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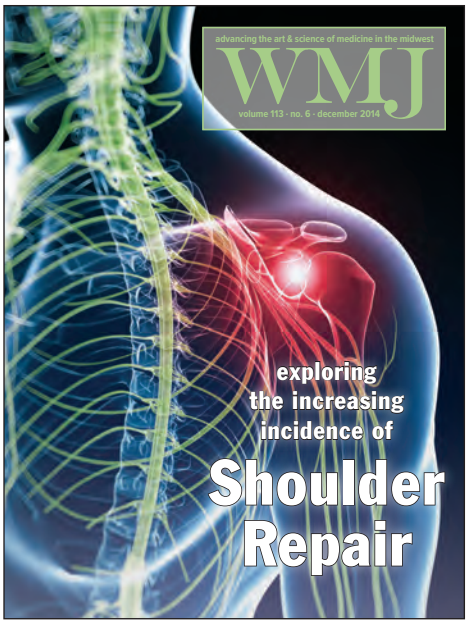

COVER THEME
Exploring the Increasing Incidence of Shoulder Repair

Recent evidence has demonstrated a profound increase in the incidence of shoulder surgery. A study in this issue of *WMJ* reports on that increase and suggests a need for better, more specific testing to evaluate best treatment options for common shoulder conditions.

Cover design by
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WMJ

EDITORIAL

ORIGINAL RESEARCH

CASE REPORTS

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Christmas and the New Year

A.W. Myers, MD, Editor; J.P. McMahon, MD, Managing Editor

Editor's note: The following editorial was originally published in WMJ, *Volume 13, p. 274, December 1914.*

We have been wont to look upon the age in which we are living as rather prosaic and undramatic and not in the least heroic. And yet when the flame of war has enabled us to view the depths of the hearts of our prosaic and undramatic-looking brothers on both sides of the battle line in Europe, we see there on every side as magnificent a heroism as the world has ever beheld.

There never has been a finer courage than has been shown, not by isolated bodies of troops here and there in the field of conflict, but by the armies of all the belligerents in the whole theatre of the war. And this has been shown in the slow, plodding work in the trenches no less than in the more dashing and spectacular phases of the war. Courage is not simply the doing of some brilliant and hazardous feat, it is the quality of mind which makes such an act possible, but it shows itself no less in the steadfast doing of the little duties, the disagreeable commonplaces of war which receive so little mention in the dispatches from the front.

In the practice of medicine we are in a constant state of war against the forces of disease and destruction. And this war is real and earnest, not a mere Fourth of July parade, although the enemy may seem as intangible and elusive as a dream.

About our work there is very little of the "pomp and circumstance of glorious war," most of it is very like that of the soldier in the trenches—plenty of cold and fatigue and watchful nights, with very little gold braid and epaulets.

The practice of medicine can be made as prosaic and commonplace as the raising of turnips, or it can be made the noblest of callings. Its whole character depends on the quality of mind with which we approach it.

It is well for us, therefore, that once a year there comes a season of at least partial detachment from our work, when we can do with advanatage as the Irish drill-sergeant said to his raw recruits: "Step out here and look at yerselves."

At this season we can take stock of ourselves and see in what direction we are traveling. We may well stop to consider whether we are beginning to feel that our patients exist and have illnesses for our benefit, or if we still realize that we exist for their good. We may well review our progress in our work during the year that is closing to see whether or not we are keeping up with the stream of progress. And above all we may well study ourselves to see what is the quality of mind with which we approach our work. Are we trying to see how well we can do our work with the accumulated store of experience which has been handed down to us through the centuries, or are we merely trying to see how much money we can make out of it?

On our answer to this first question depends the decision as to whether we belong on the firing-line or in the sutler's tent.

But if we will open our minds to the spirit of the season there will be no doubt in which group we shall be found, for in spite of the sadness of this Christmas it still brings its message of Peace and Good Will and the New Year still speaks of hope and high resolve.

The Value of Establishing Baselines

John J. Frey, III, MD, Medical Editor

The old saw about not knowing where you are going means that any road will get you there has a corollary—you can't get to a destination unless you know where you are starting. This issue of the *WMJ* includes two articles that help understand the starting point—and trends—for two important Wisconsin-focused clinical issues. The first, from Che and colleagues[1] looks at prescription use by patients statewide, and the second, from Ablove and colleagues,[2] describes the changes in the increased use of a shoulder surgery over a relatively short period of time

We are a pill-using nation, and pressure from society, pharma, and the press tries to identify every social ill from the cold to sleeplessness to erectile dysfunction as a problem that will respond to a pill. Direct-to-consumer advertising, which used to be direct-to-prescriber advertising in medical journals, has increased the likelihood of patients seeking something pharmaceutical for their problems.[3] I remember a patient contacting me about a new drug for obesity that was going to be released by the Food and Drug Administration (FDA) the next day and wondering if he could get a prescription for it. Patients often more closely follow the FDA than clinicians do.

We can't begin to change our prescribing behaviors until we understand the starting point—the baseline—for our practices. Electronic health records should help understand what we do in practice, but health systems rarely report prescribing patterns except when they are a problem—such as narcotic use—and the individual variability in a group is often surprising when we do look at reports. A few years ago, a resident at our clinic brought some studies that showed both the cost and positive effects of chlorthalidone should make it the diuretic of choice for hypertension. Most in our practice changed but then changed again after the third or fourth report of a patient with life-threatening hypokalemia as a result. We either had to add another medication or change to another diuretic. None of the other clinics were using chlorthalidone, and it was not clear to me why we had decided to use it. Regular reports of prescribing profiles would be the source of lots of interesting discussions in group practices.

I remember a patient contacting me about a new drug for obesity that was going to be released by the Food and Drug Administration (FDA) the next day and wondering if he could get a prescription for it. Patients often more closely follow the FDA than clinicians do.

So, findings from Che and colleagues are worth reading and talking about. Common medications for cardiovascular, endocrinologic, and respiratory problems—all chronic illnesses—lead the list and, fortunately, the entire list of most-prescribed medications from their study come as generics. They also did not find oxycodone in their top medications, which is surprising, given that chronic pain is becoming one of the more controversial and exasperating problems encountered in primary care. Any list of prescriptions has narcotics in the top 5 most prescribed. But the authors' explanation is enlightening: there are more prescriptions written for narcotics but for a small number of patients from the general population. The database for Che and colleagues is a representative statewide sample of patients, rather than a list from a practice. Their study emphasizes the value of looking at total populations as a starting point, rather than simply our own practices. Their study shows things that should not come as a surprise: that we take more pills as we age, that women take more pills than men, and smokers need more medication than nonsmokers. But their data also show that education, race, and family income are correlated with increased medication use. Social deter-

minants (see the article in this issue by Swain and colleagues[4]) have an effect on health—and one of those effects is on the number and cost of medications to treat problems.

Ablove and colleagues describe the increase in shoulder repair for superior labrum anterior and posterior (SLAP) injuries. A statewide database showed that the number of surgeries for SLAP repairs almost doubled in 8 years. The authors raise a number of concerns about the potential for over-diagnosis of the problem and concerns about the frequency or desirability of surgical repair. While the prevalence of bionic people is increasing and many poorly functioning older adults now walk better on new hips and knees, surgery has obvious risks and the important question is whether the long-term benefits outweigh those risks. It might if you are a major league pitcher with a shoulder injury, but might not if you are a 70-year-old whose golf swing is more restricted than you would like. Rigorous guidelines for both diagnosis and surgical vs nonsurgical treatment of SLAP injuries must be established and followed if we are to achieve the best results for patients. We know, in 2010, where the baseline was. Where should it be in another decade?

Autism in all its forms and variations has become a diagnosis that has been increasing in frequency throughout the country.[5] What was formerly not seen or not recognized is now a common part of the care of a general population. Instead of being a two-box disease—either you have it or you don't—it is a spectrum disorder, which helps clinicians think about the diagnosis more broadly. The use of screening tools for detecting autism spectrum disorders by clinicians who care for children has doubled over the period studied by Keil and her associates.[6] Clinicians who use the screening tools also have established a reliable network of referrals to consultants and to community-based programs, like the Birth to Three Program for at-risk children. It is a reassuring study that demonstrates that giving clinicians the appropriate screening tools results in their using them.

Whenever editors raise the issue of the value of a case report, we find out that they are among the most-used articles in journals, since one of their contributions is to include a mini-review of a subject. As such, whenever we have a group of case reports as we do in this issue, two on atypical presentations or associations and one on an atypical treatment, we find they will be used a great deal over time.[7-9] One of my early teachers said that the most difficult problem I would face would be distinguishing the uncommon from the common cold. Well written case reports, at times, help us make that distinction.

Finally, as 2014 comes to a close, I'd like to extend thanks—on behalf of the *WMJ* Editorial Board and staff—to everyone who reviewed manuscripts for the journal this year. In addition to being an important collegial act, manuscript review is essential to the integrity of *WMJ*. A complete list of reviewers is on p. 213, as well as information about getting involved. If you have served as a reviewer, thank you. If you haven't, please consider doing so in 2015.

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Health Care Professionals: Opportunities to Address Social Determinants of Health

Geoffrey R. Swain, MD, MPH; Katarina M. Grande, MPH; Carlyn M. Hood, MPA, MPH; Paula Tran Inzeo, MPH

Nearly all of the health-related investments in the United States are focused on health care. While access to and quality of health care is important, health is influenced far more strongly by social and economic factors such as employment, income, and education. These factors drive not only health outcomes, but also the significant health inequities experienced by many of our communities. Therefore, it is essential that professionals dedicated to improving health increase their effectiveness by addressing the "upstream" causes of health in the community and by engaging in ways to change the broad policies, systems, and environments that shape the social and economic conditions that, in turn, so strongly influence health.

