



advancing the art & science of medicine in the midwest

WMJ

volume 112 • no. 5 • october 2013

Educating tomorrow's physicians

**Helping students understand how
research informs clinical medicine**

Inspiring a generation

**CME: Heiner syndrome mimicking
an immune deficiency**



No waiting period.
Small detail. **Big difference.**

Some insurance companies say your power has to be out for at least 72 hours before they'll reimburse you for loss of business. But we both know you start losing money the second you lose power. That's why our coverage kicks in immediately. To hear more about how we handle the details that make the biggest difference, call 888-5-SOCIETY or find one of our agents at societyinsurance.com.



Small details. Big difference.™



FOR SEEING

if your cash flow is as effective as your treatments.



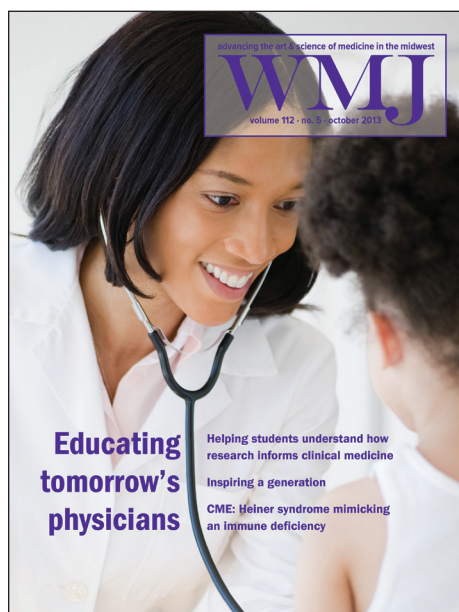
Cash Flow InsightSM | for the achiever in you[®]

Introducing Cash Flow Insight powered by PNC CFO — a suite of user-friendly online tools that can help you understand and project your practice's cash flow, so you can turn insight into action. Try it at no cost today*. Call the Cash Flow Insight Center at 855-762-2361, stop by any PNC branch or go to pnc.com/cashflowinsight

PNC | CFOSM
Cash Flow Options



*Offer requires a PNC Business Checking account and enrollment in PNC Online Banking. Offer valid during your current statement cycle period and two additional statement cycles, which constitutes your free trial period. One free trial period per customer, based on the enrollment date of the first account you enroll in Cash Flow Insight. Your free trial period for all accounts in Cash Flow Insight ends at the same time. At the end of your free trial, you will remain enrolled in Cash Flow Insight and be charged a fee of \$10/month. If you do not want to continue with Cash Flow Insight, you may opt out of the service on your Preferences page within Cash Flow Insight. Beyond the trial period, certain account types have Cash Flow Insight for no additional monthly fee, including Business Enterprise Checking, Industry Solutions Checking and Retail Businesses Checking. Cash Flow Insight and CFO: Cash Flow Options are service marks of The PNC Financial Services Group, Inc. ©2013 The PNC Financial Services Group, Inc. All rights reserved. PNC Bank, National Association. Member FDIC



COVER THEME

Educating Tomorrow's Physicians

"The education of physicians has been the subject of debate for over a century" and "begins long before the first day in medical school." So states a report in this issue of *WMJ*, which features 3 articles focusing on very different aspects of the journey to becoming a physician.

Cover design by
Mary Kay Adams-Edgette.

The mission of *WMJ* is to provide a vehicle for professional communication and continuing education for Midwest physicians and other health professionals. *WMJ* is published by the Wisconsin Medical Society.

Volume 112, no. 5 • October 2013

WMJ

EDITORIAL

Commentary

The Art of Doctoring – Inspiring a Generation 189

Robert J. Dempsey, MD

In This Issue

Making Progress, but Still a Way to Go 191

John J. Frey, III, MD, Medical Editor

ORIGINAL RESEARCH

Providing Premedical Students with Quality Clinical and Research Experience:

The Tobacco Science Scholars Program 195

James M. Davis, MD; Maggie C. Anderson; Kristin A. Stankevitz; Alison R. Manley

Barriers and Facilitators of Universal HIV Screening

Among Internal Medicine Residents 199

Meghan B. Brennan, MD; Christine Kolehmainen, MD; Joshua Barocas, MD;

Carol Isaac, PhD; Christopher J. Crnich, MD; James M. Sosman, MD

Child Abuse Pediatric Consults in the Pediatric Emergency Department

Improve Adherence to Hospital Guidelines 206

Tara Webb, MD; Thomas Valvano, MD, JD; Melodee Nugent, MA;

Marlene Melzer-Lange, MD

PUBLIC HEALTH BRIEF REPORT

Progress in Reducing Premature Deaths

in Wisconsin Counties, 2000-2010 211

Thomas Nonnweiler; Elizabeth A. Pollock, BS; Barbara Rudolph, PhD, MSSW;

Patrick L. Remington, MD, MPH

advancing the art & science of medicine in the midwest

CASE REPORTS

Heiner Syndrome Mimicking an Immune Deficiency	215
--	-----

Jerome A. Sigua, MD; Michael Zacharisen, MD

Heat-related Fatalities in Wisconsin During the Summer of 2012	219
---	-----

Megan L. Christenson, MS, MPH; Sarah Dee Geiger, PhD, MS; Henry A. Anderson, MD

YOUR PROFESSION

Looking Back...to 1938

The Whole Patient.....	188
------------------------	-----

Paul F. Doege, JG Crownhart

Dean's Corner

Clinical Implementation of Whole Genome Sequencing a Valuable Step Toward Personalized Care	224
--	-----

Joseph E. Kerschner, MD

CME Quiz

Quiz: Heiner Syndrome Mimicking an Immune Deficiency	218
--	-----

YOUR PRACTICE

Driven to Serve	226
-----------------------	-----

W. Stancil Starnes, JD

Statement of Ownership	228
------------------------------	-----

Classified Ads	228
----------------------	-----

The *WMJ* (ISSN 1098-1861) is published by the Wisconsin Medical Society and is devoted to the interests of the medical profession and health care in the Midwest. The managing editor is responsible for overseeing the production, business operation and contents of the *WMJ*. The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic, or organizational articles. All articles published herein, including commentaries, letters to the editor and editorials represent the views of the authors, for which neither *WMJ* nor the Wisconsin Medical Society take responsibility, unless clearly stated. Advertising content is the responsibility advertiser and does not imply an endorsement or sponsorship by *WMJ* or the Wisconsin Medical Society and its affiliates unless specified. *WMJ* is indexed in Index Medicus, Hospital Literature Index, and Cambridge Scientific Abstracts.

Send manuscripts to *WMJ*, 330 E Lakeside St, Madison, WI 53715. Instructions to authors are available at www.wmjonline.org, call 866.442.3800, or e-mail wmj@wismed.org.

MEDICAL EDITOR

John J. Frey, III, MD, Madison, Wis.

EDITORIAL BOARD

John J. Frey, III, MD, Madison, Wis.
Philip F. Giampietro, MD, Madison, Wis.
Louis Kleager, MD, Scottsbluff, Neb.
Kathleen R. Maginot, MD, Madison, Wis.
Joseph J. Mazza, MD, Marshfield, Wis.
Richard H. Reynertson, MD, La Crosse, Wis.
Sarina B. Schrager, MD, Madison, Wis.
Kenneth B. Simons, MD, Milwaukee, Wis.
Geoffrey R. Swain, MD, Milwaukee, Wis.
Darold A. Treffert, MD, Fond du Lac, Wis.
Steven H. Yale, MD, Marshfield, Wis.

STAFF

Kendi Parvin
Managing Editor
Mary Kay Adams-Edgette
Layout and Design
Lisa Hildebrand
Editorial Assistant
Deana Hipke
Editorial Assistant

ADVERTISING

Kelly Slack, Slack Attack Advertising,
608.222.7630 or kelly@slackattack.com.

SUBSCRIPTION RATES

Members: included in membership dues.
Non-members: \$149. Current year single copies, \$25 each. Previous years' single copies, when available, \$12 each.

Periodical postage paid in Madison, Wis, and additional mailing offices.

Published every other month, beginning in February. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917. Authorized August 7, 1918.

Address all correspondence to *WMJ*, PO Box 1109, Madison, WI 53701. Street address: 330 E Lakeside St, Madison, WI 53715; e-mail: wmj@wismed.org

POSTMASTER

Send address changes to: *WMJ*,
PO Box 1109, Madison, WI 53701

ISSN 1098-1861
Established 1903

© 2013 Wisconsin Medical Society

The Whole Patient

Paul F. Doege, Marshfield, Medical Editor; Mr JG Crownhart, Madison, Managing Editor

Editor's note: The following is an editorial published in WMJ, Volume 37, p. 1014, November 1938.

Most of the patients we physicians see day in and day out present no very serious problems from either the viewpoint of diagnosis or sound treatment. They require the skilled attention of a physician but, with respect to ordinary illnesses, our training and experience enables us rather quickly to discover the causative factors and choose the most promising treatment.

Because this is true, how frequently are we apt to treat the “case”—particularly when we are confronted with a full waiting-room — without pausing to explain to the patient in at least a few words what it is that we have found, what it is that we will do, and advising, when the facts so indicate, that there is no cause for undue apprehension.

The earlier the patient comes to us with symptoms, the more evident it should be that it is in part at least his apprehension that brings him. This is as it should be. Let us not forget that if we treat the “case” and not the patient we will lack the human touch that has always marked the true physician.



**MS STOPS PEOPLE
FROM MOVING**

**WE EXIST
TO MAKE SURE
IT DOESN'T**

JOIN THE MOVEMENT
jointhemovement.org



WMJ

**Let us hear
from you**

If an article strikes a chord or you have something on your mind related to medicine, we want to hear from you. Submit your letter via e-mail to wmj@wismed.org or send it to *WMJ* Letters, 330 E Lakeside St, Madison, WI 53715.

The Art of Doctoring – Inspiring a Generation

Robert J. Dempsey, MD

The completion of medical training and the start of a career is one of the great transitions in a physician's life. It is a time for reflection, a time for pride and satisfaction, and a time for new challenges. The following is my contribution given as the commencement address chosen by the graduating students of the 2013 class at the University of Wisconsin School of Medicine and Public Health. It is my attempt to summate what I have learned about the art of doctoring and to challenge them to fulfill the promise and possibility of their talents, their efforts, and their inspiration.

• • •

It is a great honor to be here. This is truly wonderful. As a teacher, I've often said that of all the days of the year, this is the best because it marks your accomplishment. All of you as an extended family. And that you share it with us—your teachers—that's inspiring. And indeed, inspiring doctors is exactly what I'm talking about today. But first—a teacher's confession: All of you in the front row—remember the Krebs cycle? I don't either. The back row—remember all those mnemonics you used to help yourself get through anatomy class? They don't work in the operating room. It is a bit of a dilemma. You thought you came to school to be taught medi-

• • •

Robert J. Dempsey, MD; University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Rm K4/866, Madison, WI 53792; phone 608.265.5967; fax 608.263.1728; e-mail dempsey@neurosurgery.wisc.edu.

cine, but Oscar Wilde claimed that nothing truly worth knowing can be taught. Indeed there might be a bit of truth to this. Look at politics. Arguably our greatest president and certainly our most eloquent, Abraham Lincoln, was also our least educated. Scholars think he had at least 6 months of total education. So what was the last 4 years

that doctoring is hard work, that you work too many hours—but never believe it. Whether it's me taking a brain tumor out of a child in sub-Saharan Africa, or my colleagues working to stop a resistant bacteria from becoming the world's next plague, or a generation of doctors trying to influence their patients to take control of their health to stop the modern plagues

You will be teachers for all of your patients, and you must be. But the role of a teacher in medicine goes beyond individual patients. You must also teach yourself and your peers.

about? Certainly it was not about mnemonics. It was about inspiring you to discover this thing that we call the art of doctoring. It is what Yeats called "lighting a fire, not filling a pail." It is a lifelong discovery. It may seem odd for a neurosurgeon to talk doctoring. Neurosurgeons are supposed to carry an ego so large it requires a wheelbarrow to follow them on rounds, but I think people that know my career know that it has been spent trying to bring down those barriers. I have been at this attempt to discover for myself this art of doctoring for 40 years. I hope I never stop. So let me share with you some of the lessons that I have learned myself and hope you find similar ones in your continuing education in this doctoring.

First: Great doctors are in love with their jobs. Your college classmates may tell you

of obesity and diabetes, it all starts with the patient before you who has a need and you care enough about them to do the best for them. When you do, the hours fall away and you are fully engaged in your life, and in this field you must be. You see, as students you observe, you practice, you're protected—but now, from this day forth Doctors (what a wonderful title, "Doctors"), patients will put their lives, their happiness, and their future in your hands. Great doctors are truly engaged.

Second: Great doctors are creative. Be proud of what you have learned; be proud of the techniques and practices you know. But also be totally dissatisfied with them. When the patient is before you, then nothing we do for cancer, heart disease, or Alzheimer's is good enough. I do not want you to treat me with the techniques of my professors. I do not want

you to treat my children with the techniques that I taught you—I want you to surpass me. I want you to be agents of disruptive change, not settle for just what you know so far—I want you to create a better way. This is true in all fields. Look in music. At one time, American music was dominated by something called “Dixieland” and the leader of that was a man named King Oliver, impossibly rich and famous; clearly his fame would live forever. But he mentored a 16-year-old reform school kid. He gave him a cornet, taught him music, and when Louis Armstrong played, music was never the same and the teacher was surpassed and forgotten. You need to have scientific curiosity. You need to know you can do research and show creativity. Don’t be afraid of research. Be it DNA or clinical outcomes research, you can do it. I don’t have a PhD, but I will soon have 30 years of NIH funding because when I go to my clinic, my patients ask, “How is your research going Doc?” because they know I’m working on their problem.

Third: Great doctors are teachers. This is my favorite part. Do you know what “Doctor” means? It is from the Latin “docēre,” which means teacher. You must be teachers of your patients if you wish them to take charge of their health. A great teacher knows it’s never about what they said or what material they covered. It’s what the student heard and understood. I cannot tell a patient that I’m going to go into their brain, repair a leaking blood vessel, and come out and expect to have their trust if they cannot understand what I say. You will be teachers for all of your patients, and you must be. But the role of a teacher in medicine goes beyond individual patients. You must also teach yourself and your peers. You must learn and grow if you are to create and change or the world will pass you by. And you must teach your fellow doctors. For me this was made so apparent by 1 person, 1 day, 1 place—it was a great gift for me to see. I was working in the mountains of Guatemala during the time of their civil war. I had taken care of some hundred patients that day, and as I entered the courtyard at evening, I saw a young child selling fruit. I sought permission to photograph her and that picture hangs in my office where I look at it often. Because on that day I thought, who will take care of her when in the

future she is sick and I’m not here? That day I became a teacher of doctors because we need you to go to the places we will never visit—to treat the patients we will never see, and in doing so, they will teach you.

Fourth: Great doctors have integrity. We all know the icons of Schweitzer, of Paul Farmer, of Lincoln. He fought to the death for the rights of man even though his namesake was murdered by Native Americans. He himself as a youth was attacked by slaves who attempted to murder him, but he treated people as he saw was right. But I am not talking about icons. I am talking about the true meaning of integrity. It is from the Latin for “whole.” It means you are true to the complete mission. You don’t treat the brain and forget the heart, the kidney, the social problems, or a patient’s very access to health care. You show integrity by treating the whole patient and by realizing the need to continually improve, to be creative, to serve, to teach—and to care for yourself, because how you treat your whole person is all about your integrity as a doctor as well.

Treating yourself is the root of the final and most important lesson: Great doctors are great people. I’ve always observed that great doctors really like people. I’ve never seen it work the other way around. And when it’s true, none of this is hard work. You are able to serve because you’ve taken time to develop yourself as a person and hold true to the values that brought you to medicine in the first place in a world of conflict, bureaucracy and greed (be careful of greed!). And how do you do that? By having a value system you compare to for everything you do. It is a very individual thing, but I will share with you what I value. For me it is faith, family, and patients.

Faith or moral code may be formal or informal, but it is a guide to find the right path for you. It is something to help you make sense of a world where people in Boston place bombs at the feet of children. But what I saw immediately after the explosion gives me faith and inspires me: medical personnel rushed into the blast area to give aid, while police said there may be a third bomb.

Next is family. You decide how you define that. It could be a very nontraditional family; it

could be a family of colleagues. But these are people you hold close, people in whom you can confide, people with whom you are safe, people who make you laugh when you so need to. Hold them dear. Do nothing to lose that.

Finally, most obvious is patients—the people that bring it all into focus, the true source of that inspiration and your best teachers. They inspire you to create, to teach yourself to develop your whole person, and to be in love with what you do.

I still believe in the essential goodness of men and women. It has always been about how you treat people. From the patient, to the cleaning lady you pass every day, to the CEO. You acknowledge them; you get down to their level and you listen. You explain so that they can understand, and you will inspire me. You are embarking on the greatest of professions. Cushing called it the “divine vocation,” this art of doctoring. Now go and inspire others every day to be that teacher, to look after yourself and create for future patients a world that will show how you earned that role of teacher and how you came to be called the Latin docēre, “Doctor.” Congratulations and thank you for inspiring me.

Professional Office Space

-Cedarburg-
Historic Downtown
Creekside Center
Medical Arts Building

► Close to
*Aurora Hospital-Grafton &
Columbia St. Mary's Hospital-
Mequon*

► Health & wellness neighbors

► Ready for your
custom floor plan

► Competitive Rates

For details, visit
www.creeksidecenter.info
or contact
Tom Schemberger
262-389-4858

Making Progress, but Still a Way to Go

John J. Frey III, MD, Medical Editor

This issue of the *WMJ* has the usual interesting variety of studies and reports that bring together some of the challenges facing the practicing community.

Reducing premature death is one element of measuring progress, not only for health systems, but for the society in which those health systems function. The widely used County Health Rankings developed by the University of Wisconsin Public Health Institute,¹ have been a useful tool for communities to identify issues that should be addressed to improve health. Nonnweiler and colleagues² add another type of scorecard to use as a measure of how we are doing by looking at the changes in age-adjusted premature death rates by county. Much of the prematurity can be traced to preventable causes that lend themselves to improving both public health and clinical care for communities. Their paper describes the overall data—the *what*—and it is up to us to work to find the *why*. The best news is that the counties that started out being the farthest behind have made the greatest improvements.

2012 was a record summer for heat in the state—and the world—and we could expect that heat-related stresses might increase problems for at-risk patients. Christenson and colleagues,³ in their review of cases of heat-related deaths, show that older people on psychiatric medication who lived in houses or apartments without air conditioning are at much greater risk of dying during very hot periods. This confirms the work by Klinenberg from the 1995 Chicago heat wave.⁴ While at face value the data should not surprise us, these deaths should be preventable through a combination of neighborhood action and medical systems identifying populations that are more at risk. However, when I ask physicians if they can identify their patients who are elderly, living alone, and poor, their electronic health records (EHRs) don't usually contain that information.

EHRs need to be more about populations and less about billing if they are to meet their full potential.

Webb and colleagues⁵ report on a special child abuse consultation service that improves the quality of care in emergency departments (EDs) for the terrible reality of children and families involved in domestic violence, and is able to do it in a more systematic and organized way. Emergency and community clinicians have been taught to raise the issue of possible abuse, but the process of gathering the correct information could be expedited through consultation when necessary and through the dissemination of proper guidelines to all practices that might encounter potentially abused children. This study is from an ED, but most children who are potential victims of abuse are seen in offices of pediatricians and family doctors.

Three articles in this issue address education. The study by Brennan and colleagues⁶ nicely describes some of the issues for internal medicine residents in attempting to increase screening for HIV in their practices. Interviews with residents describe patient-related and physician-related barriers and offer some suggestions for increasing screening. While there may be a great deal of controversy about the recommendation to screen the entire population for HIV, increasing screening for those who are at risk is certainly in order. A combination of education and goal setting is the likely solution, along with faculty who are supportive and encouraging.

Giving pre-professional students a meaningful experience in clinical care is becoming increasingly more problematic, with HIPAA restrictions and more complicated institutional guidelines that often don't distinguish between inpatient and outpatient experiences. The article by Davis and colleagues⁷ about getting under-

graduates to work with clinicians and researchers through the UW Center for Tobacco Research and Intervention (CTRI) points out the value that students can add to ongoing projects while learning important communication skills and bringing help to persons addicted to tobacco. It's a very win-win program and something that could be reproduced in other schools in the United States since CTRI has made much of the material available on the Web.

Finally, Dempsey⁸ offers important and searching lessons from his own life and career to graduating medical students. One of the responsibilities that "elders" have is to coach and listen, to be sure, but telling stories, and the insight those experiences bring, is the true way that teaching moves ahead. The data are important; the stories are essential.

REFERENCES

1. University of Wisconsin Population Health Institute. Robert Wood Johnson Foundation. County Health Rankings & Roadmaps. <http://www.countyhealthrankings.org>. Accessed September 23, 2013.
2. Nonnweiler T, Pollock EA, Rudolph B, Remington PL. Progress in reducing premature deaths in Wisconsin counties, 2000-2010. *WMJ*. 2013;112(5):211-214.
3. Christensen ML, Geiger SD, Anderson HA. Heat-related fatalities in Wisconsin during the summer of 2012. *WMJ*. 2013;112(5):219-223.
4. Klinenberg E. *Heat Wave: A Social Autopsy of Disaster in Chicago*. University of Chicago Press; 2002.
5. Webb T, Valvano T, Nugent M, Melzer-Lange M. Child abuse pediatric consults in the pediatric emergency department improve adherence to hospital guidelines. *WMJ*. 2013;112(5):206-210.
6. Brennan MB, Kolehmainen C, Barocas J, Isaac C, Crnich CJ, Sosman JM. Barriers and facilitators of universal HIV screening among internal medicine residents. *WMJ*. 2013;112(5):199-205.
7. Davis JM, Anderson MC, Stankevitz KA, Manley AR. Providing premedical students with quality clinical and research experience: the Tobacco Science Scholars Program. *WMJ*. 2013;112(5):195-198.
8. Dempsey RJ. The art of doctoring [commentary]. *WMJ*. 2013;112(5):189-190.

PROVEN.

LOW RATE OF
HYPOGLYCEMIA

**POWERFUL A1C
REDUCTIONS**
-0.8% to -1.5%*

MAY PROVIDE
ADDITIONAL BENEFIT
OF WEIGHT LOSS†

For adult patients with type 2 diabetes, Victoza® offers these benefits and more.
Visit **VictozaPro.com/Care** to learn how the support program helps patients get started.



*Victoza® 1.2 mg and 1.8 mg when used alone or in combination with OADs.

†Victoza® is not indicated for the management of obesity, and weight change was a secondary end point in clinical trials.

VICTOZA®
liraglutide (rDNA origin) injection

Indications and Usage

Victoza® (liraglutide [rDNA origin] injection) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.

Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

Victoza® has not been studied in combination with prandial insulin.

Important Safety Information

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate

human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

Do not use in patients with a prior serious hypersensitivity reaction to Victoza® (liraglutide [rDNA origin] injection) or to any of the product components.

Postmarketing reports, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

When Victoza® is used with an insulin secretagogue (e.g. a sulfonylurea) or insulin serious hypoglycemia can occur. Consider lowering the dose of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

Renal impairment has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment.

Serious hypersensitivity reactions (e.g. anaphylaxis and angioedema) have been reported during postmarketing use of Victoza®. If symptoms of hypersensitivity reactions occur, patients must stop taking Victoza® and seek medical advice promptly.

There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

The most common adverse reactions, reported in ≥5% of patients treated with Victoza® and more commonly than in patients treated with placebo, are headache, nausea, diarrhea, dyspepsia, constipation and anti-liraglutide antibody formation. Immunogenicity-related events, including urticaria, were more common among Victoza®-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials.

Victoza® has not been studied in type 2 diabetes patients below 18 years of age and is not recommended for use in pediatric patients.

There is limited data in patients with renal or hepatic impairment.

Please see brief summary of Prescribing Information on adjacent page.

Victoza® (liraglutide [rDNA origin] injection)**Rx Only****BRIEF SUMMARY. Please consult package insert for full prescribing information.**

WARNING: RISK OF THYROID C-CELL TUMORS: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors [see *Contraindications and Warnings and Precautions*].

