems within primary care settings. Many practices and health care systems, such as Kaiser Permanente, use the PHQ to screen for mental health problems. Results from numerous studies indicate that this measure is effective in screening for mental health problems in primary care settings; even versions with fewer items do a good job of identifying depression.

Although there are numerous resources that describe different versions of the PHQ as well as information about reliability and validity, in addition to steps on how to score the screener, there are no clear guidelines about how clinicians should go about asking patients questions about their mental health. However, the manner in which questions are asked and by whom have a profound effect on the answers that patients provide. This is especially true when asking about sensitive information. Race/ethnicity, sex, social class, and sexual orientation are additional considerations that mental health service clinicians must contend with and which make recognition and treatment of depression even more challenging. Further, mental health conditions remain highly stigmatized. This seems to be an important factor that should be addressed at the individual clinician level as well as at the system level.

Practices and health care plans should be applauded for taking steps to integrate mental health and primary care. Despite the efficacy and effectiveness of the PHQ, I wondered how probable someone suffering from depression would be to share such feelings during a similar clinical interaction. I wondered if the nurse’s preface and, more importantly, her demeanor would affect the comfort of patients who do suffer from mental health problems and give them pause about answering the questions honestly.

Is it enough to simply ask questions, especially if the person asking the question does not seem the least bit interested or enthused about doing so? If the goal is to screen patients who may be suffering from depression and other mental health problems, there must be better care in the administration of...
Fewer than It is probable that there are patients suffering from mental health problems who do not seek treatment or who are not being recognized with these problems when they interact with clinicians for medical concerns. It is important to consider whether enough care is being taken when administering depression screeners in primary care settings. Furthermore, it may be important to alert patients that they should expect to be screened for mental health issues even if they are visiting for their physical examinations.

Disclosure Statement

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Acknowledgment

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How to Cite This Article


References


COMMENTARY

Quality Over Quantity: Integrating Mental Health Assessment Tools into Primary Care Practice

document.pdf.

Mental Distress

Every day brought some fresh proof of how great was the influence of mental distress in augmenting bodily pain and sickness. Whatever circumstances were calculated to make a strong impression upon the spirits, threw them back at once from a state of convalescence, into absolute disease … . Passions and affections of the mind are wont to show their power over the body especially by the manner in which they influence the heart, even the healthy heart; rousing it to tumultuous and irregular action and engendering pain within it.

— Peter Mere Latham, 1789-1875, physician and medical educator
**COMMENTARY**

**Plant-Based Diets: A Physician’s Guide**

Julieanna Hever, MS, RD, CPT

E-pub: 07/06/2016

**ABSTRACT**

Because of the ever-increasing body of evidence in support of the health advantages of plant-based nutrition, there is a need for guidance on implementing its practice. This article provides physicians and other health care practitioners an overview of the myriad benefits of a plant-based diet as well as details on how best to achieve a well-balanced, nutrient-dense meal plan. It also defines notable nutrient sources, describes how to get started, and offers suggestions on how health care practitioners can encourage their patients to achieve goals, adhere to the plan, and experience success.

**SUMMARY OF HEALTH BENEFITS**

Plant-based nutrition has exploded in popularity, and many advantages have been well documented over the past several decades. Not only is there a broad expansion of the research database supporting the myriad benefits of plant-based diets, but also health care practitioners are seeing awe-inspiring results with their patients across multiple unique subspecialties. Plant-based diets have been associated with lowering overall and ischemic heart disease mortality; supporting sustainable weight management; reducing medication needs; lowering the risk for most chronic diseases; decreasing the incidence and severity of high-risk conditions, including obesity, hypertension, hyperlipidemia, and hyperglycemia; and even possibly reversing advanced coronary artery disease and type 2 diabetes.

The reason for these outcomes is two-fold. First, there are inherent benefits to eating a wide variety of health-promoting plants. Second, there is additional benefit from crowding out—and thereby avoiding—the injurious constituents found in animal products, including the following:

- **Saturated fats**: Saturated fats are a group of fatty acids found primarily in animal products (but also in the plant kingdom—mostly in tropical oils, such as coconut and palm) that are well established in the literature as promoting cardiovascular disease (CVD). The American Heart Association lowered its recommendations for a heart-healthy diet to include no more than 5% to 6% of total calories from saturated fat, which is just the amount found naturally in a vegan diet (one consisting of no animal products).
- **Dietary cholesterol**: Human bodies produce enough cholesterol for adequate functioning. Although evidence suggests that dietary cholesterol may only be a minor player in elevated serum cholesterol levels, high intakes are linked to increased susceptibility to low-density lipoprotein oxidation, both of which are associated with the promotion of CVD. Dietary cholesterol is found almost exclusively in animal products.
- **Antibiotics**: The vast majority (70% to 80%) of antibiotics used in the US are given to healthy livestock animals to avoid infections inherent in the types of environments in which they are kept. This is, therefore, the number one contributor to the increasingly virulent antibiotic-resistant infections of the type that sickened 2 million and killed 23,000 Americans in 2013.
- **Insulin-like growth factor-1**: In insulin-like growth factor-1 is a hormone naturally found in animals, including humans. This hormone promotes growth. When insulin-like growth factor-1 is consumed, not only is the added exogenous dose itself taken in, but because the amino acid profile typical of animal protein stimulates the body’s production of insulin-like growth factor-1, more is generated endogenously. Fostering growth as a full-grown adult can promote cancer proliferation.
- **Heme iron**: Although heme iron, found in animal products, is absorbed at a higher rate than nonheme iron, found in plant-based and fortified foods, absorption of nonheme iron can be increased by pairing plant-based protein sources with foods high in vitamin C. Additionally, research suggests that excess iron is pro-oxidative and may increase colorectal cancer risk and promote atherosclerosis and reduced insulin sensitivity.
- **Chemical contaminants formed from high temperature cooking of cooked animal products**: When flesh is cooked, compounds called polycyclic aromatic hydrocarbons, heterocyclic amines, and advanced glycation end products are formed. These compounds are carcinogenic, pro-inflammatory, pro-oxidative, and contributive to chronic disease.
- **Carnitine**: Carnitine, found primarily in meat, may be converted in the body by the gut bacteria to produce trimethylamine N-oxide (TMAO). High levels of trimethylamine n-oxide are associated with inflammation, atherosclerosis, heart attack, stroke, and death.
- **N-Glycolyneuraminic acid (Neu5Gc)**: This compound is found in meat and promotes chronic inflammation. On the other hand, there are infinite advantages to the vast array of nutrients found in plant foods. Phytochemicals and fibers are the two categories of nutrients that are possibly the most health promoting and disease fighting. Plants are the only source of these nutrients; they are completely absent in animals. Plants contain thousands of phytochemicals,
such as carotenoids, glucosinolates, and flavonoids, which perform a multitude of beneficial functions, including:

- **Antioxidation**, neutralizing free radicals
- **Anti-inflammation**
- **Cancer activity reduction** via several mechanisms, including inhibiting tumor growth, detoxifying carcinogens, retarding cell growth, and preventing cancer formation
- **Immunity enhancement**
- **Protection against certain diseases**, such as osteoporosis, some cancers, CVD, macular degeneration, and cataracts
- **Optimization of serum cholesterol**

Fibers found in whole plant foods powerfully support the gastrointestinal, cardiovascular, and immune systems through multiple mechanisms. Yet more than 90% of adults and children in the US do not get the minimum recommended dietary fiber.

Thus, it can be advantageous for physicians to recommend and support plant-based eating to achieve optimal health outcomes and possibly minimize the need for procedures, medications, and other treatments. Aiming for lifestyle changes as primary prevention has been estimated to save upwards of 70% to 80% of health care costs because 75% of health care spending in the US goes to treat people with chronic conditions. Offering this option and guiding patients through the logistics and their concerns about plant-based eating is a viable first line of therapy in the clinical setting. This article will delineate how best to achieve a well-balanced, nutrient-dense meal plan, define notable nutrient sources, describe how to get started, and offer suggestions on how physicians can encourage and work with their patients who are interested to maintain adherence and enjoy success.

**NOTABLE NUTRIENTS**

Although nutrient deficiency is a primary concern for many people when considering plant-based eating, the Academy of Nutrition and Dietetics states that "vegetarian diets, including total vegetarian or vegan diets, are healthful, nutritionally adequate, and may provide health benefits in the prevention and treatment of certain diseases." The Academy’s position paper goes on to conclude that "well-planned vegetarian diets are appropriate for individuals during all stages of the life cycle, including pregnancy, lactation, infancy, childhood, and adolescence, and for athletes." Because any type of meal plan should be approached with careful thought, it is helpful to note that plant-based diets, including calorie-restricted, weight-loss diets, have been found to be more nutritionally sound than typical dietary patterns.

A well-balanced, plant-based diet is composed of vegetables, fruits, whole grains, legumes, herbs, spices, and a small amount of nuts and seeds. Half of the plate should consist of vegetables and fruits in accordance with the US Department of Agriculture, American Cancer Society, and American Heart Association, because they are filled with fiber, potassium, magnesium, iron, folate, and vitamins C and A—almost all of the nutrients that tend to run low in the American population, according to the Scientific Report of the 2015 Dietary Guidelines Advisory Committee. Legumes are excellent sources of lysine (an amino acid that may fall short in a plant-based diet), fiber, calcium, iron, zinc, and selenium. It is ideal to consume one to one-and-a-half cups of legumes per day. Substituting meals with whole grains aids with satiety, energy, and versatility in cuisine. Nuts are nutritional nuggets, brimming with essential fats, protein, fiber, vitamin E, and plant sterols, and have been shown to promote cardiovascular health and protect against type 2 diabetes and obesity. Macular degeneration, and cholelithiasis. One oz to 2 oz (or 30 g to 60 g) of nuts per day is recommended. Seeds, too, are special in that their essential fat ratios are well-balanced, and they contain multiple trace minerals and phytochemicals. One or 2 tablespoons per day will boost overall nutrition. Opting for whole food sources of fats, as opposed to extracted fats as found in oils, is optimal to decrease caloric density and increase nutrient and fiber consumption. Herbs and spices also contain phytochemicals and help make food delicious, varied, and exciting, and should be used according to preference. Food group recommended servings per day are shown in Table 1.

**PLANT-BASED MACRONUTRITION**

All calories (kcal) come from some combination of carbohydrates (4 kcal/g), proteins (4 kcal/g), and fats (9 kcal/g). Alcohol also provides calories (7 kcal/g) but is not considered an essential nutrient. The ideal ratio of intake of these 3 macronutrients is highly controversial and debatable. There is plenty of evidence supporting health and weight management benefits of low-fat/high-carbohydrate diets, as seen in the traditional Okinawan diet and in Dean Ornish, MD’s reversal of advanced coronary artery disease and Neal Barnard, MD’s reduction of glycemia in type 2 diabetes using a plant-based diet with 10% of calories from fat. Similarly, the Mediterranean diet and many raw food diets consisting of upwards of 36% or more of calories from fat show consistently positive health advantages. Thus, it appears that it is likely the quality of the diet that is responsible for health outcomes rather than the ratio of macronutrients.

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**Table 1. Food group recommended servings per day**

<table>
<thead>
<tr>
<th>Food group</th>
<th>Recommended servings per day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables, all types, including starchy</td>
<td>Ad libitum, with a variety of colors represented</td>
</tr>
<tr>
<td>Fruits, all types</td>
<td>2-4 servings (1 serving = 1 medium piece or 1/2 cup)</td>
</tr>
<tr>
<td>Whole grains (eg, quinoa, brown rice, oats)</td>
<td>6-11 servings (1 serving = 1/2 cup cooked or 1 slice whole grain bread)</td>
</tr>
<tr>
<td>Legumes (beans, peas, lentils, soy foods)</td>
<td>2-3 servings (1 serving = 1/2 cup cooked)</td>
</tr>
<tr>
<td>Leafy green vegetables (eg, kale, lettuce, broccoli)</td>
<td>At least 2-3 servings (1 serving = 1 cup raw or 1/2 cup cooked)</td>
</tr>
<tr>
<td>Nuts (eg, walnuts, almonds, pistachios)</td>
<td>1-2 ounces</td>
</tr>
<tr>
<td>Seeds (eg, chia, hemp, and flax seeds)</td>
<td>1-3 tablespoons</td>
</tr>
<tr>
<td>Fortified plant milks (eg, soy, almond, cashew)</td>
<td>Optional, 2-3 cups</td>
</tr>
<tr>
<td>Fresh herbs and spices</td>
<td>Optional, ad libitum</td>
</tr>
</tbody>
</table>

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The Permanente Journal/Perm J 2016 Summer;20(3):15-082
Carbohydrates

The Institute of Medicine’s adequate intake of carbohydrates is \(1.5 \text{ g/kg/d}\) for infants, \(1.1 \text{ g/kg/d}\) for those aged 1 to 3 years, \(0.95 \text{ g/kg/d}\) for those aged 4 to 13 years, \(0.85 \text{ g/kg/d}\) for those aged 14 to 18 years, \(0.8 \text{ g/kg/d}\) for adults, and \(1.1 \text{ g/kg/d}\) for pregnant women. This intake is directly available throughout the plant kingdom, but those foods that are particularly rich in protein include legumes, nuts and nut butters, seeds and seed butters, soy foods, and intact whole grains.

Protein

Adequate intake of protein is based on weight and is estimated at \(1.5 \text{ g/kg/d}\) for infants, \(1.1 \text{ g/kg/d}\) for those aged 1 to 3 years, \(0.95 \text{ g/kg/d}\) for those aged 4 to 13 years, \(0.85 \text{ g/kg/d}\) for those aged 14 to 18 years, \(0.8 \text{ g/kg/d}\) for adults, and \(1.1 \text{ g/kg/d}\) for pregnant women. Protein is readily available throughout the plant kingdom, but those foods that are particularly rich in protein include legumes, nuts and nut butters, seeds and seed butters, soy foods, and intact whole grains.

Fats

Fats or fatty acids are more complicated because there are several different chemical varieties based on level and type of saturation. Each category of fatty acids performs different functions and acts uniquely in the body.

The essential fatty acids are polyunsaturated and include both omega-3 and omega-6 fatty acids. Omega-3 fats are found in their shorter chain form as alpha linolenic acid and are used as energy. They are also converted by the body to the longer-chain eicosapentaenoic acid (EPA) and then docosahexaenoic acid (DHA). Because this conversion process can be inefficient, some people may require a direct source of these longer-chain EPA and DHA in the form of a microalgae supplement. Alpha linolenic acid can be found in flaxseeds, hempseeds, chia seeds, leafy green vegetables (both terrestrial and marine), soybeans and soy products, walnuts, and wheat germ, as well as in their respective oils. A direct plant source of EPA and DHA is microalgae, through which fish acquire them. Plant sources may be superior because they do not contain the contaminants that fish contain, including heavy metals, such as mercury, lead, and cadmium, as well as industrial pollutants. Also, plant sources are more sustainable than fish sources.