The World Health Organization (WHO) has broadly defined the social determinants of health as "the conditions in which people are born, grow, live, work, and age."[1] They include an individual's socioeconomic status (SES)—including income, employment, and education—as well as multiple other factors such as social cohesion, social support, community safety, affordable housing, and food security.

Research shows strong and consistent associations between these socioeconomic factors and health outcomes.[2,3] The Milwaukee Health Report illustrates this pattern well, showing a consistent gradient on nearly every health measure, with higher education and income strongly associated with better health outcomes.[4] Further, communities with greater differences between the highest and the lowest incomes not only experience poorer health down the income gradient, but also overall poorer health than communities with incomes more equally distributed.[5]

These relationships are documented not only in research data; there are solid, plausible mechanisms proposed for why socioeconomic factors drive health outcomes.[6] In short, social determinants (a) affect people's access to health care, (b) support or constrain people's ability to practice healthy behaviors, and (c) directly affect people's physiology through chronic elevations of stress hormones, epigenetic changes, and other biologic mechanisms across the life course that can have lasting impacts across generations.[7]

The effects of socioeconomic factors on health are surprisingly strong. The County Health Rankings model (Figure), developed at the University of Wisconsin Population Health Institute (UWPHI), indicates that only 20% of the modifiable factors that influence health relate to access to quality health care, while 40% of the factors that influence health are social and economic.

While the influence of social determinants of health in driving health outcomes is clear, actions to address social determinants—particularly by physicians, other health professionals, and health care systems—have been less well explored. How can professionals dedicated to improving health continue our traditional roles of promoting healthy behaviors and delivering quality health care and also balance our repertoire by adding the skills, competencies, tools, and methods to address the socioeconomic policies, systems, and environments that so strongly influence health?

Here we discuss 2 concrete and well-studied examples of social determinants of health: income/employment and education. We then describe evidence-based examples of clinical and policy-level practices to address these determinants.[8] Finally, we offer suggestions and resources for specific actions readers can take to address not only these specific determinants, but also any of the many other social and economic factors that drive health outcomes.

DETERMINANT: INCOME/ EMPLOYMENT

There is a clear relationship between health and employment/income: people in high-income groups can live up to 6 years longer than their low-income counterparts.[2] Not only are high-income individuals more likely to have insurance and access to medical care, but they also have better access to nutritious food, more oppor-

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tunities to be physically active, and increased ability to live in safe homes and neighborhoods.[9] For most people, income is driven by employment, yet employment opportunities vary widely among communities. For example, the rate of employment for the white population of Milwaukee is 77.4%, while the rate of employment for Milwaukee's African Americans is only 44.7%.[10] Increasing employment rates and income levels typically requires systemic policy changes, and although income- and employment-based policies often do not have health improvement as a primary goal, research has shown that many such social policies play a key role in improving health outcomes.[5]

Existing antipoverty programs such as Social Security have already reduced poverty by about 80% among seniors.[11] But with poverty rates in Wisconsin hovering in the low double digits overall, and closer to 25% in some urban areas (including a child poverty rate of over 40% in Milwaukee),[12] more policy interventions are needed.

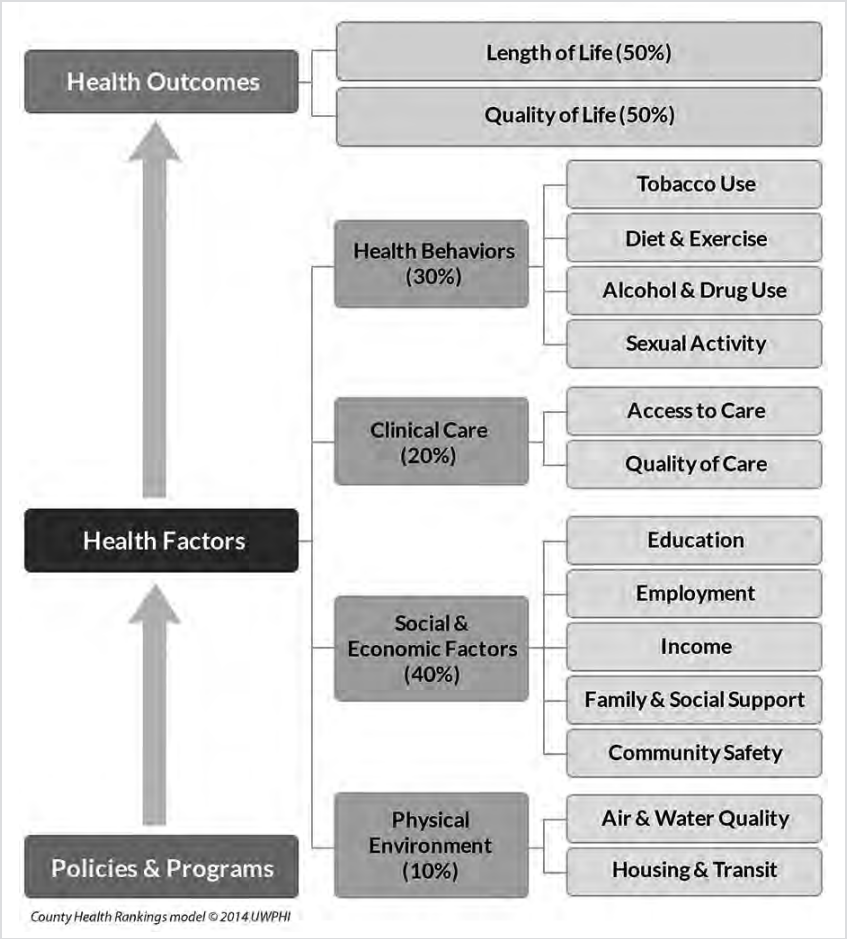
Policy Case Example

Addressing income and employment to greatly reduce poverty

A rigorous analysis by the Urban Institute and Milwaukee's Community Advocates Public Policy Institute has shown that a 4-component policy package would reduce poverty in Wisconsin by more than 50% for all age groups and all racial and ethnic groups.[8] This policy package includes: (1) expanding transitional jobs programs, (2) increasing the minimum wage and indexing it for inflation, (3) expanding the Earned Income Tax Credit (EITC) so that all low-income workers—regardless of marital status or number of children—would qualify, and (4) providing a tax credit for adults who cannot work and who receive disability income or Social Security income.

The components of this policy package have proven health benefits as well. In the case of EITC, an increase of $1000 in the tax credit income is associated with a 6.7% to 10.8% reduction in low birth weight rates for single mothers with less than a high school diploma, and an even larger impact for births to African American mothers.[13] In the case of transitional jobs (TJs), a Health Impact Assessment (HIA) conducted by UW–Madison's Population Health Institute found a host of positive health impacts of relating to expanding TJs.[14] In fact, the study found that the absence of such programs increases poor health outcomes, and that many of employment's positive effects on stress, children's physical and mental health, and family cohesion are undermined or even reversed when employment is unstable (and income inadequate). Another HIA on minimum wage policy conducted at the University of California Los Angeles (UCLA) showed that improvements in minimum wage policy could reduce mortality on the order of 1.4 deaths per 10,000 workers per year over the long term.[15]

Figure. The County Health Rankings Model



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DETERMINANT: EDUCATION

Education and poverty are closely linked—as one's educational background improves, typically so do opportunities for higher incomes, better employment opportunities, and improved living conditions.[16] As with income/employment, educational outcomes can vary widely among communities. For example, Wisconsin's 4-year graduation rate (87.5% in 2011-2012)[15] is among the best in the nation. In Milwaukee, however, the graduation rate is 61.1%; among Milwaukee students who are economically disadvantaged, graduation rates are even lower.[17] As with income, there are many policy levers by which to improve educational outcomes (and thereby improve health);[6] we will highlight only 1 example here.

Policy Case Example

Early Childhood Education Programs

WHO's Commission on Social Determinants of Health has identified early childhood education as a priority area, urging governments

Box. Examples of Social Determinants-focused Individual and Population Level Strategies

Clinical Level

Screen for socioeconomic issues in clinical interactions.
Screening for access to basic needs (food, employment, benefits, education) increases physician referrals and family contact with community resources. Screening tools such as the mnemonic IHELLP for Income, Housing Education, Legal Status, Literacy, and Personal Safety (Table) are intended to facilitate care by connecting a patient's biomedical situation to the context of his or her life.[30]

If no one on the health care team asks and providers remain ignorant of patients' social and economic realities, factors like prescription unaffordability and poor neighborhood composition will continue to adversely influence health. Conversely, screening for patient's socioeconomic issues could broadly augment clinical care over a number of clinical visits or could be leveraged in a focused way should an area be identified as a significant contributor to poor health,[31] such as altering traditional clinical prescribing practices to better fit within a patient's life conditions or providing more coordinated services overall.

Coordinate services for individual patients by partnering with social workers, health advocates, community health workers, and similar professionals.
One California-based organization, Health Leads, leverages college students to connect patients with the basic resources they need to be healthy. Information from socioeconomic screening questions results in more effective prescriptions for food, heat, and aptly targeted diet and exercise-related interventions. Through this model, students act as navigators to expand clinics' capacity to address basic resource needs often at the root of poor health and implement a net of social support within health-care settings.[32]

Population Level

Advocate for pro-health social and economic policies.
Due to their position and influence in society, health care professionals in general and physicians in particular can use their expertise, access to evidence, and credibility to help decision-makers better understand the health impact of policies far beyond those focused on clinical care quality or access. With their power, physicians can advocate for pro-health social policies such as income maintenance policies (eg, unemployment and disability insurance), education policies (eg, Head Start, universal pre-K), employment policies (eg, transitional jobs), compensation policies (eg, minimum wage/living wage), and tax policies (eg, Earned Income Tax Credit).