INDICATIONS AND USAGE: Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Important Limitations of Use:** Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise. Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis. Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. The concurrent use of Victoza® and prandial insulin has not been studied.

CONTRAINDICATIONS: Do not use in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Do not use in patients with a prior serious hypersensitivity reaction to Victoza® or to any of the product components.

WARNINGS AND PRECAUTIONS: Risk of Thyroid C-cell Tumors: Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. A statistically significant increase in cancer was observed in rats receiving liraglutide at 8-times clinical exposure compared to controls. It is unknown whether Victoza® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors could not be determined by clinical or nonclinical studies. In the clinical trials, there have been 6 reported cases of thyroid C-cell hyperplasia among Victoza®-treated patients and 2 cases in comparator-treated patients (1.3 vs. 1.0 cases per 1000 patient-years). One comparator-treated patient with MTC had pre-treatment serum calcitonin concentrations >1000 ng/L suggesting pre-existing disease. All of these cases were diagnosed after thyroidectomy, which was prompted by abnormal results on routine, protocol-specified measurements of serum calcitonin. Five of the six Victoza®-treated patients had elevated calcitonin concentrations at baseline and throughout the trial. One Victoza® and one non-Victoza®-treated patient developed elevated calcitonin concentrations while on treatment. Calcitonin, a biological marker of MTC, was measured throughout the clinical development program. The serum calcitonin assay used in the Victoza® clinical trials had a lower limit of quantification (LLOQ) of 0.7 ng/L and the upper limit of the reference range was 5.0 ng/L for women and 8.4 ng/L for men. At Weeks 26 and 52 in the clinical trials, adjusted mean serum calcitonin concentrations were higher in Victoza®-treated patients compared to placebo-treated patients but not compared to patients receiving active comparator. At these timepoints, the adjusted mean serum calcitonin values (~1.0 ng/L) were just above the LLOQ with between-group differences in adjusted mean serum calcitonin values of approximately 0.1 ng/L or less. Among patients with pre-treatment serum calcitonin below the upper limit of the reference range, shifts to above the upper limit of the reference range which persisted in subsequent measurements occurred most frequently among patients treated with Victoza® 1.8 mg/day. In trials with on-treatment serum calcitonin measurements out to 5-6 months, 1.9% of patients treated with Victoza® 1.8 mg/day developed new and persistent calcitonin elevations above the upper limit of the reference range compared to 0.8-1.1% of patients treated with control medication or the 0.6 and 1.2 mg doses of Victoza®. In trials with on-treatment serum calcitonin measurements out to 12 months, 1.3% of patients treated with Victoza® 1.8 mg/day had new and persistent elevations of calcitonin from below or within the reference range to above the upper limit of the reference range, compared to 0.6%, 0% and 1.0% of patients treated with Victoza® 1.2 mg, placebo and active control, respectively. Otherwise, Victoza® did not produce consistent dose-dependent or time-dependent increases in serum calcitonin. Patients with MTC usually have calcitonin values >50 ng/L. In Victoza® clinical trials, among patients with pre-treatment serum calcitonin <50 ng/L, one Victoza®-treated patient and no comparator-treated patients developed serum calcitonin >50 ng/L. The Victoza®-treated patient who developed serum calcitonin >50 ng/L had an elevated pre-treatment serum calcitonin of 10.7 ng/L that increased to 30.7 ng/L at Week 12 and 53.5 ng/L at the end of the 6-month trial. Follow-up serum calcitonin was 22.3 ng/L more than 2.5 years after the last dose of Victoza®. The largest increase in serum calcitonin in a comparator-treated patient was seen with glimepiride in a patient whose serum calcitonin increased from 19.3 ng/L at baseline to 44.8 ng/L at Week 65 and 38.1 ng/L at Week 104. Among patients who began with serum calcitonin <20 ng/L, calcitonin elevations to >20 ng/L occurred in 0.7% of Victoza®-treated patients, 0.3% of placebo-treated patients, and 0.5% of active-comparator-treated patients, with an incidence of 1.1% among patients treated with 1.8 mg/day of Victoza®. The clinical significance of these findings is unknown. Counsel patients regarding the risk for MTC and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness). It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate the potential risk of MTC, and such monitoring may increase the risk of unnecessary procedures, due to low test specificity for serum calcitonin and a high background incidence of thyroid disease. Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation. Although routine monitoring of serum calcitonin is of uncertain value in patients treated with Victoza®, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation. **Pancreatitis:** Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with Victoza®. After initiation of Victoza®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Victoza® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, Victoza® should not be restarted. Consider antidiabetic therapies other than Victoza® in patients with a history of pancreatitis. In clinical trials of Victoza®, there have been 13 cases of pancreatitis among Victoza®-treated patients and 1 case in a comparator (glimepiride) treated patient (2.7 vs. 0.5 cases per 1000 patient-years). Nine of the 13 cases with Victoza® were reported as acute pancreatitis and four were reported as chronic pancreatitis. In one case in a Victoza®-treated patient, pancreatitis, with necrosis, was observed and led to death; however clinical causal-

ity could not be established. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse. **Use with Medications Known to Cause Hypoglycemia:** Patients receiving Victoza® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogues) or insulin. **Renal Impairment:** Victoza® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in Victoza®-treated patients. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including Victoza®. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment. **Hypersensitivity Reactions:** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with Victoza®. If a hypersensitivity reaction occurs, the patient should discontinue Victoza® and other suspect medications and promptly seek medical advice. Angioedema has also been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to angioedema with Victoza®. **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

ADVERSE REACTIONS: Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of Victoza® has been evaluated in 8 clinical trials: A double-blind 52-week monotherapy trial compared Victoza® 1.2 mg daily, Victoza® 1.8 mg daily, and glimepiride 8 mg daily; A double-blind 26 week add-on to metformin trial compared Victoza® 0.6 mg once-daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and glimepiride 4 mg once-daily; A double-blind 26 week add-on to glimepiride trial compared Victoza® 0.6 mg daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and rosiglitazone 4 mg once-daily; A 26 week add-on to metformin + glimepiride trial, compared double-blind Victoza® 1.8 mg once-daily, double-blind placebo, and open-label insulin glargine once-daily; A double-blind 26-week add-on to metformin + rosiglitazone trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily and placebo; An open-label 26-week add-on to metformin and/or sulfonylurea trial compared Victoza® 1.8 mg once-daily and exenatide 10 mcg twice-daily; An open-label 26-week add-on to metformin trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, and sitagliptin 100 mg once-daily; An open-label 26-week trial compared insulin detemir as add-on to Victoza® 1.8 mg + metformin to continued treatment with Victoza® + metformin alone. **Withdrawals:** The incidence of withdrawal due to adverse events was 7.8% for Victoza®-treated patients and 3.4% for comparator-treated patients in the five double-blind controlled trials of 26 weeks duration or longer. This difference was driven by withdrawals due to gastrointestinal adverse reactions, which occurred in 5.0% of Victoza®-treated patients and 0.5% of comparator-treated patients. In these five trials, the most common adverse reactions leading to withdrawal for Victoza®-treated patients were nausea (2.8% versus 0% for comparator) and vomiting (1.5% versus 0.1% for comparator). Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials. **Common adverse reactions:** Tables 1, 2, 3 and 4 summarize common adverse reactions (hypoglycemia is discussed separately) reported in seven of the eight controlled trials of 26 weeks duration or longer. Most of these adverse reactions were gastrointestinal in nature. In the five double-blind clinical trials of 26 weeks duration or longer, gastrointestinal adverse reactions were reported in 41% of Victoza®-treated patients and were dose-related. Gastrointestinal adverse reactions occurred in 17% of comparator-treated patients. Common adverse reactions that occurred at a higher incidence among Victoza®-treated patients included nausea, vomiting, diarrhea, dyspepsia and constipation. In the five double-blind and three open-label clinical trials of 26 weeks duration or longer, the percentage of patients who reported nausea declined over time. In the five double-blind trials approximately 13% of Victoza®-treated patients and 2% of comparator-treated patients reported nausea during the first 2 weeks of treatment. In the 26-week open-label trial comparing Victoza® to exenatide, both in combination with metformin and/or sulfonylurea, gastrointestinal adverse reactions were reported at a similar incidence in the Victoza® and exenatide treatment groups (Table 3). In the 26-week open-label trial comparing Victoza® 1.2 mg, Victoza® 1.8 mg and sitagliptin 100 mg, all in combination with metformin, gastrointestinal adverse reactions were reported at a higher incidence with Victoza® than sitagliptin (Table 4). In the remaining 26-week trial, all patients received Victoza® 1.8 mg + metformin during a 12-week run-in period. During the run-in period, 167 patients (17% of enrolled total) withdrew from the trial: 76 (46% of withdrawals) of these patients doing so because of gastrointestinal adverse reactions and 15 (9% of withdrawals) doing so due to other adverse events. Only those patients who completed the run-in period with inadequate glycemic control were randomized to 26 weeks of add-on therapy with insulin detemir or continued, unchanged treatment with Victoza® 1.8 mg + metformin. During this randomized 26-week period, diarrhea was the only adverse reaction reported in ≥5% of patients treated with Victoza® 1.8 mg + metformin + insulin detemir (11.7%) and greater than in patients treated with Victoza® 1.8 mg and metformin alone (6.9%).

Table 1: Adverse reactions reported in ≥5% of Victoza®-treated patients in a 52-week monotherapy trial

Adverse Reaction	All Victoza® N = 497 (%)	Glimepiride N = 248 (%)
Nausea	28.4	8.5
Diarrhea	17.1	8.9
Vomiting	10.9	3.6
Constipation	9.9	4.8
Headache	9.1	9.3

Table 2: Adverse reactions reported in ≥5% of Victoza®-treated patients and occurring more frequently with Victoza® compared to placebo: 26-week combination therapy trials

Add-on to Metformin Trial			
	All Victoza® + Metformin N = 724	Placebo + Metformin N = 121	Glimepiride + Metformin N = 242
Adverse Reaction	(%)	(%)	(%)
Nausea	15.2	4.1	3.3
Diarrhea	10.9	4.1	3.7
Headache	9.0	6.6	9.5
Vomiting	6.5	0.8	0.4
Add-on to Glimepiride Trial			
	All Victoza® + Glimepiride N = 695	Placebo + Glimepiride N = 114	Rosiglitazone + Glimepiride N = 231
Adverse Reaction	(%)	(%)	(%)
Nausea	7.5	1.8	2.6
Diarrhea	7.2	1.8	2.2

Constipation	5.3	0.9	1.7
Dyspepsia	5.2	0.9	2.6
Add-on to Metformin + Glimepiride			
	Victoza® 1.8 + Metformin + Glimepiride N = 230	Placebo + Metformin + Glimepiride N = 114	Glargine + Metformin + Glimepiride N = 232
Adverse Reaction	(%)	(%)	(%)
Nausea	13.9	3.5	1.3
Diarrhea	10.0	5.3	1.3
Headache	9.6	7.9	5.6
Dyspepsia	6.5	0.9	1.7
Vomiting	6.5	3.5	0.4
Add-on to Metformin + Rosiglitazone			
	All Victoza® + Metformin + Rosiglitazone N = 355	Placebo + Metformin + Rosiglitazone N = 175	
Adverse Reaction	(%)	(%)	
Nausea	34.6	8.6	
Diarrhea	14.1	6.3	
Vomiting	12.4	2.9	
Headache	8.2	4.6	
Constipation	5.1	1.1	

Table 3: Adverse Reactions reported in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Exenatide

	Victoza® 1.8 mg once daily + metformin and/or sulfonylurea N = 235	Exenatide 10 mcg twice daily + metformin and/or sulfonylurea N = 232
Adverse Reaction	(%)	(%)
Nausea	25.5	28.0
Diarrhea	12.3	12.1
Headache	8.9	10.3
Dyspepsia	8.9	4.7
Vomiting	6.0	9.9
Constipation	5.1	2.6

Table 4: Adverse Reactions in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Sitagliptin

	All Victoza® + metformin N = 439	Sitagliptin 100 mg/day + metformin N = 219
Adverse Reaction	(%)	(%)
Nausea	23.9	4.6
Headache	10.3	10.0
Diarrhea	9.3	4.6
Vomiting	8.7	4.1

Immunogenicity: Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with Victoza® may develop anti-liraglutide antibodies. Approximately 50-70% of Victoza®-treated patients in the five double-blind clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment. Low titers (concentrations not requiring dilution of serum) of anti-liraglutide antibodies were detected in 8.6% of these Victoza®-treated patients. Sampling was not performed uniformly across all patients in the clinical trials, and this may have resulted in an underestimate of the actual percentage of patients who developed antibodies. Cross-reacting anti-liraglutide antibodies to native glucagon-like peptide-1 (GLP-1) occurred in 6.9% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 4.8% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an *in vitro* assay occurred in 2.3% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 1.0% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. Among Victoza®-treated patients who developed anti-liraglutide antibodies, the most common category of adverse events was that of infections, which occurred among 40% of these patients compared to 36%, 34% and 35% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. The specific infections which occurred with greater frequency among Victoza®-treated antibody-positive patients were primarily nonserious upper respiratory tract infections, which occurred among 11% of Victoza®-treated antibody-positive patients; and among 7%, 7% and 5% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Among Victoza®-treated antibody-negative patients, the most common category of adverse events was that of gastrointestinal events, which occurred in 43%, 18% and 19% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy of Victoza® when comparing mean HbA_{1c} of all antibody-positive and all antibody-negative patients. However, the 3 patients with the highest titers of anti-liraglutide antibodies had no reduction in HbA_{1c} with Victoza® treatment. In the five double-blind clinical trials of Victoza®, events from a composite of adverse events potentially related to immunogenicity (e.g., urticaria, angioedema) occurred among 0.8% of Victoza®-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for Victoza®-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies. **Injection site reactions:** Injection site reactions (e.g., injection site rash, erythema) were reported in approximately 2% of Victoza®-treated patients in the five double-blind clinical trials of at least 26 weeks duration. Less than 0.2% of Victoza®-treated patients discontinued due to injection site reactions. **Papillary thyroid carcinoma:** In clinical trials of Victoza®, there were 7 reported cases of papillary thyroid carcinoma in patients treated with Victoza® and 1 case in a comparator-treated patient (1.5 vs. 0.5 cases per 1000 patient-years). Most of these papillary thyroid carcinomas were <1 cm in greatest diameter and were diagnosed in surgical pathology specimens after thyroidectomy prompted by findings on protocol-specified screening with serum calcitonin or thyroid ultrasound. **Hypoglycemia:** In the eight clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 11 Victoza®-treated patients (2.3 cases per 1000 patient-years) and in two exenatide-treated patients. Of these 11 Victoza®-treated patients, six patients were concomitantly using metformin and a sulfonylurea, one was concomitantly using a sulfonylurea, two were concomitantly using metformin (blood glucose values were 65 and 94 mg/dL) and two were using Victoza® as monotherapy (one of these patients was undergoing an intravenous glucose tolerance test and the other was receiving insulin as treatment during a hospital stay). For these two patients on Victoza® monotherapy, the insulin treatment was the likely explanation for the hypoglycemia. In the 26-week open-label trial comparing Victoza® to sitagliptin,

the incidence of hypoglycemic events defined as symptoms accompanied by a fingerstick glucose <56 mg/dL was comparable among the treatment groups (approximately 5%).

Table 5: Incidence (%) and Rate (episodes/patient year) of Hypoglycemia in the 52-Week Monotherapy Trial and in the 26-Week Combination Therapy Trials

	Victoza® Treatment (N = 497)	Active Comparator (N = 248)	Placebo Comparator
Monotherapy			
	Victoza® (N = 497)	Glimepiride (N = 248)	None
Patient not able to self-treat	0	0	—
Patient able to self-treat	9.7 (0.24)	25.0 (1.66)	—
Not classified	1.2 (0.03)	2.4 (0.04)	—
Add-on to Metformin			
	Victoza® + Metformin (N = 724)	Glimepiride + Metformin (N = 242)	Placebo + Metformin (N = 121)
Patient not able to self-treat	0.1 (0.001)	0	0
Patient able to self-treat	3.6 (0.05)	22.3 (0.87)	2.5 (0.06)
Add-on to Victoza® + Metformin			
	Insulin detemir + Victoza® + Metformin (N = 163)	Continued Victoza® + Metformin alone (N = 158*)	None
Patient not able to self-treat	0	0	—
Patient able to self-treat	9.2 (0.29)	1.3 (0.03)	—
Add-on to Glimepiride			
	Victoza® + Glimepiride (N = 695)	Rosiglitazone + Glimepiride (N = 231)	Placebo + Glimepiride (N = 114)
Patient not able to self-treat	0.1 (0.003)	0	0
Patient able to self-treat	7.5 (0.38)	4.3 (0.12)	2.6 (0.17)
Not classified	0.9 (0.05)	0.9 (0.02)	0
Add-on to Metformin + Rosiglitazone			
	Victoza® + Metformin + Rosiglitazone (N = 355)	None	Placebo + Metformin + Rosiglitazone (N = 175)
Patient not able to self-treat	0	—	0
Patient able to self-treat	7.9 (0.49)	—	4.6 (0.15)
Not classified	0.6 (0.01)	—	1.1 (0.03)
Add-on to Metformin + Glimepiride			
	Victoza® + Metformin + Glimepiride (N = 230)	Insulin glargine + Metformin + Glimepiride (N = 232)	Placebo + Metformin + Glimepiride (N = 114)
Patient not able to self-treat	2.2 (0.06)	0	0
Patient able to self-treat	27.4 (1.16)	28.9 (1.29)	16.7 (0.95)
Not classified	0	1.7 (0.04)	0

*One patient is an outlier and was excluded due to 25 hypoglycemic episodes that the patient was able to self-treat. This patient had a history of frequent hypoglycemia prior to the study.

In a pooled analysis of clinical trials, the incidence rate (per 1,000 patient-years) for malignant neoplasms (based on investigator-reported events, medical history, pathology reports, and surgical reports from both blinded and open-label study periods) was 10.9 for Victoza®, 6.3 for placebo, and 7.2 for active comparator. After excluding papillary thyroid carcinoma events [see **Adverse Reactions**], no particular cancer cell type predominated. Seven malignant neoplasm events were reported beyond 1 year of exposure to study medication, six events among Victoza®-treated patients (4 colon, 1 prostate and 1 nasopharyngeal), no events with placebo and one event with active comparator (colon). Causality has not been established. **Laboratory Tests:** In the five clinical trials of at least 26 weeks duration, mildly elevated serum bilirubin concentrations (elevations to no more than twice the upper limit of the reference range) occurred in 4.0% of Victoza®-treated patients, 2.1% of placebo-treated patients and 3.5% of active-comparator-treated patients. This finding was not accompanied by abnormalities in other liver tests. The significance of this isolated finding is unknown. **Vital signs:** Victoza® did not have adverse effects on blood pressure. Mean increases from baseline in heart rate of 2 to 3 beats per minute have been observed with Victoza® compared to placebo. The long-term clinical effects of the increase in pulse rate have not been established. **Post-Marketing Experience:** The following additional adverse reactions have been reported during post-approval use of Victoza®. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure: Dehydration resulting from nausea, vomiting and diarrhea; Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis; Angioedema and anaphylactic reactions; Allergic reactions: rash and pruritus; Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death.

OVERDOSAGE: Overdoses have been reported in clinical trials and post-marketing use of Victoza®. Effects have included severe nausea and severe vomiting. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

More detailed information is available upon request.

For information about Victoza® contact: Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, NJ 08536, 1-877-484-2869

Date of Issue: April 16, 2013

Version: 6

Manufactured by: Novo Nordisk A/S, DK-2880 Bagsvaerd, Denmark

Victoza® is covered by US Patent Nos. 6,268,343, 6,458,924, 7,235,627, 8,114,833 and other patents pending. Victoza® Pen is covered by US Patent Nos. 6,004,297, RE 43,834, RE 41,956 and other patents pending.

© 2010-2013 Novo Nordisk 0513-00015681-1 5/2013



VICTOZA®
liraglutide (rDNA origin) injection

Providing Premedical Students with Quality Clinical and Research Experience: The Tobacco Science Scholars Program

James M. Davis, MD; Maggie C. Anderson; Kristin A. Stankevitz; Alison R. Manley

ABSTRACT

Undergraduate premedical students face a formidable decision as they work to determine whether to pursue a profession in medicine. Exposure to clinical medicine and research is essential to inform students what it might be like to be a physician. Undergraduates, however, face a number of obstacles to obtaining the kind of quality clinical and research experience needed to make an informed decision. Growing regulations designed to protect patient confidentiality, though undeniably important, pose a barrier to students seeking patient contact. Traditional passive physician shadowing often does not provide ample opportunities for one-on-one patient interaction or problem solving. Finally, research opportunities available to students typically are not associated with clinical work and therefore do not provide an experiential model of how empirical evidence informs medical practice. This report describes the University of Wisconsin School of Medicine and Public Health's Tobacco Science Scholars Program, a pilot program designed to address some of these barriers. While fulfilling institutional requirements for patient contact, the program provides students with an active model of clinical patient interaction and problem solving, with a research experience integrated into these clinical experiences so that undergraduates better understand how research informs clinical medicine.

INTRODUCTION

The education of physicians has been the subject of debate for over a century,¹ and as Jeffery Gross notes, “begins long before the first day in medical school.”² While considerable attention has been given to designing quality premedical academic curricula,³⁻⁸ less attention has been given to designing opportunities for premedical clinical and research experience.² Medicine is a clinical profession based in research, but undergraduates often apply to medical school with limited understanding of clinical

experience and only minimal exposure to clinically relevant research.^{9,10} It is common that students starting medical school are unfamiliar with the experience of human suffering found in medicine and have little understanding of the patient-healer relationship.¹¹⁻¹⁵ Premedical students today face several obstacles to gaining quality clinical and research experience: (1) they face restrictions to patient access in clinical settings due to regulations necessary to protect patient confidentiality;¹⁶ (2) they gain clinical experience primarily through passive physician shadowing,^{17,18} while evidence now supports active forms of patient interaction;^{9,19} and (3) undergraduate research is typically conducted in separate arenas from clinical experience, resulting in a poor understanding of how research informs clinical practice.¹⁷

Patient Confidentiality

In the last 10 years, there has been a substantial evolution in the protection of patient confidentiality, resulting in substantial limitations to patient exposure for premedical students. National guidelines, such as those of the Health Insurance Portability and Accountability Act (HIPAA),²⁰ and local guidelines on patient confidentiality, are of undisputed importance in the evolution of medical practice. Today, patient access is limited for undergraduates who obtain clinical experience through shadowing.^{12,13,19} Shadowing is a venerable tradition in which a student follows a physician through patient rounds and observes patient interactions.¹³ Often students will find a physician to shadow through a family member or friend, but these informal relationships comply only loosely with HIPAA or local confidentiality regulations.¹⁸ Recognizing the need for regulation of undergraduate clinical experience,¹⁶ many universities have cre-

• • •

Author Affiliations: Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health, Madison, Wis (Davis, Anderson, Stankevitz, Manley).

Corresponding Author: James M Davis, MD, Center for Tobacco Research and Intervention, 1930 Monroe St, Ste 300, Madison, WI 53711; phone 608.217.9405; fax 608.265.3102; e-mail jjamesdavis@hotmail.com.

Table. Tobacco Science Scholars (TSS) Program Introductory Training.