Monounsaturated fats are not essential but have been found to impart either a neutral or slightly beneficial effect on serum cholesterol levels, depending on which nutrient they are replacing. When swapped for saturated fats, trans fats, or refined carbohydrates, monounsaturated fats may lower low-density lipoprotein and raise high-density lipoprotein cholesterol. These fatty acids are found in olives, avocados, macadamia nuts, hazelnuts, pecans, peanuts, and their respective oils, as well as in canola, sunflower, and safflower oils.

Saturated fats, as mentioned above, are not essential in the diet and can promote CVD. They are found primarily in animal products but are available in some plant foods, mostly in tropical fats and oils, such as palm and coconut, and also in other high-fat foods, including avocados, olives, nuts, and seeds. If a vegan diet contains an average of 5% to 6% of kcals from saturated fat, which is what the American Heart Organization recommends for a heart-healthy diet, any added serving of animal products will significantly increase the total intake.

Trans fatty acids are laboratory-made via hydrogenation and are found in processed, fried, and fast foods. Although they were originally developed to be a healthy alternative to butter and lard, trans fatty acids were found to significantly increase CVD risk. In November 2013, the US Food and Drug Administration issued a notice that trans fatty acids were no longer considered safe and is now trying to eliminate artificially produced trans fatty acids (there are small amounts found naturally in meat and dairy products) from the food supply. Be aware that a nutritional label can state a food product contains “0 g trans fats” even if it contains up to 0.5 g per serving. Thus, advise your patients to focus on the ingredient list on food products and to avoid anything with the words “partially hydrogenated.”

Dietary cholesterol is a sterol that is found primarily in animal products. Although cholesterol is required for the production of hormones, vitamin D, and bile acids, the liver produces enough cholesterol on its own. Excessive intake of dietary cholesterol is associated with increased risk of CVD.

Phytosterols, which are similar to cholesterol, are plant-based sterols found in all plant foods (especially wheat germ, nuts, seeds, whole grains, legumes, and unrefined plant oils). Phytosterols reduce cholesterol absorption in the gut, thereby optimizing lipid profiles. Together with viscous fibers, soy proteins, and almonds, phytosterols have been found to be as effective as statins in some studies in lowering low-density lipoprotein cholesterol.

It is crucial to note that all whole foods contain all three macronutrients. It is a pervasive misunderstanding to identify a food as a “carb,” “protein,” or “fat.” Instead, these are all nutrients within a complex of other myriad constituents that are beyond the oversimplification perpetuated by the media and trendy diet fads.

Ideally, a healthful diet is loaded with wholesome carbohydrates, moderate in fat, and temperate in protein. The emphasis must be on the quality of the totality of foods coming from whole plant sources as opposed to calculations and perfect ratios.

PLANT-BASED MICRONUTRITION

All nutrients, with the exception of vitamin B₁₂, and possibly vitamin D, which is ideally sourced from the skin’s exposure to the sun’s ultraviolet rays, can be found in plants. They are also packed together with thousands of powerful disease-fighting nutrients that work synergistically to support optimal health.

Vitamin B₁₂

Cobalamin, commonly referred to as vitamin B₁₂, is the only nutrient not directly available from plants. This is because vitamin B₁₂ is synthesized by microorganisms, bacteria, fungi, and algae, but not by plants or animals. Animals consume these microorganisms along with their food, which is why this vitamin can be found in their meat, organs, and byproducts (eggs and dairy). Vitamin B₁₂ deficiency can lead to irreversible neurologic disorders, gastrointestinal problems,
and megaloblastic anemia. Among other populations, vegans who do not supplement with a reliable source of vitamin B₁₂ or breastfeeding infants of vegan mothers who are not consuming a regular reliable source of vitamin B₁₂ are at risk for deficiency.

The body can store vitamin B₁₂ for approximately three to five years, but after that, with no repletion or with inability to absorb, deficiency symptoms may persist; deficiency may also be asymptomatic. Because of this lag time and because serum tests for B₁₂ levels can be skewed by other variables, irreversible damage may occur before a deficiency is caught.

In a vegan diet, vitamin B₁₂ can be found in fortified plant milks, cereals, or nutritional yeast. However, these are not dependable means of achieving B₁₂ requirements. Although there are claims that fermented foods, spirulina, chlorella, certain mushrooms, and sea vegetables, among other foods, can provide B₁₂, the vitamin is not usually biologically active. These inactive forms act as B₁₂ analogues, attaching to B₁₂ receptors, preventing absorption of the functional version, and thereby promoting deficiency. The most reliable method of avoiding deficiency for vegans or anyone else at risk is to take a B₁₂ supplement.

Because the body can absorb only approximately 1.5 µg to 2.0 µg at a time, it is ideal to supplement with a dose greater than the Recommended Dietary Allowance (RDA) to ensure adequate intake. Plant-based nutrition experts recommend a total weekly dose of 2000 µg to 2500 µg. This can be split into daily doses or into 2 to 3 doses of 1000 µg each per week to help enhance absorption. Because vitamin B₁₂ is water soluble, toxicity is rare.

Vitamin D
Vitamin D₃, or calciferol, is also known as the "sunshine vitamin" because it is the only nutrient that is acquired from the sun. Although vitamin D is classified as and treated like a fat-soluble vitamin, it is actually a prohormone produced in the skin upon exposure to ultraviolet B sun radiation and then activated by the liver and kidneys.

Although human bodies evolved to produce vitamin D via the sun, there appears to be a worldwide epidemic of deficiency. Vitamin D is not widely available from the food supply. Sources of preformed vitamin D include fish liver oil, oily fish, liver, and in smaller doses, meat and egg yolk—foods that also contain high concentrations of saturated fat, cholesterol, and other less-than-ideal components. Vitamin D from sunshine and animal sources is in the form of cholecalciferol, or vitamin D₃. A second form called ergocalciferol, or vitamin D₂, is found in plant sources, mostly in ultraviolet B-irradiated mushrooms. However, a plant-derived version of D₃ made by lichen was recently discovered. Dietary supplements may contain either D₃ or D₂, both of which can be effective at optimizing blood levels.

More and more physicians are testing for serum levels of vitamin D using the 25-hydroxyvitamin D test. The Institute of Medicine concluded that adequate serum 25-hydroxyvitamin D levels are ≥ 50 nmol/L (≥ 20 ng/mL). If patients have suboptimal levels, emphasizing food sources (especially fortified plant milks) as well as supplements may be helpful. Dosing may be tricky because of variable responses in individuals and differences in types of vitamin D formulas. Of note, although both of the 2 forms of vitamin D—cholecalciferol (D₃) and ergocalciferol (D₂)—are effective at raising serum D levels in small doses (4000 IU or less), cholecalciferol (D₃) is superior when using large boluses. Because the supplement industry is not regulated by the Food and Drug Administration, it is “buyer beware” in the supplement market. Thus, aim to find well-reputed companies. A few organizations, such as Consumer Lab, NSF International, and US Pharmacopeia, act as independent third parties and offer seals of approval after testing products for potency and contaminants. They do not, however, test for safety or efficacy.

Calcium
Calcium, a macromineral, is the most abundant mineral in the human body. A mere 1% of the body's calcium circulates in the blood and tissues; 99% is stored in the bones and teeth. Calcium is a nutrient of concern for the general population with respect to bone mineral optimization during the lifespan. However, because bone metabolism is multifactorial and complex, it is important to emphasize consumption of ample sources of calcium as well as vitamins K and B₁₂, fluoride, magnesium, phosphorus, and potassium; to maintain serum vitamin D levels; and to ensure consistent exercise. Throughout the lifespan, dietary recommendations for adequate intake of calcium fluctuate.

Excellent plant sources of calcium include leafy green vegetables—especially bok choy, broccoli, napa cabbage, collard greens, dandelion greens, kale, turnip greens, and watercress—as well as fortified plant milks, calcium-set tofu, dried figs, sesame seeds and tahini, tempeh, almonds and almond butter, oranges, sweet potatoes, and beans.

No matter how much calcium is consumed, the amount that is actually absorbed is more significant. Many variables affect calcium levels via absorption or excretion, including:

- Overall consumption determines how much is absorbed. Only about 500 mg can be absorbed at a time, and absorption decreases as calcium intake increases
- Age. Calcium absorption peaks in infants and children, as they are rapidly growing bone, and then progressively decreases with age
- Phytates, compounds found in whole grains, beans, seeds, nuts, and wheat bran, can bind with calcium as well as with other minerals and inhibit absorption. Soaking, sprouting, leavening, and fermenting improve absorption
- Oxalates are constituents found in some leafy green vegetables, such as spinach, Swiss chard, collard greens, parsley, leeks, and beet greens; berries; almonds; cashews; peanuts; soybeans; okra; quinoa; cocoa; tea; and chocolate. They may also somewhat inhibit absorption of calcium and other minerals, but some may still be absorbed. Emphasizing variety in the foods eaten on a regular basis encourages adequate absorption
- Serum vitamin D levels must be within optimum range in order for the body to absorb calcium
- Excessive intake of sodium, protein, caffeine, and phosphorus (as from dark sodas) may enhance calcium excretion.
Iron

Ironically, iron is one of the most abundant metals on Earth and yet iron deficiency is one of the most common and widespread nutritional deficiencies. It is the most common deficiency in the world and is a public health problem in both industrialized and nonindustrialized countries. It is particularly prevalent in women of childbearing age, pregnant women, infants, children, teenage girls, and anyone experiencing bleeding, such as people with ulcers, inflamed intestines caused by malabsorptive disorders, or heavy menstruation. Iron-deficiency anemia is no more common in vegetarians than in nonvegetarians.

Because plant-sourced iron is nonheme iron, which is susceptible to compounds that inhibit and enhance its absorption, the recommendation for vegetarians and nonvegetarians is to aim for slightly more iron than nonvegetarians. Fortunately, this is easy to do with the wide array of iron-rich food choices in the plant kingdom. Leafy greens and legumes are excellent sources of iron and a multitude of other nutrients, so it is advantageous to include these foods often. Other good choices include soy products, dark chocolate, blackstrap molasses, sesame seeds, tahini, pumpkin seeds, sunflower seeds, raisins, prunes, and cashews.

Iron absorption may be diminished in the presence of phytates, tannic acids from tea, calcium in dairy, fiber, polyphenols in coffee and cocoa, and certain spices (eg, turmeric, coriander, chilies, and tamarind). To minimize this, separate iron-rich foods from these nutrients as much as possible. An example is to drink coffee or tea separately from meals or to mix up meal combinations. One of the best tips for optimizing iron absorption is to eat iron-rich foods in combination with foods high in vitamin C and organic acids. This improves solubility, thereby facilitating absorption. Examples of such optimizing food combinations are a green smoothie with leafy greens (iron) and fruit (vitamin C) or salad greens (iron) with tomatoes (vitamin C).

Iodine

Dietary sources of the trace mineral iodine are unreliable and fluctuate geographically because of varying soil qualities. It is crucial for vegans to be mindful of consuming a source of iodine to avoid thyroid issues. Sources of iodine include iodized salt and sea vegetables. However, it is important to note that iodine is not found in sea salts, gourmet salts, or other salty foods. One half-teaspoon of iodized salt provides the daily recommended 150-µg dose. Also, iodine levels in sea vegetables fluctuate dramatically, with some (especially dulse and nori) containing safe amounts and others (such as kelp) harboring toxic doses. Hijiki, also spelled hiziki, should be avoided owing to its excessive arsenic levels. A preexisting iodine deficiency, a selenium deficiency, or high intake of goitrogens (antinutrients found in cruciferous vegetables, soy products, flaxseeds, millet, peanuts, peas, pine nuts, spinach, sweet potatoes, and strawberries) can interfere with iodine absorption. There is no need to avoid goitrogenic foods as long as iodine intake is sufficient. If a patient does not enjoy sea vegetables or is minimizing intake of salt, an iodine supplement may be warranted.

Selenium

Selenium is a potent antioxidant that protects against cellular damage and also plays a role in thyroid hormone regulation, reproduction, and DNA synthesis. Brazil nuts are an especially rich source of selenium in the plant kingdom. Although selenium content varies depending on the source, an average ounce (approximately 6 to 8 nuts) can provide 777% of the RDA. When accessible, one Brazil nut a day is an ideal way of meeting selenium recommendations. Other plant sources include whole grains, legumes, vegetables, seeds, and other nuts.

Zinc

Zinc supports immune function and wound healing; synthesis of protein and DNA; and growth and development throughout pregnancy, childhood, and adolescence. Because of the presence of phytates, bioavailability of zinc from plants is lower than from animal products. Zinc deficiency may be difficult to detect in blood tests but can show up clinically as delayed wound healing, growth retardation, hair loss, diminished immunity, suppressed appetite, taste

### Table 2. Sources of notable nutrients

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Food sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>legumes (beans, lentils, peas, peanuts), nuts, seeds, soy foods (tempeh, tofu)</td>
</tr>
<tr>
<td>Omega-3 fats</td>
<td>seeds (chia, hemp, flax), leafy green vegetables, microalgae, soybeans and soy foods, walnuts, wheat germ</td>
</tr>
<tr>
<td>Fiber</td>
<td>vegetables, fruits (berries, peaches, papaya, dried fruits), avocado, legumes (beans, lentils, peas), nuts, seeds, whole grains</td>
</tr>
<tr>
<td>Calcium</td>
<td>low-oxalate leafy greens (broccoli, bok choy, cabbage, collard, dandelion, kale, watercress), calcium-set tofu, almonds, almond butter, fortified plant milks, sesame seeds, tahini, figs, blackstrap molasses</td>
</tr>
<tr>
<td>Iodine</td>
<td>sea vegetables (arame, dulse, nori, wakame), iodized salt</td>
</tr>
<tr>
<td>Iron</td>
<td>legumes (beans, lentils, peas, peanuts), leafy greens, soybeans and soy foods, quinoa, potatoes, dried fruit, dark chocolate, tahini, seeds (pumpkin, sesame, sunflower), sea vegetables (dulse, nori)</td>
</tr>
<tr>
<td>Zinc</td>
<td>legumes (beans, lentils, peas, peanuts), soy foods, nuts, seeds, oats</td>
</tr>
<tr>
<td>Choline</td>
<td>legumes (beans, lentils, peas, peanuts), bananas, broccoli, oats, oranges, quinoa, soy foods</td>
</tr>
<tr>
<td>Folate</td>
<td>leafy green vegetables, almonds, asparagus, avocado, beets, enriched grains (breads, pasta, rice), oranges, quinoa, nutritional yeast</td>
</tr>
<tr>
<td>Vitamin B12</td>
<td>fortified foods (nutritional yeast, plant milks), supplement (2500 µg per week)</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>fruits (especially berries, citrus, cantaloupe, kiwi fruit, mango, papaya, pineapple), leafy green vegetables, potatoes, peas, bell peppers, chili peppers, tomatoes</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>sun, fortified plant milks, supplement if deficient</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>leafy green vegetables, sea vegetables, asparagus, avocado, broccoli, Brussels sprouts, cauliflower, lentils, peas, natto (a traditional Japanese food made from soybeans fermented with Bacillus subtilis var natto)</td>
</tr>
</tbody>
</table>
abnormalities, or skin or eye lesions. Consider advising patients to aim for 50% or greater than the RDA of zinc daily by including legumes, cashews and other nuts, seeds, soy products, and whole grains. Preparation methods such as soaking, sprouting, leavening, and fermenting will improve absorption. Table 2 provides a convenient chart highlighting excellent sources of notable nutrients.