In addition to developing relationships with and educating policy-makers directly (eg, participating in Doctor Day at the Wisconsin Capitol), physicians can exert their influence through media appearances (eg, television interviews, radio show call-ins, and writing op-eds and letters to the editor), by becoming involved in local policy leadership (eg, school board, board of health, city council, county board), by supporting educational and workplace initiatives, and by working in other venues to change public attitudes on various issues. Physicians and other health care professionals also can provide significant support to community efforts—via partnering with community and faith-based organizations with overlapping interests, education sector leaders, business leaders, and public health and safety officials—because of the content expertise as well as the credibility and standing in society that they bring to the table.

Work collectively with peers.
Clinicians can and should advocate within their group practice/hospital/HMO for a community/population health perspective emphasizing the importance of addressing the social determinants of health. As group practices and hospitals are increasingly held accountable for community health outcomes, effective interventions addressing "upstream" socioeconomic factors are crucial for success.

Work collectively with professional associations.
The more medical and other health professional groups become involved in addressing social determinants of health, the higher the impact on policy change and eventual improvement in health outcomes. The American Academy of Pediatrics (AAP), for example, has put poverty high on its advocacy agenda for 2013-2014, and has convened a workgroup to review current opportunities related to expanding access to basic needs such as food, housing and transportation, and promoting positive early brain and child development and school readiness and success.[33]

Be both patient and persistent.
Physicians and other health care professionals should view policy change as incremental and occurring at various windows of opportunity, not under any 1 political environment. Health care providers can help open these windows of opportunity by building policy and advocacy capacity within their organizations, creating and elevating the evidence-base for social policy, and educating their own organizations, policy-makers, and the public on these issues.

to invest in it.[14] Similarly, Wisconsin's State Health Plan—Healthiest Wisconsin 2020 (HW2020)—cites strong and consistent evidence for early childhood education's positive influence on health over the life course.[2] Children who attend high-quality early learning programs see gains later in life including improved graduation rates and earnings, as well as decreased rates of crime and teen pregnancy.[18] Additionally, randomized controlled preschool intervention trials have shown that early childhood education is associated with improved adult health status, lower behavioral risk factors, and lower criminal activity,[19,20] and that these early childhood programs are cost-effective.[21] The quality of these programs can be improved through interventions such as smaller teacher-child ratios, increasing the number of teachers with 4-year college degrees in early childhood education, increasing home visits with families, and more monitoring by government or accrediting agencies.[22] Expanding the reach and quality of early childhood education programs such as Head Start and Early Head Start, therefore, is a social determinants-based policy approach with potential for great impact on health outcomes.[23]

IMPLICATIONS FOR PRACTICE

Today, 4 in 5 physicians believe that unmet social needs are leading to worse health among Americans, yet the same percentage also feel unable to address health concerns caused by the unmet social needs of their patients.[24] The Affordable Care Act's new payment structures encourage physicians, hospitals and other health care professionals to form networks known as Accountable Care Organizations (ACOs) to increase the coordination and quality of care.[25] ACOs currently are thought of as focusing on individual-level quality care that matters (eg, improvement in health measures among clinical populations such as average hemoglobin A1c among all diabetics in a health care system). However, health care systems will see improved patient outcomes, and thus improved reimbursement, if they also become involved in addressing the upstream social determinants of health in the

communities where their patients live, work, and play.

Medical school curricula are beginning to emphasize the role of physicians as population health and social determinants policy advocates.[26] At least 9 medical schools now integrate population and community health coursework with traditional clinical science curricula.[27] Some also include the importance of advocacy and policy work for medical professionals. Both Wisconsin medical schools are innovating in this area; the University of Wisconsin School of Medicine and Public Health incorporates policy advocacy in its innovative Integrative Case Series for medical students in their first 2 years,[28] and the Medical College of Wisconsin features an Urban and Community Health Pathway whose core sessions include a focus on social determinants.[29]

In practice, physicians and other health care professionals can address the social determinants of health at both the individual and population levels. See Box for examples.

On the individual patient-care level, clinicians can implement broader and deeper screening for social determinants (Table). Elevating the importance of gathering information on a patient's socioeconomic context to that of conducting his or her physical examination or developing an evidence-based treatment plan will increase the effectiveness of individual level patient care. Clinicians also can partner with allied health professionals and community partners to address patients' socioeconomic needs.

On the continuum between the individual and population levels, physicians also can provide support to local community-based organizations whose mission focuses on addressing the social and economic needs of community members. Such physician support could range from providing volunteer clinical services (eg, sports physicals at Boys and Girls Clubs or YMCAs/YWCAs) to serving on the advisory boards of advocacy or social service organizations.

Physicians also might consider working with community coalitions. Coalitions are comprised of many partners such as community-based organizations, government agencies, and private sector partners who are collaborating on a common goal. Physician perspectives can bring added depth to coalition strategies, and such engagement can provide a platform for policy and systems change.

On the population level, health care professionals should advocate for pro-health socioeconomic policies, work collectively with peers and professional organizations, and be both patient and persistent in working to bring about policy change (Box).

To be effective change agents, physicians don't need to become policy experts on income/employment, education, or any other social determinants-related policy. What physicians and other health care professionals bring to the table is unparalleled credibility and expertise in the area of health. Thus, when physicians and their colleagues bring their health-related voices to the table, it strengthens the arguments of advocates who are already experts in policy fields related to the social determinants of health.

It would, of course, be extremely helpful for health professionals to partner with policy advocates. It would also be ideal for each group practice or hospital system to designate a specific person whose job is to advocate for pro-health social and economic policies.

In any case, clinicians' participation in the policy advocacy process makes such changes far more likely to succeed—all for the ultimate benefit of patients, communities, and population health.

Table. The "IHELLP" Mnemonic

Examples of Potential Social History Questions (Using the "IHELLP" Mnemonic) to Address Basic Needs

Domain/Area	Examples of Questions
	Income
General	Do you ever have trouble making ends meet?
Food income	Do you ever have a time when you don't have enough food?
	Do you have WIC?[a]
	Do you have food stamps?
	Housing
Housing	Is your housing ever a problem for you?
Utilities	Do you ever have trouble paying your electric / heat / telephone bill?
	Education
Appropriate education placement	How is your child doing in school?
	Is he/she getting the help to learn what he/she needs?
Early childhood program	Is your child in Head Start, preschool, or other early childhood enrichment?
	Legal Status
Immigration	Do you have questions about your immigration status?
	Do you need help accessing benefits or services for your family?
	Literacy
Child literacy	Do you read to your child every night?
Parent literacy	How happy are you with how you read?
	Personal Safety
Domestic violence	Have you ever taken out a restraining order?
	Do you feel safe in your relationship?
General safety	Do you feel safe in your home?
	Is your neighborhood safe?

[a]WIC includes Supplemental Nutrition Assistance Program (SNAP) for Women, Infants, and Children.
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CONCLUSION

The role of physicians and other health care professionals in both individual care provision and individual behavior change is crucial. However, social determinants of health make up a stronger percentage of the modifiable

drivers of health outcomes than either health care or health behaviors.

To be most effective at improving the health of families and communities and to ensure the greatest impact for investment of resources, health professionals need to expand their repertoire of skills and activities both with their individual patients and in the policy arena.

Medical education training programs focusing on physicians' clinical and policy-level responsibilities for addressing social determinants are emerging.[31,34] But currently-practicing physicians and other health professionals must also work both individually and collectively to address social determinants within their practices, their communities, their states, and beyond.

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The Incidence and Demographics of Shoulder Repair in Wisconsin, 2002-2010

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ABSTRACT

Importance: Recent evidence has demonstrated a profound increase in the incidence of shoulder surgery. Superior labral anterior and posterior (SLAP) repair is a common procedure that has been noted in other studies to be increasing.

Objective: The purpose of this study is to report the incidence and demographics of a single shoulder surgery code in the state of Wisconsin in order to evaluate whether it is being performed in increasing numbers relative to population.

Methods: In a retrospective review of the Wisconsin Hospital Association statewide database for the years 2002-2010, we queried one ICD-9 procedure code: 81.83, other repair of shoulder (not replacement or repair of recurrent dislocation). This code was selected because it would include SLAP repair and exclude most other common shoulder surgeries. The data retrieved includes ICD-9 diagnosis codes, county of surgery, patient age, and gender.

Results: The number of surgeries performed in Wisconsin over the course of the study increased by 91.4% between 2002 and 2010, starting at 5649 in 2002 and rising to 10,812 by 2010. The incidence of surgeries increased 83.1% over this time period: from 103.8 per 100,000 in 2002 to 190.1 per 100,000 in 2010. The ratio of male to female surgeries remained nearly constant at 3:2 throughout the length of the study. The mean patient age at time of surgery increased 2.6 years, from 48.3 in 2002 to 50.9 in 2010.

Conclusions: The increase in number of shoulder surgeries is well beyond expectations based on population growth. The relatively high percentage of females does not correspond with reported gender ratios in other studies of similar shoulder procedures. The high mean age of patients and the large number of surgeries in older patients also is concerning. More educational effort needs to be given regarding the diagnosis and treatment of common shoulder conditions.

INTRODUCTION

Several studies have demonstrated an increase in the frequency of common shoulder surgical procedures.[1-3] Superior labrum anterior and posterior (SLAP) repair is a prominent example.[2,3]

SLAP tears involve an injury to the glenoid labrum. The glenoid labrum is a ring of fibrous and fibrocartilaginous tissue that encircles the glenoid cavity. Since the head of the humerus and the glenoid cavity differ in size, the labrum serves to increase the area of articulation and deepen the glenoid fossa, both of which increase joint stability. The labrum is also the site of attachment of the tendon of the long head of the biceps brachii muscle and the glenohumeral ligaments.[4] In 1985, Andrews et al described lesions of the glenoid labrum, mostly in the anterosuperior portion, identified in a group of throwing athletes.[5] In 1990, Synder et al introduced the term SLAP for lesions involving the superior portion of the glenoid labrum, which cause shoulder pain and instability.[6] The mechanism of injury is either axial loading or axial distraction of the arm causing labral tearing.