1. Proof of immunizations to Rubella, Hepatitis B, Rubeola, Mumps, Varicella, and TB test.
2. Permission from the University of Wisconsin School of Medicine and Public Health to enroll in the course.
3. Letter from undergraduate advisor stating that student is enrolled and in good standing.
4. Letter from TSS Program to the local hospital indicating the activities of the student.
5. Letter from the supervising physician stating they accept the student into the clinical program.
6. Waiver of Liability and Pledge of Confidentiality to local hospital.
7. HIPAA certification through the Institutional Review Board.
8. Human Subjects Research Training Certification through the Institutional Review Board.
9. Institutional Review Board approval of student as key personnel on the research project.
10. Training in TSS program guidelines for clinical patient interaction.

ated shadowing programs for premedical students that ensure compliance with federal and local regulations. When available, these programs are prized and highly utilized by premedical students.^{13,21}

Active vs Passive Clinical Experience

Although shadowing experiences vary widely, the role of the shadowing student is typically passive and is not designed to provide one-on-one patient interaction or engage the student in problem solving.¹⁷ There are a small but growing number of institutions that have recognized the limitations of passive clinical experience and are providing more active clinical programs for premedical students.^{13,17,22} Programs that emphasize active clinical learning for undergraduates include the Patient Perspectives Program (Charlotte, North Carolina), the Minneapolis Heart Institute Foundation Summer Research Internship Program (Minneapolis, Minnesota), the Stewart F. Alexander Premedical Program (Westwood, New Jersey), the Dartmouth Health Experience Learning Program (Hanover, New Hampshire), and the St. Jude's Pediatric Oncology Education Program (Memphis, Tennessee). These programs have demonstrated that active learning experience greatly enhances student decision making when considering a medical career and provides deeper sense of purpose and motivation with regard to other coursework.^{13,19,21,23,24}

Research Experience

Today, essentially all medical schools require or recommend that applicants have research experience.²⁵ Understanding the nature of evidenced-based medicine (EBM) requires an understanding of empirical methodology, not only through reading textbooks, but through active participation in research.²⁶⁻²⁸ EBM is a philosophy of providing therapies based on empirical results instead of tradition or opinion²⁹ and today is considered the foundation of quality medical care.^{30-32,33} An ideal way to facilitate an understanding of EBM would be to involve the student in clinical research that directly applies to the patients he or she encounters in clinical rounds. If a program provides an integrated research and clinical experience, a student can participate in the research required to develop a therapy, and then observe the clinical uti-

lization of this therapy, thereby gaining an experiential understanding of evidence-based practice.

Program Description and Objectives

The University of Wisconsin School of Medicine and Public Health, Center for Tobacco Research and Intervention (UW-CTRI) is in its second year piloting the UW-Tobacco Science Scholars Program (TSS). TSS is a 1-credit, 1-semester program designed to shepherd students

through required HIPAA and local institutional regulations, provide active-model clinical experience, and provide a fully integrated research experience. Because the program is sponsored by volunteer faculty, there are no costs or funding required. The curriculum contains 4 components—introductory training, clinical experience, research experience, and a capstone presentation. Research and clinical rotations focus on tobacco-related illness to promote an experiential understanding of EBM. TSS course objectives are to (1) provide the student with access to patients in an active learning model, (2) provide the student with access to research that will help the student understand the connection between research and clinical medicine, and (3) provide the student with a better understanding of the medical field as a possible future profession.

TSS Introductory Training

Introductory training in TSS is a week-long process whereby an administrator will provide a student with necessary forms and instructions to meet requirements for patient contact and research outlined by HIPAA, the University of Wisconsin Institutional Review Board, and a local community hospital (Table). Without guidance, completion of these multiple steps is often prohibitive to most undergraduates. An additional component of introductory training is comprehensive TSS training on hospital dress code, restrictions on physical contact with patients, inappropriate patient questions, and guidelines for interactions with physicians and staff during rounds. Once introductory training is complete, students not only satisfy required institutional regulations but gain a somewhat nuanced understanding of clinical etiquette.

TSS Clinical Experience

The TSS clinical experience involves rounding with a volunteer physician of any specialty encountering tobacco-related illness during their clinical rotations at a local community hospital. Rounds last for 4 hours, take place every 2 weeks throughout the semester, and typically involve 3 to 4 patient encounters. The physician first selects a patient with a reasonable disposition and requests permission of the patient for a student encounter. If the patient agrees to speak to the student, then the student goes into

the patient's room and asks rehearsed open-ended questions and takes notes while the patient speaks. After the student has seen each patient, she or he provides a brief verbal history to the physician. At the end of each rounding day, the student reads about the pathophysiology and treatment on 1 of the patient diagnoses, with preference given to smoking-related illnesses. The student then writes a rudimentary patient history with discussion of relevant pathophysiology and treatment and provides a brief presentation to the attending physician. In this way, the student engages in patient interaction and problem solving. The total time spent in rounds for each student or faculty is approximately 40 hours per semester. Several physicians have volunteered to participate in the TSS program and have provided positive feedback on students in areas of clinical etiquette and presentation.

TSS Research Experience

The TSS research experience is conducted at UW-CTRI. The research experience is 1 semester and provides students with regular access to the study's principal investigator and a limited de-identified data set (for example, data on a self-report questionnaire). Students are asked to conduct a simple data analysis and are given instruction on how to find means, standard deviations, *t* tests and ANOVAs. After analyses are complete, the student meets with one of the UW-CTRI doctoral-level research faculty, who spends an hour advising the student on how to refine their analysis and better understand clinical implications of the research. Five members of the research faculty at UW-CTRI have volunteered to help guide TSS students in analyzing and understanding data.

TSS Presentation

At the end of the semester, students are required to provide a presentation to staff at UW-CTRI containing 2 components. The first component is a clinical presentation of a patient history with a relevant pathophysiology and treatment plan; the second component is a presentation of data from smoking-related research. The 2 parts of the presentation typically share a theme. For example, the clinical component might provide a description of a smoker with anxiety, and the research component might provide a description of data from an anxiety scale taken by smokers who are trying to quit. Evaluation of the student is based on faculty assessment of a student's clinical work, research understanding, and final presentation.

TSS Program Response

The TSS program is available to undergraduates with strong academic standing and interest in becoming a physician. As a volunteer program, TSS initially was piloted with only 1 available position, although 3 positions currently are available and larger numbers are expected in the future. When the TSS program was first offered, 49 students applied, and in its second semester 71

students applied, representing a significant portion of the UW premedical class. A survey was provided to students approximately 1 year after the TSS experience, while some were in medical school. The questions included Likert scale 1-10 responses and written answers reflecting course objectives. The following are mean (*m*) responses to scale questions and examples of written responses:

Objective 1) Provide the student with access to patients in an active learning model. Questions: Did TSS provide you with direct access to patients: *m* = 9.33, *SD* = .58; Did TSS provide an active rather than passive clinical experience: *m* = 8.67, *SD* = 2.31. Written response:

My role with patients was one close to that of an actual medical student. I learned history taking skills that I am currently learning in medical school and received more real-life patient contact than most of my peers.

Objective 2) Provide the student with access to research that will help the student understand the connection between research and clinical medicine. Questions: Did TSS provide you with a hands-on research experience: *m* = 9.00, *SD* = 1.00. Did TSS help you understand the connection between research and clinical practice: *m* = 10.00, *SD* = 0.00. Written responses:

The most useful research skill gained was being able to extrapolate data findings from different areas of the project to develop one central conclusion.

I feel that the experience gave great insight into the way physicians utilize medical resources to solve medical dilemmas and gain further insight into specific medical conditions.

Objective 3) Provide the student with a better understanding of the medical field as a possible future profession. Question: Did TSS provide you with a deeper understanding of the medical field: *m* = 9.67, *SD* = .58. Written responses:

I would leave my shift with a smile. I talked about my experience for months after completion of the program. Being a Tobacco Science Scholar made me confident in my decision to become a doctor.

I strongly believe that the TSS program allowed me to excel in my first year of medical school. I have a leg up on other students in terms of having confident patient interactions and it was second nature to me already to be presented with a disease and instantly look for the relevant research on the topic.

CONCLUSION

The undergraduate who is considering the medical profession faces a decision of considerable complexity with limited opportunities for exposure to the profession. Presently, shadowing is the primary method through which students gain clinical experience necessary to approach this decision. The University of Wisconsin

Tobacco Science Scholars Program is one of a number of programs attempting to meet these goals. TSS is in its infancy, but strong student response to the program shows there is demand for this type of experience. Feedback among program completers has been positive, and survey responses suggest that TSS is meeting its intended objectives. Additional study is warranted to better understand the effect of this program on communication skills with patients, and ability to apply research skills, and understand EBM principals. Most universities that conduct clinically relevant research potentially could develop a similar program. We hope that our experience with this pilot program might be helpful to those with a desire to develop quality premedical education.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

- Flexner A. *Medical Education in the United States and Canada*. New York, NY: Carnegie Foundation for Higher Education; 1910.
- Gross JP, Mommaerts CD, Earl D, De Vries RG. Perspective: after a century of criticizing premedical education, are we missing the point? *Acad Med*. 2008;83(5):516-520.
- Cooke M, Irby DM, Sullivan W, Ludmerer KM. American medical education 100 years after the Flexner report. *N Engl J Med*. 2006;355(13):1339-1344.
- Finnerty EP, Chauvin S, Bonaminio G, Andrews M, Carroll RG, Pangaro LN. Flexner revisited: the role and value of the basic sciences in medical education. *Acad Med*. 2010;85(2):349-355.
- Institute of Medicine (US). Committee on Quality of Health Care in America. Crossing the quality chasm: a new health system for the 21st century. Washington, DC: National Academy Press; 2001.
- Larson EB, Fihn SD, Kirk LM, et al. The future of general internal medicine. Report and recommendations from the Society of General Internal Medicine (SGIM) Task Force on the Domain of General Internal Medicine. *J Gen Intern Med*. 2004;19(1):69-77.
- Sales CS, Schlaff AL. Reforming medical education: a review and synthesis of five critiques of medical practice. *Soc Sci Med*. 2010;70(11):1665-1668.
- Shusterman M. 100 years after Flexner: Reconsidering premedical education [editorial]. *TuftsScope*. 2010;9(2):10-11.
- Gerbens DA, Stid MA, Foulds KL. A collaborative internship program for premedical students. *Acad Med*. 1998;73(8):827-828.
- Holmboe ES. Faculty and the observation of trainees' clinical skills: problems and opportunities. *Acad Med*. 2004;79(1):16-22.
- Young KW. The effect of medical school admissions on undergraduate pre-medical education: a case for change. *The Advisor*. 1986;6:14-20.
- Engel MF. Achieving "narrative flow": Pre-medical education as an essential chapter of a physician's story. *J Med Humanit*. 2005;26(1):39-51.
- Alexander SF, Lyon LJ, Nevins MA, Ycre LR Jr, Thayer HS. Ten years of orienting college students to careers in medicine. *JAMA*. 1992;267(24):3330-3331.
- Dornan T. Osler, Flexner, apprenticeship and 'the new medical education'. *J R Soc Med*. 2005;98(3):91-95.
- Moffat KJ, McConnachie A, Ross S, Morrison JM. First year medical student stress and coping in a problem-based learning medical curriculum. *Med Educ*. 2004;38(5):482-491.
- Kitsis EA. Shining a light on shadowing. *JAMA*. 2011;305(10):1029-1030.
- Chuck JM. Do premedical students know what they are getting into? *West J Med*. 1996;164(3):228-230.
- O'Connell VG, J. The Premedical Student: Training and Practice Expectations. *Medical Education Online*. 2006;11.
- Willenbring BD, McKee KC, Wilson BV, Henry TD. The Minneapolis Heart Institute Foundation Summer Research Internship Program: the benefits of preprofessional experience for prospective physicians. *Minn Med*. 2008;91(8):47-49.
- Pub L No. 104-191. Health Insurance Portability and Accountability Act of 1996. <https://www.cms.gov/Regulations-and-Guidance/HIPAA-Administrative-Simplification/HIPAAGenInfo/downloads/HIPAAALaw.pdf>. Accessed September 10, 2013.
- Wagner AK, Stewart PJ. An internship for college students in physical medicine and rehabilitation: effects on awareness, career choice, and disability perceptions. *Am J Phys Med Rehabil*. 2001;80(6):459-465.
- Lovetchio K, Dundes L. Premed survival: understanding the culling process in pre-medical undergraduate education. *Acad Med*. 2002;77(7):719-724.
- Gronemeyer SA. The impact of predoctoral pediatric oncology education. *J Cancer Educ*. 2005;20(1):16-22.
- Almy TP, Cohen RD, Ham TH, Hornig EO, Price J. Health-related experiential learning for college undergraduates. *J Med Educ*. 1983;58(5):404-410.
- Association of American Medical Colleges. Medical School Admission Requirements (MSAR). <https://www.aamc.org/students/applying/requirements/msar/>. Accessed September 10, 2013.
- Stoeckle JD, Ronan L, Ehrlich C, Roberts D. The uses of shadowing the doctor--and patient: on seeing and hearing their work of care. *J Gen Intern Med*. 1993;8(10):561-563.
- Bauer KW, Bennett JS. Alumni perceptions used to assess undergraduate research experience. *J Higher Educ*. Mar-Apr 2003;74(2):210-+.
- Lopatto D. Survey of Undergraduate Research Experiences (SURE): first findings. *Cell Biol Educ*. 2004;3(4):270-277.
- Sackett DL, Rosenberg WMC, Gray JAM, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it isn't. *BMJ*. 1996;312(7023):71-72.
- Fiore MC, Baker TB. Smoking cessation treatment and the good doctor club. *Am J Public Health*. 1995;85(2):161-163.
- Carey JC. Significance of case reports in the advancement of medical scientific knowledge. *Am J Med Genet A*. 2006;140(19):2131-2134.
- Fichman RG, Kohli R, Krishnan R. The role of information systems in healthcare: current research and future trends. *Inform Syst Res*. 2011;22(3):419-428.
- Riegelman RK, Garr DR. Evidence-based public health education as preparation for medical school. *Acad Med*. 2008;83(4):321-326.

Barriers and Facilitators of Universal HIV Screening Among Internal Medicine Residents

Meghan B. Brennan, MD; Christine Kolehmainen, MD; Joshua Barocas, MD; Carol Isaac, PhD; Christopher J. Crnich, MD; James M. Sosman, MD

ABSTRACT

Background: Adoption of universal HIV screening has been low despite national recommendations.

Objective: To describe the barriers and facilitators to adoption of universal HIV screening in a low-prevalence setting.

Design: Qualitative, thematic analysis of focus group discussions among internal medicine residents who introduced universal HIV screening into their primary care practice in Madison, Wisconsin.

Approach: Deductive and inductive codes constructed a hybridized thematic analysis model. Deductive codes stemmed from a knowledge-attitude-behavior framework for physician nonadherence to guidelines. Inductive codes emerged from the focus group discussions and were embedded into broader deductive codes to provide an HIV-specific model.

Key Results: Residents were knowledgeable and had positive attitudes toward recommendations for universal HIV screening. Residents felt the majority of their patients were receptive to HIV screening, especially when introduced with normalizing techniques and reference to an expert authority such as the Centers for Disease Control and Prevention (CDC). They still perceived patient discussions as challenging due to stigma surrounding HIV and patients' perceptions of being at low risk. Residents employed individualized electronic medical record cues as a memory aid to discuss the issue.

Conclusion: This qualitative study of internal medicine residents training in an area with low HIV prevalence suggests that stigma and patient perception of being at low risk are barriers that should be addressed to effectively integrate universal HIV screening into primary care.

INTRODUCTION

In 2006, the The Centers for Disease Control and Prevention (CDC) endorsed universal HIV screening as opposed to risk-based testing.¹ Specifically, they recommend a 1-time HIV screen for low risk adults less than 65 years old in populations where the estimated

• • •

Author Affiliations: University of Wisconsin Department of Medicine, Madison, Wis (Brennan, Kolehmainen, Barocas, Crnich, Sosman); University of Wisconsin Center for Women's Health Research, Madison, Wis (Brennan, Kolehmainen, Isaac); Geriatric Research, Education and Clinical Center, William S. Middleton Memorial Veterans Hospital, Madison, Wis (Brennan, Kolehmainen).

Corresponding Author: Meghan Brennan, MD, 700 Regent St, Ste 301, Madison, WI 53715; phone 608.263.9770; fax 608.265.6423; e-mail mb-brennan@medicine.wisc.edu.

prevalence of HIV is greater than 0.1%. The American College of Physicians published similar guidelines 3 years later.² This shift was motivated by an effort to identify the estimated 236,400 Americans who are unaware they are infected with HIV.³ Although they may represent only 20% of all HIV-positive Americans, this undiagnosed subset accounts for approximately half of the estimated 56,000 new transmissions each year.⁴ Diagnosing infection is the first step in a test-and-treat strategy currently employed to prevent HIV infection.⁵ Therefore, identifying these infected individuals early has important personal as well as population health benefits.

Despite guidelines recommending universal HIV screening, adoption among primary care providers has been low. Only 45% of Americans aged 18-64 reported ever having been tested for HIV, and half of the general internists participating in a recent national survey reported increasing

their screening rates after publication of the guidelines.^{6,7} Recent studies addressing the slow integration of universal HIV screening into primary care provide preliminary explanations for observed low-screening rates, but a detailed understanding of the factors that affect HIV screening in primary care is still lacking.⁷⁻⁹ Screening initiatives have often focused on metropolitan, high-risk populations and emergency department settings rather than suburban, low-prevalence communities utilizing primary care clinics.^{10,11} Little is known about HIV screening in low prevalence communities, where physicians may encounter unique barriers or facilitators. Much of the US Midwest typifies this less urban and understudied region with the nation's lowest HIV screening rates.¹² This study aims to explore the barriers and facilitators perceived by internal medicine residents as they adopt HIV screening into their primary care practice in a Midwestern community with an estimated 0.2% prevalence of HIV.¹³

Table 1. Questions Included in the Focus Group Interview Guide

Tell me about the last patient you screened for HIV in your primary care clinic.
Can you remember a patient you didn't screen, but wish you had?
Do you think most residents know the 2006 CDC guidelines?
How do you approach screening? What works well and what doesn't?
How do you bring it up?
How do different types of patients respond? Is it fairly predictable?
Why do you think patients decline screening?
Has it ever been awkward? What types of things do you do to keep it from becoming awkward?
What are some barriers to screening?
What has made screening easier?
Do you think the perception that we work with a low-prevalence community affects physician's likelihood to screen?
What role could the electronic medical record play in HIV screening?
According to the annual chart review, HIV screening has gone up quite a bit—almost doubled. How did you guys do it, and what motivated you?

Table 2. Barrier/Facilitator Matrix Coding^a**Time****Barrier (12 quotes)**

"The person today, for example, is a person I would like to screen. She's a sexually active 19 year old but she has horrifically controlled type 1 diabetes. I only had a half an hour, so I spent most of the time trying to convince her to take her insulin. I said at the end, 'You know, there are all these things that I'd like to talk to you about, but we need to have another visit.' I had to pick the thing that was likely to kill her first."

Facilitator (2 quotes)

Facilitator: "So do you think time plays a factor at all in screening?"

Resident: "No, because most of my visits are about prevention. That's what it's all about—get them on statins, blood pressure meds, screening, and colonoscopies."

^aUsing Nvivo, the barrier and facilitator nodes were cross-referenced to each inductive and deductive node. In the example above, 12 quotes described time as a barrier, while 2 described it as a facilitator. An initial query displays only the number(s), 12 or 2. However, Nvivo will generate a list of all the quotes if an investigator clicks on the cell. For illustrative purposes, only 1 example quote was included in each cell.

METHODS

Participants

All University of Wisconsin (UW) internal medicine residents with primary care clinics in Madison, Wisconsin were eligible to participate. This group offers an important perspective for 3 reasons: (1) they serve a low-prevalence community; (2) they work in a region with the lowest HIV screening rates; and (3) in the prior year, they doubled their HIV screening rates after this topic was added to a self-audit. Incorporating universal screening into residents' practice patterns should increase the likelihood that they will continue to screen as they become the next generation of clinicians.^{14,15} The UW residency program requires trainees to perform a self-audit of preventive health services offered during their continuity clinics. Topics include immunizations, cancer

and metabolic screenings, and alcohol and tobacco counseling. In 2010, universal HIV screening was added to the required self-audit without announcing the change to resident physicians. No additional teaching regarding HIV screening was added to the established curriculum. The following year, HIV screening rates increased from 18% to 40% (unpublished data). HIV screening at all clinics is done using standard blood draws with ELISA assays followed by confirmation Western blot. Patients must give explicit verbal consent.

Recruitment

All internal medicine residents at UW were recruited to participate in focus groups regarding "HIV screening in outpatient primary care settings" via e-mail solicitations and announcements at educational lectures. Three separate focus groups, with 4 to 6 volunteer participants each, were conducted to foster open discussion and obtain thematic saturation.¹⁶ Dinner was provided during the focus groups, but participants received no other compensation or incentive. The study was approved by the University of Wisconsin Health Sciences IRB.

Data Collection

Hour-long focus groups were conducted between December, 2011 and January, 2012. Participants were grouped by their primary care clinic location—a university or VA clinic. Residents at university clinics composed 2 focus groups, while residents at Veterans Administration (VA) clinics composed a separate focus group. A recent graduate of the UW residency program (CK) led the focus groups using a standardized interview guide with probing questions for clarification (Table 1). Questions were formulated based on: (1) Cabana's guideline nonadherence framework, (2) previously published survey results examining physicians' perceptions of barriers towards HIV screening, and (3) informal discussions with residents and recent graduates of the program.^{7-9,17,18} The guide was piloted using a mock focus group of local physicians who had graduated from the residency program in the previous year. All focus groups were audio recorded, transcribed verbatim, and de-identified to preserve confidentiality. Residents refrained from using patient identifiers. Transcriptions were reviewed for accuracy by an investigator (MB) who observed the focus groups and loaded into NVivo (QSR International Pty Ltd, Doncaster, Victoria, Australia) for analysis.

Data Analysis

Two investigators (MB and CK) independently coded the 3 transcripts line-by-line using a hybrid of inductive and deductive thematic analysis.^{20,21} This process generated an HIV screening-specific conceptual model in 2 steps. First, 14 deductive nodes were derived a priori from Cabana's guideline nonadherence framework.¹⁷ Second, 2 investigators (MB and JB) derived inductive HIV-specific nodes by analyzing the first transcript, which were

embedded as sub-categories within broad deductive nodes derived in step 1 (Figure). Resident demographics and HIV screening barriers/facilitators were also coded, which allowed matrices to facilitate analysis (Table 2). Inter-rater reliability was 95% across all 3 focus group transcripts. Main themes that emerged from the coded text were discussed until consensus was reached. Investigators conducting primary analysis (MB, JB, and CK) were either currently enrolled in, or recent graduates of the residency program, providing local expertise needed to generate credible interpretations.

RESULTS

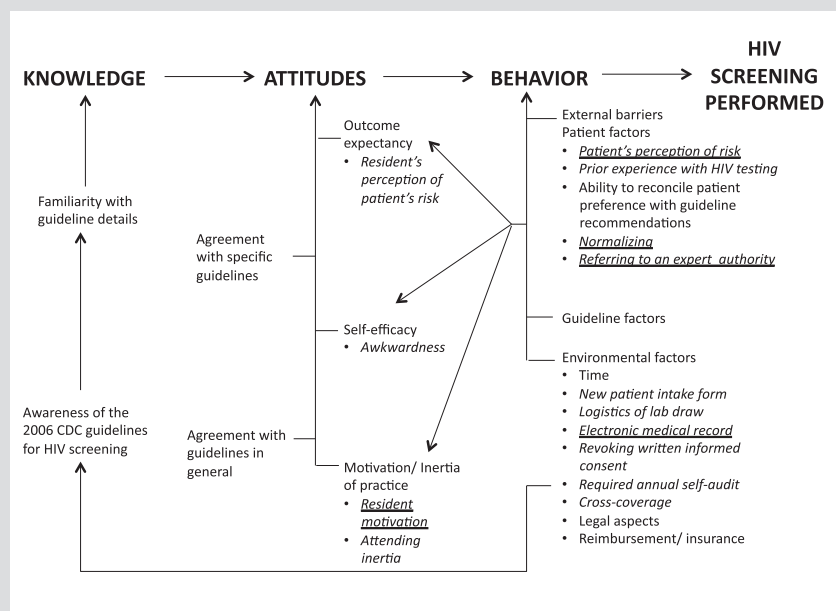
Fifteen of 74 eligible internal medicine residents participated, representing 20.3% of the UW residency program (Table 3). Thirteen participants were exposed to the self-audit that was associated with an increase in HIV screening within the residency program. Each focus group lasted approximately 1 hour, yielding a total of 187 minutes of dialogue and 115 pages of transcription. Four themes regarding routine HIV screening emerged during analyses: (1) integration into standard practice, (2) resident perceptions of patients' attitudes, (3) strategies for opening the discussion with patients, and (4) use of electronic medical record (EMR) cues (Figure). Each is described below with illustrative quotes.