HELPING PATIENTS GET STARTED
To support patients to delve into this therapeutic nutrition plan to help them prevent or manage chronic disease and improve or maintain their state of health, it is crucial to provide optimistic, simple, and strategic guidance. See Sidebar: Six-Step Guide for Initiating and Maintaining a Nutrition Dialogue with Patients.

GUIDE FOR INITIATING AND MAINTAINING A NUTRITION DIALOGUE WITH PATIENTS
1. During the first part of an office visit when interviewing patients regarding wellness behaviors (typically covering exercise and smoking), include questions about diet, such as the following:
   • Do you eat at least 7 to 9 servings of vegetables and fruits every day?

2. When discussing a patient’s treatment plan, include diet as a viable option with positive effects (eg, improved gastrointestinal function, decreased risk for chronic diseases, and better outcomes for existing conditions).
3. Advocate simple suggestions to start off. Instead of overwhelming a patient with drastic renovations to their current way of eating, begin with a few changes that can be made within reason. Some examples include the following:
   • Incorporate leafy green vegetables with at least two meals or snacks each day (enjoy a salad, add broccoli to pasta, try a green smoothie for breakfast or a snack).
   • Start reducing intake of red and processed meat to once per week or less.
   • Opt for whole grains over refined (eg, brown rice instead of white rice, whole grain pasta instead of white pasta, 100% whole grain or sprouted bread).

4. Educate patients on both the risks and better outcomes for existing conditions).
5. Offer patients educational support (see Sidebar: Suggested Educational Support). Information in the form of pamphlets, onsite nutrition counseling, in-house cooking classes, and articles on the Internet (see Sidebar: Suggested Internet Nutrition Resources) is ideal because there are multiple points of reference and communication for patients.
6. Maintain a plan for follow-up and continued encouragement. It is common for people to lose motivation, and to become frustrated over time, particularly if there is not a strong support system in place (see Sidebar: Tips for Patient Motivation). Engage patients by ensuring they are enrolled in classes, have family or friends participating alongside them, are connected to others in similar phases of transition, and have access to continued information, as designated above.

Suggested Internet Nutrition Resources

Website

- www.nlm.nih.gov
- http://vegetariannutrition.net
- http://nutritionfacts.org
- www.pcrm.org
- www.brendadavisrd.com
- www.veganhealth.org
- http://plantbaseddietitian.com
- www.theveganrd.com
- www.vrg.org/nutrition/
- https://fnic.nal.usda.gov/lifecycle-nutrition/vegetarian-nutrition
- www.vegansociety.com

Label-Reading Protocol

- Ignore misleading marketing terminology on labels (eg, “excellent source of,” “free of,” “natural”)
- Focus solely on ingredient list and ignore rest of packaging
- Strive to purchase foods with:
   - Only recognizable ingredients
   - Few total ingredients listed
   - Absence of artificial colors/flavorings/sweeteners, refined sugars, preservatives, stabilizers, thickeners, or any unrecognizable names

Six-Step Guide for Initiating and Maintaining a Nutrition Dialogue with Patients

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Plant-Based Diets: A Physician’s Guide

CONSIDERATIONS

1. Enjoy 2 to 4 servings of fruit per day.
2. Include colorful vegetables with each meal.
3. Try making a plant-based meal and then an entire plant-based day by prioritizing previously loved plant-based dishes (eg, pasta primavera, bean and rice burrito, bean chili).
4. Aim to eat a rainbow every day (foods naturally red, orange, yellow, green, and blue/purple).

For those patients eager to make more dramatic changes, encourage switching to eating a combination of vegetables, fruits, legumes, and whole grains, according to the recommendations above.

4. Educate patients on both the risks associated with inadequate intake of produce and regular consumption of refined sugars and animal products as well as the advantages of emphasizing whole plant foods. Enlist all health care practitioners on the patient’s team to be aware of diet modification goals. One way to simplify this is by charting progress and goals.

5. Offer patients educational support (see Sidebar: Suggested Educational Support). Information in the form of pamphlets, onsite nutrition counseling, in-house cooking classes, and articles on the Internet (see Sidebar: Suggested Internet Nutrition Resources) is ideal because there are multiple points of reference and communication for patients.

It is also important to educate patients on the importance of reading labels (see Sidebar: Label-Reading Protocol).

6. Maintain a plan for follow-up and continued encouragement. It is common for people to lose motivation, and to become frustrated over time, particularly if there is not a strong support system in place (see Sidebar: Tips for Patient Motivation). Engage patients by ensuring they are enrolled in classes, have family or friends participating alongside them, are connected to others in similar phases of transition, and have access to continued information.

CONCLUSION

Ultimately, it is a win-win situation—for patients, and for health care practitioners—to have plant-based eating as a powerful tool in the toolbox. Pharmaceuticals are an important tool in a physician’s armamentarium, particularly in treating acute illness, but lifestyle changes, eg diet, can be an important and powerful tool in treating chronic illness. To facilitate lower health care costs and likely better health outcomes, let food be medicine and the route of the future.

Disclosure Statement

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

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3. Rosell M, Appleby P, Spencer E, Key T. Weight gain over 5 years in 21,966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-

Suggested Educational Support

- Informational sheets, such as pamphlets and handouts, of meal options, recipes, nutrient sources (as in Table 2), sample meal plans, benefits of eating healthfully, additional resources, and advice on the Internet in this guide will support the patient in pursuing plant-based eating at home.
- Individual nutrition counseling as prescribed by a physician provides encouragement, reinforces positive outcomes, and helps address needs and concerns.
- Cooking classes, available in many communities, led by plant-based chefs or registered dietitians are excellent tools for successful adaptation of healthy cooking patterns in the home. Demonstrations and interactive methods whereby participants are able to prepare food or at least taste samples and receive recipes to take home will inspire adherence.
- Articles on the Internet (see Sidebar: Internet Nutrition Resources) and other online resources (or even nutrition-specific Web sites) are opportunities to provide patients with ready-to-go information and perhaps a 24-hour interactive resource.

Tips for Patient Motivation

- Focus on optimism. Encourage every positive choice because food is deeply personal and making significant changes is challenging for most people. Every bite matters.
- Encourage the conversation with patients who are interested. The single person most people trust for advice and recommendations on health, diet, and wellness is their physician. It is an honor and special occasion to be able to open up the dialogue from a place of caring and support and without judgment. Offer advice and an ear to help propel patients onto the path of long-term health.
- Make it fun. Recalculating diet is similar to learning a new language. Initially, a few new ingredients are discovered, which is like learning some new words. Then enjoyable recipes and meals become part of the repertoire, which is similar to learning some phrases in the new language. Finally, the knowledge base expands so greatly that it becomes second nature to choose and prepare plant-based meals, akin to speaking the language fluently. Health care practitioners are ideally situated to easily guide patients toward fluency and success in this new language.
COMMENTARY

Plant-Based Diets: A Physician's Guide


Plant-Based Diets: A Physician’s Guide


63. Food Rules

Eat food.
Not too much.
Mostly plants.

— Food Rules, Michael Pollan, b 1955, American author, journalist, activist, and professor of journalism
The Use of Narrative as a Treatment Approach for Obesity: A Storied Educational Program Description

Marcus Griffith, MD; Jeana Griffith, PhD; Mellanese Cobb, MPH; Vladimir Oge, MPH

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ABSTRACT

Introduction: Childhood obesity is a health care crisis according to the leading pediatric advocacy groups (National Medical Association, American Academy of Pediatrics, and American Diabetes Association) and the White House. The problem has reached epidemic proportions for all children, but it has an even greater impact on racial minorities. The subject of childhood obesity can lead to a host of medical, psychological, and social problems, including low self-esteem and discrimination.

We wrote an interventional children's book and workbook (The Tale of Two Athletes: The Story of Jumper and The Thumper) and developed a three-step intervention based on the narrative. The intervention's purpose is to increase public awareness, reduce stigma, and to help members of underserved communities become more comfortable discussing obesity.

Methods: In classrooms and other community settings, a storied education program is presented to students of various ages. Interactive storytelling is the first step: live narration with direct listening and active participation. Didactic information on obesity is shared, including a sociocultural explanation for why the issue is more problematic among racial minorities. The audience is then introduced to the story of Jumper and The Thumper, two larger-than-life characters who experience different outcomes as a result of their choices about diet and exercise. True examples are described during the narration about these two young men, accompanied by cartoons and photographs for visual emphasis.

The next step is reading: audience members are provided with a book to reinforce what was learned. Readers are allowed to more closely examine the importance of making healthy choices.

Practicing positive behaviors and decision making through games and exercises from the companion workbook is the final step. These activities help children and their families live a healthier lifestyle. The goal is that these three steps, linked to a common narrative, will have a meaningful impact on obesity by creating behavioral change.

Results: Children, parents, and health care professionals have stated their enthusiastic response to the information and message that they have made positive changes in children's eating and exercise habits. The program has been presented in community forums, churches, medical meetings, and elementary schools in at-risk communities.

Conclusion: New strategies must be developed to lead, uplift, and empower through health and wellness education and through community collaboration if we are to change the direction of course toward this devastating condition that affects our most valuable commodity—our children. This community-based educational approach is a means to help recognize and treat obesity in underserved communities.

INTRODUCTION

Obesity is a health care crisis according to leading medical and patient advocacy groups (Centers for Disease Control and Prevention, American Academy of Pediatrics, American Medical Association, and National Medical Association) and the White House. Obesity is defined by excess body fat, which is not the same as overweight. A person may be overweight because of extra muscle, bone, water, and/or fat. Although obesity rates have reached epidemic proportions, there is a lack of culturally competent interventions to educate the public and to prevent and combat this condition. We developed an innovative, culturally competent approach with narrative to address this deficiency.

The statistics on obesity in both children and adults are alarming; however, facts, figures, and epidemiologic information do not tell the whole story. Obesity has grown into such an enormous public health problem that even the untrained observer can recognize that it is out of hand. The challenges faced in elementary school lunchrooms are one clue to this growing problem. According to the National Health and Nutrition Examination Survey, more than 33% of adults and 17% of youths in the US are obese. Rates of obesity among children and adolescents have tripled since 1980, with an estimated 12.5 million children and adolescents aged 2 to 19 years identified as obese or overweight.

The problem of obesity in children and adolescents is perhaps one of the most pressing public health concerns in the US. Studies suggest that individuals who experience problems with excess weight during childhood are commonly overweight or obese as adults. The best method for preventing this potentially lifelong problem is to control it during childhood through education and behavioral intervention.

Obesity may have the greatest impact on racial minorities. Minority populations and low-income communities appear to have the highest risk. The 2001 report The Surgeon General’s Call to Action to Prevent and Decrease Overweight and Obesity was...
The Use of Narrative as a Treatment Approach for Obesity: A Storied Educational Program Description

one of the first to call attention to obesity as a major health problem. More recently, First Lady Michelle Obama launched the Let’s Move initiative to examine root causes and offer practical solutions.13

Obesity is believed to be a preventable illness that many believe will one day have greater rates of morbidity and mortality than any other health condition. Because racial minorities experience higher rates of obesity than whites, this disease state is linked to health care disparities in the US. According to a 2001 Institute of Medicine report, racial and ethnic disparities exist regardless of socioeconomic status.12 The reported data suggest that racial and ethnic minorities tend to receive a lower quality of health care than whites, even when analyses control for access-related factors, such as insurance status and income. Key epidemiologic indices on these differences include higher morbidity and mortality from the leading causes of death, poorer quality of care, and worse outcomes.12

A COMMUNITY-BASED EDUCATIONAL APPROACH

A critical service line in the battle against obesity is the need for new methods of communication between health care organizations and underserved communities. Traditional strategies for communicating messages about obesity and other chronic diseases have failed to improve population health, as evidenced by worsening rates. New, culturally competent interventions must be developed so as to build relationships between people from different races, cultures, and ethnicities. The spectrum of health-related problems linked to obesity is well documented; it includes diabetes, hypertension, respiratory problems, and depression. Low self-esteem, depression, and social discrimination associated with childhood obesity are frequently unaddressed.13 Battling the medical complications of obesity and forming solutions for associated emotional distress has been the focus of my (MG’s) work. On the eve of the grand opening of my (MG’s) medical practice, in 1994, I got the sad news that my best friend had died from a massive heart attack. I had always dreamed of becoming a physician and running my own office. I had imagined that this day would be filled with a sense of accomplishment and excitement; but instead, it was overshadowed with grief. That night I experienced a profound sense of loss, and I made a commitment to fight obesity. When I opened my office the following day, I began to incorporate that fight into my daily clinical practice. Over the years, I have continued to explore new education and prevention strategies designed for clinical and community settings.

I (MG) wrote the story of Jumper and The Thumper several years later, while working in a mental health treatment center for children and adolescents with severe behavioral and emotional problems. The vast majority of the patients were African American, low-income, and were obese or overweight. The children learned about diet, nutrition, and exercise as components for improving their mental and physical health. As we worked with dieticians, encouraged a reduction in television and video game time, and promoted increased physical activity, our activities reinforced the guidelines on obesity recommended by the American Academy of Pediatrics.13

During the last several years I (MG) traveled throughout the US and received a number of awards for my work on obesity. The work began through telling a story about how a dear friend lost his life because of complications from obesity. I then used the story as a platform to develop a community-based educational program to address both the mental and the physical health problems associated with obesity. The intervention’s purpose is to increase public awareness, to reduce stigma, and to help constituents of underserved populations become more comfortable discussing obesity. The program also incorporates nutrition, exercise, and other behavioral strategies to combat weight gain. Community-based educational programs that teach the benefits of healthy eating, nutrition, and exercise have proved to be effective tools for controlling weight and promoting positive behavioral change.14

The initiative centers around a children’s book that my wife and I (MG) wrote, entitled The Tale of Two Athletes—The Story of Jumper and The Thumper. The story in the book is told through the eyes of a little girl named Jasmine who attended one of my presentations at a community event in Seaside, CA. Jasmine is battling childhood obesity and heard the story The Tale of Two Athletes. This inspirational story is based on my lifelong friendship with Joe Drake, a professional football player who died prematurely because of obesity. Recently, after reading a magazine article on the number of football players who have died from obesity-related complications, I discovered from an ESPN story that Joe was the heaviest player in the history of the National Football League to die.15

Following the presentation, Jasmine sought me (MG) out and asked if I could help her. She told me that she had also struggled with her weight all through her life and could relate to many of the points in the story. As we talked, Jasmine was curious about the two characters, Jumper and Marcus Griffith, MD, telling the story of The Tale of Two Athletes at the Boys and Girls Club in Seaside, CA.
The Thumper, and wanted to know more about their lives. She stated that she would never forget the story and did not want to end up like The Thumper. Jasmine made a promise that she would begin trying to live a healthier lifestyle. In addition to children, adults struggling with obesity are receptive to the program’s message. The interactive narrative, based on a true story, attempts to inspire change and create solutions. It is an alternative approach for examining the causes of obesity and forming solutions, especially in the context of racial minorities and underserved communities.