The reported incidence of SLAP lesions in shoulder arthroscopies has varied in different reports, ranging from 1.2% to 11.8%.[7-9] One possible explanation for this variation is controversy over what constitutes a SLAP tear.[10,11] Many variants occur in normal labral anatomy[4,12,13] and SLAP tears can be difficult to diagnose, even arthroscopically. No reliable diagnostic physical examinations are considered sufficient for diagnosis, and magnetic resonance imaging (MRI) techniques are able to identify only certain types of labral tears or associated pathology.[14]

Treatment is controversial. While most surgeons are able to come to agreement over treatment options for patients with both SLAP lesions and biceps pathology, appropriate treatment of other types of lesions without obvious biceps pathology or degenerative labral changes is not clear.[14] When the long head of the biceps is pathologic, SLAP tears can be addressed by either transfixing the biceps tendon in place (tenodesis) or transection (tenotomy). Due to these factors, it appears that SLAP tears often are overdiagnosed and fixed unnecessarily. Most reported SLAP repairs

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occur in younger predominantly male patients. Arthroscopic SLAP repairs seem to be increasingly common, which is concerning given the above factors and uncertainty regarding appropriate indications for and benefits of the surgery.

The purpose of this study is to analyze the incidence and demographics of this code in the state of Wisconsin in order to evaluate whether the incidence is increasing relative to state population.

METHODS

This study was carried out using information from the Wisconsin Hospital Association (WHA) statewide database for the years 2002-2010. WHA collects both inpatient and outpatient data from all surgical centers in the state of Wisconsin. The data includes International Classification of Diseases revision 9 (ICD-9) procedure and diagnosis code, county of surgery, and patient age and gender. Because it is a public database and the data is de-identified, the study is exempt from review by the institutional review board.

We identified one ICD-9 procedure code: 81.83, other repair of shoulder (not replacement or repair of recurrent dislocation). This code was selected because it would include superior labrum anterior and SLAP repair—a common procedure that has been noted in other studies to be increasing—but excludes most other common shoulder procedures, including repair of dislocation, arthroplasty, rotator cuff repair, labral repair for dislocation, acromioplasty, biopsy, and synovectomy, as well as biceps tenotomy and tenodesis. Inclusion criteria for the study included any patient who had this code submitted as a principal or secondary procedure. Patients were limited to facilities in the state of Wisconsin, excluding VA hospitals. Within each year's data set, the numbers of male and female surgeries and patient age were noted.

The population information for the state of Wisconsin during the 2002-2010 period was taken from the US Census Bureau. Statistics were reported on procedure volumes, incidence rates, and demographic variables. Pearson correlation coefficient squared (R-squared values) were determined between selected variables (rate, age, gender, and diagnosis code) and time. A value of 1.0 means that 100% of the variability in the given variable can be explained by time. *P*-values were determined for the association between each value and time.

RESULTS

The number of procedures performed each year in the state of Wisconsin increased by 91.4% (*P*-value <0.001) between 2002 and 2010, starting at 5649 in 2002 and rising to 10,812 by 2010. On the basis of the population of the state of Wisconsin, the incidence of procedures increased 83.1% (*P*-value <0.001) over this time period: from 103.8 per 100,000 in 2002 to 190.1 per 100,000 in 2010 (Figure 1).

The ratio of male to female surgeries remained nearly constant at 3:2 throughout the length of the study (*P*-value 0.491) (Figure 2). The mean patient age at time of procedure increased 2.6 years (5.4%) (*P*-value <0.001), from 48.3 in 2002 to 50.9 in 2010 (Figure 3). This difference was not statistically significant (Figure 4).

An audit of our own institution demonstrated high correlation between current procedural terminology (CPT) codes for SLAP repair and this ICD-9 procedure code.

DISCUSSION

The purpose of this study is to evaluate the incidence and demographics of shoulder surgery in Wisconsin from 2002 through 2010. We postulated the rate was increasing. We sought to gather more data regarding the patients receiving shoulder surgery in order to determine how the gender ratio and age of patients compared to other studies.

The incidence of this surgery almost doubled during the course of the study. The male to female ratio was initially 3:2 and remained fairly consistent. The mean patient age increased from 48.3 to 50.9. The female patients were slightly older than male patients.

The ICD-9 procedure code 81.83 is designated for other repair of shoulder, not including arthroplasty, repair of dislocation, biceps tenodesis, and biceps tenotomy and should include all SLAP repairs and exclude most other common shoulder procedures. There has been very little change in the observed incidence of SLAP lesions, and the reported rate of SLAP surgeries as a percentage of overall surgeries has remained fairly low. Snyder et al reported rates of SLAP lesions of 6% of symptomatic shoulders noted at the time of arthroscopy.[8] Weber et al reported on the incidence rates, complications, and outcomes in orthopedic Part II board candidates.[3] In a 6-month surgical reporting period, Part II board candidates (orthopedic surgeons who have passed the Part I written board certification examination and sit for a practice-based oral examination) noted that SLAP repairs represented 9.4% of all reported shoulder surgeries. Of the SLAP repairs reported by Part II candidates, 78.4% were in males and 21.6% were in females with average ages of 36.4 for males and 40.9 for females.[3]

The results of this study are worrisome. The number of shoulder repairs relative to population was very high at the beginning of the study and nearly doubled by the end. The high percentage of females does not correspond with gender ratios in any other similar shoulder studies.[3,6,8,15] The average ages of both men and women were much higher than any other report.[2,3,6,8,15-17] Even if every case reported under this code was not a SLAP repair, there is no evidence supporting the numerical growth of any type of shoulder surgical repair over the course of this study. SLAP repair is not benign and carries a risk for complications, including stiff-

Figure 1. Number of Surgeries per 100,000 Patients

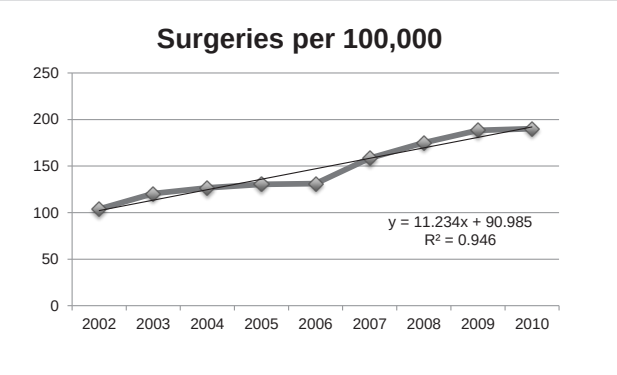


Figure 2. Male to Female Ratio (y-axis) vs Year (x-axis)

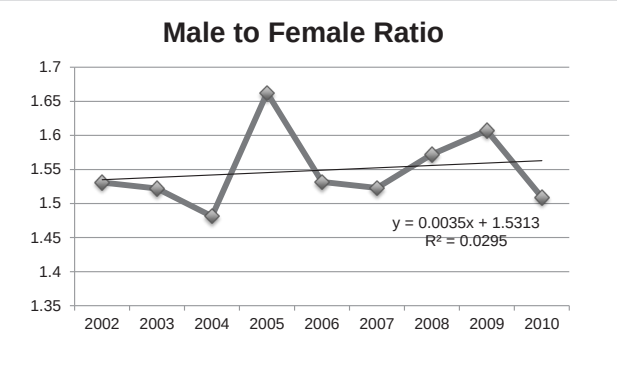


Figure 3. Patient Age (y-axis) vs Year (x-axis)

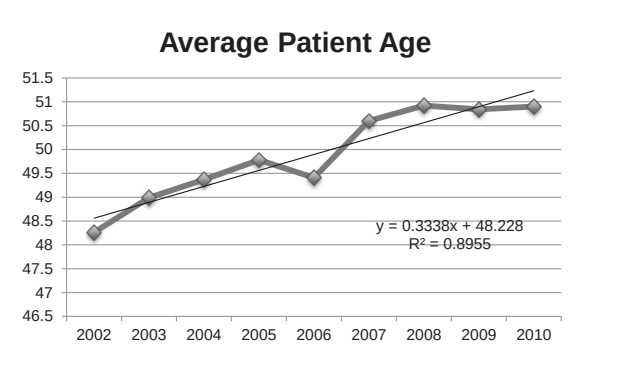
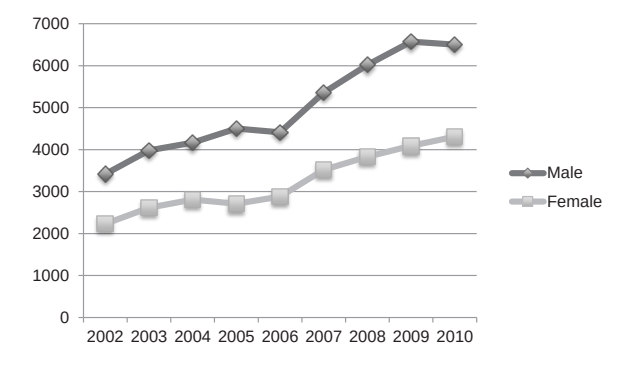


Figure 4. Number of Procedures (y-axis) vs Year (x-axis)



ness, rotator cuff tears next to arthroscopic portals, and articular cartilage damage.[3]

An obvious limitation of this study is the use of ICD-9 procedure codes, which are less specific than CPT codes, and the lack of more specific patient information. We are unable to report clinical outcomes or complication rates. We do not know how accurate the codes were and to what extent possible miscoding affected the results. Unfortunately, the only reason the information was available was due to the lack of specific patient identifiers. However, prior studies have demonstrated fairly high accuracy for coding of primary diagnosis and procedures using ICD-9 procedure codes.[18,19]

This data reinforces and emphasizes the findings of Weber et al. It is likely that SLAP tears are over-diagnosed and almost certain that too many SLAP repairs are being performed, particularly in older patients and, potentially in this study, in women. MRI findings of SLAP pathology should be viewed with circumspection and need to be correlated with clinical findings. There is still a need for better, more specific physical tests to confirm symptomatic SLAP pathology and treatment needs to reflect the age and needs of the patient. It also illustrates the need to evaluate the incidence of other common shoulder procedures. Educational efforts in both residency and fellowship need to be directed towards understanding indications for this and other procedures.