Integration of HIV Screening Into Standard Practice

Overall, residents' knowledge and attitudes towards universal screening were positive. Some residents endorsed universal screening because they felt their patients did not always divulge risk factors, and universal screening allowed these patients to be tested at least once. One resident remarked, "The social history in general—people don't tell you everything." Twelve of the 15 residents explicitly stated that they incorporated universal HIV screening into their standard practice. However, lack of time during the clinical encounter led residents to prioritize HIV screening among a list of preventive health actions based upon their assessment of which were mostly likely to pose the most risk to their patient. Using this approach, residents introduced HIV screening less often or encouraged patients to consent less frequently than they would have for other screening tests when they felt that patient was at low risk.

It's lower on my priority list for, say, a healthy 55-year-old man. I go through all their preventive issues, but if they come in with 6 chief complaints for a 1-hour physical, that's one of the things I may not get to along with a living will or

Figure. Conceptual Framework and Nodes for Qualitative Analysis



Cabana's framework for physician guideline nonadherence was modified for the 2006 Centers for Disease Control and Prevention guidelines recommending universal HIV screening.¹⁷ Deductive codes are set in normal type. Inductive nodes are set in italicized type. The 4 main themes that emerged can be linked directly to underlined nodes.

health care power of attorney. Those are lower on my preventive screening list, as opposed to cholesterol or colonoscopies. I would say about 25% of the time I don't get to it.

Some also felt that because the guidelines recommended a 1-time screen within a broad age range for low-risk patients, there was less urgency to accomplish this screening as opposed to other annual preventive services. Institutional benchmarks also entered into this prioritization.

Since this is for a person who is not at high risk, for once-in-a-lifetime screening, there is a lot less urgency to get it done at this visit than there is for screening diabetes or screening cholesterol, where you have annual performance measures.

In sum, residents prioritized HIV screening within a panel of other preventive health actions based upon (1) their assessment of the patient's HIV risk, (2) potential benefits of other preventive services, (3) institutional benchmarking, and (4) a long time-frame over which to accomplish HIV screening.

Participants also commented on a "concerted effort" among residents to increase their collective HIV screening rates. They had clearly discussed the topic over the course of the last year, both with regard to their chart review results and patient responses to screening. For instance, the same difficult patient encounters were described in multiple focus groups without any overlap in participants. However, residents did not specifically credit peer opinion leaders or informal discussion when describing how HIV screening became a part of their community practice.

Table 3. Internal Medicine Resident Characteristics

Characteristic	Participating residents n=15 (%)	Total residency program, n= 74 (%)
Year of training		
First year	1 (6.7)	23 (31.1)
Second year	8 (53.3)	27 (36.5)
Third year	6 (40.0)	24 (32.4)
Gender		
Female	10 (66.7)	36 (48.6)
Anticipated career practice		
Primary care	5 (33.3)	22 (29.7)
Subspecialty	9 (60.0)	40 (54.0)
Undecided	1 (6.7)	12 (16.3)
Primary care clinic site		
University clinic	11 (73.3)	43 (58.1)
Veterans Administration clinic	4 (26.7)	31 (41.9)

Resident Perceptions of Patients' Attitudes Toward Universal HIV Screening

Nine of 15 residents reported that patients generally were receptive to HIV screening. Resident descriptions of patients who were agreeable to screening fell into 4 categories: patients who (1) felt they were at such low risk there was no reason to decline because the test was going to be negative, (2) wanted comprehensive preventive services, (3) were already familiar with routine screening, and (4) deferred to physician discretion. Residents practicing at VA clinics noted a particular openness to screening; younger veterans were habituated to routine HIV screening during active service, older veterans often deferred to the physician's judgment, and none were concerned about cost or insurance ramifications. In both clinic settings, a subset of patients declined HIV screening.

When asked why some of their patients refused, all residents mentioned at least 1 of 2 interconnected themes: social stigma and low perceived risk. One resident thought her patients equated having HIV with "being a bad person." Residents reported their patients often justified their decision not to be screened with statements such as, "I haven't done anything wrong," or "[I've] been very well behaved." Most residents felt their patients were aware HIV could be transmitted through heterosexual intercourse. However, this knowledge did not seem to translate into heterosexual patients perceiving themselves to be at risk. One resident summarized, "I think most people think [sex] is dangerous for everybody else." Some patients took offense to screening, since HIV may be associated with ostracized behaviors. When this occurred, the patient-physician interaction became more awkward and time consuming as the resident had to expend a significant amount of effort re-establishing rapport. Residents could not predict which patients would refuse HIV testing. For example, residents recalled mixed responses from married patients.

There was this one woman (patient) who said "Oh—there's no way," kind of like "I can't believe you are asking me." But she wasn't angry. She just explained, "No, I've only had one partner—my husband."

I have been surprised by the number of people (patients) who are married and very willing to get HIV tested. I always feel like I am saying something about them or their spouses, but I haven't found that.

One resident reported some married patients were willing to be screened, but were concerned their spouse would find out the test was performed because it implied infidelity regardless of the result. Those patients preferred to be contacted directly with the result rather than include it in a letter with other lab values. Interactions with older patients were similarly varied and unpredictable.

I always find it more uncomfortable with my older patients. They think "What kind of a person do you think I am?" when I ask their sexual history and offer HIV screening.

I was actually surprised. I had a conversation with a guy, an older veteran and his wife, and they were both all about getting screened for HIV. I just brought it up and sort of coached it, saying, "This is something we recommend doing at least once." They were both, "Yeah, that's a great idea," really enthusiastically.

Residents found it particularly difficult to predict and plan for potential patient resistance to HIV screening. Three residents who anticipated awkward encounters reported that preconceived expectations often materialized because of provider, rather than patient, embarrassment. One resident remarked, "If I think they will be offended, I might ask it in a way that makes them feel awkward because my face turns red." Another stated that this phenomenon decreased with repetition. The more residents screened, the more comfortable they were asking patients about HIV.

Strategies for Opening the Discussion: Normalizing Screening and Referring to Expert Authorities

All participating residents developed a standard opening line when introducing HIV screening to their patients. Residents either used (1) normalizing, (2) a reference to authority, or (3) both, to reduce the social stigma associated with HIV screening. Nine residents normalized screening by either stating they screen everyone in their practice or that HIV screening was similar to screening for other diseases, like diabetes or colon cancer.

Everybody in my clinic seems to have diabetes, so they know what an A1C is...I have one patient who just understands it that way—like any other chronic condition, you just have to screen for it.

Normalizing HIV screening helped unlink the screening from the stigma surrounding HIV and reframe it using paral-

lels to other chronic disease that patients could easily grasp and accept. Seven residents referred to an expert authority, such as the institution where they worked or, more commonly, the CDC: “I start out ‘Have you ever been screened? The CDC recommends it. Would you like me to screen you today?’” By referring to an expert authority or explicitly stating they screened everyone, residents removed the implication that they personally were judging their patients.

[Universal screening] is very helpful because you can make a blanket statement [to your patient]. I know it has helped my screening rates. I know it helps the provider approach the subject.

I think one of the benefits of trying to make [HIV testing] more routine and mainstream is normalizing it as a screen... The more we try to put it out there and make it a more normal thing...makes it easier for everybody, including the patients. They don't get as scared.

Electronic Medical Record Cues

All residents worked at clinics that had fully integrated electronic medical records (EMR); however, no EMR had a standard HIV screening reminder. Fourteen of the 15 residents explicitly stated they created automated prompts within the EMR as a reminder to screen patients for HIV, and most included HIV screening as a prepopulated text in the preventive care section of their clinic note templates.

I have a section on health maintenance [in the EMR] for all my patients. I document when I asked last, what their response was, and if they'd ever been screened before. So I tend to bring it up [with my patients].

One resident embedded an HIV screening reminder into her EMR preventive screening template to help normalize her approach to this subject. She turned the computer screen toward the patient and went through her preventive section. She felt that having the patient see HIV screening was on a standardized list helped them accept that she truly asked everyone.

Five residents felt giving interns EMR note documentation templates that included HIV screening would be beneficial. Some residents expressed concerns including the “clunkiness” of other institution-wide EMR reminders, pop-up reminders occurring at inopportune times, and EMR reminder-fatigue. However, most residents endorsed the importance of a standardized approach to EMR prompts and the sense of institutional backing.

DISCUSSION

This qualitative study describes barriers and facilitators faced by internal medicine resident physicians while attempting to increase HIV screening rates. In contrast to an earlier study of New York City internal medicine trainees, the majority of residents in this study were aware of and endorsed the 2006 CDC recommenda-

tions.⁸ Most intended to offer HIV screening to their patients. However, despite high awareness and intent, residents completed screening with only 40% of their primary care patients (unpublished data). Provider knowledge and positive attitudes are necessary but often insufficient for guideline adoption.²¹

In our study, residents identified lack of time, perceived patient resistance, and lack of standardized screening as barriers to the integration of universal HIV screening into their primary care practice. Other physicians have consistently reported lack of time as a barrier to universal HIV screening.^{8,18} In our study, residents attempted to address time constraints by prioritizing preventive services based on the likelihood that a specific patient would benefit. However, applying this approach within a low-prevalence community practice can lead to suboptimal HIV screening rates.

Residents perceived resistance to HIV screening from a significant minority of their patients. Most published reports largely ignore this subset and, instead, highlight the majority who accept universal HIV screening.²² However, it is important to understand how encounters with patients who refuse HIV testing may influence future screening. First, physicians are more likely to remember difficult encounters. Negative recall bias has curbed physician adoption of other guidelines, even when presented with compelling risk-to-benefit ratios.²¹ Second, negative encounters may lead physicians to inappropriately equate declining an HIV screen with patient reluctance to discuss the topic. This is an important distinction, especially in the era of shared patient-doctor decision-making. The difference is easily blurred when introducing a new screening practice. Although it may be understandable for residents to feel that they did not successfully offer HIV screening if a patient declined the screening test, this may lead to decreased provider self-efficacy and reluctance to recommend HIV screening in subsequent patient encounters. Providers need strategies to mitigate the first and objectively view the second when adopting screening.

Residents in our study attributed patients' resistance to screening to stigma and low perceived risk, barriers that have been reported previously.²³ Residents mentioned that some of their patients equated HIV-positive people with socially stigmatized groups of which they were not a part. Residents tempered these potential concerns by referring to an expert authority and normalizing HIV screening. A focus group of veteran patients directly stated that acceptance would be best if parallels were drawn to other preventive screening tests and if it was explicit that patients were not being screened because of risk factors.⁹ The techniques developed by residents in our study addressed precisely those patient preferences expressed in the prior study and demonstrate their perceived importance among a different patient population. This approach also begins to address apprehensions expressed by a minority of patients regarding the stigma of HIV screening.

Although residents initiated HIV screening with no standard-

ized reminder, they addressed this shortcoming by developing individualized EMR cues. Most constructed provider-specific HIV screening sections within their EMR clinic note templates. This approach avoided pop-up boxes that can occur at inopportune times and lead to EMR-associated provider fatigue.²⁴ Although computerized reminders can facilitate new clinical practices, residents were concerned about the streamlining and navigability of such a system.

Our study has several limitations. We did not purposively sample the population of internal medicine residents on baseline attitudes toward HIV screening. It is possible that residents who participated in this study held more positive attitudes toward HIV screening and had developed more robust strategies for promoting screening among their patients than their nonparticipating peers. Study results may therefore represent an under-saturated description of the barriers to HIV screening in primary care. Moreover, because our study was performed in a single residency program, our findings may not be representative of the experiences in other settings.

Although several participants made reference to the influence of social networks during focus groups, this facet deserves further investigation. The influence of social networks has been shown to play an integral part in the diffusion of guidelines.^{21,25} In our study, social networks may have played a significant role in forming community consensus regarding the importance of HIV screening, by motivating residents to prioritize it and include it on the list of preventive services.

In summary, this study provides a contemporary examination of resident physicians who have successfully implemented universal HIV screening. Most previous provider-level studies have been derived from survey responses, which are unable to capture in-depth detail. Prior studies focused on either patient attitudes before universal HIV screening was successfully introduced or on physicians' perceptions of barriers and facilitators using a sample with a low proportion of providers who had adopted universal screening. This study also provides insight regarding resident physicians' self-reported knowledge, facilitators, and barriers to routine, clinic-based HIV screening. These physicians are the next wave of practicing clinicians, and national guidelines adopted and reinforced during residency are more likely to be integrated into provider practices than those learned after training.¹⁴ Although this study addressed clinicians serving a low-prevalence community, these residents perceived high patient acceptance of universal HIV screening recommendations. Finally, physicians in this study endorsed tailoring their EMRs to provide memory cues so that HIV screening is addressed uniformly. Although some patient barriers exist, universal HIV screening generally was acceptable to patients when the topic was normalized and reference was made to an expert or institutional author-

ity. Physicians serving populations with an estimated prevalence of HIV greater than 0.1% may wish to incorporate these strategies—normalizing, referring to an expert authority, and utilizing an electronic medical record reminder—when introducing universal HIV screening to their practice.

Acknowledgements: The authors would like to thank the internal medicine residents of the University of Wisconsin, who so graciously donated their time and frankly discussed their experiences. Molly Carnes, MD, Marissa Manwell, and Laura Thibodeau offered valuable critiques of the manuscript.

Funding/Support: Supported by the UW Department of Medicine and the Division of Infectious Disease, as well as the VA Women's Health Research Fellowship for their support. This is GRECC Manuscript number 2013-11.

Financial Disclosures: None declared.

Prior Publication: These findings were communicated in poster format at the 2012 National Summit on HIV and Viral Hepatitis Diagnosis, Prevention, and Access to Care, Washington DC, November 27, 2012.

REFERENCES

1. Branson BM, Handsfield HH, Lampe MA, et al. Revised recommendations for HIV testing of adults, adolescents, and pregnant women in healthcare settings. *MMWR Recomm Rep*. 2006;55(RR-14):1-17.
2. Qaseem A, Snow V, Shekelle P, Hopkins R, Owens DK. Screening for HIV in health-care settings: a guidance statement from the American College of Physicians and HIV Medicine Association. *Ann Intern Med*. 2009;150(2):125-131.
3. Cohen SM, Van Handel MM, Branson BM, et al. Vital Signs: HIV prevention through care and treatment—United States. *MMWR Morb Mortal Wkly Rep*. 2011;60(47):1618-1623.
4. Althoff KN, Gange SJ, Klein MB, et al. Late presentation for human immunodeficiency virus care in the United States and Canada. *Clin Infect Dis*. 2010;50(11):1512-1520.
5. Gardner EM, McLees MP, Steiner JF, del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis*. 2011;52(6):793-800.
6. Johnson AS, Heitgerd J, Koenig LJ, et al. Vital signs: HIV testing and diagnosis among adults—United States, 2011–2009. *MMWR Morb Mortal Wkly Rep*. 2010;59(47):1550-1555.
7. Korthuis PT, Berkenblit GV, Sullivan LE, et al. General internists' beliefs, behaviors, and perceived barriers to routine HIV screening in primary care. *AIDS Educ Prevention*. 2011;23(3 Suppl):70-83.
8. Jain CL, Wyatt CM, Burke R, Sepkowitz K, Begier EM. Knowledge of the Centers for Disease Control and Prevention's 2006 routine HIV testing recommendations among New York City internal medicine residents. *AIDS Patient Care STDs*. 2009;23(3):167-176.
9. Bokhour BG, Solomon JL, Knapp H, Asch SM, Gifford AL. Barriers and facilitators to routine HIV testing in VA primary care. *J Gen Intern Med*. 2009;24(10):1109-1114.
10. d'Almeida KW, Kierzek G, de Truchis P, Vu SL, Pateron D, Renaud B. Modest public health impact of nontargeted human immunodeficiency virus screening in 29 emergency departments. *Arch Intern Med*. 2012;172(1):12-20.
11. Haukoos JS, Hopkins E, Conroy AA, et al. Routine opt-out rapid HIV screening and detection of HIV infection in emergency department patients. *JAMA*. 2010;304(3):284-292.
12. Ohl ME, Perencevich E. Frequency of human immunodeficiency virus (HIV) testing in urban vs rural areas of the United States: results from a nationally representative sample. *BMC Public Health*. 2011;11:681-688.
13. AIDS/HIV Program, Wisconsin Department of Health Services. Wisconsin AIDS/HIV surveillance annual review: cases reported through December 31, 2011. Available at: <http://www.dhs.wisconsin.gov/aids-hiv/stats/index.htm>. Accessed September 10, 2013.

14. Cox ED, Smith MA, Bartell JM. Managing febrile infants: impact of literature recommendations published during a physician's residency. *Eval Health Prof.* 2005;28(3):328-348.
15. Berkenblit GV, Sosman JM, Bass M, et al. Factors affecting clinical educator encouragement of routine HIV testing among trainees. *J Gen Intern Med.* 2012;27(7):839-844.
16. Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. *Field Methods.* 2006;18(1):59-82.
17. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA.* 1999;282(15):1458-1465.
18. Burke RC, Sepkowitz KA, Bernstein KT, et al. Why don't physicians test for HIV? A review of the US literature. *AIDS.* 2007;21(12):1617-1624.
19. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: a hybrid approach of inductive and deductive coding and theme development. *Int J Qualitative Methods.* 2006;5(1):80-92.
20. Boyatzis RE. *Transforming Qualitative Information: Thematic Analysis and Code Development.* Thousand Oaks, CA: Sage; 1998.
21. Borbas C, Morris N, McLaughlin B, Asinger R, Gobel F. The role of clinical opinion leaders in guideline implementation and quality improvement. *Chest.* 2000;118(2 Suppl):24S-32S.
22. Stefan MS, Blackwell M, Crawford KM, et al. Patients' attitudes toward and factors predictive of human Immunodeficiency virus testing of academic medical clinics. *Am J Med Sci.* 2010;340(4):264-267.
23. Weis K, Liese AD, Hussey J, et al. A routine HIV screening program in a South Carolina community health center in an area of low HIV prevalence. *AIDS Patient Care and STDs.* 2009;23(4):251-258.
24. Patterson ES, Doebbeling BN, Fung CH, Militello L, Anders S, Asch SM. Identifying barriers to the effective use of clinical reminders: bootstrapping multiple methods. *J Biomed Informatics.* 2005;38(3):189-199.
25. Gabbay J, le May A. Evidence based guidelines or collectively constructed "mindlines?": ethnographic study of knowledge management in primary care. *BMJ.* 2004;329(7473):1013-1017.

Child Abuse Pediatric Consults in the Pediatric Emergency Department Improve Adherence to Hospital Guidelines

Tara Webb, MD; Thomas Valvano, MD, JD; Melodee Nugent, MA; Marlene Melzer-Lange, MD

ABSTRACT

Background: Little data describes the role of child abuse pediatricians in consultation for physical abuse patients the pediatric emergency department.

Objectives: To compare adherence in the emergency department to hospital physical abuse guidelines and need to return for testing between 2 groups: those receiving a child abuse consultation in the pediatric emergency department vs those who received standard emergency department care with subsequent child abuse review.

Methods: We reviewed 471 records of visits to the pediatric emergency department for physical abuse. Data collected included demographics, studies performed, whether patients need to return after child abuse review, child abuse subpoenas, child abuse testimony in court.

Results: Patients who received a child abuse consult in the emergency department or inpatient were more likely to be younger and to have more severe injuries. In cases where a consult was obtained, there was 100% adherence to emergency department clinical guidelines vs 66% when no consult was obtained. In addition, in cases that did not receive a child abuse consult, 8% had to return to the hospital for labs or radiographs after their emergency department visit.

Conclusions: Child abuse consultation in the pediatric emergency department improves compliance with clinical guidelines and decreases the likelihood that patients will need to return for further testing.

INTRODUCTION/OBJECTIVES

Child physical abuse is a widespread problem in the United States, with approximately 80,000 cases reported each year.^{1,2,3} Many of these children present to the emergency department (ED) for evaluation of these injuries. There is currently little data to demonstrate the frequency and number of these visits, though

• • •

Author Affiliations: Medical College of Wisconsin, Department of Pediatric Emergency Medicine, Milwaukee, Wis (Webb, Melzer-Lange); Medical College of Wisconsin, Department of Quantitative Health Sciences, Milwaukee, Wis (Nugent); Oregon Health and Science University, Department of Pediatrics, Child Abuse and Neglect, Portland, Ore (Valvano).

Corresponding Author: Tara Webb, MD; Medical College of Wisconsin, MS C550, PO Box 1997, Milwaukee, WI 53201; phone 414.266.6673; fax 414.266.2635; e-mail twebb@mcw.edu.

children who are ultimately diagnosed with physical abuse tend to be frequent users of the pediatric ED in general.⁴

As child abuse (CA) pediatrics is a relatively new specialty,⁵ the role of these physicians in caring for physical abuse patients in the pediatric ED is not clearly defined. In some institutions, these physicians are contacted regarding all cases of physical abuse; however, in our pediatric ED, physical abuse cases are not routinely evaluated in the ED by child abuse pediatricians. The need for specialist consultation is determined based on the ED physician's level of suspicion for abuse or if there is diagnostic uncertainty. If a specialty consult is not obtained while the patient is in the ED, the chart is later reviewed by a child abuse pediatrician to determine if the patient needs additional follow-up.

Due to the importance of proper detection and management of physical abuse in children, the American Academy of Pediatrics (AAP) has developed a set of guidelines for the evaluation of suspected physical abuse in children.⁶ Since not all children are initially evaluated by the specialist, a set of step-by-step hospital guidelines (based on recommendations in the AAP guidelines for management of physical abuse) is available for work-up of physical abuse patients in our ED. ED physicians have been educated on the presence of the guidelines, which are periodically updated based on updated AAP recommendations. Secondly, though 1 prior study has looked at the percentage of court subpoena and testimony for physical abuse patients,⁷ no studies have looked specifically at patients in the ED.

The aims of this study are: (1) to compare adherence to hospital guidelines and the need for patients to return to the hospital for further testing in patients that receive child abuse specialist consults versus those that receive standard ED care, and (2) to describe the frequency of subpoenas and court testimony by

treating physicians in cases with specialty consult vs those where no consult was obtained.

METHODS

Study Population

A retrospective record review was performed for physical abuse on visits to an urban pediatric ED from January 1, 2005 to December 31, 2006. The study was performed beginning in 2008, and this data was the most recent data available that included information on court appearances and subpoenas. Patients were identified as patients who were logged in an Access (Microsoft Corporation, Redmond, Washington) database maintained by the child abuse pediatrics department as having received a social work consult in the ED for physical abuse. All patients who present to the ED with injuries concerning for physical abuse receive a social work consult, which is a standard of care for an abuse evaluation in our ED and a social worker is available in the ED 24 hours a day. The Access database also contained information on demographics, follow-up, and court involvement for each patient. Data also was obtained from paper/electronic medical records. The diagnosis of physical abuse was either suspected during the ED evaluation, or patients presented to the ED for evaluation of abuse as self-referrals, primary doctor referrals, or referrals from child protective services. Records of patient visits were excluded if the patient already had been evaluated in the ED for the same injury. A total of 471 records were included in the study, which represented 0.4% of all ED visits during a 2-year time period. The institutional review board of the Children's Hospital of Wisconsin approved this study.