One of the activities that generated the most excitement resulted from the relationship that we formed with the park rangers at Davidson-Arabia Nature Preserve in DeKalb County, GA. Two park rangers and I (MG) led three groups of patients on a series of nature hikes through the forest in an effort to increase exercise and to create exposure to a new experience. We instructed the patients on the importance of exercise and appreciation of nature. Staff members from the day treatment program also participated to help ensure safety. To my surprise, many of the children had never been outside of the city or spent time in the woods. The healing power of nature was quite evident as the children had never been outside of the city or spent time in the woods. The healing power of nature was quite evident as they experienced the outdoors. I made sure that the children with the most severe behavioral issues were placed in my group, with the appropriate accompanying staff. No major issues were encountered.

One rainy day when we were unable to go outside for our nature hike, a young man shared with me the pain he experienced because of excess weight. I (MG) asked him to write down his feelings, and he entitled his story “My Life as an Obese Child.” His name just happened to be Joseph—the same name as my late friend. I was inspired to create a story and use it as a component of a comprehensive obesity program at the center (up until the book was written the story was told from memory in the old tradition of story telling). I told the story about Jumper and The Thumper so as to convey a powerful message about obesity, from and about someone the children knew.

The story about my (MG’s) relationship with Joe Drake continues to be integral to my personal and professional life. On February 28, 2012, I closed my private practice after 18 years of service and accepted a position with Kaiser Permanente in GA. Coincidently, as I was closing my office for the final time and was saying goodbye to my patients, the first copy of the published book arrived. Closing my office and simultaneously receiving the first printed copy of The Tale of Two Athletes was a powerfully emotional experience, especially considering what had happened the night before opening my office in 1994. The moment of closure marked for me a beginning and an end at the same time. Although it was an end to my private practice, a new opportunity began in my quest to honor my friend in the fight against obesity through the telling of The Tale of Two Athletes.

### NARRATIVES—A THREE-STEP APPROACH

I (MG) developed a three-step approach based on The Tale of Two Athletes to educate the community about obesity. Storytelling is the primary concept that moves from active listening to live narration as the first step. Live narration aims to make an impact on the audience through direct listening and active participation. Didactic information on obesity is shared, including statistics, easy-to-understand epidemiologic information, and a sociocultural explanation for why the issue is more problematic among racial minorities. Jumper and The Thumper are then introduced to the audience as two larger-than-life characters who experience different outcomes resulting from their choices in diet and exercise. The true examples about the young men are described during the narration, accompanied by cartoons and photographs to enhance the visual experience and highlight the realities of the problem. At the end of the story, when The Thumper dies, the true names of the characters and a photograph of the characters are revealed. The audience then realizes that the narrator is Jumper, which hopefully inspires them and impresses on them the importance of diet, nutrition, and exercise in the battle against obesity.

The next step of the educational process is reading the book to reinforce what was learned in the live community educational program. The book provides more intimate details about the two young men and allows the reader to more closely examine and identify with the characters and to realize the importance of making healthy choices.

The final step of the program uses the companion workbook that my wife and coauthor, Jeana Griffith, PhD, wrote to personalize the story for each reader. Participants practice positive behaviors and decision making through games and
exercises that help them set goals for physical activity and a healthier diet. The hope is that these three steps, linked to a common narrative, will make a meaningful impact for creating behavioral change related to obesity.

The use of narratives and storytelling is now recognized as a culturally competent approach for reaching racial minorities and underserved populations. This method may be a more effective process for sharing health information in communities where traditional health education has failed. Storytelling may also be a means of easing the disconnect between healthcare professionals and underserved communities.

The intention is to offer a culturally competent message that allows the audience to see, hear, understand, and feel what obesity is all about and that they are not alone in their struggles. The story about the two characters, Jumper and Thumper, offers an opportunity for the participants to build a relationship with the characters and the storyteller. An expectation is that the listeners will become immersed in the story and identify with the message. This process, which Banks describes, emphasizes the importance of building trust between the presenter and the audience, using the experiences within the story to create “a sense of oneness.”

Furthermore, the companion workbook to *The Tale of Two Athletes* is an example of how stories can incorporate games to engage audiences and reinforce learning.

The researchers developed this initiative as they observed similarities between disadvantaged communities in developing African nations and the US. Gilliam et al combined traditional storytelling with technologies of social media and game design to reshape adolescent sexual health behaviors. They believe that stories and games can be used to communicate information about other preventable illnesses where traditional health messaging has been unsuccessful.

DISCUSSION

Storytelling has been used since the beginning of human communication as a means to preserve history, culture, ideas, and teaching. Ideally it is an interactive process between the storyteller and the audience that helps listeners to conceptualize and makes the message more meaningful. I (MG) have been using a narrative approach in my obesity education programs as a means of conveying health information to diverse populations (African-American and Hispanic populations). I have attempted to construct a program that engages the audience and inspires behavioral change through humor, didactic material, and a true, compelling story.

Health interventions typically focus on changing individual behavior through traditional health policy and communications. These approaches have done little to reduce the differences in prevalence, mortality, and burden of chronic diseases in underserved communities. Examples include heart disease, diabetes, preterm births, human
immunodeficiency virus, and obesity, which continue to disproportionately affect African Americans, Hispanic, Native Americans, and low-income communities.  

CONCLUSION

Next steps are to expand programs by obtaining grants and sponsorships to promote it. We hope the three-step approach of active listening to the narrative, reading the book, and practicing what was learned by using the workbook will serve as an additional model in the fight against obesity. Up to this point, the program has been funded by the article’s authors. The resources to get it done were inspired by the love of a friend and all those who have lost someone because of obesity.

Disclosure Statement

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How to Cite this Article


References


Powerful Drugs

In medicine, as in stagecraft and propaganda, words are sometimes the most powerful drugs we can use.

— Anonymous; Sara Murrah Jordan’s obituary in The New York Times
I wasn’t even scheduled to work that morning; I had just gone into the office for a meeting. Chatting with coworkers on my way out the door, I was told there was someone asking for me at the reception desk. So it was there, in front of a waiting room full of patients, that I received the papers notifying me of the lawsuit. “Have a nice day,” the woman called out to me as she left.

Over the next months, as the legalities played out, I struggled to keep moving. My confidence evaporated. I’d been taught that physicians who build good relationships are less likely to be sued, so I had obviously failed. I didn’t know how I could face my patients—I felt like a fraud. I couldn’t sleep. I lost my appetite. Sometimes my experience felt surreal, especially when my attorney told me: “This case will not affect your life in any way.”

I wondered if I would lose my job, my license, my home. Even worse, I wondered if I had lost the trust of my colleagues.

I met a coworker who had survived a lawsuit; she had been as stressed as I was, and knowing that my reaction was not abnormal reassured me. I began to practice strategies to help myself cope, and life slowly improved.

As much as we hate to think about it, most physicians, about 60%, will be sued at some point in their career. Not everyone will be as unnerved as I was, but physicians typically do feel intense strain when faced with a lawsuit. Our trust in ourselves and in our patients is shaken. We practice more defensively. We are more likely to suffer depression and burnout. We may feel anxious, depressed, angry, and afraid. Here I offer ten techniques for coping that really work.

RESIST ISOLATION

Asking for help can be tough for physicians; we’re used to being the ones people come to for help, not the ones who need help. You will be advised not to talk with anyone about the case, but you’ve got to know that you’re not alone. Conversations with certain people are protected from discovery. Ask your attorney for advice here, but typically it is acceptable to talk to family members, counselors, and your personal physician. And you can generally feel safe discussing your emotions while avoiding the medical details of the case.

Some liability insurance providers cover psychological counseling costs, so make sure to ask about this option. If you think you might benefit from talking to someone who has had a similar experience, check to see if your organization or insurance provider offers a peer support team.

It’s common for physicians undergoing litigation to contemplate suicide. If you’re having thoughts of suicide, pick up the phone and call someone immediately: 911, your physician, a counselor, your spiritual advisor, or a friend or family member. Don’t do anything until you’ve spoken with someone. Keep a list in your phone of people you can call for support. If you are so depressed or anxious that you can’t stop the negative thoughts, if you’re not eating or not sleeping, or if you feel overwhelmed, medication may be helpful. Do not prescribe for yourself; talk to a physician you can trust. It could save your life.

USE YOUR STRENGTHS

We all developed skills for managing stress as we made our way through college, medical school, and residency. Remind yourself that you have these tools, and turn to them now. Focus, persistence, preparation, not taking things personally—we know how to do these things.

RETRAIN YOUR BRAIN

We all have habitual thought patterns, places our minds go when under stress. But you can create new patterns for yourself. Use your rational mind to respond to the sometimes overwhelming fears that come up; this is a technique that clinicians tend to practice a lot. When the ugly thoughts begin to spiral, and you start thinking that you’re obviously a fraud, and no one should trust you to care for them, stop and remind yourself of the patients you’ve helped, the procedures that went well, and the successes you’ve had. These new neural pathways will become more ingrained as you continue to practice them.

Research by Martin Seligman, MD, shows that a simple gratitude exercise increases happiness and resilience (read his book Flourish or go to http://giga.berkeley.edu/practice/three-good-things). Take a few moments each evening to consider what went well and write it down. At first all you may be able to come up with is that you have clean sheets, or that you had a really great piece of chocolate for dessert. But as you begin to look for the good, you see it more, even when life seems bleak. I look forward to this “what went well” exercise at the end of my day.

TAKE CARE OF YOURSELF

It’s important to make room in your hectic schedule for some downtime. Staying busy can make you feel more in control. It can distract you and keep you from fixating on the case. But you need all your strength right now, so you’ve got to preserve that. Sleep is crucial, to give your
You Are Not Alone: Ten Strategies for Surviving a Malpractice Lawsuit

NARRATIVE MEDICINE

The unexpected good news is that I feel healing that I have to offer my patients. The unexpected good news is that I feel more engaged now with my work than ever. I’m more clear about the help and healing that I have to offer my patients. I have confidence that I can survive what I thought was the worst thing that could happen to me in my career. Stress, both personal and professional, is inevitable. These techniques help me cope.

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Brain time to recover from the stress of each day. Exercise helps release stress. Eating well fuels your body and brain (but give yourself enough slack to turn to comfort food when you most need it—I might not have survived without mint Newman-O’s). Take some relaxation time, whether it’s for a massage, bedtime reading to your kids, a hot bath, yoga, or meditation (research has shown the effectiveness of Jon Kabat-Zinn, MD’s mindfulness-based stress-reduction program, for example). Just be careful about using alcohol or drugs to check out—they can quickly cause more problems than they solve when used to self-medicate.

GIVE YOURSELF A BREAK
Physicians tend to be perfectionists, and being sued seems only to reinforce the expectation to be perfect. Much of the time we are our worst critics, and we say things to ourselves that we’d never say to a colleague. Show yourself the same compassion you’d show your child, patient, or best friend. Read Kristin Neff, MD’s work for more information on self-compassion (http://self-compassion.org/).

SET PRIORITIES
It’s important to do things that make you feel like you’re living in line with your values: be a great parent to your kids, volunteer to do work you care about, spend time with your religious community. Find some activities that engage you enough to distract you from your worries and that feed your soul.

APPROACH LAW AS A FOREIGN CULTURE
As physicians we’re used to having time pressures. Review the stat labs now! Call the patient before you go home! Get to the OR immediately! Things move much differently in the legal world. Scheduling a meeting may take days, weeks, or even months. Phone calls may not be returned the same day. It can be frustrating to just wait when you’re used to taking care of things quickly.

Your attorney is there to help you navigate. But just as a patient may be surprised to find out that they need an IV to have surgery whereas you take it for granted, you may find the legal process confusing and your attorney unaware of your uneasiness. So ask questions, and ask for preparation. If you’ve never given a deposition before, ask to have the process explained in detail. Again, use your strengths and prepare as you would prepare for oral board exams. You can even do a practice run, answering questions in front of a video camera. If you think that might help you, ask your attorney to arrange it.

There will be times of relative quiet, and then a period that is acutely stressful, like the deposition. I realized that I needed to approach those episodes the way I would a crash C-section—push aside the emotions and just do it.

The case will require your time and energy, but be reassured that generally your liability insurance will cover the financial aspects.

REGAIN PERSPECTIVE
Almost every day in my work, and every time I do my volunteer shift with people living on the streets, I am reminded of the relative ease of my life. My problems still feel big to me, but not insurmountable.

USE DISTRACTION
If your thoughts are stuck in a negative spiral, use distraction to pull yourself out of the descent: movies, audiobooks, printed books, intense exercise, time with your kids, a hobby that engages you, a call to a friend; find something that works for you. I learned to queue up an audiobook for my drive to work, so that I didn’t start my day in worry, and to listen to a guided meditation if I woke up feeling anxious during the night.

FOCUS ON WHAT YOU CAN CONTROL
In the legal process, as in life generally, there are some things you can control but many more things you cannot. As physicians we tend to believe that we’re in charge, so it can be hard for us to accept that there are things we can’t control. But acceptance can bring relief. After one very long and frustrating day, my attorney said to me, “We gotta focus on what we can control.” And he’s right: stressing and obsessing about what someone else may do doesn’t help. We’ve all heard the Serenity Prayer: “God, grant me the serenity to accept the things I cannot change, the courage to change the things I can, and the wisdom to know the difference.” Make this your mantra.

I encourage you to experiment to see what works for you. None of these strategies will make the lawsuit, or the stress, disappear. For me, they took the edge off and made the situation bearable when I wasn’t sure that bearing it was possible. My case is over now, and I wish I could tell you that there was a nice, neat ending—but there wasn’t; it was messy and lasted much longer than I had hoped. The unexpected good news is that I feel more engaged now with my work than ever. I’m more clear about the help and healing that I have to offer my patients. I have confidence that I can survive what I thought was the worst thing that could happen to me in my career. Stress, both personal and professional, is inevitable. These techniques help me cope.

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The Handshake Layer Cake: Meeting and Regretting Difficulties for a Non-French Surgeon in France

Colin G Murphy, MCh, FRCSI

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“I’m not shaking hands with you,” my friend and colleague says loudly. With a dramatic flourish, he withdraws his hand and hides it behind his back, pointing his chin and lower lip towards me in a classic Gallic pout. No one else present bats an eyelid. The chomping of lunch and chewing the fat continues around the table, and I am left offering my hand to empty space. This response is slightly better than the "Aaaggh, salaud" (“Agh, bastard”) I received a few days earlier when committing the same social faux pas. Twice in one week—not good.