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Promoting Routine Use of Developmental and Autism-Specific Screening Tools by Pediatric Primary Care Clinicians

Arianna Keil, MD; Christine Breunig, MS; Sharon Fleischfresser, MD, MPH; Elizabeth Oftedahl, MPH

ABSTRACT

Introduction: In 2006, the American Academy of Pediatrics published a policy statement recommending routine developmental screening for all children. Most clinicians at that time were using informal methods to monitor child development.

Methods: Outreach to Wisconsin primary care clinicians designed to promote use of validated developmental screening tools began in 2006. A survey of 157 Wisconsin primary care clinicians was conducted in late 2012 to assess routine use of developmental and autism-specific tools.

Results: As compared with a similar survey conducted in 2007, where only 25% of clinicians reported use of a validated developmental screening tool, over 55% of clinicians in this survey reported routine use of validated developmental and autism-specific screening tools within well-child care.

Conclusion: Outreach to clinicians and their care teams, in conjunction with policy statements from national professional organizations and supporting evidence, can contribute to quality improvement in well-child care delivery.

INTRODUCTION

The American Academy of Pediatrics (AAP) published a policy statement on developmental screening and surveillance in July 2006.[1] In this statement, AAP recommends that all children receive screening of their development with a formal, validated tool at 9 months, 18 months, and 24 or 30 months of age. In addition, AAP recommends children receive screening with a validated tool any time developmental surveillance elicits concerns.

In 2007, AAP published a policy statement on screening for autism spectrum disorders.[2] Similar to the policy statement on developmental screening, AAP recommends universal screening for autism spectrum disorders. It is recommended that all children receive screening with a validated, autism-specific instrument at 18 months and 24 months. Early identification of delays that result in timely access to high-quality, developmentally appropriate services assists children in achieving their full developmental potential.[3,4,5]

At the time the AAP policy statements were released, most pediatric primary care clinicians in Wisconsin and across the country were not using validated tools to monitor children's development.[6] A survey conducted in 2007 of 173 Wisconsin pediatricians and family physicians found that nearly 74% never used a validated developmental screening tool as part of well-child care delivery.[7] Clinicians commonly used non-validated checklists, often composed of individual items from the Denver II Developmental Screening Test (Denver Developmental Materials, Inc, Denver, Colorado).

Integrating routine developmental screening for all children within a practice setting is a significant undertaking. As with many other quality improvement efforts, those clinics taking an office-systems approach to screening are more successful at implementing screening and sustaining it over time.[8] In addition, an academic detailing model of educational outreach to clinicians conducted at their site has been shown to be an effective way to promote both understanding and behavior change on a variety of topics, including developmental screening.[9]

Outreach to Wisconsin primary care clinicians designed to promote routine use of validated developmental and autism-specific screening tools began in the fall of 2006 and continues currently. Over the past 7 years, funding for this outreach has come from several publicly funded grants. This survey was conducted to determine if rates of routine use of developmental and

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Table 1. Respondent Demographics

Distribution of survey respondents by professional role (n = 155)	
	Respondent number
Family physicians	83 (53.5%)
Pediatricians	63 (40.6%)
Other primary care clinicians	9 (5.9%)
Distribution of survey respondents by length of time in practice (n = 156)	
0-5 years	30 (19.2%)
6-10 years	24 (15.4%)
11-15 years	25 (16.0%)
16+ years	77 (49.4%)
Distribution of survey respondents by practice location (n = 140)	
Northern region	15 (10.7%)
Northeast region	24 (17.1%)
Southern region	54 (38.6%)
Southeast region	32 (22.9%)
Western region	15 (10.7%)

autism-specific screening tools had changed following outreach to clinicians.

METHODS

From September 2006 to February 2013, primary care clinicians and care team members from 138 primary care clinics across Wisconsin participated in voluntary trainings designed to promote routine use of validated developmental and autism-specific screening tools within well-child care. Training availability was promoted through the Wisconsin Academy of Family Physicians (WAFP), the Wisconsin Chapter of the AAP, and informally by word of mouth. Clinics contacted project staff to arrange a training at their site. Prior to each training, clinicians were asked to complete a brief 10-question pre-assessment describing their current use of developmental and autism-specific screening tools, as well as their awareness of community resources for children with concerning screening results. A similar postassessment was conducted 9 to 12 months following the training. The results of those assessments are not discussed in this article.

The 60- to 90-minute training was delivered onsite at clinics, at a time convenient for clinicians and care team members, generally before clinic hours or over the lunch hour. Clinicians and care team members (such as nurses, medical assistants, and receptionists) were encouraged to attend, so that all team members understood the importance of screening and their role in the process.

The presentation outlined AAP recommendations for developmental and autism-specific screening, as well as literature supporting routine use of validated tools to refine risk of delay. Information was shared on the Ages and Stages Questionnaire, 3rd Edition (ASQ-3 or ASQ),[10] a validated, parent-completed developmental screening instrument, as well as the Modified Checklist for Autism in Toddlers (M-CHAT).[11] These instruments were selected for their solid psychometric properties, parent-completed nature, suitability for use in primary care settings, and use by other community partners serving children with delays. Each participating clinic received a set of ASQ-3 questionnaires and a user's guide, along with copies of the M-CHAT.

Trainings were performed in collaboration with local professionals serving children with delays and their families. Professionals from Wisconsin's Regional Centers for Children and Youth With Special Health Care Needs, along with Wisconsin's Part C Early Intervention Program, shared information on their programs. Wisconsin's Regional Centers are funded through the Wisconsin Department of Health Services Title V Children and Youth with Special Health Care Needs Program. Wisconsin's Part C Early Intervention Program (known as the Wisconsin Birth to 3 Program) is funded through the Wisconsin Department of Health Services.

In 2012, a survey was developed for Wisconsin primary care clinicians to assess rates of routine use of developmental and autism-specific screening tools within well-child care. The 11-question electronic survey was sent to over 300 clinicians who had participated in developmental screening trainings, as well as members of the WAFP via program listservs in November 2012. In early December 2012, the same survey was sent to the Wisconsin Chapter of AAP members through its listserv. The survey was closed December 30, 2012.

RESULTS

Survey Respondent Demographics.

One hundred fifty-seven clinicians completed some or all of the survey. The number of clinicians completing each item varied; percentages were calculated using the total number of respondents for each individual question. Eighty-three (53.5%) respondents were family physicians and 63 (40.6%) were pediatricians; the remaining respondents were nurse practitioners or physician assistants (Table 1). Seventy-seven respondents (49.4%) had been practicing for 16 or more years, 30 respondents had been practicing for less than or equal to 5 years, 25 for 11 to 15 years, and 24 for 6 to 10 years. The vast majority provided primary care to pediatric patients (n = 143 respondents, 91.7%), and only 4 respondents had fellowship training in developmental pediatrics or neurology.

The greatest number of respondents practiced in a non-university hospital or clinic practice (n = 27 respondents, 21.4%), followed by a group or health maintenance organization (HMO) practice with either 3 to 5 clinicians or 6 to 10 clinicians (both 24 respondents), a group or HMO practice with 11 or more clinicians (20 respondents), and a university hospital or clinic practice (18 respondents). Fewer respondents practiced in a community health center (9 respondents) or a solo or 2-clinician practice (4 respondents). Over 60% of the respondents practiced in the southern or southeastern portion of the state (54 and 32, respec-

tively), as defined by the 5 Wisconsin public health regions.[12] Twenty-four respondents practiced in the northeast, and 15 respondents practiced in both the northern and western regions of Wisconsin.

Most respondents practiced in either a suburban (48 respondents) or urban, non-inner city (45) community setting. Nearly a quarter of respondents practiced in a rural community setting (31), defined as a population less than 2500 people. The fewest respondents practiced in an urban, inner city setting (10).

Use of Screening Tools and Referral Patterns

Three of the 11 survey questions asked about routine use of validated developmental and autism-specific screening tools within well-child care, as well as referral option selection for children with concerning screening results. Respondents were asked to select "almost always," "sometimes," or "never" to describe their practice patterns on these topics.

The majority of respondents "almost always" used an informal checklist of developmental milestones (84 respondents), while 76 respondents "almost always" used clinical impression (history and physical exam) without use of a screening instrument or checklist (Figure 1). Over half of respondents (66) "almost always" used a formal developmental screening tool, and an even greater number (74) "almost always" used the specific developmental screening tool ASQ.

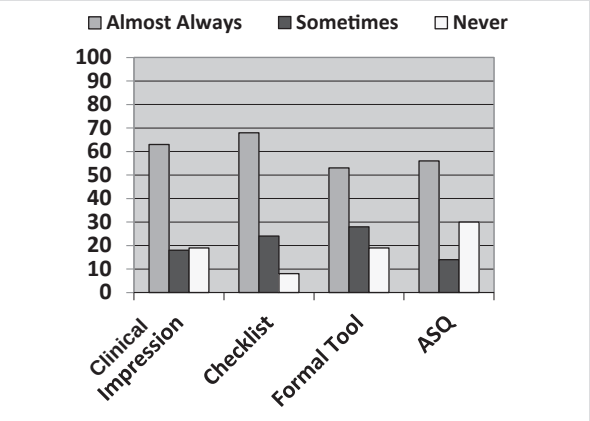
Similar to use of validated developmental screening instruments, the majority of respondents "almost always" used clinical impression (77 respondents) or an informal checklist of developmental milestones (74 respondents) to identify children who may have an autism spectrum disorder (Figure 2). Over half of respondents (73) "almost always" used the autism screening instrument M-CHAT; 53 respondents "almost always" used some type of formal tool to identify this population. Another autism screening tool, the Communication and Symbolic Behavior Scale: Developmental Profile (CSBS:DP),[13] was used less frequently by respondents. Only 6 respondents "sometimes" used this instrument.