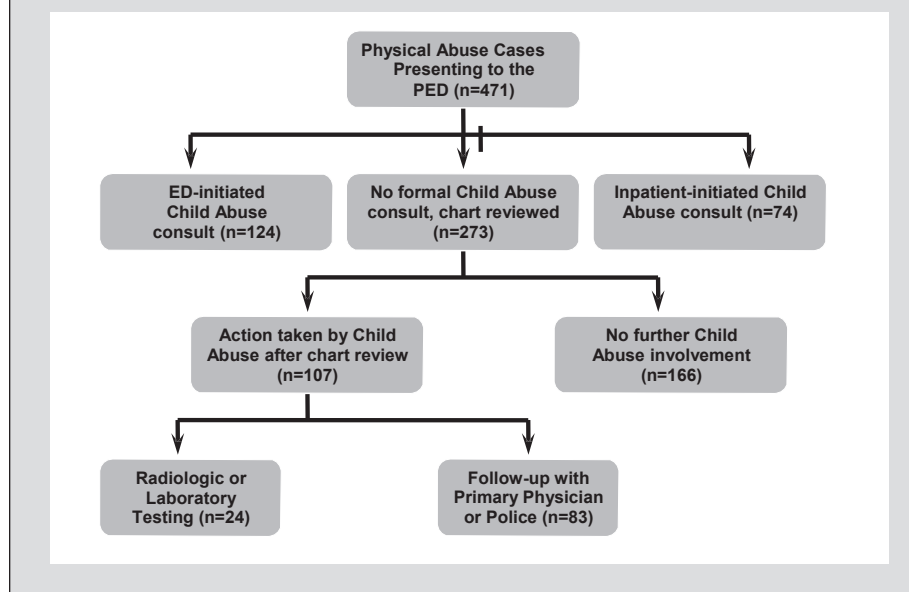
Clinical and Legal Characteristics

Data extracted from the records included demographic data, laboratory and radiographic studies performed in the ED, child abuse pediatrician consultation (in ED, inpatient, or none), whether the patient needed to return to the hospital for additional testing after chart review by child abuse pediatricians, whether patients required follow-up for legal issues, and whether child abuse pediatricians were subpoenaed or testified in court. An Abbreviated Injury Score (AIS) was calculated for each subject using methodology as described by Greenspan et al.⁸

Groups

Patients presenting to the pediatric ED can follow 1 of several different management pathways. All children seen in the ED for whom there are concerns of physical abuse receive a social work

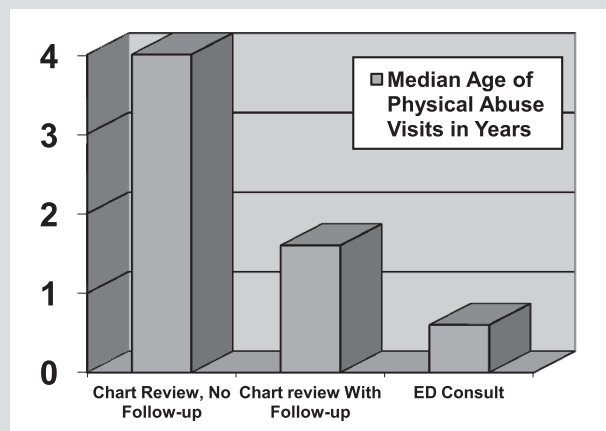
Figure 1: Management Options for Physical Abuse Cases that Present to the Pediatric Emergency Department (PED).



consult and are evaluated by an ED physician. After evaluation by the physician, either a child abuse consult is requested in the ED, the child is admitted and receives the child abuse consult as an inpatient, or no child abuse consult is requested. For patients who do not receive a consult, all charts are reviewed later by a child abuse pediatrician who determines whether additional follow-up is necessary (Figure 1). If additional laboratory or radiologic testing is required after chart review, the patient or their primary doctor is contacted to arrange this testing. Information on the need for additional testing was obtained from medical records and a database maintained by the child abuse pediatricians. Only patients that needed to return for testing that could have been performed as part of the initial evaluation were recorded as patients that needed to return to the hospital; patients who needed to return for routine follow-up (such as repeat skeletal surveys in 2 weeks or follow-up of prior abnormal studies) were not included in this category. Aside from laboratory or radiologic testing, CA pediatricians also follow up on legal issues such as providing reports to police for this group of patients or arranging follow-up with the patients' primary physicians.

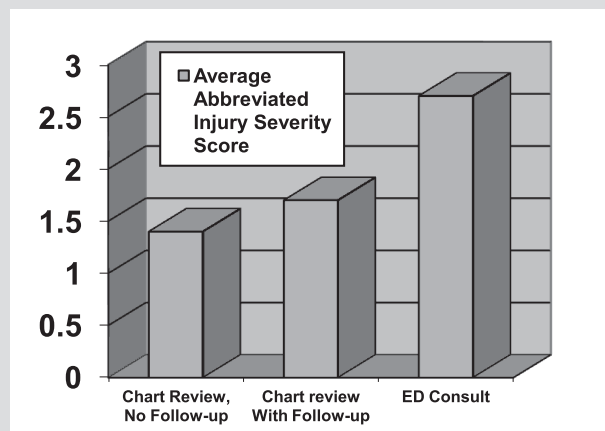
To determine the differences in management of these patients, comparisons were made among 3 groups: ED consults, chart review (no ED child abuse consult) with follow-up required, and chart review (no ED child abuse consult) with no follow-up required. Patients who were admitted to the hospital and received a child abuse consult as inpatients were excluded, since the testing performed in the ED was only part of the workup performed during their hospital stay and some studies were deferred to be done during their inpatient stay. The primary record reviewer (TW) reviewed each record to determine the number of indi-

Figure 2: Age by Child Abuse Specialist Involvement.



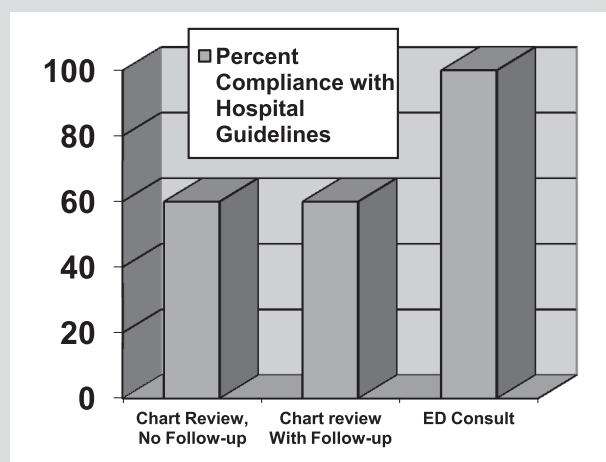
Patients who received child abuse specialist consults in the emergency department or as inpatients were significantly younger than patients who did not receive consults ($P < 0.001$).

Figure 3: Injury Severity by Child Abuse Specialist Involvement.



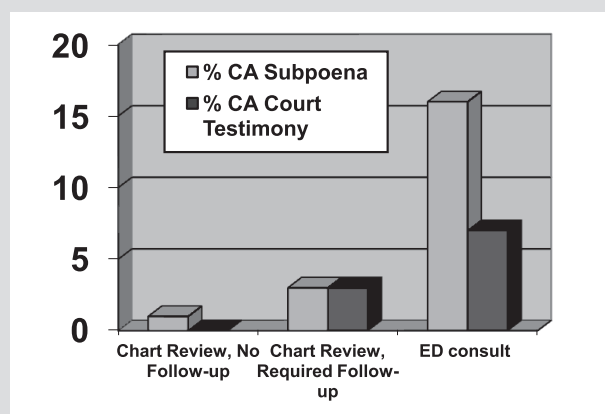
As expected, children with more severe injuries (calculated based on abbreviated injury severity score) were more likely to receive child abuse consults ($P < 0.001$).

Figure 4: Compliance With Hospital Guidelines.



Patients with child abuse consults had significantly increased compliance with hospital guidelines. ($P < 0.001$)

Figure 5: Child Abuse Specialist Subpoena and Court Testimony.



Child abuse pediatricians received subpoenas on 16% of the patients they consulted on in the emergency department (ED). They appeared in court to testify for 7% of ED consults. No ED physicians were subpoenaed or testified in court over this time period.

cated studies (based on hospital guidelines) performed and the number of tests indicated but not ordered. A percent compliance was calculated with number of tests ordered in the numerator and total number of tests indicated in the denominator. For example, if a 6-month old came to the ED for an arm fracture, the guidelines recommend that a head CT and skeletal survey should be obtained. If only 1 of these tests were performed on the patient, the percent compliance would be recorded at 50%.

Data Analysis

Statistical analyses were performed using SPSS software (IBM Corporation, Armonk, New York). Data was analyzed using the Mann Whitney test for continuous data, the χ^2 test for proportions, and the Kruskal-Wallis test for >2 continuous variables (such as the comparisons among the 3 groups by specialty consult).

RESULTS

Demographics

The median age for physical abuse visits was 1.7 years, significantly lower than the median age of 3 years for all ED visits. Patients evaluated in the ED for physical abuse did not have a significantly different racial or ethnic distribution when compared to all ED visits ($P = .470$) though they did have a significantly lower median family income (calculated by ZIP code of residence) ($P < 0.001$).

Use of Specialty Consults

Comparisons by Age

Comparisons of median age of patients receiving child abuse physician consults showed that younger patients were more likely to receive consults than older patients. The median age of

patients who received consults in the ED was 0.6 years. In the patients who did not receive consults, younger patients tended to need more follow-up from the specialists, with a median age of 1.6 years in patients that needed follow-up compared to 4.0 years in patients who did not need follow-up (Figure 2).

Comparisons by Injury Severity

Patients receiving consults had more severe injuries ($P < 0.001$) with a mean AIS of 2.7. Patients who did not receive ED consults but required follow-up had a mean score of 1.4, and patients who did not receive ED consults and did not need follow-up had a mean AIS of 1.6 (Figure 3).

Compliance with Clinical Guidelines

Comparisons of the 3 groups showed that, when no consult was obtained, ED physicians had approximately 66% compliance with the testing recommended by clinical guidelines. When a consult was obtained in the ED, there was 100% compliance with the guidelines ($P < 0.001$) (Figure 4).

Patients Returning to the Hospital for Further Testing

In the group of patients who did not receive a consult, 8% of patients needed to return to the hospital for additional testing (24 patients). See Table 1 for additional testing required for these patients. No patients who received a child abuse consult in the ED needed to return for additional testing.

Court Subpoenas and Testimony by Physician Specialists

Frequencies of court subpoenas and testimony of child abuse pediatricians were recorded. In patients who received consults in the ED, child abuse pediatricians received subpoenas 16% of the time and provided court testimony 7% of the time. The CA pediatricians testified as expert witnesses on 1% of the group that did not receive a consult (3 patients for whom they had recommended follow-up testing). No ED physicians were subpoenaed or testified in court over this time period (Figure 5).

DISCUSSION

Child abuse and neglect recently has been recognized as a specialty, approved by the American Board of Pediatrics in 2005 and accepted by the American Board of Medical Specialties in 2006. As reported by Block and Palusci,⁵ the specialty was developed in response to a relative paucity of research in this important area and the rapid advances in the field that make it difficult for a general pediatrician to stay updated. In addition, child abuse pediatricians bring greater understanding of the workings of the legal system and knowledge of current state legislation.⁵

There are no previous published studies addressing the use of child abuse pediatricians in the ED. The goal of this study was to determine the contributions of the CA pediatricians to cases of physical abuse in the ED. As reported earlier, since not all children in our ED receive consults, we were able to compare the children with child abuse involvement directly to groups of

patients in our ED who did not receive consults. With respect to demographic comparisons, younger children were more likely to receive specialty consults, likely because this population tends to have more severe injuries such as nonaccidental head trauma. Our data shows patients with higher AIS scores also were more likely to receive consults, so there may have been a significant overlap between these 2 populations.

As hypothesized, adherence to the guidelines varied with the level of involvement of the child abuse pediatricians. After the charts of patients who did not receive consults in the ED were reviewed by the specialists, a significant number of patients needed to return to the hospital for additional testing or radiological evaluation. Since this testing should have been performed as part of the initial workup in the ED as part of the physical abuse guidelines, it is concerning that patients who do not receive a consult may have undiagnosed injuries during their initial visits and may be at risk for further abuse. However, we were able to demonstrate improvements in the adherence to clinical guidelines and the reduced need for patients to return to the hospital for further testing in patients who received CA consults.

In addition, the recorded data on court testimony and subpoenas by the child abuse specialists is similar to that published by Palusci et al in 2001.⁷ While both studies look at rates of court subpoena and testimony in child abuse experts, the Palusci study was performed before a formal pediatric specialty in the field of child abuse existed and showed rates of court subpoenas of 13% of patients evaluated, while our study shows slightly higher court subpoenas on 16% of patients evaluated in the ED and 18% of patients evaluated as inpatients. Our study also showed a slightly higher percentage of court appearances in patients evaluated by the child abuse pediatricians (7% of ED consults compared to 4.5% of total evaluations in the Palusci study). It is unclear from the Palusci study whether the child abuse experts were evaluating only outpatients or were also performing consults in the ED. Possible explanations for our higher rates of subpoenas and court appearances could be related to higher acuity of care resulting in patients with more severe injuries or may be simply due to differences in the legal system in different jurisdictions.

Possible limitations of our study are that our inclusion criteria may have inadvertently excluded some physical abuse patients. First, though we perform social work consults on abuse patients as a standard of care, it is possible that a rare patient may not have received a consult. Secondly, not all cases of physical abuse that present to the ED are detected, so patients who had unrecognized abuse would not have been included in the study. Third, though we were able to demonstrate that a significant number of patients needed to return to the hospital for additional testing, incomplete data was available regarding the results of this testing, so we were unable to determine if any new injuries were detected as a result of the additional testing. Also, given the retrospective nature of the study, it is difficult to determine whether the

involvement of the child abuse physicians and improved guideline adherence resulted in improved outcomes for the patients.

Another limitation is that child abuse policies and procedures vary among institutions. In institutions that have different protocols for consultation, the information reported in our study may not be applicable or relevant to their clinical practice. Also, the study data reflects physician practice specific to our geographic area, which may vary in other hospitals and locations. Finally, not all institutions have child abuse specialists available and do not have the ability to consult these physicians regarding patient management. Though this study has demonstrated significant improvements in adherence to hospital guidelines when child abuse physicians were involved in patient care, similar adherence could be achieved potentially with better education of ED physicians regarding established AAP or local hospital guidelines.

CONCLUSION

This study shows that consultation of child abuse pediatricians can improve adherence to physical abuse guidelines and decrease the need for patients to return to the hospital for further testing. Future directions will be to determine whether these indicators of improved clinical practice result in an improvement in diagnosis of physical abuse and prevention of future injury. In addition, a prospective study aimed at determination of the effect of specialist involvement on legal and child protective service outcomes is needed to examine the contribution of these specialists to ongoing management of physical abuse patients and prevention of further injuries.

Funding/Support: None declared.

Financial Disclosures: None declared.

REFERENCES

1. US Department of Health and Human Services, Administration for Children and Families. Victims by Maltreatment Type. *Child Maltreatment 2007*: 25. <http://www.acf.hhs.gov/programs/cb/pubs/cm07/cm07.pdf>. Accessed September 11, 2013.
2. US Department of Health and Human Services, Administration for Children and Families. Perpetrators. *Child Maltreatment 2007*:65-67. <http://www.acf.hhs.gov/programs/cb/pubs/cm07/cm07.pdf>. Accessed September 11, 2013.
3. US Department of Health and Human Services, Administration for Children and Families. Children. *Child Maltreatment 2007*:23-30. <http://www.acf.hhs.gov/programs/cb/pubs/cm07/cm07.pdf>. Accessed September 11, 2013.
4. Keshavarz R, Kawashima R, Low C. Child abuse and neglect presentations to a pediatric emergency department. *J Emergency Medicine*. 2002;23(4):341-345.
5. Block RW, Palusci VJ. Child abuse pediatrics: a new pediatrics subspecialty. *J Pediatr*. 2006;148(6):711-712.
6. Kellogg N, Committee on Child Abuse and Neglect. Evaluation of suspected physical abuse. *J Pediatr*. 2007;119(6):1232-1241.
7. Palusci VJ, Hicks RA, Vandervort FE. "You are hereby commanded to appear": pediatrician subpoena and court appearance in child maltreatment. *J Pediatr*. 2001; 107:1427-1430.
8. Greenspan L, McLellan BA, Greig, H. Abbreviated injury scale and injury severity score: a scoring chart. *J Trauma*. 1985;25(1):60-64.

Progress in Reducing Premature Deaths in Wisconsin Counties, 2000-2010

Thomas Nonnweiler; Elizabeth A. Pollock, BS; Barbara Rudolph, PhD, MSSW; Patrick L. Remington, MD, MPH

ABSTRACT

Background: Measuring trends in a county's premature death rate is a straightforward method that can be used to assess a county's progress in improving the health of the population.

Methods: Age-adjusted premature death rate data from Wisconsin Interactive Statistics on Health for persons less than 75 years of age were collected for the years 2000-2010. Overall 10-year percent change was calculated, compared, and ranked for all Wisconsin counties during this time period. Progress was assessed as excellent (25.0% or greater decline), very good (20.0%-24.9% decline), good (10.0%-19.9% decline), fair (0.0%-9.9% decline), or poor (any increase).

Results: Overall, premature death rates in counties declined by 16.8% over the 10-year period 2000-2010 in Wisconsin. Trends varied by county, with 8, 15, 37, 9, and 3 counties having excellent, very good, good, fair, and poor progress, respectively. The most improvement was seen in Kewaunee County (decreasing 38.3%) and the least progress in Lafayette County (increasing 4.8%). Trends in premature death rates were not related to the county's initial death rate, population, rurality, or income.

Conclusions: Although premature death rates declined overall in Wisconsin during the 2000s, this progress varied across counties and was not related to baseline mortality rates or other county characteristics.

Wisconsin from 1999 to 2009, showing an average annual reduction of 1% per year in premature death rates.¹⁰ This report also showed that death rates have declined in all age groups under the age of 75 (declines of 0.3% for infants; 3.1% for ages 1-14; 1.2% for ages 15-24; 0.1% for ages 25-44; 1.1% for ages 45-64; and 2.9% for ages 65-74).¹⁰

Measuring trends in premature death rates is a direct way to assess progress in improving the overall health in Wisconsin, and for each of Wisconsin's counties. The purpose of this report is to assess trends in premature death rates in Wisconsin's counties and to allow comparisons across counties. This information can be used by communities to assess progress of past public health and health care interventions and set goals for future efforts.

INTRODUCTION

The goal of Healthiest Wisconsin 2020 is "Everyone Living Better, Longer."¹ One way to monitor progress toward this goal is to track death rates in Wisconsin, by cause of death, and by age, race, gender, or place. In the past, the *WMJ* has published numerous assessments of trends in death rates in Wisconsin.²⁻⁹ A recent report published by the University of Wisconsin Population Health Institute tracked progress in death rates in

• • •

METHODS

Age-adjusted (to the 2000 US population) death rates for those less than 75 years of age were used as the measure of premature death for Wisconsin and each of its 72 counties. We measured changes in deaths only under the age of 75 in an attempt to understand trends in death rates that are ideally preventable, and we used overall age-adjusted death rates, as this measure shows less random year-to-year fluctuation than measures of "years of potential life lost," making it better suited for the measurement of trends over time. Data were obtained for the years 2000-2010 for all counties from the Wisconsin Interactive Statistics on Health (WISH) website.¹¹ Microsoft Excel¹² was used to create trend lines for the state and for each county. An exponential trend line was created for the state and for each county, which assumes a constant percent change in rate over time. To achieve more precise estimates and smooth the data to reduce errors, this regression line was used to calculate predicted premature death rates for 2000 and 2010. From these predicted rates, the 10-year

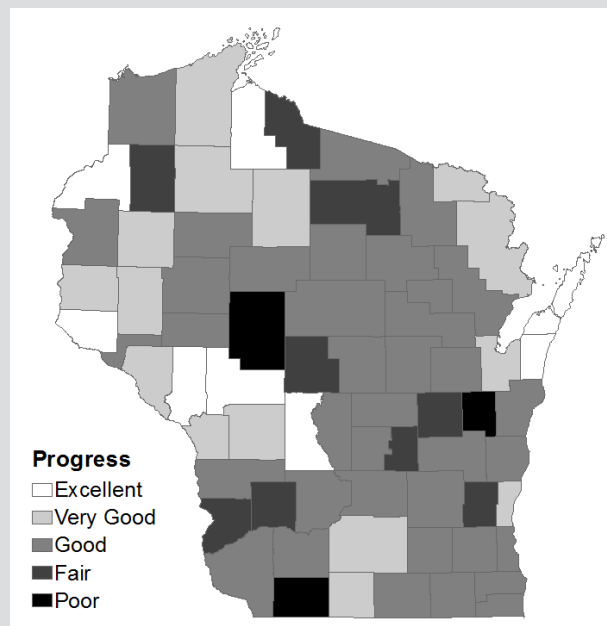
Author Affiliations: University of Wisconsin–Madison (Nonnweiler); UW Department of Population Health Sciences, Madison, Wis (Pollock); UW Population Health Institute, Madison, Wis (Rudolph); Population Health Sciences and Associate University of Wisconsin–Madison (Remington).

Corresponding Author: Patrick Remington, MD, MPH, School of Medicine and Public Health, 4263 Health Science Learning Center, 750 Highland Ave, Madison, WI, 53705; phone 608.263.1745; e-mail plreming@wisc.edu.

Table 1. Summary of Trends in Premature Death Rates (Age-adjusted <75 Years) in Wisconsin, 2000-2010

10-year percent change	Progress	Number of Counties (%)
25% or greater reduction	Excellent	8 (11.1%)
20% to 24.9% reduction	Very good	15 (20.8%)
10% to 19.9% reduction	Good	37 (51.4%)
0% to 9.9% reduction	Fair	9 (12.5%)
+0.1% or greater increase	Poor	3 (4.2%)

Figure 1. Progress Toward Reducing Premature (< 75 years) Death Rates in Wisconsin, by County, 2000-2010.



percent reductions in premature mortality for each county were calculated, ranked (from 1-72), and rounded to the nearest decimal point.

A scale was developed to further describe and communicate a county's progress in reducing premature death rates. Healthy People 2020 has recommended that communities establish 10-year targets of a 10% improvement for measures of health outcomes and factors¹³—or approximately 1% per year. Different levels of progress were assigned the categories “excellent,” “very good,” “good,” “fair,” and “poor.” We defined inadequate population health progress as the percent of counties whose progress was only fair or poor (ie, did not meet the Healthy People 2020 goal of a 10% reduction in 10-year death rates).

Finally, baseline county characteristics used in this analysis (2000 premature death rates) and data from the 2000 US Census (population, percent rural, and median income) were correlated with overall percent change (2000-2010) in death rate in an attempt to detect any association between initial mortality rate and county characteristics and progress in mortality rate over the last 10 years.

RESULTS

The overall premature death rate for people under 75 years of age in Wisconsin declined by 16.8% over the 10-year period 2000-2010. Trends for each county, however, varied greatly across the state. A 4.8% overall increase in the premature death rate in Lafayette County was the highest for any county in Wisconsin, while Kewaunee County saw the largest reduction in the 10-year premature death rate with a decline of 38.3%. Of Wisconsin's 72 counties, 60 (83%) met the goal of a 10% or greater reduction in premature death rate during the 2000-2010 period. As shown in Table 1, 8 counties were rated as “excellent,” 15 counties were rated “very good,” and 37 counties were rated “good.” Twelve of the 72 counties did not meet the goal of at least a 10% decrease in 10-year premature mortality—with 9 counties rated “fair,” while 3 counties were rated “poor.” Table 2 displays a listing by county according to trend rank, and Figure 1 illustrates a map of county by 10-year percent change progress category.

The 8 counties with excellent progress—a 10-year decline of 25% or greater—were Kewaunee, Door, Trempealeau, Pierce, Jackson, Burnett, Ashland, and Juneau counties. Counties with only fair or poor progress—less than a 10% decrease or any increase—included Lafayette, Clark, Calumet, Washburn, Richland, Winnebago, Wood, Crawford, Oneida, Green Lake, Iron, and Washington counties.

In general, less healthy counties at baseline (in 2000) did slightly better in improving their premature mortality rates than did the more healthy counties at baseline, although this association was small (correlation coefficient of -0.244, $R^2=0.06$). No additional apparent association was found between baseline county characteristics (population of county, percent rural population, median income) and overall percent change in mortality rate between 2000 and 2010 (correlation coefficients -0.03, -0.05, and -0.07 respectively).