These are two of the more aggressive responses to this particular social blésoir and pointed reminders of the highly codified systems of salutations here in France. Just when this Irishman abroad thinks he has the natives cracked, he realizes the magnitude of his ignorance for a new social situation. Happily these rebukes are usually followed, and were immediately in the two above cases, by a grin, a pppffffhhhhhh, or a backsnap.

There are kinder rebukes: “HEEEEY, on croise les doigts cette fois-ci?” (“Hey, how ‘bout we shake fingers this time instead?”), or a big, exaggerated outstretched hand followed by withdrawing the hand to do the thumb-to-nose and wiggling fingers maneuver—like we did when we were kids—and a "OOOH, on se connaît déjà nous!" (“Hey, we already know each other!”). It is strange to see grown Frenchmen doing this at you at work and stranger still that you get used to it.

Typically the regret conundrum develops like this: say you see a colleague walking down the corridor, maybe with a patient. You shake hands in passing and give a Bonjour/Ca va?/Ça va, the absolute-scraping-the-barrel-bare-minimum of conversational interactions. Then at lunch you walk into the Café En Face (my colleagues rarely seem to eat in the hospital cafeteria—unsurprising given the quality of the plat du jour at the local café), say with a different colleague, where seven doctors are sitting down eating away and chatting animatedly. You don’t interrupt, but you both start at the head of the table and work your way around shaking hands or giving les bises (the cheek-kissing of a female colleague). Sixth of seven at the table is the colleague you greeted earlier that morning in passing in the corridor. He is deep in chat, holding court. What do you do? Your colleague ahead of you has just shaken his hand (first greeting of the day for those two), and not wanting to make a fuss or interrupt the flow of invective of your seated colleagues, you might be tempted to offer your hand to him, again. Big mistake. Prepare to be taken to task.

You have just created a scene as now he stops talking, leans back in his chair affecting deep insult, and pointedly refuses to shake hands.

The best strategy for the regret scenario is very much person and situation dependent. I am becoming a big fan of the index-finger shake, which can be done with the same familiar and safe nonverbal cues as a full handshake: approaching his or her personal space, making eye contact, and lifting your hand, but only the index finger is offered for a playful sword-cross style greeting. It is perfectly acceptable for this all to be done without speaking.

For regretting a senior colleague you don’t know well enough yet to tutoyer (to address someone in French using the familiar form of the pronoun “you”—“tu”—rather than the more formal form of “vous”), I copy my own boss who does an elegant head nod and an “On s’est déjà vu” (“We’ve already met”). This avoids committing to a second-person singular familiar/second-person singular respectful pronoun and obviates the need to offer either hand or index finger.

Maybe the index-finger shake is the informal fist-pump to the more formal handshake? I’m going to have to watch my French gangster movies again to be sure, but it seems one doesn’t regret a senior ranking surgeon with the index shake, or thumb-to-nose-with-fingerwiggle. Layers on layers. And so different from home. Coming from a culture where work greetings are mostly nonverbal, this represents a quantum change. Eye contact and a nod are considered eminently sufficient for both greeting and regretting. Verbal greetings are also acceptable; for colleagues a clipped, “Morning” or “Doctor”; for the consultant surgeon a “Mr/Ms O’Brien,” usually with eye contact and a nod (if feeling particularly effusive one could add in a temporal “Good morning/afternoon Mr/Ms O’Brien”). Tactile greetings in Irish hospitals are almost unheard of. On one six-month rotation, the only physical contact I had with any of my bosses was a backsnap from the senior ranking surgeon on the morning he came in late for the morbidity and mortality conference after I stood to vacate the chair nearest the exit door for him.

But it’s not just the handshakes. Les bises is another minefield and much more complex than handshakes. I frequently cringe at the different ways I achieve social awkwardness at work by getting even the primary greeting wrong, let alone the regretting. We have all done it: offer the cheek when she puts out the hand or vice versa. At work, after a few months here and meeting the same folks daily, playing l’etranger card just isn’t an option anymore. Reluctance to experiment with social greetings with female work colleagues means, happily, that I can’t shed any light on the regret avec bises conundrum, but here is...
The Handshake Layer Cake: Meeting and Regretting Difficulties for a Non-French Surgeon in France

On mature reflection, when it comes to the regret dilemma, it is probably better to receive the playful rebuke for attempting to steal a second handshake than the sharp word for none at all, but it is infinitely better, as with most operative procedures, to get it right the first time.

Who You Are

What you see and hear depends on where you are standing; it also depends on what sort of person you are.

— CS Lewis, 1898-1963, British novelist, poet, academic, medievalist, literary critic, lay theologian, broadcaster, lecturer, and Christian apologist
Disconnection

Ahmed Obeidat, MD, PhD

It was a very familiar object that I asked her to identify. She started to look, feel, think, and she said, “It has buttons, numbers, and glass, but I cannot put them together. I am unsure!” I then pushed a button and asked again. With an assertive voice, she said, “It’s a radio.” I asked, “What else could it be?” With a tentative voice, she said, “A video player?” I whispered, “You are so close, it’s a television.”

Then, I asked her to identify numbers. She said “four” instead of “three” and “one” instead of “five.” Despite her confidence, her answers appeared random. I asked her to read the letters of my name as spelled on my hospital ID. She spelled “TLOPZ” for “AHMED”; no pattern that I could identify. I then pointed to my black jacket and asked her to identify what it was, including what color. She said, after a thoughtful pause, “I have seen it before, but I am unsure.” She started to cry but then felt my jacket with her hand and readily said, “Oh, it’s your jacket, and it is blue.” The last task I asked her to perform was to write a sentence. I was thrilled that she wrote in beautiful script, “Doctor, I want to know what is wrong with me.”

Yes, this was alexia (word blindness), without agraphia, associated with color anomia and visual/color agnosia (the inability to interpret visual information and color). All implied a disconnection tragedy in her young brain. She was a creative writer in her third decade of life who had battled lupus and antiphospholipid syndrome for 12 years. Now her disease ravaged her left visual cortex and further interrupted the connection between her intact right occipital lobe and the dominant hemisphere, leaving her blind to her own words. Apart from alexia, anomia, and visual agnosia, she had no other language problems; she was able to express her ideas in speech and in writing, and could fully comprehend spoken English. I quantified her deficits using the National Institutes of Health stroke scale assessment. Though the examination earned her only 2 points, 1 for the field cut, and 1 for the naming difficulty, her disability was beyond what this scale could convey. Nevertheless, her coming to our attention after a day of symptoms precluded the use of a clot buster medication. She was praying that her difficulties represented migraine with visual disturbances. But symptoms lasted longer than they should and her ophthalmologist asked her to go to the Emergency Department to be evaluated. I wondered whether an early arrival might have made me consider treating with tissue plasminogen activator despite her low stroke scale assessment score.

I feel safe carrying the stroke scale card in my pocket daily; it reflects an inventory of brain functions that makes such a complicated machine comprehensible and under control. The naming page reminds us to look for subtleties. Being able to name glove, key, chair, cactus, feather, and hammock can be very reassuring, whereas losing that ability is worrisome. Moreover, being able to tell the story of the inattentive mother and her sneaky kids reaching for the cookie jar helps us ferret out the elusive signs of language and speech disorders. But, it is challenging to diagnose alexia without agraphia; it may pass unnoticed. Sometimes, even if observed, it can still be overlooked and blamed on its frequent fellow traveler, “homonymous hemianopia.” Alexia without agraphia is very disabling, very frustrating, and much more important than its corresponding low stroke scale assessment score. The sum total of our decision to treat or not weighs what we can’t always capture by a number. The decision to treat or not emphasizes the concept of art in our daily practice of medicine.

Several months after the event, she lives with her loving parents; she is gradually coping with her loss. I talked to her again but this time away from the Emergency Department.

She said, “I lost some capabilities. For example, I am not driving anymore: it is hard to read the signs or even follow the navigation system directions. Occasionally, I ask for help when I want to dress for an important event. Otherwise, a perfectly matching outfit means little to me. I believe in the beauty of each color and the beauty of each soul.” I then asked about her writing. She looked at me and smiled. She said, “I still enjoy writing and I love it even more now! I write on my small notebook and then listen to my mother’s voice carrying my own words; she reads them out loud, once, twice, three times and sometimes even more; I enjoy and then refine!” She went on to say, “I feel that I am learning again. I believe that my perception and my ability to read are going to eventually come back, but I also know that it might be long before that moment arrives!”

During that visit, I asked her to read some simple sentences; I was so excited to observe her success. She was able to read a few letters and some simple words. Although it was still difficult for her to name the colors or group them on the basis of their similarities, she made some improvement. I can see her young, talented brain marching on the path to recovery perhaps through a “detour” bypassing the “disconnection.”

Finally, by observing her voyage, I gained significant insight into the intricacies of brain connections, and most importantly, the consequences of such seemingly minor deficits in a person’s life.

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CASE REPORTS

Metastatic Renal Cell Carcinoma Presenting as Painful Chewing Successfully Treated with Combined Nivolumab and Sunitinib

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ABSTRACT

Introduction: Metastatic renal cell carcinoma (RCC) to the head and neck is rare. It is the third-most common cause of distant metastasis to the head and neck, after breast cancer and lung cancer. Several drugs are available to treat metastatic RCC including high-dose interleukin and targeted therapy. Immunotherapy with nivolumab was recently approved by the US Food and Drug Administration (FDA) as a second-line treatment for patients with metastatic RCC.

Case Presentation: We present a case of metastatic RCC in a 71-year-old man with a single complaint of a 1-year history of pain while chewing food. Positron emission tomography-computed tomography showed diffuse metastatic disease. Nivolumab, off-label use before its recent FDA approval, was combined with sunitinib and resulted in an excellent and ongoing response.

Discussion: RCC is the third-most common cause of distant metastasis to the head and neck. The patient described in this case did not have any symptoms commonly seen in RCC, such as painless hematuria, weight loss, anorexia, fatigue, or anemia, despite the bulk of his disease. The other important aspect of this case is the almost complete response of his metastatic disease to the combination of nivolumab and sunitinib that was used off label before the FDA issued the approval. Future clinical trials should look at combining immunotherapy with targeted therapy in metastatic RCC.

INTRODUCTION

Renal cell carcinoma (RCC) is more common in men than in women, with an overall annual incidence of approximately 3.7%.1 The median age of onset is around 64 years.1 Approximately 62,000 new cases and 14,000 deaths caused by RCC occur annually.1 Up to 30% of patients with RCC present with metastatic disease.1 Most patients are asymptomatic until the disease is advanced. The classic triad of flank pain, hematuria, and a palpable abdominal mass is present in only 9% of patients. Several risk factors are thought to play a role in the etiology of RCC; these include smoking, hypertension, obesity, renal cystic disease, use of nonsteroidal anti-inflammatory drugs and other analgesics, chronic hepatitis C infection, and history of kidney stones.2-5

High-dose interleukin (HDIL-2) is the only therapy that provides a potential cure in a minority of patients.6 Several targeted therapies are approved as first-line for those patients who are not fit for HDIL-2.6 The recent advent of immunotherapy with checkpoint inhibitors has brought hope to patients with metastatic renal cell carcinoma. In this case we discuss a unique presentation of metastatic renal cell carcinoma. Also we report an excellent sustained tumor response to combined sunitinib and nivolumab.

CASE PRESENTATION

A 71-year-old man presented with pain while chewing, progressively worse, during the last year. He initially saw his dentist, and an oral exam did not reveal any abnormalities. Pain medications were prescribed for use as needed. His symptoms gradually got worse, so he was referred to an otolaryngologist.

Soft tissue neck computed tomography (CT) with contrast revealed a 5-cm intensely enhancing mass with extensive vascular supply in the left masticator space (Figure 1). Fine needle aspiration of the
mass showed large cells with clear vesicular cytoplasm. These cells were reactive to paired box gene 8 (PAX8) and pankeratin, whereas the supporting cells were reactive to smooth muscle actin. These findings were suggestive of metastatic renal cell carcinoma (RCC). Full-body positron emission tomography (PET)-CT confirmed the above findings but also revealed masses at the inferior pole of the left kidney, retroperitoneal lymphadenopathy, and bilateral lung nodules (Figure 2A). The differential diagnosis based on the location of the mass included schwannoma, hemangioepithelioma, angiosarcoma, lymphoma, and metastatic carcinoma, particularly lung carcinoma and RCC. Sunitinib, an inhibitor of cellular signaling that targets multiple receptor tyrosine kinases, was initiated at 50 mg orally daily (4 weeks on and 2 weeks off). His pain was controlled with opioids, but we discussed with him palliative radiation therapy to the left masticator space mass in case his pain became resistant to opioids. Follow up PET-CT postsunitinib therapy showed an interval progression of his disease (Figure 2B). Nivolumab, an anti-program death receptor 1 inhibitor, was not approved yet by the US Food and Drug Administration, but we decided to add it to sunitinib, and the combined treatment resulted in almost complete response (Figure 2C). Table 1 illustrates a timeline of his follow-up visits, diagnostic tests, and interventions.

**DISCUSSION**

Surpassed only by breast cancer and lung cancer, RCC is the third-most common cause of distant metastasis to the head and neck. Head-and-neck metastasis is the presenting complaint for 7.5% of patients with RCC. However, only 1% of patients with RCC have metastasis confined to the head and neck. A retrospective chart review of 21 cases of metastasis of RCC to the head and neck found that the most common sites of metastasis were bone (n = 6), skin and subcutaneous tissue (n = 6), and lymph nodes (n = 5). A head-and-neck metastasis may occasionally be the presenting sign in a patient with RCC or may follow the primary diagnosis by many years. Our patient did not have any symptoms commonly seen in RCC, such as painless hematuria, weight loss, anorexia, fatigue, or anemia, despite the bulk of his disease. It was only pain while chewing food that led to the diagnosis of metastatic RCC. CT scan with contrast is the imaging modality of choice in demonstrating the vascularity and extent of the lesion.

The pathology revealed cells that are reactive to PAX8 and pankeratin. PAX8 and paired box gene 2 (PAX2) are transcription factors important for fetal development of several organs, including kidney, müllerian organs, brain, and eye. Both are good markers for renal cell tumors. Almost all RCCs are positive for PAX8, which is frequently expressed by lymphoma (100%), nephrogenic adenoma (100%), parathyroid tumors (62%), thyroid tumors (100%), and müllerian organ-derived tumors (92%).