Given a child with a concerning screening result, the majority of respondents (115) "almost always" referred the child to the Wisconsin Birth to 3 Program (Figure 3). Providers referred to Early Childhood Special Education (ECSE) regularly, but less frequently than Birth to 3; 51 respondents referred "almost always" to ECSE, and 49 "sometimes" referred to the Birth to 3 program.

Respondents most commonly "sometimes" referred to private therapy or to a developmental specialist (80 and 73 respondents, respectively). Over a quarter (47 respondents) "almost always" referred to a developmental specialist, and 18 respondents "almost always" referred such children to private therapy.

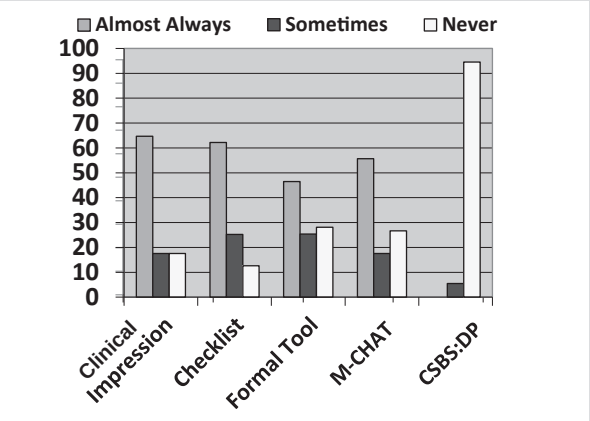
Tools like the ASQ offer parent-guided learning activities designed to promote child development in specific domains. Forty-nine respondents (40.5%) "almost always" provided

Figure 1. Strategies Used to Identify Children with Developmental Delays in Wisconsin (n=137)



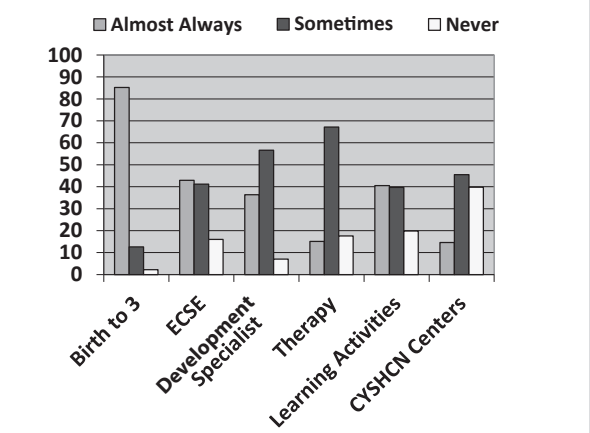
Abbreviations = ASQ, Ages and Stages Questionnaire.

Figure 2. Strategies Used to Identify Children with Autism Spectrum Disorders in Wisconsin (n=136)



Abbreviations = M-CHAT, Modified Checklist for Autism in Toddlers; CSBS:DP, Communication and Symbolic Behavior Scale: Developmental Profile.

Figure 3. Referrals Following a Concerning Screening Result in Wisconsin (n=137)



Abbreviations = ECSE, Early Childhood Special Education; CYSHCN, Children and Youth with Special Health Care Needs Program.

Table 2. Perceived Barriers to Developmental Screening (n = 135)

	Agree (%)	Slightly Agree (%)	Neutral (%)	Slightly Disagree (%)	Disagree (%)
Lack of training on use of a validated screening tool	27 (20.0)	39 (28.9)	17 (12.6)	19 (14.1)	33 (24.4)
Lack of time for developmental screening	29 (21.6)	56 (41.8)	13 (9.7)	13 (9.7)	23 (17.2)
Lack of office staff to perform the screen	26 (19.3)	44 (32.6)	16 (11.9)	26 (19.3)	23 (17.0)
Language barriers (staff cannot speak the family's language)	12 (8.9)	29 (21.5)	26 (19.3)	23 (17.0)	45 (33.3)
Inadequate reimbursement for conducting a formal developmental screen	29 (21.5)	32 (23.7)	33 (24.4)	16 (11.9)	25 (18.5)
Lack of confidence in the validity of screening instruments	4 (3.0)	17 (12.6)	25 (18.5)	34 (25.2)	55 (40.7)
Lack of referral options for children with concerning screens	19 (14.1)	28 (20.7)	15 (11.1)	34 (25.2)	39 (28.9)
Lack of understanding of community partners serving children with delays	14 (10.4)	30 (22.2)	16 (11.9)	37 (27.4)	38 (28.1)

such learning activities to parents of children with concerning screening results. Eighteen respondents (14.6%) "almost always" referred the family to their Regional Center for Children and Youth With Special Health Care Needs, while 56 (45.5%) "sometimes" did.

The last survey question asked about perceived barriers to providing high-quality developmental screening in respondents' practices. Reponses to this question were formatted in a typical 5-level Likert item manner (Table 2). Barriers most commonly selected by respondents included lack of time (41.8% "slightly agreed," n = 56), lack of office staff (32.6% "slightly agreed," n = 44), and lack of training on use of a validated tool (28.9% "slightly agreed," n = 39). Respondents most commonly did not consider the following barriers to screening: lack of confidence in the validity of the screening instruments (40.7% "disagreed," n = 55), language barriers (n = 45 "disagreed"), lack of referral options for children with concerning screens (n = 39 "disagreed"), and lack of understanding community partners serving children with delays (38 respondents "disagreed"). Respondents were divided on whether inadequate reimbursement for conducting a formal screen was a barrier; they most commonly were neutral on this issue (24.4%, n = 33).

DISCUSSION

Routine use of validated tools within well-child care is more effective than surveillance alone for the early identification of children with delays.[8,14] Surveillance alone identifies some children with delays, particularly those with medical complications or those with significant delay. Validated tools do a superior job overall at identifying children with more subtle delays, particularly fine motor, cognitive, and personal social delays.

As compared with a similar survey of Wisconsin primary care clinicians conducted in 2007, more clinicians are now using validated tools to monitor children's development, along with informal checklists and clinical impression. Six years ago, 74% of survey respondents indicated that they "never" used a validated tool, whereas this survey found that only 19% "never" routinely use developmental screening tools, and 28% "never" use an autism-specific tool.

Of those clinicians using tools, the ASQ and the M-CHAT were the most commonly used instruments. These correspond with the tools shared during physician outreach in this area, as well as tools used by community partners. Few clinicians used another autism-specific tool listed on the survey, the CSBS:DP. As compared with the M-CHAT, the CSBS:DP distinguishes children with communication-only delays from those with deficits in the areas of symbolic play and social reciprocity. It is a more complicated and extensive instrument than the M-CHAT, however, and may present more challenges to use in a busy primary care setting.

Referral patterns for children with concerning screening results are complex and likely are influenced by many factors, including perceived severity of delay, parent preference, insurance coverage, and relationships with other professionals serving children with delays. The vast majority of clinicians referred children with concerning screening results to the Wisconsin Birth to 3 Program. This state- and federally-funded program offers full developmental assessments for children with suspected delays. Children with at least a 25% delay (or a diagnosed condition with at least a 50% likelihood of delay) are eligible for Birth to 3 programming, which emphasizes family-centered goals and intervention activities. Birth to 3 Program partners attended over 90% of the onsite physician trainings on developmental screening. In many cases, these trainings helped strengthen already well-established relationships.

Respondents referred children with concerning screening results regularly to ECSE, but less frequently than Birth to 3. Like Birth to 3 programs, ECSE programs conduct developmental assessments for children with suspected delays and offer developmentally appropriate supports and services for those children determined to be eligible. They serve children aged 3-5 years through local public schools.

Birth to 3 Program professionals and professionals from regional centers co-present at physician trainings on developmental and autism-specific screening. Regional centers were "almost always" selected as a referral source by 15% of respondents and "sometimes" by 46%. These free and confidential resources for families and providers may be underutilized for children with

concerning screening results. Professionals from the regional centers offer guidance on health benefits coverage, local resources, and statewide support networks available to families raising children with unique health care needs.

CONCLUSION

Although a causal relationship cannot be established between the trainings offered to over 130 clinics statewide on this topic and increased use of validated tools, a strong correlation between them appears to exist. The academic detailing model of outreach has been demonstrated to be an effective strategy for modifying clinician understanding and behavior. Including community partners serving children with delays as well as care team members also may promote successful implementation of screening. Momentum for this work built gradually over time; for instance, clinicians initially were asked if they were interested in participating in screening trainings, whereas later unsolicited requests for training came in regularly. In the long term, a model to consider is the Child Health and Development Institute of Connecticut,[15] which provides a stable source of funding and programming from which ongoing support of this kind can be offered to primary care clinicians in practices statewide.

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Overall Prescription Medication Use Among Adults: Findings from the Survey of the Health of Wisconsin

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ABSTRACT

Purpose: To analyze overall prescription medication use patterns among study participants in a representative statewide sample of Wisconsin adults.

Methods: We analyzed data on 1572 participants from the 2008-2010 cycles of the Survey of the Health of Wisconsin (SHOW). SHOW is a statewide population-based survey that collects health information, including prescription medications, from 21 to 74 year olds. Prescription medication use was examined according to demographic and socioeconomic characteristics.

Result: Almost 55% of participants reported using at least 1 medication in the past month and 14% reported using at least 5 medications. The top 5 medications reported were lisinopril, hydrochlorothiazide, simvastatin, levothyroxine, and metoprolol. Overall prescription medication use increased significantly with age. Medication use was greater among females, former smokers, adults with body mass index (BMI) ≥ 30, or with low family income, and non-hispanic blacks. Adults having health insurance, drug coverage, or a regular source of care were more likely to report medication use.