DISCUSSION

This report shows that overall Wisconsin is showing good progress in reducing premature death rates, with an overall reduction of 16.8% from 2000 to 2010. This exceeds the expectations of the Healthy People 2020 goal of a 10% improvement in 10 years.¹³ Of Wisconsin's 72 counties, 60 counties (83.3%) had good, very good, or excellent progress, meeting or exceeding the 2020 goal of 10% improvement in a decade. Our findings are consistent with national findings of declining death rates since 1935. The age-adjusted death rate (for the population under 75 years of age) has decreased 41% between 1969 and 2010 in the United States.¹⁴ This equates to an average decline of about 12% per decade; therefore, the 16.8% reduction in premature death rates observed over the past decade in Wisconsin has been slightly better than the average 10-year declines over the past 4 decades in the United States.

Table 2. Age-adjusted Premature (<75 Years) Death Rates, Ranks, Trends, and Progress in Wisconsin Counties, 2000-2010

	2000 Death Rate ^a	2000 Rank	2010 Death Rate ^a	2010 Rank	Percent Change (2000- 2010)	Percent Change 95% CI	Trend Rank		2000 Death Rate ^a	2000 Rank	2010 Death Rate ^a	2010 Rank	Percent Change (2000- 2010)	Percent Change 95% CI	Trend Rank
Wisconsin	353		294		-16.8%	(-16.7, -16.9)		Fond du Lac	337	34	287	30	-14.9%	(-14.3, -15.5)	37
Kewaunee	329	27	203	1	-38.3%	(-35.0, -44.1)	1	Polk	340	35	290	33	-14.6%	(-14.2, -15.3)	38
Door	326	25	212	2	-35.0%	(-32.4, -35.0)	2	Vilas	354	47	303	44	-14.3%	(-13.4, -15.7)	39
Trempealeau	391	57	271	22	-30.6%	(-28.7, -30.6)	3	Waukesha	276	2	236	7	-14.2%	(-13.9, -14.5)	40
Pierce	318	20	227	4	-28.6%	(-27.3, -30.5)	4	Marquette	435	68	374	70	-14.0%	(-12.7, -16.2)	41
Jackson	430	66	313	50	-27.2%	(-25.4, -29.9)	5	Kenosha	402	63	347	67	-13.6%	(-13.5, -13.8)	42
Burnett	391	58	287	32	-26.5%	(-24.1, -30.4)	6	Waushara	380	54	329	60	-13.4%	(-12.8, -14.4)	43
Ashland	458	70	341	65	-25.6%	(-23.1, -29.5)	7	Adams	405	64	351	68	-13.3%	(-12.8, -13.9)	44
Juneau	432	67	324	56	-25.1%	(-24.0, -26.7)	8	Jefferson	341	38	296	40	-13.1%	(-13.0, -13.4)	45
Ozaukee	282	3	212	3	-24.9%	(-23.8, -26.4)	9	Waupaca	397	60	346	66	-12.7%	(-12.1, -13.6)	46
Florence	320	21	244	8	-23.9%	(-19.3, -36.6)	10	Vernon	334	31	293	36	-12.3%	(-11.8, -13.1)	47
Dane	304	12	231	6	-23.9%	(-23.6, -24.2)	11	Dodge	357	50	313	52	-12.3%	(-11.9, -12.9)	48
Sawyer	445	69	339	64	-23.9%	(-22.2, -26.6)	12	Marathon	294	8	258	16	-12.3%	(-12.0, -12.6)	49
Green	346	41	264	20	-23.8%	(-22.6, -25.4)	13	Columbia	335	32	294	37	-12.3%	(-12.0, -12.7)	50
Buffalo	324	23	249	9	-23.4%	(-20.8, -28.0)	14	Langlade	337	33	297	41	-12.0%	(-10.8, -13.9)	51
St. Croix	301	11	231	5	-23.3%	(-23.2, -23.4)	15	Sauk	348	43	307	47	-11.8%	(-11.7, -11.8)	52
Barron	354	48	274	23	-22.6%	(-21.3, -24.3)	16	Manitowoc	314	18	278	26	-11.5%	(-10.8, -12.3)	53
La Crosse	346	40	269	21	-22.3%	(-21.6, -23.2)	17	Portage	284	4	251	10	-11.4%	(-11.0, -12.0)	54
Marinette	393	59	306	46	-22.2%	(-20.7, -24.3)	18	Grant	333	30	295	39	-11.3%	(-10.7, -12.2)	55
Bayfield	373	53	291	34	-22.0%	(-20.1, -25.1)	19	Menominee	612	72	543	72	-11.3%	(-9.4, -15.5)	56
Brown	322	22	253	12	-21.5%	(-21.1, -22.0)	20	Forest	365	51	325	58	-11.0%	(-9.6, -13.4)	57
Price	365	52	287	31	-21.5%	(-18.7, -26.2)	21	Eau Claire	288	7	257	14	-10.7%	(-10.5, -11.1)	58
Monroe	414	65	331	61	-20.2%	(-19.4, -21.2)	22	Oconto	329	26	295	38	-10.2%	(-10.0, -10.5)	59
Dunn	315	19	252	11	-20.1%	(-19.3, -21.3)	23	Douglas	390	56	351	69	-10.0%	(-9.5, -10.6)	60
Racine	389	55	313	51	-19.6%	(-19.1, -20.2)	24	Washington	286	5	258	15	-9.8%	(-9.8, -9.9)	61
Rock	399	62	325	59	-18.6%	(-18.1, -19.1)	25	Iron	350	46	317	54	-9.4%	(-6.8, -15.4)	62
Rusk	397	61	325	57	-18.2%	(-16.1, -21.7)	26	Green Lake	347	42	317	53	-8.8%	(-8.0, -10.1)	63
Iowa	340	36	280	28	-17.7%	(-16.5, -19.6)	27	Oneida	325	24	309	48	-4.8%	(-4.4, -5.4)	64
Walworth	332	29	274	24	-17.5%	(-17.0, -18.0)	28	Crawford	349	45	334	62	-4.4%	(-3.8, -5.4)	65
Sheboygan	343	39	283	29	-17.3%	(-16.7, -18.1)	29	Wood	287	6	275	25	-4.1%	(-3.8, -4.6)	66
Milwaukee	461	71	385	71	-16.5%	(-16.2, -16.7)	30	Winnebago	312	17	304	45	-2.3%	(-2.2, -2.5)	67
Lincoln	356	49	298	42	-16.3%	(-15.0, -18.3)	31	Richland	309	15	303	43	-2.2%	(-2.0, -2.4)	68
Shawano	349	44	292	35	-16.1%	(-15.2, -17.4)	32	Washburn	341	37	336	63	-1.5%	(-0.9, -1.8)	69
Taylor	309	14	260	19	-15.8%	(-14.5, -18.1)	33	Calumet	251	1	258	17	2.9%	(1.5, 5.0)	70
Outagamie	306	13	260	18	-15.2%	(-14.9, -15.5)	34	Clark	310	16	322	55	4.1%	(3.4, 5.2)	71
Pepin	298	9	253	13	-15.1%	(-13.6, -19.4)	35	Lafayette	298	10	313	49	4.8%	(4.0, 6.3)	72
Chippewa	330	28	280	27	-15.1%	(-14.9, -15.4)	36								

^aPredicted from the 10-year regression line.

While these results are certainly encouraging, it is of concern that 16.7% of counties failed to meet the goal. This is an area that needs attention, and the counties with less than satisfactory progress could perhaps consider this during their community health assessment process, in an effort to meet the goal for 2020. One potential approach to seek improvement for those counties that showed inadequate progress to meet the Healthy People 2020 goal could be to look to *County Health Rankings & Roadmaps* and the “Areas to Explore” component suggested specifically for their community.¹⁵ The “Areas to Explore” highlight potential health factors specific to each county that may have the greatest potential opportunity for improvement, or measures for which there are meaningful differences between their county’s values and the

state average or national benchmark. Subsequently, the county could utilize the “What Works for Health” database found on the *County Health Rankings & Roadmaps* website to examine and assess potential evidence-based policies and programs to implement in order to address the specific health-related challenges that face their community.¹⁵

It is also important to note the lack of any distinct association between mortality improvement and baseline mortality or county characteristics, indicating that any county at baseline can improve regardless of initial death rate, size, how rural they are, or income. In other words, counties have an equal opportunity to improve premature death rates. This is an encouraging result suggesting that any county can improve irrespective of their start-

ing point, and that counties should not be discouraged by these baseline characteristics in seeking progress. It should be noted, however, that correlations are not necessarily predictors of future results; rather, they are retrospective metrics. Future research will need to establish differences by county in approaches to lowering premature death rates and continue to monitor their relative successes, such as by conducting case studies examining the characteristics of counties that have great improvements in health outcomes over time.

It is important to recognize limitations of this study, including random error due to small population sizes. The use of 10 years of data for the trend analysis, however, tends to smooth out random variation found where death counts are small, and our use of an exponential trend methodology, which also holds the amount of change constant, suggests that the errors would be small. Finally, this study did not account for changes in health outcomes that may result from changes in population demographics, beyond changes in the age of the population.

This study provides Wisconsin counties with critical information on where they stand in terms of reducing premature deaths through trend analysis and comparison to the goals set by Healthy People 2020. This early look at how they are progressing will allow counties to adopt programs and policies that could potentially reduce premature death rates by 2020. Using an exponential trend methodology over a 10-year period provides empirical evidence of change or lack thereof, which can provide a strong marker for the future and could serve to ignite further action to reduce premature deaths in all counties.

Acknowledgments: The authors would like to thank Anne Roubal, MS, at the University of Wisconsin–Madison for her assistance with the mapping component of the paper, and the peer reviewers for their time and thoughtful suggestions.

Funding/Support: This research was supported in part through a grant from the Robert Wood Johnson Foundation in support of the County Health Rankings, and through support of the Population Health Institute from the UW School of Medicine and Public Health.

Financial Disclosures: None declared.

REFERENCES

1. Wisconsin Department of Health Services. Wisconsin State Health Plan: Healthiest Wisconsin 2020. <http://www.dhs.wisconsin.gov/hw2020/>. Accessed September 9, 2013.
2. Mansfield CJ, Wilson JL, Kobrinski E, Mitchell J. Premature mortality in the United States: the roles of geographic area, socioeconomic status, household type, and availability of medical care. *Am J Public Health*. 1999;89(6):893-898.
3. Schumann CL, Hoxie NJ, Vergeront JM. Wisconsin trends in pneumonia and influenza mortality, 1980-2003. *WMJ*. 2006;105(1):40-46.
4. Edwards NM, Umland M, Ahrens D, Remington PL. The silent epidemic among Wisconsin women: chronic obstructive pulmonary disease trends, 1980-2000. *WMJ*. 2005;104(4):50-54.
5. Insinga RP, Reither EN, Remington PL, Stephenson-Vine L. Trends in malignant melanoma incidence and mortality in Wisconsin, 1979-1997. *WMJ*. 2001;100(6):27-31.
6. Haas SA, Jehn LR, Meek PD. Regional variation in stroke mortality in Wisconsin, 1989-1998. *WMJ*. 2002;101(3):28-31.
7. Said A, Guan H. A decline in adult mortality, ages 45-64, in Wisconsin over the last 20 years: is it enough? *WMJ*. 2003;102(8):47-51.
8. Dawson K, Gordon BJ, Guend A. Progress in reducing stroke mortality in Wisconsin, 1984-1998. *WMJ*. 2002;101(3):32-36,48.
9. Pfister J, Chou C. Progress in reducing mortality among persons 65 to 74 years of age in Wisconsin. *WMJ*. 2003;102(8):52-56.
10. Remington PL, Roubal AM, Catlin BB, Timberlake K. Making Wisconsin the Healthiest State. *Wisconsin Health Trends: 2011 Progress Report*. University of Wisconsin Population Health Institute; 2012. <http://uwphi.pophealth.wisc.edu/publications/other/wisconsin-health-trends-2011-progress-report.pdf>. Accessed September 9, 2013.
11. Wisconsin Department of Health Services. Wisconsin Interactive Statistics on Health (WISH). <http://www.dhs.wisconsin.gov/wish/>. Accessed September 9, 2013.
12. Excel for Mac 2011 [computer program]. Version 14.3.6. Redmond, WA: Microsoft Corporation; 2010.
13. US Department of Health and Human Services. Healthy People 2020. <http://healthypeople.gov>. Accessed September 9, 2013.
14. Hoyert DL. 75 Years of Mortality in the United States, 1936-2010. Centers for Disease Control and Prevention. NCHS Data Brief, March 2012. <http://www.cdc.gov/nchs/data/databriefs/db88.pdf>. Accessed September 9, 2013.
15. University of Wisconsin Population Health Institute. County Health Rankings & Roadmaps. <http://www.countyhealthrankings.org/app/wisconsin/2013/rankings/outcomes/overall/by-rank>. Accessed September 9, 2013.

Heiner Syndrome Mimicking an Immune Deficiency

Jerome A. Sigua, MD; Michael Zacharisen, MD

ABSTRACT

Heiner syndrome is a rare but reversible non-IgE mediated hypersensitivity to cow's milk resulting in an atypical pulmonary disease in infants and young children. There is often a delay in diagnosis in this disorder due to its unusual presentation with heterogeneous manifestations. Such infants usually have chronic or recurrent upper or lower respiratory tract symptoms, suggestive of recurring infections such as otitis media or pneumonia. The patchy infiltrates on chest x-ray are commonly mistaken for pneumonia, yet are refractory to antibiotic treatment. Systemic features such as fever, vomiting, diarrhea, and failure to thrive further contribute to the difficulty in making a prompt diagnosis. Only a few case reports have been published. We report a case of this unique milk-induced pulmonary syndrome in a hospitalized 12-month-old child, which illustrates the importance of considering this diagnosis in any child with unexplained lung infiltrates.

CASE PRESENTATION

A 12-month-old Hmong boy, born full term without complications in Wisconsin with a normal newborn screen, was hospitalized in a tertiary medical center with a suspected multifocal pneumonia that was refractory to outpatient antibiotic treatment. He had a 2-month history of persistent cough with occasional sputum production, dyspnea without wheeze, progressive anorexia, and intermittent fevers. He did not have vomiting or diarrhea but had lost approximately 3 pounds.

His past medical history was otherwise unremarkable; he had normal growth and development and was reaching appropriate developmental milestones. There was no family history of known

immune deficiencies or autoimmune disorders. There was no pet or animal exposure, nor travel outside of his immediate home.

A chest x-ray (CXR) from 2 months prior when his symptoms began was remarkable for a right upper lobe infiltrate (Figure 1A). At that time, he had a concurrent right otitis media and was treated as an outpatient with amoxicillin for a projected 10-day course. His cough worsened before he completed this antibiotic, therefore his treatment was changed to cefdinir

to complete 10 days. His cough did not abate after completing this course. A repeat CXR showed a persistent yet improved right upper lobe infiltrate (Figure 1B), therefore his antibiotic treatment was extended with a course of azithromycin for 5 days. One week later a repeat CXR appeared largely unchanged. He was treated with amoxicillin/clavulanate for an additional 10 days. His symptoms improved mildly, though incompletely, so his treatment with amoxicillin/clavulanate was extended for an additional 20 days. Despite adherence to this regimen, he continued to cough with occasional post-tussive nonbloody emesis. He had no nasal discharge, wheeze, or hemoptysis. His oral intake gradually diminished. He developed intermittent fevers to 101°F-102°F twice weekly. He did not have rash, reflux, vomiting, changes in his bowel habits, or blood in his stools.

On arrival to the emergency department, he was febrile with a temperature of 101.5°F and hypoxemic with an oxygen saturation of 88% on room air. Physical examination was unrevealing other than mild rhonchi noted in his right upper and left lower lung fields. CXR showed an increased right upper lobe consolidation with left basilar and retrocardiac air space opacities that were significantly worse compared to his previous CXR (Figure 1C). Laboratory studies revealed a leukocytosis with mild eosinophilia (white blood cell [WBC] 13.6 K/uL, absolute eosinophil count 816 K/uL), a profound microcytic anemia (hemoglobin 7.1 g/dL, MCV 52 fL), and a mild thrombocytosis (platelets 582,000 K/uL). Iron studies were consistent with iron deficiency anemia (low iron 17 ug/dL, elevated total iron-binding capacity [TIBC]

• • •

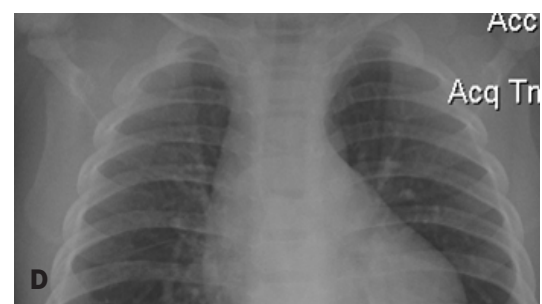
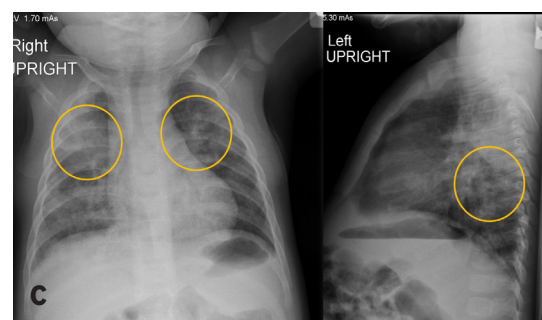
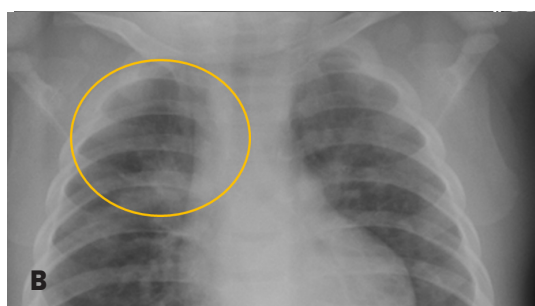
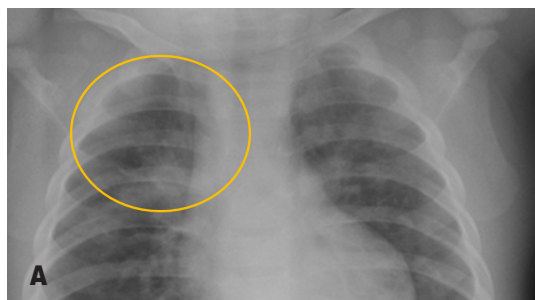
Author Affiliations: Department of Pediatrics, Division of Asthma, Allergy, and Immunology, Medical College of Wisconsin, Milwaukee Wis (Sigua); Department of Pediatrics, University of Colorado School of Medicine, Denver, Colo (Zacharisen).

Corresponding Author: Jerome A. Sigua, MD, Department of Pediatrics, Division of Asthma, Allergy, and Immunology, Medical College of Wisconsin, 9000 W Wisconsin Ave Ste 440, Milwaukee, WI 53226; phone 414.266.6840; fax 414.266.6437; e-mail jsigua@mcw.edu.

CME

CME available. See page 218 for more information.

Figure 1. Chest X-ray Findings Over Time



- A.** Two months prior to hospitalization at symptom onset after cow's milk reintroduction, showing a dense right upper lobe (RUL) infiltrate.
- B.** One month later after persistent antibiotic treatment, showing improved but incomplete resolution of the previous infiltrate.
- C.** During hospital admission, showing relapse of the RUL infiltrate, with new infiltrates in the left upper lobe and retrocardiac areas.
- D.** Two months after strict cow's milk avoidance, revealing dramatic resolution of the previously identified infiltrates.

554 ug/dL, low ferritin 7.9 ng/mL). Inflammatory markers were mildly elevated (erythrocyte sedimentation rate [ESR] 13 mm/hr, C-reactive protein [CRP] 1.1 mg/dL). Blood cultures were without growth.

Due to concern for an atypical or fungal pneumonia, pulmonary hemorrhage, or pulmonary hemosiderosis, a bronchoscopy was performed, which on gross inspection appeared normal other than mild edema and erythema of his bronchi and bronchioles. Bronchoalveolar lavage (BAL) cytology revealed 1600 red blood cells and 1600 nucleated cells of predominant neutrophils and few foamy macrophages. There were no iron-laden macrophages seen. Bacterial and fungal cultures, mycoplasma PCR, viral studies, and acid-fast bacilli smear of the BAL were negative. Additionally, blastomyces and histoplasma serologies were negative. He was continued on treatment with amoxicillin/clavulanate, with clindamycin added for additional microbial coverage; however, his clinical status remained unchanged.

Recurrent aspiration essentially was excluded by a normal swallow evaluation. Because an infectious cause could not be determined, a vasculitis or autoimmune disorder was considered. An anti-nuclear antibody (ANA) test was positive at a titer of 1:640 with a speckled pattern. More specific tests including anti-double-stranded DNA (anti-DS DNA) for systemic lupus erythematosus and anti-glomerular basement membrane (anti-GBM) antibodies for Goodpasture's Syndrome were negative.

An immunology consultation was requested by the primary team for concern of an immunodeficiency. Further history obtained by the consulting service indicated that cow's milk formula at birth elicited nonbloody diarrhea, therefore prompting a switch to a soy-based formula that was better tolerated. At age 10 months, cow's milk formula was reintroduced. Within 1 week of this transition, his chronic cough, dyspnea, intermittent fevers, and progressive anorexia had started.

With this additional history, there was a high index of suspicion for a milk-induced pulmonary syndrome known as Heiner syndrome (HS), especially given the precise correlation of cow's milk reintroduction with subsequent symptom onset. First, a basic screen of his immune function was undertaken. He demonstrated normal tetanus antibody titers of 1.487 IU/mL (>0.150 IU/mL), elevated IgG 1739 mg/dL (174-857 mg/dL), normal IgA 56 mg/dL (10-75 mg/dL), and slightly elevated IgM 107 mg/dL (22-95 mg/dL). A serum specific IgE to cow's milk was negative. Serum precipitating IgG antibodies to all 9 cow's milk protein fractions tested were strongly positive.

Even prior to return of the milk precipitin assay results, a cow's milk-free diet was initiated due to a strong suspicion of HS. Within 1 to 2 days, he exhibited full recovery from his cough, dyspnea, fever, and anorexia. He was discharged home shortly thereafter on a strict soy-based diet. Two months later, a repeat CXR showed complete resolution of the previously identified

pulmonary opacities and infiltrates (Figure 1D). Collectively, all of these findings were strongly suggestive of HS.

DISCUSSION

In 1962, Heiner first reported the presence of precipitating antibodies to several cow's milk antigens in the sera of 7 infants who had presented with varied manifestations including chronic cough, lung infiltrates, diarrhea, failure to thrive, and anemia. Such patients improved after either transitioning to a diet with denatured milk or complete elimination of cow's milk.¹

The precise mechanism responsible for this syndrome is still poorly understood. Whether or not the precipitating antibodies to milk are themselves causative of this disease is not known; however, a type III hypersensitivity or immune complex deposition reaction has been strongly suspected. Heiner and his colleagues had previously demonstrated the presence of IgG, C3, fibrin, and milk antigen deposition on immunofluorescence studies of lung tissue biopsies in a couple of infants.² Additionally, a cell-mediated reaction has also been postulated as contributing to the pathogenesis of this disease.³

Approximately 1% of healthy asymptomatic children are estimated to have precipitating IgG antibodies to milk,⁴ while 4% to 6% of children with chronic respiratory tract disease are thought to have these milk precipitins.⁵ Among those children with HS, approximately 10% are believed to have the severe form of the disease with pulmonary hemosiderosis. Although the onset of symptoms usually occurs before the age of 1 year, it has been reported to occur as late as age 5.²

HS is primarily a clinical diagnosis with no specific confirmatory test. Features of this disorder include upper or lower respiratory tract symptoms such as cough, rhinitis, dyspnea, or wheeze, gastrointestinal symptoms such as vomiting or diarrhea, failure to thrive, fever, CXRs with patchy and fleeting opacities or infiltrates, and varying degrees of peripheral eosinophilia or iron deficiency anemia. Although common, the presence of iron-laden macrophages on bronchial or gastric aspirates is not exhibited by all such children. A majority of children, however, will demonstrate the presence of precipitating IgG antibodies to cow's milk.⁶ Some may even have evidence of serum specific IgE to cow's milk.¹ Rarely, hepatomegaly, splenomegaly, or nonspecific lymphadenopathy can be seen.⁵ What ultimately unifies and supports the diagnosis of HS is resolution of all of the above findings after strict cow's milk avoidance, which our patient exhibited.