Tumors that may be negative or infrequently positive for PAX2, including chromophobe RCC, oncocyotma, and sarcomatoid RCC, are often positive for PAX8. Several drugs are available to treat metastatic RCC. Patients with good Karnofsky performance status (≥ 80%) and intact organ function are treated with high-dose interleukin-2 (HDIL-2) up front. HDIL-2 can induce long-term remissions in approximately 10% of patients. This treatment is associated with an approximately 4% mortality rate, so it is extremely important to select patients who are fit for this therapy. Several targeted therapies were approved as first-line for those patients who are not fit for HDIL-2, but treatment is based on risk groups. The Memorial Sloan-Kettering Cancer Center prognostic score stratifies patients with metastatic RCC into poor, intermediate, and favorable risk categories on the basis of the number of adverse clinical and laboratory parameters present. Poor prognostic factors include a Karnofsky performance status of less than 80 (80 indicates normal activity with effort and some signs or symptoms of disease), time from diagnosis to treatment less than 12 months, serum lactate dehydrogenase more than 1.5 times the upper limit of normal, corrected serum calcium greater than 10 mg/dL, and hemoglobin less than the lower limit of normal. Patients in the favorable-risk group have no poor prognostic factors, those in the intermediate-risk category have 1 or 2 adverse prognostic factors, and patients with poor-risk RCC have more than 2 poor prognostic factors. Patients in the favorable or intermediate-risk group are treated with sunitinib, pazopanib, or interferon alpha plus bevacizumab, whereas the front-line treatment for those in the poor risk group is temsirolimus alone. Axitinib and sorafenib has been approved as second-line treatment, for use after other targeted therapy or cytokine therapy have failed.
Activating the immune system appears to be a promising strategy to treat metastatic RCC. Since 2011, 2 novel classes of immunotherapy drugs have been approved: the cytotoxic T lymphocyte antigen 4 (CTLA-4) inhibitor ipilimumab and the program death receptor 1 inhibitors pembrolizumab and nivolumab. In melanoma the combination of ipilimumab and nivolumab resulted in an objective response rate of 61%. In a phase I trial, patients with metastatic RCC received nivolumab in combination with sunitinib (50 mg, 4 weeks on, 2 weeks off) or pazopanib (800 mg daily), until progression/unacceptable toxicity. The starting dosage of nivolumab was 2 mg/kg intravenously every 3 weeks with planned escalation to 5 mg/kg intravenously every 3 weeks. Objective response rate was 52% among patients receiving nivolumab and sutent and 45% among those receiving nivolumab and pazopanib. Almost half the responses occurred by the first assessment, which is week 6 of treatment. The investigators concluded that nivolumab plus sutent or pazopanib showed encouraging results.

### Table 1. Timeline of the case

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<th>Date</th>
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| April 20, 2015| **Chief complaint:** A 71-year-old man with no past medical history presented with painful chewing during the past 1 year.  
**Family history:**  
Father died from lung cancer at the age of 86.  
Mother died from pancreatic cancer at the age of 69.  
**Physical examination:** Mild left cheek swelling.  
**Previous imaging:** An outside-hospital, soft-tissue neck CT with contrast dated March 12, 2015 revealed a 5-cm intensely enhancing mass with extensive vascular supply in the left masticator space.  
**Previous intervention:** A CT-guided biopsy of the mass dated April 2, 2015 confirmed metastatic renal cell carcinoma (clear cell type).  
**Current intervention:** Ordered whole-body PET-CT scan to complete the staging. | PET-CT: At least a 3.7-cm mass within the left pterygopalatine fossa, SUV 2.4. A minimum of 10 nodules are seen scattered throughout both lungs; the largest measures 33 x 28 mm, SUV 6.2.  
Liver: Approximately 2.1-cm focus in the posterior aspect of segment VIII, SUV 3.1. Right suprarenal fossa: approximately 9 x 6-cm mass, SUV 2.7.  
Left kidney, inferior pole: Approximately 9-cm mass, SUV 5.0 | Sunitinib 50 mg orally daily (4 weeks on, 2 weeks off). |
| May 19, 2015  | **Tolerating medication without problems. States that he has some left cheek swelling that comes and goes**        | None                                                                                | Sunitinib was approved by his insurance and shipped to patient. Medication started May 1, 2015. |
| July 7, 2015  | Left cheek swelling that comes while off Sunitinib and goes away while on Sunitinib                        | PET-CT: At least a 4.1 x 2.5-cm mass within the left pterygopalatine fossa, SUV 5.5. A minimum of 10 nodules are seen scattered throughout both lungs; the largest measures 36 x 29 mm, SUV 6.3.  
Liver: Approximately 5-cm focus in the posterior aspect of segment VIII, SUV 5.1. Right suprarenal fossa: Approximately 10.5 x 5.4-cm mass, SUV 5.3.  
Left kidney, inferior pole: Approximately 6.9-cm mass, SUV 5.6. These findings are consistent with progression of his disease. | We decided to get nivolumab off label use. We told the patient to continue taking sunitinib because he had been on it for only 2 months. |
| August 5 - September 15, 2015 | Patient was seen every 2 weeks while on nivolumab                                                          | None                                                                                | Completed 4 cycles of nivolumab. |
| September 21, 2015 | **Tolerating treatment well with combined sunitinib and nivolumab**                                           | PET-CT: Complete opacification of the left maxillary sinus, SUV 6.3. A minimum of 10 nodules are seen scattered throughout both lungs, most of which appear slightly improved; the largest measures 28 mm, SUV 5.5. There is interval improvement in previously documented hypermetabolic right hepatic focus, which on today’s study has an SUV of 2.9 (prior SUV 5.1). Stable to slight morphologic and metabolic improvement in previously documented left and right renal masses. | Continue sunitinib and nivolumab, restage disease in 3 months. |
| December 15, 2015 | **Tolerating treatment well with combined sunitinib and nivolumab**                                          | PET-CT: Decreased extent and metabolic activity of left masticator space metastasis, SUV 3.7. Decreased size of the left lower pole renal mass. Decrease in size, and metabolic activity of lung, right adrenal, retroperitoneal soft tissue and lymph node metastases. | Continue combined sunitinib and nivolumab, restage disease in 3 months. |
| March 8, 2016 | **Tolerating treatment well with combined sunitinib and nivolumab**                                           | PET-CT: Improving metabolic activity in the left masticator space, SUV 2.7 (prior SUV 3.6). Stable to slight improvement in the previously documented subcentimeter right lung nodules and 1.7-cm left upper lobe mass. | Continue combined sunitinib and nivolumab, restage disease in 3 months. |

CT = computed tomography; PET = positron emission tomography; SUV = standardized uptake value.
antitumor activity and a manageable safety profile in patients with metastatic RCC. The decision to add nivolumab (off-label use) in our patient was based on the results of the above phase I trial. Three months later (November 23, 2015), the FDA approved nivolumab on the basis of results of an open label, randomized study that showed an overall survival advantage of nivolumab over everolimus in patients with metastatic RCC who failed antiangiogenic agents. Those treated with nivolumab lived an average of 25 months compared with 19.6 months in those treated with Afinitor. Additionally, 21.5% of those treated with nivolumab experienced a complete or partial shrinkage of their tumors, which lasted an average of 23 months, compared with 3.9% of those taking everolimus, lasting an average of 13.7 months.

Our patient appears to be tolerating the combination of nivolumab and sunitinib. His follow-up PET-CT showed improvement in his disease (Table 1).

CONCLUSIONS
Metastatic cancer to the head and neck is rare. Breast cancer, lung cancer, and RCC are the most common causes of distant metastasis to the head and neck. In our case, pain while chewing food was the only presenting symptom of metastatic RCC. Immunotherapy with interleukin-2 or interferon-alpha, biologic, or targeted therapy are all viable options for patients with metastatic RCC. Most recently the FDA approved nivolumab in the second-line setting after patients have failed antiangiogenic agents. Our patient had an almost complete response after patients have failed antiangiogenic therapy and immunotherapy in the front-line setting among patients with metastatic RCC.

ACKNOWLEDGMENT
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REFERENCES

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

Flexibility
Fixity of purpose requires flexibility of method.
— Harold G Wolff, 1898-1962, American physician, neurologist, and scientist
A 76-year-old man who underwent emergent tracheostomy placement presented on postoperative day 10 with massive hemorrhage concerning for tracheoinnominate fistula and was treated with median sternotomy and ligation of the innominate artery.

Discussion: This presentation describes a concise diagnosis and treatment plan for a rare event. The key to good outcomes is quick diagnosis and urgent surgical intervention.

Introduction
Tracheoinnominate fistula (TIF) is a devastating complication of tracheostomy with 100% mortality reported in the absence of treatment. Here we report the case of a 76-year-old man who survived ligation of the innominate artery.

Case Presentation
A 76-year-old man with a history of recurrent papillary thyroid cancer, modified radical neck dissection, and previous neck radiation that was complicated by bilateral recurrent laryngeal nerve injury, underwent emergent tracheostomy. On postoperative day 8, less than a teaspoon of blood emanated from the tracheostomy site after coughing. This was thought to be related to granulation tissue around the stoma, thus bronchoscopy was not performed. Massive hemorrhage through the tracheostomy occurred on day 10. Direct tamponade through the neck incision (Utley maneuver) was immediately lifesaving. Massive transfusion protocol was activated and thoracic and vascular surgical services were emergently consulted. Median sternotomy with ligation of the innominate artery was performed. The innominate artery was extremely friable, consistent with postradiation changes, and was ligated and divided with the addition of a pericardial patch and pledged 2-0 prolene sutures owing to the poor quality of the artery. The patient was stabilized and returned to the intensive care unit fully neurologically intact. On postoperative day 2, with the patient medically stable in the intensive care unit, he returned to the operating room for formal revision of the innominate stump owing to concern over its friability from extensive radiation changes, as well as to prevent its constant contact with tracheal secretions. The stump was debrided, ligated, and buttressed with a pedicled left pectoralis major muscle flap to prevent refistulization. On postoperative day 3, he became hypotensive longer than 10 minutes owing to intermittent atrial fibrillation. He was later noted on examination to have a left-sided hemiparesis. A moderate right middle cerebral artery hemispheric infarct was visualized on urgent computed tomography scan of the brain. On the basis of imaging and timing of onset of hypotension, the cause of the stroke was determined to be ischemia from prolonged hypotension, rather than a direct result of decreased perfusion after ligation. Over time he regained his strength and was fully alert and communicative. The patient was transferred to the ward and is currently doing well in a rehabilitation facility.

Discussion
TIF is a rare but devastating complication of tracheostomy. The incidence of TIF is reported from 0.1% to 1%. There is 100% mortality if no intervention is pursued. TIF occurs within the first 3 weeks after tracheostomy in 72% of the patients that develop this condition but may occur years after the surgical procedure. Risk factors for TIF include tracheal infection, steroid use, creation of the tracheostomy below the third tracheal ring, pressure necrosis caused by overinflation of the cuff or malposition, and chest deformity leading to a high-riding innominate artery. Surgical texts dictate immediate repair or ligation of the innominate artery; however, there are only sporadic case reports available in the literature.

Diagnosis and Management of Initial Hemorrhage
Bleeding from the tracheostomy site is relatively common, though true TIF is rare. “Early” bleeding occurs within hours after tracheostomy and is generally caused by failure of local hemostasis or underlying coagulopathy. Incidence of TIFs, however, peaks 1 to 2 weeks postoperatively and may manifest as a “sentinel bleed,” wherein there is a brief episode of bright red, often pulsatile bleeding from the tracheostomy site. Unfortunately, only 35% of patients with TIF exhibit this pathognomonic sign, making preemptive diagnosis challenging.

Confirming the diagnosis of TIF can be difficult and may include bronchoscopy, arteriography, or computed tomography angiography with 3-dimensional reconstruction.
reconstruction. Taken together, these studies have only a 20% to 30% sensitivity to confirm the diagnosis1 and therefore a high clinical suspicion must be employed to improve mortality. Any tracheostomal bleeding and/or hemoptysis beyond the first 48 postoperative hours must be considered a sentinel bleed and investigated for the possibility of TIF.2 Even with prompt identification, surgery is associated with a greater than 50% mortality owing to both perioperative hemorrhage and infectious complications.3 Overall prognosis remains poor, with 56% of survivors reported dead within 2 months,3 probably because of the high prevalence of associated comorbidities within this critically ill population.

Early Control of Hemorrhage

When patients present with massive hemorrhage, a stepwise progression of bedside interventions can be rapidly applied to temporize bleeding, maintain a patent airway, and bridge patients to definitive therapy.1,2 The most common site of TIF is at the level of the endotracheal cuff; therefore, overinflation of the tracheostomy cuff should be attempted first. This technique is successful in nearly 85% of cases.1 In patients in whom it is not, the tracheostomy should be replaced with auffed endotracheal tube distal to the site of the bleeding.1 If hemorrhage persists, the Utley maneuver can be employed wherein a finger is placed into the airway, with or without extension of the incision, and the innominate artery is compressed against the posterior sternum. Furukawa and colleagues6 describe prompt control of the tracheostomy hemorrhage by insertion of a tracheostomy cannula with a wired silastic tube and an adjustable wing, and overinflating the cuff to provide hemostasis. This resulted in control of hemorrhage in 7 of 7 patients in their case series.

Innominate Artery Ligation

Once TIF has been identified as the cause of hemorrhage, surgical texts describe division of the innominate artery and the separation of the oversewn ends from the trachea. By ligating only the innominate artery, the subclavian and carotid circulation are left in continuity. Innominate artery ligation has an estimated 10% risk of neurologic deficit.4 This number is roughly supported by case reports in the literature, although this is probably because of a reporting bias in favor of successful patient outcomes.

One of the largest case series of TIF ligation by Furukawa and colleagues6 describes excellent results seen in 7 pediatric patients with existing severe neurologic deficits. Operative repair was approached by collar incision with partial sternotomy and innominate artery division. Cerebral blood flow was monitored by the blood pressure difference in the bilateral upper extremities and by near-infrared spectroscopy. Only 1 of 7 patients was noted to have evidence of decreased cerebral perfusion after innominate artery clamping, and an innominate to right carotid artery bypass was performed. The tracheal fistula was left adherent to the innominate artery in all but 1 patient, in whom a pericardial covering was placed between the trachea and innominate artery. Long-term follow-up confirmed no new neurologic deficits including any vascular, tracheal, or new computed tomography findings postoperatively. Overall survival was an impressive 84% at 37 months,5 compared with the reported 15% to 71% cited elsewhere in the literature.6

In the case presented in this report, ligation was accomplished via median sternotomy, which allowed full exposure of the supra-aortic trunk. This was particularly useful in the context of an infected, postradiation operative field. However, this approach also carries the risk of both mediastinitis and wound infection. A 39% incidence of sternal wound complications has been reported in patients with tracheostomy and median sternotomy.7

Recent technologic advancements in interventional radiology and endovascular techniques have allowed clinicians to pursue less invasive options to manage TIF. Troutman et al3 managed to successfully deploy an endovascular stent graft via the right common carotid artery in addition to a carotid to subclavian bypass. The patient survived the initial event; however, after three months the patient succumbed to recurrent hemoptysis and subsequent cardiac arrest. Troutman et al3 concluded that endovascular stent management of TIF offers a less invasive option and can substitute as a bridge for poor surgical candidates with the potential for becoming better surgical candidates. The main advantage to endovascular management of TIF is less morbidity. The limitations to the use of endovascular stent grafting include 1) inadequacy of resources and expertise at smaller community-based hospitals; 2) inadequate landing zones for stent placement, necessitating an additional surgical bypass to maintain flow; and 3) lack of data because of so few cases.