Conclusion: The prevalence of prescription medication use in a general population sample in Wisconsin was high. Age, gender, race, BMI, family income, smoking history, health insurance, prescription drug coverage, and having a regular source of health care were associated with prescription medication use.

INTRODUCTION

Prescription medications have become a significant component of health care expenditures. According to data from the 2007-2008 National Health and Nutrition Examination Survey (NHANES), the percentage of Americans who took at least 1 prescription medication in the past month increased from 43% to 48% during the last decade; the proportion of those using at least 5 prescription medications increased from 6% to 11%, and 53% of women and 43% men used at least 1 prescription medication in the past month.[1] Prescription drug spending was estimated at $234.1 billion in 2008, more than double the spending in 1999.[1]

The rapid increase in medication use does not appear to result in a proportionally equivalent degree of improved health outcomes, in part because medications are not always prescribed or used appropriately.[2,3] Clinically indicated medications may be omitted, while inappropriate medications may be prescribed even though the potential risks outweigh the clinical benefits.[3,4] For instance, aspirin was reported to be underused in high cardiovascular disease (CVD) risk groups, but overused in low CVD risk groups among Wisconsin adults.[5] A survey of Iowa Medicare beneficiaries found that 51% of respondents had received at least 1 potentially inappropriate prescription medication.[6] Older adults are particularly vulnerable to medication-related problems because they are more likely to use multiple medications due to chronic diseases. According to another recent study, "a higher number of concurrent medicines is the only significant predictor of inappropriate medicine use."[7] Inappropriate prescribing of medications among the elderly is now considered a major public health issue, and advocates are calling for new prescribing criteria.[4,7]

Without sufficient knowledge about the prescription medication use patterns at a state or national level, it would be nearly impossible to determine whether or not medications have been prescribed appropriately and which areas public health policies should target. However, population-based studies of prevalence of prescription medication use are scarce. The most recent studies utilizing medication data from the National Social Life,

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CME available. See page 238 for more information.

Health and Aging Project (NSHAP) and NHANES have shed some light on the current medication use pattern among elderly, obese adults and the general US population.[1,8,9] However, more granular data (eg, at the state level) that can support more targeted and regional evaluation of health care system variations are lacking. The goals of this study are to identify the most commonly used prescription medications, to estimate the prevalence of prescription medication use, and to examine socio-demographic factors related to prescription medication use in a representative sample of Wisconsin adults.

METHODS

Data Source

As described elsewhere in detail,[10] the Survey of the Health of Wisconsin (SHOW) is an annual examination survey of representative household-based samples of the adult (21 to 74 years old) population of Wisconsin. SHOW collects data on a breadth of health and health care determinants, including a detailed inventory of prescription medications and medication use.[10] SHOW mimics NHANES, but is focused locally with the purpose of guiding public health and health care programs aimed at improving the health of Wisconsin residents. The present analyses are based on information collected from 1572 participants from the 2008-2010 cycles of SHOW. The study was approved by the UW-Madison Health Sciences Institutional Review Board.

Prescription medication use data were recorded during the household interview by direct observation and information abstraction from medication bottles. The participants were asked: "In the past 30 days, have you used a prescription medication? Include only those products prescribed by a health professional such as a doctor, a nurse practitioner, or a dentist." If the answer was yes, then the field surveyors continued with the following request: "I would like to see the containers for all the prescription medications that you used or took in the past 30 days." The field surveyors then entered medication names from medication bottles directly into secure laptop computers.

The information collected during the household interview includes insurance status and type, prescription drug coverage, and source of care. During the interview, participants were asked: "During the last 12 months, how many months did you have health insurance?" If they answered anything other than "0" they were asked about the type of health insurance (Medicare, Medicaid/Badger Care/Healthy Start/Family Medicaid, Military Health Care, private health plan, or other), prescription drug coverage (covers all of the costs, some of the costs, or none of the costs), and where they most often go to seek medical care or advice when they feel sick.

Data Processing and Revision

The medication data were reviewed and cleaned by a registered pharmacist. Data entry inconsistencies and errors (abbreviations, shortened names, and misspellings) were corrected manually and a revised database was created. Next, all brand name medications were translated into generic names, so that the same medications could be aggregated and frequency analyses could be performed. Lexicomp (Walters Kluwer Health, Philadelphia, Pennsylvania, http://www.lexi.com) was used as a resource to identify medication spellings and brand or generic names.[11]

Prescription medication use frequency was measured as the aggregate of all medications inventoried by SHOW field surveyors, and specific medication counts were calculated based on the number of unique generic name medications inventoried (Table 1). For the analysis of precription ingredients, medications that are combination products were treated as single entities and all components were added up (Table 2). For example, simvastatin and simvastatin/ezetimibe (Vytorin) are both counted toward the use of simvastatin. When evaluating the number of prescription drugs taken by a participant, a combination formula (eg, lisinopril/hydrochlorothiazide) is counted as 1 medication.

Statistical Analysis

Medication use was calculated for each participant based on a series of binary variables. Two binary variables representing medication use were developed. One variable indicates if a participant was taking at least 1 medication (≥1) and the other if a participant was taking at least 5 medications (≥ 5). A continuous number representing the total count of medications taken by each participant also was calculated by summing up all medication counts per respondent.

Microsoft Excel (Microsoft, Redmond, Washington) was used for frequency analyses. All additional statistical analyses were conducted using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina), taking into account the complex sampling design of the SHOW study. The prevalence of medication use and 95% confidence intervals were calculated weighting each observation according to the cluster and stratified sampling design (PROC SURVEYFREQ). The statistical significance of difference in prevalence across different subgroups was assessed using standard chi-squared tests. Logistic regression (PROC SURVEYLOGISTICS) was used for analyses of prescription drug use by health care factors adjusted for demographic variables (age, gender, race/ethnicity). When appropriate, variables were entered as ordinal covariates in the logistic regression model to test the statistical significance of a linear trend.

RESULTS

Overall, 54.2% of the participants took at least 1 prescription medication in the past month, and 13.5% took at least 5 prescription medications. Prescription medications and prescription ingredients used by at least 2% of the participants are listed in Table 1 and Table 2, respectively.

Table 1. Most Commonly Used Prescription Medications

Generic name	Medication Class	Prevalence (%)
Lisinopril	ACEI	7.7
Simvastatin	Antilipemic agent	7.6
Levothyroxine	Synthetic thyroid hormone	7.3
Hydrochlorothiazide	Diuretic	5.4
Metoprolol	β-blocker	5.2
Metformin	Antidiabetic agent	4.2
Omeprazole	Proton pump inhibitor	4.1
Albuterol	β2-agonist	3.7
Atenolol	β-blocker	3.6
Furosemide	Diuretic	3.2
Amlodipine	Calcium-channel blocker	3.0
Citalopram	Antidepressant, SSRI	2.7
Atorvastatin	Antilipemic agent	2.6
Bupropion	Antidepressant	2.5
Sertraline	Antidepressant, SSRI	2.4
Warfarin	Anticoagulant	2.4
Fluticasone	Corticosteroid	2.4
Fluoxetine	Antidepressant, SSRI	2.3
Cyclobenzaprine	Muscle relaxant	2.0
Fluticasone/salmeterol	Corticosteroid/long-acting β2 agonist	2.0
Aspirin	Salicylate	2.0

Data from Survey of the Health of Wisconsin (SHOW), 2008-2010. Generics and brands are combined.
Abbreviations = ACEI, angiotensin-converting-enzyme inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 2. Most Commonly Used Prescription Ingredients

Generic name	Medication Class	Prevalence (%)
Lisinopril	ACEI	9.2
Hydrochlorothiazide	Diuretic	8.9
Simvastatin	Antilipemic agent	8.4
Levothyroxine	Synthetic thyroid hormone	7.3
Metoprolol	β-blocker	5.2
Metformin	Antidiabetic agent	4.7
Fluticasone	Corticosteroid	4.4
Albuterol	β2-agonist	4.2
Omeprazole	Proton pump inhibitor	4.1
Atenolol	β-blocker	3.7
Acetaminophen	Analgesic	3.6
Amlodipine	Calcium-channel blocker	3.5
Furosemide	Diuretic	3.2
Hydrocodone	Analgesic, opioid	3.2
Citalopram	Antidepressant, SSRI	2.7
Atorvastatin	Antilipemic agent	2.7
Bupropion	Antidepressant	2.5
Sertraline	Antidepressant, SSRI	2.4
Warfarin	Vitamin K antagonist	2.4
Fluoxetine	Antidepressant, SSRI	2.3
Aspirin	Salicylate	2.1
Cyclobenzaprine	Muscle relaxant	2.0
Salmelterol	Long-acting β2-agonist	2.0

Data from Survey of the Health of Wisconsin (SHOW), 2008-2010.
Abbreviations = ACEI, angiotensin-converting-enzyme inhibitor; SSRI, selective serotonin reuptake inhibitor.

Lisinopril, simvastatin, levothyroxine, hydrochlorothiazide (HCTZ), and metoprolol were the top 5 prescription medications used by sample participants. They also were identified as the top 5 prescription ingredients. One-third of HCTZ was used in various combination products. As a result, use of HCTZ—including that used in combination products—was much higher than the use of HCTZ excluding these products (8.9% vs 5.4%). Lisinopril was the most commonly prescribed medication and ingredient. Nearly 16% of lisinopril was combined with HCTZ. Less than 1% of the participants used combination products for simvastatin (ezetimibe/simvastatin and niacin/simvastatin). Levothyroxine and metoprolol were prescribed as single products.