Recovery after elimination of cow's milk is usually immediate, with a typical time range of 5 to 21 days.⁵ It is not clear how long one should avoid cow's milk, since it has been reported that subsequent early reintroduction or challenge with cow's milk can lead to recurrence of symptoms.⁶ In general, it is believed that most can tolerate cow's milk within a few years. Prior to reintroduction, some children are able to tolerate denatured or heated milk.⁴

If left undiagnosed and untreated, delayed manifestations of alveolar hypoventilation, pulmonary hypertension, or cor pulmonale can occur.⁵ Death from massive acute pulmonary hemorrhage was reported in a 5-year-old boy with suspected HS.⁷

CONCLUSION

Our case illustrates how Heiner syndrome, often overlooked, can resemble an infection or immune deficiency, contributing to its misdiagnosis, delayed intervention, and increased medical expenses. Interestingly, our patient's elevated ANA may represent a novel finding that has not been previously reported. While it is essential to perform a basic immune evaluation in individuals presenting with recurrent, severe or unusual infections, HS in particular should be considered in the differential diagnosis in any child with unexplained pulmonary infiltrates to avoid harmful consequences.

Funding/Support: None declared.

Financial Disclosures: None declared.

Planners/Reviewers: The planners and reviewers for this journal CME activity have no relevant financial relationships to disclose.

REFERENCES

1. Heiner DC, Sears JW, Kniker WT. Multiple precipitins to cow's milk in chronic respiratory disease. *Am J Dis Child.* 1962;103:634-654.
2. Lee SK, Kniker WT, Cook CD, Heiner DC. Cow's milk-induced pulmonary disease in children. *Adv Pediatr.* 1978;25:39-57.
3. Stafford HA, Polmar SH, Boat TF. Immunologic studies in cow's milk-induced pulmonary hemosiderosis. *Pediatr Res.* 1977;11(8):898-903.
4. Holland NH, Hong R, Davis NC, West CD. Significance of precipitating antibodies to milk proteins in the serum of infants and children. *J Pediatr.* 1962;61:181-195.
5. Boat TF, Polmar SH, Whitman V, Kleinerman JI, Stern RC, Doershuk CF. Hyperreactivity to cow milk in young children with pulmonary hemosiderosis and cor pulmonale secondary to nasopharyngeal obstruction. *J Pediatr.* 1975;87:23-29.
6. Moissidis I, Chaidaroon D, Vichyanond P, Bahna SL. Milk-induced pulmonary disease in infants (Heiner Syndrome). *Pediatr Allergy Immunol.* 2005;16(6):545-552.
7. Williams S, Craver RD. Cow's milk-induced pulmonary hemosiderosis. *J La State Med Soc.* 1989;141(8):19-22.

Quiz: Heiner Syndrome Mimicking an Immune Deficiency

EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be able to:

1. Recognize the signs and symptoms typical of Heiner syndrome.
2. Understand some of the factors which may be involved in the etiology and pathogenesis of Heiner syndrome.
3. Understand the importance of a careful history of exposure to cow's milk in infants and young children with pulmonary and gastrointestinal signs and symptoms..

PUBLICATION DATE: October 16, 2013

EXPIRATION DATE: October 16, 2014

QUESTIONS

1. The following symptoms and signs may be seen in Heiner syndrome:
 - A. Respiratory tract involvement including cough, rhinitis, dyspnea, wheezing and lung infiltrates.
 - B. Gastrointestinal symptoms including vomiting or diarrhea.
 - C. Renal involvement with hematuria.
 - D. Fever and failure to thrive.
 - E. Eosinophilia and iron deficiency anemia.

☐ All of the above
☐ A and B only
☐ A, B, and C only
☐ A, B, D and E only
☐ A, C and D only
2. Heiner syndrome is characterized by the following:
 - A. Pulmonary infiltrates unresponsive to antibiotic therapy.

...

You may earn CME credit by reading the designated article in this issue and successfully completing the quiz (75% correct). Return completed quiz to *WMJ* CME, 330 E Lakeside St, Madison, WI 53715 or fax to 608.442.3802. You must include your name, address, telephone number, and e-mail address.

The Wisconsin Medical Society (Society) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The Wisconsin Medical Society designates this journal-based CME activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

- B. The presence of precipitating antibodies in the sera to several cow's milk androgens.
 - C. Usually a delayed recovery, often over several months, following elimination of cow's milk from the diet.

☐ All of the above
☐ None of the above
☐ A and B only
☐ A and C only
☐ B and C only
3. Which of the following statements is false?

☐ The presence of iron-laden macrophages on bronchial or gastric aspirates is common in Heiner syndrome.
☐ Up to 10% of healthy asymptomatic children are estimated to have precipitating IgG antibodies to cow's milk.
☐ The etiology of Heiner syndrome is thought to be a type III hypersensitivity or immune complex deposition reaction.
☐ Pulmonary hemosiderosis may occur in 10% of children with Heiner syndrome.
☐ Heiner syndrome is a clinical diagnosis that is supported by a resolution of signs and symptoms after strict cow's milk avoidance.
 4. In the present case, which of the following features were observed:
 - A. Leukocytosis, eosinophilia, and iron deficiency anemia.
 - B. An elevated IgG.
 - C. Precipitating IgG antibodies cow's milk protein fractions.
 - D. A positive antinuclear antibody (ANA) test.
 - E. Iron-laden macrophages on bronchoalveolar lavage (BAL).

☐ All of the above
☐ A, B, C and D only
☐ A, B and C only
☐ A, C and E only
☐ B and C only
 5. This case serves to demonstrate the importance of a thorough medical history by eliciting a prior history of gastrointestinal symptoms on exposure to cow's milk while a soy-based formula was better tolerated.

☐ True ☐ False

Heat-related Fatalities in Wisconsin During the Summer of 2012

Megan L. Christenson, MS, MPH; Sarah Dee Geiger, PhD, MS; Henry A. Anderson, MD

ABSTRACT

Background: The hottest year on record for the contiguous United States was 2012. July 2012 ranked as Wisconsin's fourth warmest July, which has profound implications for heat-related mortality.

Methods: We conducted a case series of 27 heat-related fatalities in Wisconsin during summer 2012. Data from death certificates supplemented by coroner reports were analyzed to characterize factors that increase vulnerability to heat-related fatality.

Results: The 2012 heat-related fatalities occurred in both urban and rural counties. All cases had 1 or more known risk factors: 100% lacked functioning residential air conditioning; 70% were over age 65; 75% had a cardiovascular disease; and 52% had a mental health condition. Of the 14 cases with a mental health condition, half were known to be taking psychotropic medication. None of the decedents had been in air conditioning immediately prior to death, and 8 (36%) had been using fans.

Conclusions: Air conditioning is known to be a strong protective factor in preventing heat-related deaths whereas fans have not been shown to be significantly protective across all exposure situations. Prevention efforts should stress reducing social isolation by encouraging checks by friends, neighbors, or police. Prevention messages should also warn patients on psychotropic medications that the medication could increase their risk of heat-related illness or fatality.

INTRODUCTION

The year 2012 was the hottest on record for the contiguous United States.¹ Extreme heat threatens public health by causing a variety of heat-related illnesses and injuries as well as death. Wisconsin reflected record-setting highs across the nation: July 2012 was the state's fourth warmest July and the warmest on record for Milwaukee.²

Previous studies of heat-related fatalities in Wisconsin focused on the heat wave of 1995,³⁻⁶ which attributed 154 fatalities to

heat,⁴ 91 (59%) of which occurred in Milwaukee.³ Subsequent public health action led to community heat response plans in Milwaukee. After implementation of a Milwaukee heat plan, an evaluation of a heat wave in 1999 found a significant decrease in fatalities.⁶

From 2000 to 2010, the annual number of heat-related deaths in Wisconsin ranged from 1 to 24. The aim of this case series is to characterize heat-related mortality by examining the demographics and risk factors of the cases of heat-related fatalities that occurred in Wisconsin during summer 2012.

METHODS

Study Design and Case Definition

We conducted a descriptive case series of heat-related fatalities in Wisconsin during summer 2012 by collecting data from 3 sources. First, we utilized a database

that tracked possible and probable heat deaths reported to the Wisconsin Division of Public Health in real time during the 2012 summer season. Second, death certificates for all probable and confirmed heat-related fatalities were collected from the Wisconsin Vital Records Office (N = 33). Heat-related fatalities were identified by querying terms such as "hyperthermia," "heat," "exposure," "sun stroke," and "heat stroke" in the database of death certificates. Death records with an ICD-10 code of X30 were also extracted; this diagnosis code is assigned to cases with exposure to excessive natural heat. For the purposes of this study, deaths were considered heat-related if heat (eg, heat stroke, environmental heat stress, environmental exposure to heat, extreme heat, heat exposure), hyperthermic, or hyperthermia were listed as the primary, underlying, or contributing cause of death on the death certificate. Third, we requested full death investigation reports from coroners and medical examiners who reported one or more heat fatalities.

• • •

Author Affiliations: Wisconsin Department of Health Services, Division of Public Health, Bureau of Environmental and Occupational Health, Madison, Wis (Christenson, Geiger, Anderson).

Corresponding Author: Henry A. Anderson, MD, 1 W Wilson St, PO Box 2659, Madison, WI, 53701-2659; phone 608.266.1253; fax 608.266.1253; e-mail henry.anderson@dhs.wisconsin.gov.

Figure 1. Timeline of Wisconsin's Heat-related Deaths in 2012.

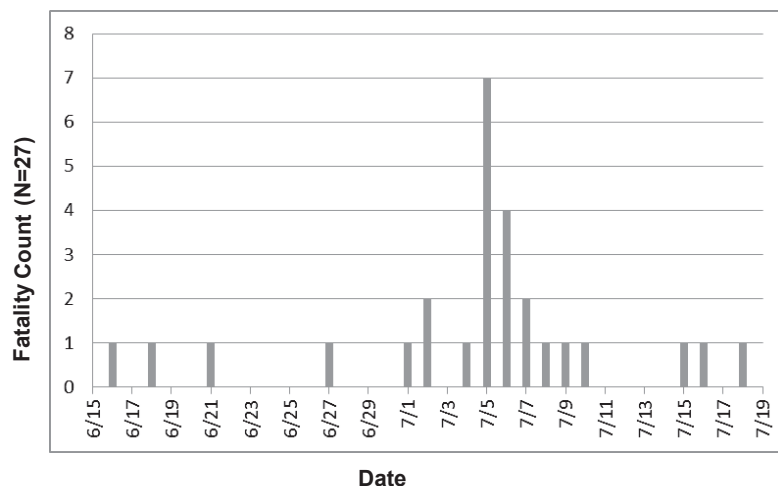
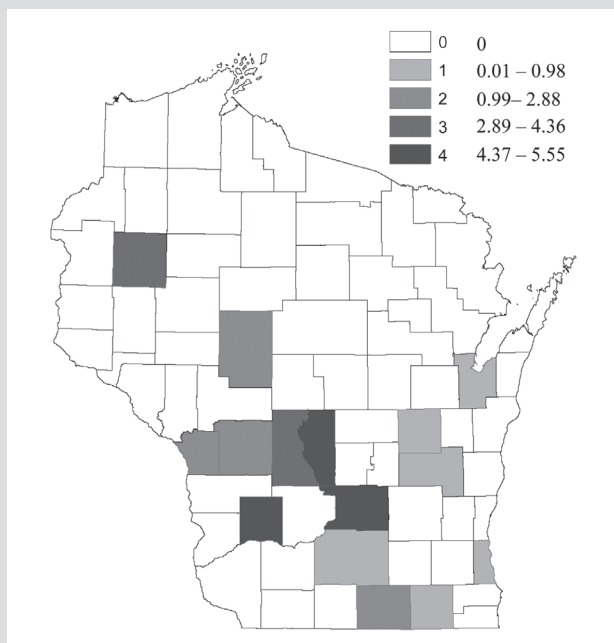


Figure 2. 2012 Heat-related Death Rate by County (per 100,000 population).



Rate calculated using 2011 Department of Health Services population estimates.

Key Variables

Demographic variables from the death certificates were entered into a Microsoft Access (Microsoft Corporation, Redmond, Washington) database, including gender, age, race, and education level. Relevant health conditions were coded into 3 categories: cardiovascular diseases (eg, coronary heart disease, heart failure, myocardial infarction, and hypertension), mental health (eg, schizophrenia, depression, hoarding), and substance abuse (current or historical drug and/or alcohol use). These variables were

chosen based on the existing body of literature (including academic studies as well as public health practice reports) and feasibility of extracting and coding data from our sources. Death certificate data were supplemented by information extracted from the coroner reports, including fan/air conditioning use (not present, unknown, present but not functioning, functioning and used, and functioning but not used), comorbidities (cardiovascular diseases, mental health, and substance abuse), and other circumstances at time of death. If the coroner report indicated that the residence temperature was greater than 80°F but did not specify air conditioning use, it was coded as not present. Though poverty has been linked to heat-related fatalities,⁷ unfortunately, neither data source

included information on income level or poverty status.

RESULTS

Investigation of 6 of the originally reported fatalities did not confirm the death as a “case.” Excluding these 6 resulted in a study sample size of 27. We achieved a 94% coroner response rate for supplemental coroner reports. Figure 1 shows that heat fatalities occurred between June 16 and July 18 with a peak of 7 deaths on July 5. Figure 2 displays fatality rates by county in a state map of Wisconsin, with darker shading indicating increasing fatality rate.

Table 1 presents characteristics of the study population along with comparison statistics for the Wisconsin general population. “The breakdown of heat as a primary or underlying cause versus contributing cause of death was 70% and 30%, respectively. The split between genders was almost equal and the majority of decedents (81.5%) were white, which is not significantly different from the proportion of whites in Wisconsin’s general population. Approximately 74.1% of the sample had cardiovascular disease and 51.9% experienced 1 or more mental health conditions (22.2% were schizophrenic, and hoarding was mentioned in 18.5% of the cases). About 56% of the sample was aged 65-84, highly significantly different from the 11.6% in the general population ($P < 0.001$). Table 2 shows the availability and use of cooling techniques among the decedents. None of the decedents had been using air conditioning at the time of death, and 8 (36.4%) had been using a fan.

Case Reports

We are highlighting 4 of the 27 total cases due to noteworthy characteristics, including risk factors particularly consistent with existing literature, situations which highlight an opportunity for improving public health prevention efforts, and/or extenuating

circumstances. Along with each case profile, we also offer key messages for future prevention efforts.

Case 1. On July 2, 2012, a 75-year-old woman died in the car where she had been primarily living, in the driveway of her home. She was reported to be a hoarder on the medical examiner’s investigation report. Police performed 2 welfare checks (at 1:30 AM and 2 PM) on the date of death before a neighbor found her deceased at 10:30 PM. The heat index indicated on the death certificate was 115°F (at 10:30 PM). The decedent’s adult daughter was away on her honeymoon at the time of death.

Comment: Welfare checks, commonly recommended by state and local public health, were ineffective in preventing this death though we do not know if the decedent was offered help. A welfare check is when a community member requests that the police check on the safety of someone. Local health departments and law enforcement should consider joint efforts to provide recommendations for those living in unsafe environmental conditions, including affordable cooling methods if air conditioning is not an option.

Case 2. On July 6, 2012, a 48-year-old male correctional institute inmate was found dead in his 95°F cell. The decedent had been treated the previous day for heat-related issues. Hyperthermia was the immediate cause of death while significant conditions contributing to the death included chronic psychotic illness and hepatitis C with cirrhosis. The decedent was taking 3 psychotropic medications that can create an increased risk for hyperthermia.

Comment: Institutions that do not have air conditioning should consider implementing special protections such as additional cool showers, fluids, electrolytes, and cold packs for inmates on drugs that could predispose them to heat injury or death.

Case 3. On July 18, 2012, a 62-year-old Hispanic woman was found deceased in her 90°F apartment. She was unclothed and appeared to have fallen from her recliner chair with her asthma inhaler nearby. She had last been seen by her son 2 days prior. The window air conditioning unit in her apartment was inoperable. The immediate cause of death was acute exacerbation of asthma. She had a history of hypertension and mesothelioma, as well as other comorbid conditions. With only a primary education level, the decedent was illiterate.

Comment: Written public health messaging (at least in English) would have been ineffective in preventing this heat-related death. Vulnerable individuals with health conditions such as asthma and other pulmonary conditions that can be exacerbated by heat could benefit from a personalized heat-readiness plan.

Case 4. On July 22, 2012, an 86-year-old man was found deceased in his recliner at home, wearing only socks and a t-shirt. Neighbors had not seen him for 2 weeks, so date of death was estimated to be between July 15-18. The man had no immedi-

Table 1. Demographic Characteristics

	Study Sample	Wisconsin General Population, 2010	P-value ^a
	N (%)	N (%)	—
Total	27 (100)	5,686,986 (100)	—
Women	14 (51.9)	2,864,586 (50.4)	0.88
Age, years			
<20	0 (0)	1,502,196 (26.4)	<0.001
20-44	1 (3.7)	1,833,912 (32.2)	<0.001
45-64	7 (25.9)	1,573,564 (27.7)	0.84
65-84	15 (55.6)	658,809 (11.6)	<0.001
85+	4 (14.8)	118,505 (.02)	0.068
Race/ethnicity			
White	22 (81.5)	4,902,067 (86.2)	0.54
Black/African American	2 (7.4)	359,148 (6.3)	0.83
American Indian	1 (3.7)	54,526 (1.0)	0.46
Hispanic	2 (7.4)	336,056 (5.9)	0.77
Education level^b			
Primary (0-8 years)	4 (14.8)	133,010 (3.5)	0.10
Secondary (9-12 years)	16 (59.3)	1,508,717 (39.7)	0.042
College (>12 years)	7 (26.0)	2,158,568 (56.8)	<0.001
Lived alone	15 (55.6)		-
Comorbidities			
Cardiovascular disease	20 (74.1)		-
Mental health	14 (51.9)		-
Substance abuse	3 (11.1)		-
Autopsy performed	10 (37.0)		-
Role of heat in cause of death			
Primary or underlying	19 (70.4)		-
Contributing	8 (29.6)		-

^aStatistical significance tested using a 2-sample z-test for the difference in proportions

^bTotal for Wisconsin general population is age 25 and older: N=3,800,295
Note: blank cells indicate that information unavailable for comparison.

Table 2. Availability and Use of Cooling Techniques (N=22)^a

	A/C (%)	Fan (%)
Not present	15 (68.2)	1 (4.5)
Unknown	3 (13.6)	11 (50.0)
Present		
Not functional	2 (9.1)	0 (0)
Functional		
Used	0 (0)	8 (36.4)
Not used	2 (9.1)	2 (9.1)

^aN=5 excluded (for Table 2 only), due to outdoor heat exposure.

ate family and lived alone without air conditioning or fans. The many observed signs of neglect included mice, envelopes with checks waiting to be cashed, and a kitchen sink filled with rancid water. The only food in the residence was 1 slice of cheese, cheese spread, and coleslaw which had been expired for almost a year.

Comment: Social isolation played a key role in this heat fatality. Social services, local public health, and police could work

together to identify socially isolated individuals with a goal of checking on their safety and providing education on heat risk factors.

DISCUSSION

Risk and protective factors

Though a relatively low number of deaths are attributable to heat compared to other causes of death such as those associated with prevalent chronic diseases, heat-related fatalities are almost always preventable. Therefore, identifying effective interventions targeting vulnerable populations is crucial.

Prevalent cardiovascular disease in our sample (74.1%) is consistent with existing literature.^{8,9} This is especially true among elderly populations who have a limited ability to thermoregulate their body temperature compared to younger populations.¹⁰

About 52% of our sample had at least 1 mental illness; half of the 14 mental health cases were taking psychotropic medication while the other half were either not taking medication or it was unknown. Two case-control studies of heat-related fatalities found that mental illness is a significant risk factor for heat-related mortality.^{9,11} The literature suggests that antipsychotic drugs can predispose users to heat-related illness by interfering with thirst and ability to thermoregulate.^{12,13} Furthermore, vulnerability to heat can be exacerbated by deficits in self-care, characteristic of individuals with depression and schizophrenia.¹³ Such barriers can lower the likelihood of pursuing preventive measures such as showers and cooling shelters. In addition, patients with schizophrenia can be disproportionately affected by heat-related fatalities; 22% of the fatalities in our sample were schizophrenic compared to worldwide prevalence of schizophrenia of around 0.5%.¹⁴ Of the 6 schizophrenic cases in our sample, 5 (83%) were under the age of 65. A case-control study by Kaiser et al found a similarly high percentage of heat fatality cases with schizophrenia: 4 (24%) of the 17 cases were schizophrenics,¹¹ while another study found that deaths due to schizophrenia increased by more than 2-fold during heat waves.¹⁵

Our study of fatalities underscores the importance of social support networks, specifically for social isolates and shut-ins. Fifty-six percent of the study sample lived alone. Studies show that living alone, a potential indicator of social isolation, is a risk factor for heat-related fatalities.^{9,16} Our case series suggested that it is not only important to check on isolated individuals to make sure they are not in heat distress but also to ensure that current living conditions are safe.

Complete lack of air conditioning across our sample also was striking. Many other studies have found that air conditioning is a strongly protective factor against heat-related death.^{9,11,16} Efficacy of fans, on the other hand, is situation dependent and some studies have shown them to be not significantly protective.^{9,11,17}

Strengths

In addition to collecting death certificate data on the heat-related fatalities, we completed a thorough follow-up of each case to obtain the coroner/medical examiner death investigation report. These reports provided valuable contextual information about the circumstances of the deaths (94% response rate). To our knowledge, this is the first study to note hoarding as a potential mental health risk factor for heat-related fatality. Small sample size and lack of baseline comparison rates prevent us from attributing significance to this observation, but future analytical studies should consider the topic for further investigation.

Limitations

One limitation of our study is variability in the case definition used for heat-related death by coroners and medical examiners across the state. A uniform definition for heat-related death that has been posited by the National Association of Medical Examiners is one "...in which exposure to high ambient temperature either caused the death or significantly contributed to it."¹⁸ It also recommends determining the diagnosis from "...circumstances surrounding the death, investigative reports concerning environmental temperature, and/or measured antemortem body temperature at the time of collapse." Despite efforts to standardize the definition, varying criteria are used in the determination of heat-related death in Wisconsin. For example, 37% of our study's cases involved an autopsy. Also, some collected a rectal temperature of the decedent while others noted the ambient temperature or conducted a toxicology analysis. Because of this inconsistent determination, we cannot rule out the possibility of selection bias, potentially resulting in an underestimate of heat-related fatalities.

CONCLUSION

The case studies and descriptive statistics from our study help inform state- and local-level preparation for future heat waves. Local agencies should partner in community heat response planning to broaden awareness and involvement. Given that three-fourths of the sample had cardiovascular disease outcomes and half suffered from mental health conditions, intervention strategies should target these high-risk groups. Providers should be encouraged to provide verbal warnings to mental health patients taking psychotropic medications that are known to affect the body's ability to cool itself, as well as to educate cardiovascular patients about their elevated risk to heat-related mortality. Other heat planning strategies could include targeted and individualized heat response plans from social services for socially isolated and vulnerable individuals.

Short-term prevention efforts should emphasize the importance of air conditioning and other cooling strategies. Although visiting an air conditioned place has been associated with lower heat-related mortality,¹⁶ results are mixed.⁹ Further research is

needed to assess cooling center effectiveness among those most vulnerable to extreme heat. Fans should not be emphasized as the main preventive strategy since they are not significantly protective across all heat exposure situations.^{16,17} However, since fans may be the only option for some individuals and can be effective in certain situations, messaging should include instructions for correct fan usage, including use when temperatures are below the high 90s. Other simple cooling techniques should also be recommended, such as loose and light-colored clothing, plenty of cool liquids, cool baths, and limited caffeine and alcohol consumption.¹⁹ Long-term prevention strategies such as green infrastructure and increased tree canopy cover should also be considered for their sustainable cooling effects.²⁰

In addition, the current study reinforces need for a consistently used case definition for heat-related fatalities by coroners and medical examiners. Standardization would ensure that heat-caused fatalities are correctly identified and characterized in order to improve future public health prevention efforts.