TIF is a rare but devastating sequela of a common surgical procedure. With early recognition, rapid control of hemorrhage, and prompt intervention, disruption of the innominate artery through division and ligation is a viable repair option that has been shown to produce sustained survival with minimal risk of neurologic deficit.

Disclosure Statement

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

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How to Cite this Article


References

Monoarticular Poncet Disease after Pulmonary Tuberculosis: A Rare Case Report and Review of Literature

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ABSTRACT

Introduction: Tuberculosis is a major health problem worldwide, more so in Asian countries and especially India. Being a communicable disease, it can affect the lives of many people. Tuberculosis has varied manifestations and can affect almost every part of the human body. Pulmonary tuberculosis is the most common form. Poncet disease (tuberculous rheumatism) is a polyarticular arthritis that occurs during acute tuberculosis infection in which no mycobacterial involvement can be found or no other known cause of polyarthritis is detected.

Case presentation: We describe an atypical presentation of active pulmonary tuberculosis with monoarticular Poncet disease of the right knee in a 24-year-old woman.

Discussion: The diagnosis of Poncet disease is mainly clinical with exclusion of other causes. It generally presents as an acute or subacute form; however, chronic forms have been described in the literature.

INTRODUCTION

Tuberculous arthritis is a monoarticular, infectious, and destructive disease. However, tuberculous rheumatism, popularly known as Poncet disease, is a nondestructive parainfective polyarthritis occurring in patients with active tuberculosis (TB), which resolves completely with antituberculosis therapy. The diagnosis of this entity is largely clinical and is made by excluding other causes of polyarthritis in a patient with documented active TB. Monoarticular involvement in tubercular rheumatism has not been previously described, to our knowledge. We describe a rare and atypical presentation of Poncet disease with involvement of only the right knee.

CASE PRESENTATION

A 24-year-old woman presented with complaints of continuous fever for 15 days, which was associated with sudden-onset swelling of her right knee for 5 days. There was a history of anorexia. There was no history of cough, burning micturition, vaginal discharge, abdominal complaints, or trauma. There was no history of TB, and the patient was sexually inactive. Results of the physical examination revealed swelling in the right knee, which was not tender. The temperature over the swelling was normal. The remaining findings of the examination were normal.

The laboratory tests showed a leukocyte count of 10.4 × 10^9/L (10,400/μL; 65% of segmented neutrophils), erythrocyte sedimentation rate of 32 mm/h, and C-reactive protein level of 159 mg/dL. The Mantoux test result was strongly positive (16 × 12 mm). The urinalysis result was normal, and urine culture and blood culture were negative. The antinuclear antibody test result was normal, and the test results for rheumatoid factor were negative. Sexually transmitted diseases were ruled out, and the serologic test result for human immunodeficiency virus was negative. The serum uric acid level was 5.8 mg/dL. Fifty milliliters of synovial fluid was aspirated from the knee joint. The analysis of the synovial fluid showed a leukocyte count of 5 × 10^9/L with a differential count of polymorphs being 55% and leukocytes being 45%. The synovial fluid was negative for TB using polymerase chain reaction. There were no crystals and the cultures were sterile.

The chest x-ray film was normal. Contrast-enhanced computed tomography scan of the chest revealed multiple enlarged pretracheal lymph nodes. The chest x-ray film was normal. Contrast-enhanced computed tomography scan of the chest revealed multiple enlarged lymph nodes in the pretracheal region (Figure 1) and the prevascular and precarinal regions. However, the contrast-enhanced computed tomography scan of the abdomen was normal. The x-ray film of the right knee joint showed periarticular soft-tissue swelling, and active TB with no changes (Figure 2). Fine-needle aspiration
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Monoaarticular Poncet Disease after Pulmonary Tuberculosis: A Rare Case Report and Review of Literature

The etiopathogenesis of Poncet disease is proposed to be molecular mimicry and thermal shock proteins.6

Our patient had active pulmonary tuberculous findings on a computed tomography scan and swalling of the right knee, which was found to be inflammatory, without any evidence of organism in the synovial fluid. Thus, a diagnosis of Poncet disease was made. Our patient responded to the antitubercular drugs, and her knee swelling was reduced over two weeks.

Although Poncet disease has been described as a polyarthritis, a review of the literature reveals it to be an often pauciarticular, symmetrical arthritis predominantly involving the large joints.1,7,8 The tuberculous septic monoarthitis, in which the mycobacterium can be isolated from the culture of the affected joint, is a known entity. However, to the best of our knowledge, monoarticular Poncet disease has not been described in the literature.

This lack of reporting may be because of a scarcity of data and a lack of knowledge about this entity called Poncet disease.

CONCLUSION

Poncet disease has been described in the literature as polyarticular disease without any evidence of organism isolated from the synovial fluid. However, because of a scarcity of data and lack of knowledge, we may be missing quite a few cases of monoarticular Poncet disease. Thorough research and sharing of knowledge may be required for the discovery of such a rare presentation.

Disclosure Statement

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

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How to Cite this Article


References


Figure 3. Fine-needle aspiration cytology of pretracheal lymph nodes reveals epithelioid cell granulomas.

Figure 4. Timeline of history, relevant investigations, and treatment of patient with Poncet disease.

Medical History
No history of TB
On examination: right knee swelling
Swelling of right knee: 5 days
Abscess
Arthritis

Synovial fluid analysis
Leukocyte count: 5 x 10^6/mm^3
Differential count: L 55%, M 45%
TB-PCR negative
No crystals
Cultures including mycobacterial sterile
CECT of chest
Multiple lymph nodes in pretracheal (Figure 1); prevascular and pericardial regions
X-rays of right knee
Periarticular soft tissue swelling, and there were no changes of active tuberculosis (Figure 2)

FNAC of pretracheal lymph nodes
Epithelioid cell granulomas
AFB from epithelioid cell granulomatous lymph node material was positive

Treatment
Patient started antitubercular therapy
On follow-up, the patient became afebrile and joint swelling decreased
Knee swelling disappeared
Patient in continued phase of treatment and symptom free

AFB = acid-fast bacilli; CECT = contrast-enhanced computed tomography; FNAC = fine-needle aspiration cytology; L = leukocytes; PCR = polymerase chain reaction; TB = tuberculosis.
CASE REPORT

A 69-year-old woman presented to the Neurology Department with 2 months of progressive psychomotor slowing, inability to concentrate, and periods of disorientation. Her past medical history was unremarkable, and she was taking no medication. There was no history of trauma. On neurologic examination she was alert but taking a long time to answer, apathetic, distractible, and hypophonic with right visual and sensitive hemiextinction and left hemiparesis. Montreal Cognitive Assessment Exam score was 11/30. A computed tomography scan of the brain (Figure 1) showed possible convexity subarachnoid hemorrhage that the brain magnetic resonance imaging (MRI)/MRI angiography (Figures 2 and 3) revealed to be engorged cerebral vessels. Hyperintensity in the deep white matter of the cerebral hemispheres was also present. Cerebral angiography (Figure 4) revealed a dural arteriovenous fistula (DAVF) of the superior sagittal sinus and torcula (Cognard classification IIIb).

The patient underwent endovascular embolization, with combined transarterial (n-butyl-cyanoacrylate) and transvenous (coils) approach, resulting in proximal occlusion of the superior sagital sinus, torcula, and transverse sinus (Figure 5). Posttreatment angiography revealed near complete DAVF occlusion (Figure 6). Control MRI revealed a marked decrease of the deep white matter hyperintensity and no engorged cerebral veins (Figures 7 and 8). The patient’s mental status improved postprocedure (Montreal Cognitive Assessment Exam score, 20/30), and she progressively came back to her baseline.
DISCUSSION

DAVFs are abnormal arteriovenous connections within the dura, usually located within the walls of a dural sinus or an adjacent cortical vein, and account for 10% to 15% of all intracranial arteriovenous lesions.2-4 The initiating events which lead to their development are not clear, but the literature reports association with trauma, infection, recent surgery, and dural sinus thrombosis.2-4 A wide variety of signs and symptoms, which can vary because of lesion location and pattern of venous drainage, may arise from DAVFs, namely, pulsatile tinnitus, ophthalmoplegia, proptosis, chemosis, retro-orbital pain, decreased visual acuity, seizures, Parkinsonism, cerebellar symptoms, apathy, and dementia.2-4

CONCLUSION

Our patient with DAVF presented with encephalopathy with diffuse white matter changes related to venous ischemia. Her symptoms partially reverted with endovascular treatment.

DAVF should be considered in patients with encephalopathy. This relatively nonspecific clinical picture may delay the diagnosis and result in further deterioration. A high level of suspicion should be maintained in patients who present in the context of unexplained intracranial hemorrhage without significant risk factors (trauma, hypertension, or anticoagulation) or in possible subarachnoid hemorrhage in a nonaneurysmal pattern. This should prompt imaging with MRI and angiography, which are the gold standard for diagnosis. DAVF recognition is essential because these patients are potentially treatable.

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

How to Cite this Article

References
Image Diagnosis: Pott Puffy Tumor

Diane Apostolakos, MD, MS; Ian Tang, MD

CASE REPORT

A 20-year-old man was admitted to our hospital with complaints of frontal headache, sinusitis, and fever for one week. He had a history of allergic rhinitis and recurrent sinus infections. At admission his temperature was 40°C and his pulse rate was 140 beats per minute. On physical examination, the center of his forehead had a soft, tender, warm, swollen area that caused an obvious bulge. The initial imaging study, a computed tomography scan, failed to clearly show the intracranial pathology. A magnetic resonance imaging study of the patient’s head with intravenous contrast revealed osteomyelitis of the frontal bone with localized swelling and underlying epidural empyema (Figures 1 and 2). This finding confirmed the diagnosis of Pott puffy tumor, which is defined as forehead swelling, usually from the anterior extension of frontal sinusitis, and associated osteomyelitis of the frontal bone.1,2

The patient was seen by otorhinolaryngology as well as neurosurgery; he declined the recommended surgery and consequently remained febrile with a maximum temperature of over 38°C for 6 consecutive days. He continued to have occasional fever spikes and was not discharged until hospital day 39. During hospitalization he was treated with intravenous ampicillin and sulbactam every 6 hours. At discharge, his treatment was changed to oral metronidazole and daily intravenous ceftriaxone via a central catheter. He received a total of 3 months of antibiotic treatment and remained well after the antibiotic treatment was completed.

DISCUSSION

Sir Percivall Pott (1714-1788), a surgeon at St Bartholomew’s Hospital in London, first described Pott puffy tumor in 1760.3 It was called a tumor because tumor refers to one of the four historic manifestations of inflammation noted by Aulus Cornelius Celsus (c. 25 BC-c. 50 AD): rubor (redness), tumor (swelling), calor (warmth), and dolor (pain). Originally described as a complication of head trauma, Pott puffy tumor typically occurs as a complication of frontal sinusitis. The extracranial manifestations frequently include subperiosteal or subgaleal abscesses. Intracranial complications may include epidural empyema, subdural empyema, intraparenchymal abscess, cavernous sinus thrombosis, or meningitis.4

A review of 53 cases of Pott puffy tumor4 indicated that sinusitis, head trauma, or cranial surgery are the usual predisposing factors; the majority of cases occurred in younger males. Culture results indicated the frequent pathogens were Streptococcus species (47%), anaerobic species (28%), and Staphylococcus aureus (22%). Almost half of the cultures revealed mixed infections with more than one isolate. Epidural and subdural empyema were the most frequently reported intracranial complications.5

Pott puffy tumor is treated with surgery and antibiotics. Surgical treatment includes drainage of the frontal sinus and other areas of infection. Broad-spectrum antibiotics that have good central nervous system penetration must be started on diagnosis. Prolonged antibiotic treatment is required after surgery because osteomyelitis is usually present.6

Disclosure Statement

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

How to Cite this Article


References

Tubo-ovarian abscess (TOA) and hydrosalphinx are complications, though uncommon, of pelvic inflammatory disease (PID). Both TOA and hydrosalphinx can lead to significant morbidity and, rarely, mortality, and both necessitate treatment to reduce short- and long-term complications. Risk factors of TOA include younger age, multiple sexual partners, nonuse of barrier contraception, and a history of PID. The clinical manifestations of TOA are similar to PID—lower abdominal pain, fever, chills, and vaginal discharge, with the addition of pelvic mass noted on examination or imaging. Women with TOA present with fever and chills (50%), nausea (26%), vaginal discharge (28%), abnormal vaginal bleeding (21%), and acute lower abdominal pain (89%).

Women with a presentation consistent with TOA should be evaluated with a complete history; pelvic examination; laboratory testing for complete blood count, erythrocyte sedimentation rate, and C-reactive protein; cervical testing for gonorrhea and chlamydia; and pregnancy testing to guide antimicrobial therapy. In severe cases, TOA can rupture and leak, causing sepsis. This increases mortality and requires emergent surgical intervention.

The most useful diagnostic imaging studies include transvaginal ultrasonography and computed tomography. Compared with ultrasonography, computed tomography has increased sensitivity to detect thick-walled, rim-enhancing adnexal masses, pyosalphinx, and mesenteric stranding, as well as changes suggestive of ruptured TOA. On computed tomography scan with contrast, a pyosalphinx is visualized as a dilated, fluid-filled fallopian tube without rim enhancement (Figures 1 and 2).

Although TOA is a complication of PID, Neisseria gonorrhoeae and Chlamydia trachomatis are infrequently isolated from abscess fluid. Instead, these organisms weaken normal host defenses, facilitating invasion and infection of the upper genital tract by aerobic streptococci, Escherichia coli, aerobic streptococci, Prevotella, Bacteroides fragilis, and Peptostreptococcus. Cephapemycin or cefotetan and doxycycline or gentamicin and clindamycin are preferred, although local antibiotic resistance patterns should be considered. Transition to oral antibiotics (clindamycin or metronidazole with doxycycline) can usually be initiated within 24 hours to 48 hours of clinical improvement to complete the 14-day treatment course. The majority of small abscesses (< 9 cm in diameter) resolve with antibiotic therapy alone.

The aim of therapeutic management is to be as noninvasive as possible. However, if this approach fails to yield clinical improvement within 3 days, reassessment of the antibiotic regimen, with consideration for laparoscopic, laparotomy, and hysterectomy, or image-guided abscess drainage is necessary. Because of its association with shorter hospitalization and improved pain control, image-guided percutaneous abscess drainage is an attractive alternative to surgical intervention in the management of TOA. The clinician should inform, evaluate, test, and treat the patient’s sexual partners.

Disclosure Statement

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

References

Image Diagnosis: Gastric Migration of Hookworms in a Patient with Anemia

Chalapathi Rao Achanta, MD

CASE REPORT
A 65-year-old man presented to our hospital with 4 months of fatigue and weakness. He denied any bleeding manifestations and had pallor on examination. Laboratory test results showed hemoglobin of 8.2 gm/dL with microcytosis and low iron stores. There was no peripheral eosinophilia. Liver and renal function tests were normal. Upper endoscopy was ordered for evaluation of iron deficiency anemia.

The patient’s esophagus was normal, but there were motile hookworms in the gastric antrum (Figure 1) and heavy loads of hookworms in the duodenum (Figure 2). His stool examination showed hookworm eggs. The patient received 400 mg of oral albendazole therapy along with iron therapy. At 3-month follow-up, his anemia was corrected, and he was symptom free.

DISCUSSION
Ancylostoma duodenale and Nector americanus are the common species of hookworm that attach to the small intestinal mucosa. Some 570 million to 740 million people are estimated to be infected with hookworms worldwide, and infection rates in India range from 16% to 30% of the population. Although the majority of the infected population remain asymptomatic, 10% of those infected suffer from anemia, bringing them to medical attention. Infestation impairs the physical, intellectual, and nutritional development of children.

The adult female hookworm releases eggs, which are passed in stool. Rhabditiform larvae are released in soil after hatching and undergo two molts before reaching an infective third-stage filariform larvae. These larvae can survive for 3 to 4 weeks in contaminated soil under favorable climate conditions. They penetrate human skin upon contact and reach the lungs through the heart via blood circulation. Once these larvae penetrate the pulmonary alveoli, they ascend the bronchus to the pharynx. From there they are swallowed and reach the small intestine, where they mature to adult worms.

Adult hookworms inhabit the small intestine and ingest intestinal epithelial and red blood cells, causing iron-deficiency anemia. On average, daily intestinal blood loss is estimated to be between 0.01 mL to 0.3 mL depending on the parasite species. Very rarely, these worms migrate and reach the gastric antrum. According to Thomas et al, retrograde jejunoduodenogastric reflux results in the gastric migration of hookworms, especially in cases of high worm burden. Treatment includes either a single dose of oral albendazole 400 mg or oral mebendazole 100 mg twice daily for 3 days. Treatment success ranges from 69% to 92% depending on the regimen used. Concomitant iron therapy is necessary to replace lost iron stores.

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

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Achanta CR. Image diagnosis: Gastric migration of hookworms in a patient with anemia. Perm J 2016 Summer;20(3):15-201. DOI: http://dx.doi.org/10.7812/TPP/15-201

References
CLINICAL MEDICINE

Image Diagnosis: Encephalopathy Resulting from Dural Arteriovenous Fistula

Ana Filipa Santos, MD; Célia Machado, MD; Sara Varanda, MD; João Pinho, MD; Manuel Ribeiro, MD; Jaime Rocha, MD; Ricardo Maré, MD

CASE REPORT

A 69-year-old woman presented to the Neurology Department with 2 months of progressive psychomotor slowing, inability to concentrate, and periods of disorientation. Her past medical history was unremarkable, and she was taking no medication. There was no history of trauma. On neurologic examination she was alert but taking a long time to answer, apathetic, distractable, and hypophonic with right visual and sensitive hemiextinction and left hemiparesis. Montreal Cognitive Assessment Exam score was 11/30. A computed tomography scan of the brain (Figure 1) showed possible convexity subarachnoid hemorrhage that the brain magnetic resonance imaging (MRI)/MRI angiography (Figures 2 and 3) revealed to be engorged cerebral vessels. Hyperintensity in the deep white matter of the cerebral hemispheres was also present. Cerebral angiography (Figure 4) revealed a dural arteriovenous fistula (DAVF) of the superior sagittal sinus and torcula (Cognard classification IIIb).

The patient underwent endovascular embolization, with combined transarterial (n-butyl-cyanoacrylate) and transvenous (coils) approach, resulting in proximal occlusion of the superior sagittal sinus, torcula, and transverse sinus (Figure 5). Posttreatment angiography revealed near complete DAVF occlusion (Figure 6). Control MRI revealed a marked decrease of the deep white matter hyperintensity and no engorged cerebral veins (Figures 7 and 8). The patient’s mental status improved post procedure (Montreal Cognitive Assessment Exam score, 20/30), and she progressively came back to her baseline.

Figure 1. Computed tomography scan of the brain showing possible convexity subarachnoid hemorrhage.

Figure 2. Coronal-view T2-weighted magnetic resonance image of the brain. The white arrows indicate engorged cerebral veins visible over the surfaces of the hemispheres bilaterally.

Figure 3. Axial-view T2-weighted magnetic resonance image of the brain. The white crosses indicate the increased signal that is diffusely present within the deep white matter of the cerebral hemispheres.

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DISCUSSION

DAVFs are abnormal arteriovenous connections within the dura, usually located within the walls of a dural sinus or an adjacent cortical vein, and account for 10% to 15% of all intracranial arteriovenous lesions.\(^2,^4\) The initiating events which lead to their development are not clear, but the literature reports association with trauma, infection, recent surgery, and dural sinus thrombosis.\(^2,^4\) A wide variety of signs and symptoms, which can vary because of lesion location and pattern of venous drainage, may arise from DAVFs, namely, pulsatile tinnitus, ophthalmoplegia, proptosis, chemosis, retro-orbital pain, decreased visual acuity, seizures, Parkinsonism, cerebellar symptoms, apathy, and dementia.\(^2,^4\)

CONCLUSION

Our patient with DAVF presented with encephalopathy with diffuse white matter changes related to venous ischemia. Her symptoms partially reverted with endovascular treatment. DAVF should be considered in patients with encephalopathy. This relatively non-specific clinical picture may delay the diagnosis and result in further deterioration. A high level of suspicion should be maintained in patients who present in the context of unexplained intracranial hemorrhage without significant risk factors (trauma, hypertension, or anticoagulation) or in possible subarachnoid hemorrhage in a nonaneurysmal pattern. This should prompt imaging with MRI and angiography, which are the gold standard for diagnosis. DAVF recognition is essential because these patients are potentially treatable.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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Future Challenges of Robotics and Artificial Intelligence in Nursing: What Can We Learn from Monsters in Popular Culture?

Henrik Erikson, RNT, PhD; Martin Salzmann-Erikson, RN, MHN, PhD

ABSTRACT
It is highly likely that artificial intelligence (AI) will be implemented in nursing robotics in various forms, both in medical and surgical robotic instruments, but also as different types of droids and humanoids, physical reinforcements, and also animal/pet robots. Exploring and discussing AI and robotics in nursing and health care before these tools become commonplace is of great importance. We propose that monsters in popular culture might be studied with the hope of learning about situations and relationships that generate empathic capacities in their monstrous existences. The aim of the article is to introduce the theoretical framework and assumptions behind this idea. Both robots and monsters are posthuman creations. The knowledge we present here gives ideas about how nursing science can address the postmodern, technologic, and global world to come. Monsters therefore serve as an entrance to explore technologic innovations such as AI. Analyzing when and why monsters step out of character can provide important insights into the conceptualization of caring and nursing as a science, which is important for discussing these empathic protocols, as well as more general insight into human knowledge. The relationship between caring, monsters, robotics, and AI is not as farfetched as it might seem at first glance.

INTRODUCTION
It is highly likely that artificial intelligence (AI) will be implemented in medical technologic equipment for clinical monitoring and decision making. This change will probably happen rapidly and on a global scale, because digitalization and globalization are intensely connected via the Internet. For this reason, the ethics of robotics and AI must be well developed for these posthuman creations to make decisions within the frame of acceptable human ethics and values of nursing. One paradox is the question of how we can understand and explore these AIs before we must embrace them as facts in everyday health care services.

Monsters in popular culture could be scrutinized with the hope of learning about situations that generate empathic capacities. If everyone who encounters a fictional monster—in a book, play, motion picture, or video game—and who engages in caring activities reported their observations, together these observations might show important patterns relating to empathic abilities in posthuman creations. Cataloging and analyzing situations in which monster characters actually become nurturing and caring can be important for understanding how humans care as well as for understanding care in relation to posthuman venues. Are these situations of protection, sheltering, or friendship? Questions about empathy in relation to robotics and AI have been addressed by researchers. Usually, this relationship is presented from the perspective of humans’ empathy for robots. However, the dimension we are interested in is the reverse: the empathic capacities that robotics and AI can demonstrate for humans. The knowledge generated will bring clues as to what the relationship is between empathy and AI and will contribute to our understanding so that it will be useful for a future where the impact of digitalization has to be taken into account in nursing/caring theories. This is one attempt to capture understanding about empathic intelligences in virtual creations, that is, robots, machines, and cyborgs (empathic protocols). From this perspective, we ask the question of whether monsters can help us relate to AI and to nursing robots.

LINK BETWEEN MONSTERS AND ARTIFICIAL INTELLIGENCE
Monsters do relate to robotics and sometimes to “evil” machines that combine the two into one appearance. One example in popular culture is found in the Terminator film series, in which machines have reached far beyond the point that is often referred to as technologic singularity. Technologic singularity is a critical moment, a point when AI surpasses biological intelligence. In the Terminator series, the machines develop, improve, and reproduce themselves without human involvement, and their goal is to drive their creators—the humans—to extinction. However, in the 1940s, Isaac Asimov wrote Runaround, in which he developed the Laws of Robotics:

1. A robot may not injure a human being, or through inaction, allow a human being to come to harm.
2. A robot must obey the orders given it by humans, except where such orders conflict with the First Law.
3. A robot must protect its own existence as long as such protection does not conflict with the First or Second Law.
4. (Added later, known as the zeroth law): No robot may harm humanity or, through inaction, allow humanity to come to harm.

We are entering an era when the vast digitalization of health care in everyday life and the fictional Laws of Robotics just presented are discussed as reality. Health care institutions and the nursing discipline face paradigmatic changes that are related to digital technology. For the discipline of...
nursing, the relationship to technology and AI is sparse, so these changes will represent a giant leap. We argue that it is also highly relevant and timely for nursing science to monitor and to debate AI and Robotics in the same fashion as other areas, such as medicine.

The International Robot Fair concluded with a World Robot Declaration proposition that next-generation robots will 1) be partners that coexist with human beings, 2) assist human beings both physically and psychologically, and 3) contribute to the realization of a safe and peaceful society. Even though robots equipped with AI in popular culture often are portrayed as embodied monsters, this might not be the reality in the near future. However, and more importantly, AI is developing rapidly, and several research projects predict that technologic singularity is no more than 30 years away. Today's robots are starting to be implemented in health care facilities, in forms such as surgical robots and in nursing homes. As posited in the World Robot Declaration, next-generation robots assist humans physically. One important aspect of AI and robotics for nursing is that nurses might be first-hand partners, working in nursing in institutions with robots in the near future. Nurses might interact with household robots in patients' homes rather than with the patients themselves.

**CHALLENGES OF ROBOTICS AND ARTIFICIAL INTELLIGENCE IN NURSING**

Even if there is a connection between monsters and robots, one does not ordinarily think of monsters and nursing in the same framework, nor of robotics and empathy. The relationship between caring monsters, robotics, and AI is not as farfetched as it might seem at first glance. Both robots and monsters are posthuman creations. Just like the robot, monsters are also connected to cultural and historic contexts. Monsters represent our fears, and they stand on the threshold of human becoming, always representing "the other." These representations suggest that monsters ask us how we perceive the world; they ask us to reevaluate our cultural assumptions about ethnicity, gender and sexuality, our perception of difference, and our tolerance toward expression.

More generally, monsters ask us why we created them. Maybe for that reason, popular culture is full of monsters in TV series, books, and movies.

**IMPLICATIONS FOR NURSING PRACTICE**

When various nursing robots become common practice in institutional settings, they will have a major impact on nursing work, the nursing profession, and health care in general. Nursing robots will redefine ideas about nurses in general as well as ideas about nursing attributes and conceptual frameworks of comfort and safety in particular. Staying abreast of developments regarding redefinitions of nursing and its underlying beliefs, values, and assumptions is relevant to also understanding the implications of AI and robots in health care. We therefore state that we can turn to monsters and their evolutionary existence for preparing ourselves and improving our understanding of AI and robotics.

What we can see in our project Caring Monsters, so far is that monsters are
It is important to address the issue that monsters are creations of storytellers and writers who have their own ideas and messages about AI and robotics. However, the storytellers’ motivations are not necessarily the same as the readers’ and viewers’ ideas, nor the larger social interpretations that the monster itself creates. In other words, the writers’ and creators’ motivations do not always match with the ideas their work provokes. We can apply this logic in the context of AI; the motivation behind researchers creating AI might not be the same as the interpretation of the resulting AI itself. Monsters exist outside and beyond storytellers’ and writers’ motivations. For this reason, we have chosen to look at the monsters themselves, not the creators’ motivations and intentions. By stating this, we recognize the understanding of reality as the projection of an ongoing construction and reconstruction from the points of reference that we experience through life and that doubt and self-negotiation are vital human values that also seem to be crucial in the evolutionary history of monsters.

Disclosure Statement

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

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Section A.

Article 1. (page 18) A Pharmacist-Staffed, Virtual Gout Management Clinic for Achieving Target Serum Uric Acid Levels: A Randomized Clinical Trial

What is the recommended goal for urate-lowering therapy in patients with chronic, recurrent gout?

- a. a serum uric acid level < 7.0 mg/dL
- b. an allopurinol dose of 300 mg/day
- c. a serum uric acid level < 6.8 mg/dL
- d. a serum uric acid level < 6.0 mg/dL

Which of the following statements is false about urate-lowering therapy in patients with gout?

- a. adherence rates to urate-lowering therapy are low compared with many other chronic conditions
- b. physicians often fail to monitor and to appropriately escalate urate-lowering therapy
- c. most gout patients are on appropriate urate-lowering therapy
- d. rarely prophylaxis with colchicine or a nonsteroidal anti-inflammatory drug is appropriate in the first several months even after achieving the target level with allopurinol or other urate-lowering treatments

Article 2. (page 51) Improving Care in Older Patients with Diabetes: A Focus on Glycemic Control

What is the first-line therapy for treatment of glycemic control in older adults with diabetes (assuming no contraindications to the medication)?

- a. glipizide
- b. glyburide
- c. metformin
- d. insulin
- e. pioglitazone

What is an appropriate hemoglobin A\(_1c\) range in a 74-year-old patient on glipizide and metformin with comorbidities of hypertension and hyperlipidemia?

- a. 5.5 to 5.9
- b. 6.0 to 6.4
- c. 6.5 to 6.9
- d. 7.0 to 7.9

Section B.

Referring to the CME articles, how likely is it that you will implement this learning to improve your practice within the next 3 months?

Objective 1
Integrate learned knowledge and increase competence/confidence to support improvement and change in specific practices, behaviors, and performance.

- 5 = highly likely
- 4 = likely
- 3 = unsure
- 2 = unlikely
- 1 = highly unlikely
- 0 = I already did this

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.

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Section C.

What other changes, if any, do you plan to make in your practice as a result of reading these articles?

Section D. (Please print)

Name ________________________________

Title ________________________________

E-mail ________________________________

Address ________________________________

Signature ________________________________

Date ________________________________

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