Temperatures are rising globally, making prevention of heat-related fatalities a continuing challenge. The public health workforce should consider allocating resources to crafting and enacting effective intervention strategies to minimize preventable heat-related fatalities.

Acknowledgements: We would like to thank Michelle Smith from the Wisconsin Vital Records Office for acquiring the death certificates used in this study, and all coroners and medical examiners who submitted their heat-related fatality investigation reports. Many thanks to Rusty Kapela at the National Weather Service for providing temperature data for the summer months of 2012. Also, thank you to Dr Carrie Tomasallo and Chuck Warzecha for providing editorial comments.

Funding/Support: This study was supported in part by an appointment to the Applied Epidemiology Fellowship Program administered by the Council of State and Territorial Epidemiologists (CSTE) and funded by the Centers for Disease Control and Prevention (CDC) Cooperative Agreement Number 5U38HM000414-5. Partial funding was also supplied by the Wisconsin Population Health Service Fellowship, supported by the Wisconsin Partnership Program of the UW School of Medicine and Public Health.

Financial Disclosures: None declared.

REFERENCES

- 2012 was warmest and second most extreme year on record for the contiguous US [press release]. *Science Daily*. January 8, 2013. <http://www.sciencedaily.com/releases/2013/01/130108131149.htm>. Accessed September 10, 2013.
- National Weather Service. July 2012 one of the warmest on record. August 8, 2012. http://www.crh.noaa.gov/news/display_cmsstory.php?wfo=mkx&storyid=85769&source=2. Accessed September 10, 2013.
- Centers for Disease Control and Prevention. Heat-related mortality—Milwaukee, Wisconsin, July 1995. *MMWR Morb Mortal Wkly Rep*. 1996;45(24):505-507.
- Nashold RD, Jentzen JM, Peterson PL, Remington PL. Heat-related deaths during the summer of 1995, Wisconsin. *WMJ*. 1996;95(6):382-383.
- Knobeloch L, Anderson H, Morgan J, Nashold R. Heat-related illness and death, Wisconsin, 1995. *WMJ*. 1997;96(5):33-38.
- Weisskopf MG, Anderson HA, Foldy S, et al. Heat wave morbidity and mortality, Milwaukee, Wis, 1999 vs 1995: an improved response? *Am J Public Health*. 2002;92(5):830-833.
- Klienberg E. *Heat Wave: A Social Autopsy of Disaster in Chicago*. University of Chicago Press; 2002.
- Henschel A, Burton LL, Margolies L, Smith JE. An analysis of the heat deaths in St. Louis during July, 1966. *Am J Public Health*. 1969;59(12):2232-2242.
- Naughton MP, Henderson A, Mirabelli MC, et al. Heat-related mortality during a 1999 heat wave in Chicago. *Am J Prev Med*. 2002;22(4):221-227.
- Basu R, Samet JM. Relation between elevated ambient temperature and mortality: a review of the epidemiologic evidence. *Epidemiol Rev*. 2002;24(2):190-202.
- Kaiser R, Rubin CH, Henderson AK, et al. Heat-related death and mental illness during the 1999 Cincinnati heat wave. *Am J Forensic Med Pathol*. 2001;22(3):303-307.
- Stollberger C, Lutz W, and Finsterer J. Heat-related side-effects of neurological and non-neurological medication may increase heatwave fatalities. *Eur J Neurol*. 2009;16(7):879-882.
- Batscha CL. Heat stroke: keeping your clients cool in the summer. *J Psychosoc Nurs Ment Health Serv*. 1997;35(7):12-17.
- Bhugra, D. The global prevalence of schizophrenia. *PLoS Med*. 2005;2(5):0372-0373.
- Hansen A, Peng B, Nitschke M, Ryan P, Pisaniello D, Tucker G. The effect of heat waves on mental health in a temperate Australian city. *Environ Health Perspect*. 2008;116(10):1369-1375.
- Semenza JC, Rubin CR, Falter KH, et al. Heat-related deaths during the July 1995 heat wave in Chicago. *N Engl J Med*. 1996;335(2):84-90.
- Kilbourne EM, Choi K, Jones TS, Thacker SB. Risk factors for heat stroke: a case-control study. *JAMA*. 1982;247(24):3332-3336.
- Donaghue ER, Graham MA, Jentzen J, Lifschultz BD, Luke JL, Mirchandani HG. Criteria for the diagnosis of heat-related deaths: National Association of Medical Examiners. Position paper. National Association of Medical Examiners Ad Hoc Committee on the Definition of Heat-Related Fatalities. *Am J Forensic Med Pathol*. 1997;18(1):11-14.
- The Centers for Disease Control and Prevention. Tips on managing heat and heat-related illnesses. <http://www.cdc.gov/media/pressrel/r2k0803.htm>. Updated October 17, 2000. Accessed September 10, 2013.
- Adler M, Harris S, Krey M, Plocinski L, Rebecchi J. City of Boston Environmental Department. Tufts University Department of Urban and Environmental Policy and Planning. Preparing for Heat Waves in Boston: A Cool Way to Attack Global Warming. May 7, 2010. http://www.cityofboston.gov/Images_Documents/Preparing%20for%20Heat%20Waves%20in%20Boston_tcm3-31986.pdf. Accessed September 10, 2013.



Clinical Implementation of Whole Genome Sequencing a Valuable Step Toward Personalized Care

Joseph E. Kerschner, MD

Three years have passed since a team of physicians and researchers at the Medical College of Wisconsin (MCW) and Children's Hospital of Wisconsin first used next generation sequencing to diagnose Nic Volker, a young boy battling an unknown and unresponsive intestinal disease. Based on the findings and emerging research that supported a link between his mutated XIAP gene and GI disease, the team proceeded with a cord blood transplant to resolve his debilitating symptoms.

The success of the treatment was transformative for Nic, and it had a similar, long-term impact on the Human and Molecular Genetics Center at MCW and on our appreciation for the importance of the clinical implementation of genome sequencing. This spring, MCW, in partnership with Children's Hospital of Wisconsin and Froedtert Hospital, became the first in the world to offer complete whole genome sequencing in an end-to-end clinical program.

This is not a pilot program; we are practicing this form of personalized medicine today with a focus on cases in which conventional medicine has failed to yield a diagnosis or elucidate the cause of disease symptoms. The genomic medicine clinic has sequenced 23 pediatric patients and 2 adult patients to date and obtained a definitive diagnosis in 27% of the cases. As

more genomes are sequenced and we discover the significance of currently unknown genetic variants, the value of the field to identify causative agents of disease will multiply.

While MCW leverages the expertise of its faculty, software technology, and bioinformatics to pioneer clinical implementation, we recognize that the decreasing cost and the increasing speed of sequencing and analysis will result in

commentary July 17 in *Science Translational Medicine* on their experience converting a research sequencing lab into a fully functioning clinical program.¹ In "Genomics in Clinical Practice: Lessons from the Frontlines," the authors describe the practical, technological, economical, and ethical barriers to deploying clinical genomics with the hope that it may serve as a guide to peers considering the

...genome sequencing is a tool capable of improving the practice of medicine. It holds the power to help patients who have exhausted standard options for care.

many, if not most, hospitals and diagnostic laboratories implementing whole genome sequencing in the future. Practicing physicians will need competencies in using data from genome sequencing. For example, they will need to understand how to use the data, how to engage in meaningful conversations with their patients about the decisions they will face, and what to do with the new wealth and volume of information.

It is in the spirit of sharing knowledge with other practitioners that MCW's clinical genomics team, led by Howard Jacob, PhD, the Warren P. Knowles Professor in Human and Molecular Genetics and Director of the Human and Molecular Genetics Center, published a

launch of similar programs.

As physicians, we tend to think of cases in terms of "what can we do?" for a particular patient. Is the information we obtain from examination, family history, or testing clinically actionable? At MCW, our philosophy as it pertains to genomic sequencing is that a diagnosis is indispensable, even if better clinical outcomes cannot be realized.

In their commentary, Dr Jacob and his associates recount the case of a child experiencing liver failure. The team, however, discovered 2 mutations in a gene with known associations to incurable neurological deterioration, and neurological symptoms were beginning to manifest. The results were not clinically actionable with

• • •

Dr Kerschner is dean of the medical school and executive vice president of the Medical College of Wisconsin.

respect to treatment, but the parents were able to make the best choice for their child's quality of life by declining a liver transplant, which also made the donor organ available for another patient.

Whole genome sequencing presents new ethical questions that have generated much debate, though little clear consensus. Determining what data is returned to the patient, their family, or their physician is among the most disputed subjects, particularly in light of guidelines published by the American College of Medical Genetics (ACMG) recommending that mutations discovered through clinical exome and genome sequencing on any of 57 genes associated with 55 specific diseases be reported to the ordering physician. ACMG recommends incidental findings — those unconnected with the original purpose for ordering the sequencing — be reported regardless of patient preferences.²

It is our belief and our practice that prior to ordering sequencing, the physician and the

patient should determine whether secondary results will be returned and how the information will be managed.

In addition to considering what information the patient wants to receive, there are ethical ramifications surrounding who else is permitted to access the information. Disease heredity makes genomic results significant to a patient's biological family members, and they may or may not want to know the information. Protecting privacy is paramount, since a person's genome is more unique and personally identifying than a fingerprint.

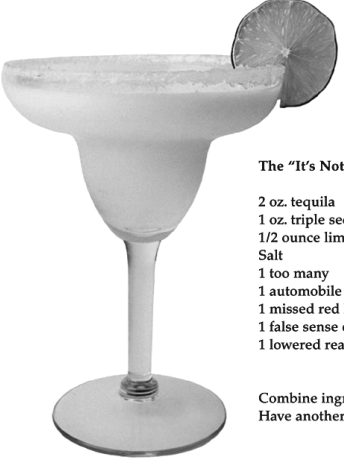
The increasing clinical utility of genomic information, however, demands that we resolve to face these challenges. How does a sequencing clinic deliver 6.4 billion new data points to a doctor who averages less than 8 minutes of contact time per visit, and how is that information managed? Who pays for sequencing and under what conditions?

These questions require answers, but the medical value of the genome makes the effort

fully worthwhile. As a quantitative family history, genome sequencing is a tool capable of improving the practice of medicine. It holds the power to help patients who have exhausted standard options for care. With further discovery and refinement, we envision its eventual efficacy in identifying disease risk and developing preventive medicine plans based on genetic risk to the benefit of patients everywhere.

REFERENCES

1. Jacob HJ, Abrams K, Bick DP, et al. Genomics in clinical practice: lessons from the front lines [commentary]. *Sci Transl Med*. 2013; 5(194):194cm5. <http://stm.sciencemag.org/content/5/194/194cm5.full>. Accessed September 20, 2013.
2. Green RC, Berg JS, Grody WW, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med*. 2013;15(7):565-574. https://www.acmg.net/docs/ACMG_Releases_Highly-Anticipated_Recommendations_on_Incidental_Findings_in_Clinical_Exome_and_Genome_Sequencing.pdf. Accessed September 20, 2013.



The "It's Not Like I'm Drunk" Cocktail

- 2 oz. tequila
- 1 oz. triple sec
- 1/2 ounce lime juice
- Salt
- 1 too many
- 1 automobile
- 1 missed red light
- 1 false sense of security
- 1 lowered reaction time

Combine ingredients. Shake.
Have another. And another.

Never underestimate 'just a few.'
Buzzed driving is drunk driving.

Ad Council

U.S. Department of Transportation

Representing Medical Professionals in Licensing & Regulatory Matters



Hal Harlowe
Attorney

Included on lists for Best Lawyers® in America and Wisconsin Super Lawyers®. Rated AV (top rating) by Martindale-Hubbell.

Former Dane County D.A. Hal Harlowe heads Murphy Desmond's Professional Licensing team. He represents physicians and other medical professionals in:

- Defending against investigations and disciplinary complaints
- Obtaining licensure

As former Chair of the Governor's Task Force on Licensed Professionals, Hal's knowledge of the process can help you defend your professional license and protect your reputation and career.

Contact Hal Harlowe at 608.257.7181 or hharlowe@murphydesmond.com



Madison & Janesville • www.murphydesmond.com



Driven to Serve

W. Stancil Starnes, JD

Editor's note: The Wisconsin Medical Society helped form PIC WISCONSIN in 1986 to ensure the availability of medical professional liability insurance for Wisconsin physicians. Today the Society continues to endorse ProAssurance Wisconsin Insurance Company (formerly PIC WISCONSIN) to provide professional liability insurance coverage with unmatched success in claims defense.

In my desk drawer there is an old letter that both haunts and drives me. I want to share the story with you and tell you why that letter in my drawer is so important to you and your colleagues.

First, a bit of background. The vision of ProAssurance's founding CEO, Dr Derrill Crowe, was to provide every ProAssurance policyholder an unequaled level of service and the strongest defense against non-meritorious claims. In my 35 years of practicing law before succeeding Dr Crowe, I was fortunate to be entrusted to deliver on those promises, defending hundreds of ProAssurance-insured physicians who will attest our dedication to those ideals is real and meaningful.

• • •

Stan Starnes is the Chairman and Chief Executive Officer of ProAssurance Corporation, the parent company of ProAssurance Casualty Company (formerly PIC Wisconsin). ProAssurance is one of the nation's largest writers of medical professional liability insurance and is rated "A+" (Excellent) by A.M. Best and "A" (Strong) by Fitch Ratings. ProAssurance has been recognized as one of the 50 best property casualty insurers in America by virtue of its inclusion in the Ward's 50® rankings for 7 straight years.

Early in my law practice, I was assigned a case of an emergency department physician who responded to a code in the hospital where he was on duty. During recovery following an unremarkable surgery, the plaintiff's breathing became obstructed and a code was called. My client responded, but was unable to intubate the patient. Ultimately a surgeon was successful in performing a tracheostomy, but the plaintiff had been without oxygen too long and emerged in a persistent vegetative state.

During the subsequent trial, the hospital settled the case for a significant amount of money, and my client was offered settlement terms that he felt were acceptable. He requested ProAssurance settle the case and a small amount of money was paid on his behalf. The judge closed the case and in turn, I closed my file and ProAssurance closed its file. But the physician learned that his file would be open the rest of his life.

That's when I received *the* letter.

The letter began by thanking me and ProAssurance for providing an excellent defense and strong support during the tedious, trying years before trial. ProAssurance had done everything it promised and more, he said in his opening paragraph.

But his second paragraph hit me like a ton of bricks. He wrote, "You should never have

let me settle that case." And he was right. My client had done nothing wrong—and in fact he had gone above and beyond anything required of him in an effort to save a person's life.

To this day, that letter haunts me, and its message drives me to ensure that everyone at ProAssurance understands that when we are fighting a non-meritorious lawsuit alongside one of our physicians, or trying to reach a fair settlement in the infrequent case of true negligence, we must—and will—have our insured's ultimate welfare foremost in our mind.

As a physician, you understand your reputation as a caring, compassionate, and effective healer is something you have worked your whole life to achieve. Think of the thousands of hours of study and rigorous training and the experience gained through thousands of patient encounters. Then think about the possible impact of a short-term decision made by your medical professional liability carrier.

I often re-read that letter I received from my client. Every time I read it, I am reminded of the great burden we carry when we promise you to provide a committed defense of a non-meritorious claim and pledge to deliver you the cutting-edge services that will help you take control in an uncertain world where medicine is changing in ways you never could have imagined when you cracked the first book in medical school.

As I have said before, Wisconsin is on the leading edge of many of the changes in delivering medical care in America. I know of no other state in which so many forward thinking physicians and health care administrators have

grouped themselves together to deliver quality care in such an efficient manner.

As we work to craft new products and resources for this brave new world of health care, we are developing a bridge that spans the continuum of care—embracing the unique economic and practice needs of physicians who remain in more traditional practice settings, while preparing to meet the full scope of liability challenges faced by evolving multispecialty and even multistate groups.

ProAssurance is uniquely qualified to walk with you as new liability challenges emerge and new demands are made on you. Our financial strength is unquestioned, our experience is unparalleled, and our commitment to you through Treated Fairly® is proven every day by our employees, our agents, and our partnership with organized medicine in Wisconsin.

My promise to you is that neither I, nor anyone else at ProAssurance will ever forget why we are driven to serve you.

Mastering Medicare in 2014

October 29: Madison • October 30: Brookfield • October 31: Green Bay

The Wisconsin Medical Society's annual fall Medicare seminar will provide the information you need about the most up-to-date changes and challenges for Medicare in 2014: Topics include:

- Medicare Physician Fee Schedule Update & Hot Topics
- Meet Your New MAC! NGS Medicare
- Tips for navigating the NGS Medicare website and free web application NGSConnex.
- Quality Resource Utilization Reports (QRURs).
- Public reporting on websites such as Physician Compare.

Learn how these issues will directly affect your practice.

Visit www.wisconsinmedicalsociety.org/resources/education for more information.


Wisconsin Medical Society



EOE/AA/LEP

Gundersen Lutheran Medical Center, Inc. | Gundersen Clinic, Ltd.

WHERE A LANDSCAPE OF OPPORTUNITIES AWAITS

PHYSICIANS

Gundersen Health System is a physician led, integrated healthcare system employing over 450 physicians. Based in La Crosse, Wis., our mission is to distinguish ourselves through excellence in patient care, education, research and improved health in the communities we serve.

Currently seeking BC/BE physicians in these areas and more:

- Family Medicine
- Emergency Medicine
- Psychiatry
- Neurology
- Dermatology
- Internal Medicine

Gundersen offers generous loan forgiveness, competitive salary, excellent pension, and more. Most importantly, you will find a rewarding practice and an excellent quality of life.

Cathy Mooney (608)775-3637
camooney@gundersenhealth.org
gundersenhealth.org/MedCareers

GUNDERSEN
HEALTH SYSTEM®
La Crosse, Wisconsin

MEDICAL CLINIC SPACE

Historic Cedarburg Location

Washington Avenue

Private Entrance

Common Reception Area

Nine Exam Rooms

Lab Area

Office Consultation Room

Medical Records Storage

Nurse's Station

Competitive Rates

Easy Access

Aurora Medical Center—Grafton

Columbia St. Mary's Hospital—Ozaukee

***Up To Six
Months
Free Rent!***

CEDARBURG SQUARE OFFICE COMPLEX

Contact Ed at 262.377.4170

www.cedarburg-square.com

Index to Advertisers

Cedarburg Square Office Complex	228
Creskide Center	190
Gundersen Health System	227
Murphy Desmond SC	225
Novo Nordisk – Victoza	192
PNC Bank	185
ProAssurance Group	BC
Society Insurance	IFC
Wisconsin Medical Society Education Department	227
Wisconsin Medical Society Insurance and Financial Services	IBC



Advertise in WMJ— Call Kelly Slack, Slack Attack Communications, 5113 Monona Dr, PO Box 6096, Madison, WI 53716; phone 608.222.7630; fax 608.222.0262; e-mail kelly@slackattack.com.

Statement of Ownership

UNITED STATES POSTAL SERVICE® (All Periodicals Publications Except Requester Publications)

1. Publication Title: WMJ

2. Publication Number: 1098-1861

3. Filing Date: October 1, 2013

4. Issue Frequency: Published 6 times per year

5. Number of Issues Published Annually: 6

6. Annual Subscription Price: \$149

7. Complete Mailing Address of Known Office of Publication (Not printer) (Street, city, county, state, and ZIP+4®):
Wisconsin Medical Society, 330 E. Lakeside St.
PO Box 1109, Madison, WI 53701-1109 (Dane County, WI)

Contact Person: Kendi Parvin
Telephone (include area code): (608) 442-3748

8. Complete Mailing Address of Headquarters or General Business Office of Publisher (Not printer):
Wisconsin Medical Society, 330 E. Lakeside St.
PO Box 1109, Madison, WI 53701-1109 (Dane County, WI)

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor (Do not leave blank):
Publisher (Name and complete mailing address):
Rick Abrams, JD, Publisher, Wisconsin Medical Society
330 E. Lakeside St., PO Box 1109, Madison, WI 53701
Editor (Name and complete mailing address):
John J. Frey, MD, Medical Editor, Wisconsin Medical Society
330 E. Lakeside St., PO Box 1109, Madison, WI 53701
Managing Editor (Name and complete mailing address):
Kendi Parvin, Managing Editor, Wisconsin Medical Society
330 E. Lakeside St., PO Box 1109, Madison, WI 53701

10. Owner (Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual owner. If the publication is published by a nonprofit organization, give its name and address.):
Full Name: Wisconsin Medical Society
Complete Mailing Address: 330 E. Lakeside St., PO Box 1109, Madison, WI 53701

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box: ☒ None

Full Name: Complete Mailing Address:

12. Tax Status (For completion by nonprofit organizations authorized to mail at nonprofit rates) (Check one):
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☒ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months (Publisher must submit explanation of change with this statement)

PS Form 3526, September 2007 (Page 1 of 3) (Instructions Page 3) PSN 7530-01-000-9031 PRIVACY NOTICE: See our privacy policy on www.usps.com

13. Publication Title: WMJ

14. Issue Date for Circulation Data Below: October 1, 2013

15. Extent and Nature of Circulation

		Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
a. Total Number of Copies (Net press run)		9,292	8,750
(1)	Mailed Outside-County Paid Subscriptions Stated on PS Form 3541 (Include paid distribution above nominal rate, advertiser's proof copies, and exchange copies)	8,585	7,823
(2)	Mailed In-County Paid Subscriptions Stated on PS Form 3541 (Include paid distribution above nominal rate, advertiser's proof copies, and exchange copies)	121	725
(3)	Paid Distribution Outside the Mails Including Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Paid Distribution Outside USPS®	0	0
(4)	Paid Distribution by Other Classes of Mail Through the USPS (e.g. First-Class Mail®)	0	0
c. Total Paid Distribution (Sum of 15b (1), (2), (3), and (4))		8,706	8,548
(1)	Free or Nominal Rate Outside-County Copies Included on PS Form 3541	0	0
(2)	Free or Nominal Rate In-County Copies Included on PS Form 3541	0	0
(3)	Free or Nominal Rate Copies Mailed at Other Classes Through the USPS (e.g. First-Class Mail)	18	12
(4)	Free or Nominal Rate Distribution Outside the Mail (Carriers or other means)	140	120
e. Total Free or Nominal Rate Distribution (Sum of 15d (1), (2), (3), and (4))		158	132
f. Total Distribution (Sum of 15c and 15e)		8,864	8,680
g. Copies not Distributed (See Instructions to Publishers #4 (page #3))		428	70
h. Total (Sum of 15f and g)		9,292	8,750
i. Percent Paid (FSC divided by 15f times 100)		98.2	98.5

16. Publication of Statement of Ownership
☒ If the publication is a general publication, publication of this statement is required. Will be printed in the October 2013 issue of this publication.
☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner
Kendi Parvin, Managing Editor
Date: October 1, 2013

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties).

PS Form 3526, September 2007 (Page 2 of 3)



*With more than 30 years of
dedicated service, our focus is on the insurance
needs of Wisconsin's medical community.*



Wisconsin Medical Society
Insurance & Financial Services, Inc.

For more information on our products and services contact us at
866.442.3810 or visit www.wisconsinmedicalsociety.org/insurance.

“As physicians, we have so many unknowns coming our way...

One thing I am certain about is my malpractice protection.”

Medicine is feeling the effects of regulatory and legislative changes, increasing risk, and profitability demands—all contributing to an atmosphere of uncertainty and lack of control.

What we do control as physicians:
our choice of a liability partner.

I selected ProAssurance because they stand behind my good medicine and understand my business decisions. In spite of the maelstrom of change, I am protected, respected, and heard.

**I believe in fair treatment—
and I get it.**

Proudly Endorsed by



Wisconsin **Medical** Society
Insurance & Financial Services, Inc.



PROASSURANCE.
Treated Fairly



Professional Liability Insurance & Risk Management Services

ProAssurance Group is rated **A+ (Superior)** by A.M. Best.
ProAssurance.com • 800.282.6242