Prescription Medication Usage Patterns

Table 3 reports the estimated prevalence of prescription medication use in various subgroups. When age, gender and race were controlled for, prescription medication use increased consistently with age in both categories (≥ 1 medication and ≥ 5 medications). More than 74% of adults aged 60-74 used prescription medications in the past month; in contrast, only about 36% of people aged 21-39 used medications; 27% of subjects aged 60-74 used ≥ 5 medications, but only 3% aged 21-39 used ≥ 5 medications.

Gender, body mass index (BMI), education, family income, smoking history, and race also were correlated with prescription medication use. Women were significantly more likely to use ≥ 5 medications than men (16.3% vs 10.8%). An association between BMI and any prescription medication use was also found. The prevalence of using ≥ 5 medications was 5 times greater among adults with BMI ≥ 30 compared to those with BMI < 25 (18.4% vs 3.0%). An inverse relationship was observed between family income and medication use. Use of ≥ 5 medications was lower as income became higher. Former smokers were about twice as likely to take ≥ 5 medications as those who never smoked (15.2% vs 8.1%). Use of ≥5 medications was more common in blacks than in whites (22.2% vs 13.1%).

Table 4 presents the relationship between health care access and utilization factors and prescription medication use. Factors include insurance status, prescription drug coverage, insurance type, and usual source of care. When age, gender, and race were controlled for, the prevalence of using ≥ 5 medications for those with health insurance doubled compared to those without health insurance for the previous 12 months (5.5% vs 10.8%), though a statistically significant trend could not be seen due to the wide confidence intervals. Among people with health insurance for the past year, those having partial or all prescription drug coverage were almost twice as likely to use ≥ 1 medications and about 3 times as likely to use ≥ 5 medications as those who did not have coverage. Type of insurance and regular source of care also appeared to affect medication use. Less than 10% of people on private insurance or Medicare coverage used ≥ 5 medications in the last month. In comparison, almost 28% of Medicaid beneficiaries used ≥ 5 medications. People who visit a doctor's office, a

hospital outpatient department, or a community health center as their usual place for care were more likely to use prescribed medications as those without a regular source of care (60.1% or 54.1% vs 26.3%).

DISCUSSION

This is the first paper describing overall prevalence of prescription drug use in a statewide, population-based sample of Wisconsin adult residents (2008-2010). It provides information for comparison with national trends and to support additional monitoring of medication use over time. Our results are consistent with recent national trends and show an even higher prevalence of prescription medication use than that found in national surveys such as NHANES.[1]

The top 10 medications among SHOW participants were prescribed for cardiovascular disorders, diabetes, hypothyroidism, gastric, and respiratory disorders. Hydrocodone was only the 14th most prevalent prescription medication in our study, a result in apparent contrast with a 2006-2010 national survey conducted by IMS Health, where the combination pain medication hydrocodone and acetaminophen was the most commonly prescribed medication.[12] A possible explanation for this discrepancy may be the different way prescription medications were counted in SHOW and in the IMS Health survey. The national counts reported by IMS Health represent the number of prescriptions dispensed, while our counts represent the number of survey participants who use them. Compared to medications prescribed for other chronic disorders, narcotics are more likely to be prescribed in small quantities at a time due to regulations or providers' precautions. This may lead to an increased number of prescriptions dispensed to a limited number of patients, but are not ones that would be found regularly in a medicine cabinet—the main source for identification of prescription drugs used in our study.

Among key factors predicting medication use among this population sample, age was found to be an important determinant in the number of prescription medications used. More than a quarter of all SHOW participants ages 60-74 used 5 or more medications in the past month. It is also common for older adults to use prescription medications along with over-the-counter medications or dietary supplements.[8] These factors pose increased risk of inappropriate prescribing, misuse, drug-related adverse events, and drug-drug interactions among older adults.[1,6,8] It has been reported that polypharmacy strongly predicts adverse outcomes and may even increase the risk of mortality.[3,13-15] A study examining the frequency of medication errors in patients taking ≥5 medications in Austria reported inappropriate medication use in 93% of patients, dosing errors in 56% of patients and "category X interactions" (the most dangerous potential drug-drug interactions) in 2.4% of patients.[3] Concurrent use of multiple medications in the elderly should, therefore, be carefully monitored and programs targeting health care providers as well as seniors to promote safe and appropriate medication use should be strongly supported.

Table 3. Adjusted Prevalence[a] of Using at Least 1 or at Least 5 Prescription Medications

	≥1 Prescription Medication		≥5 Prescription Medications	
	Percent (95% CI)	*P*-value	Percent (95% CI)	*P*-value
Age (years)[b]				
21-39	36.0 (30.8, 41.1)	<0.001	3.4 (1.8, 5.0)	<0.001
40-59	62.2 (55.4, 69.0)		13.5 (10.2, 16.8)	
60-74	69.2 (63.6, 74.7)		27.5 (23.5, 31.4)	
Gender[b]				
Men	49.0 (43.4, 54.6)	0.001	10.8 (8.6, 13.0)	0.002
Women	59.4 (53.9, 64.9)		16.3 (13.5, 19.1)	
Race[b]				
Non-Hispanic white	56.0 (51.1, 60.9)	0.20	13.1 (10.9, 15.2)	<0.001
Non-Hispanic black	52.2 (43.6, 60.9)		22.2 (13.6, 30.9)	
Hispanic	33.4 (21.2, 45.7)		11.8 (1.9, 21.7)	
Other	41.0 (23.8, 58.2)		10.5 (2.0, 19.0)	
Education[c]				
<High school	64.5 (54.4, 73.4)	0.39	10.1 (6.3, 15.9)	0.02
High school	56.1 (33.3, 76.6)		13.3 (4.4, 33.7)	
Some college	56.5 (35.7, 75.3)		12.1 (4.6, 28.2)	
≥College	55.2 (34.0, 74.6)		7.2 (2.5, 18.7)	
BMI (kg/m²)[c]				
<25	46.9 (38.3, 55.7)	<0.001	3.0 (1.6, 5.6)	<0.001
≥25 and <30	46.4 (31.4, 62.2)		8.7 (2.5, 26.2)	
≥30	70.6 (53.8, 83.2)		18.4 (5.9, 44.9)	
Family income[c]				
Don't know	62.9 (34.5, 84.5)	0.19	6.8 (4.0, 11.3)	0.001
<25,000/year	62.5 (41.3, 79.8)		16.7 (4.5, 46.1)	
25,000-49,999/year	56.1 (34.7, 75.5)		16.9 (5.8, 40.0)	
50,000-99,999/year	54.0 (34.7, 72.2)		9.5 (3.0, 26.0)	
≥100,000/year	55.3 (45.6, 64.6)		9.6 (3.0, 27.0)	
Smoking[d]				
Current	51.3 (36.0, 66.4)	0.11	12.9 (5.6, 27.0)	0.004
Former	62.5 (46.8, 75.9)		15.2 (7.8, 27.5)	
Never	53.8 (47.0, 60.5)		8.1 (6.0, 10.8)	

Data from Survey of the Health of Wisconsin (SHOW), 2008-2010.
[a] Weighted and adjusted for sampling design. Education, BMI, family income, and smoking also were adjusted for age (continuous), gender, and race (non-Hispanic white and other).
[b] *P*-value for Rao-Scott chi-square test using design adjusted, survey weighted frequencies.
[c] *P*-value for trend in ordinal independent variable tested using design adjusted, survey weighted logistic regression.
[d] *P*-value for Wald chi-square test in nominal independent variables tested using design adjusted, survey weighted logistic regression.

Similar to the NHANES 2007-2008 findings,[1] the prevalence of overall medication use was higher among women than men in SHOW. Other studies have found that prescription medication use was higher in women than men across all age groups.[8] NHANES also reported that whites consumed the highest number of medications and Mexican Americans the lowest.[1] In this Wisconsin sample, Hispanics lagged behind non-Hispanic whites in use of ≥1 prescription medication. Blacks had the highest prevalence of using ≥5 medications. Future studies should explore the

Table 4. Adjusted Prevalence[a] of Medication Use According to Access to Health Insurance and Usage Characteristics

	≥1 Prescription Medication		≥5 Prescription Medications	
	Percent (95% CI)	*P*-value	Percent (95% CI)	*P*-value
Health Insurance[b]				
0 month	37.2 (27.2-48.5)	<0.001	5.5 (2.1-14.1)	0.24
1-11 months	47.2 (22.6-73.3)		11.0 (1.1-57.8)	
12 months	58.9 (36.7-78.0)		10.8 (1.5-48.8)	
Prescription Drug Coverage[b]				
All	66.9 (54.2-77.0)	<0.001	10.9 (6.3-18.3)	0.01
Some	59.7 (35.5-80.0)		11.5 (3.6-31.2)	
None	36.2 (16.0-62.7)		3.9 (0.8-17.0)	
Insurance Type[c]				
None	36.9 (27.3-47.6)	<0.001	5.4 (2.1-13.0)	<0.001
Medicaid	71.1 (45.4-87.9)		27.7 (4.7-75.0)	
Private/Medicare	56.9 (35.7-75.8)		9.1 (1.4-40.4)	
Usual Source of Care[c]				
Emergency department	27.8 (14.4-47.0)	<0.001	16.9 (6.0-39.4)	0.05
Physician's office	60.1 (21.6-89.2)		10.3 (1.1-54.7)	
Other (hospital out-patient department, community health center, etc)	54.1 (15.9-88.0)		16.8 (1.5-73.0)	
No regular source of care	26.3 (6.0-66.7)		5.4 (0.4-46.2)	

Data from Survey of the Health of Wisconsin (SHOW), 2008-2010.
[a] Weighted and adjusted for sampling design, as well as age (continuous), gender, and race (non-Hispanic white and other).
[b] *P*-value for trend in ordinal independent variable tested using design adjusted, survey weighted logistic regression.
[c] *P*-value for Wald chi-square test in nominal independent variables tested using design adjusted, survey weighted logistic regression.

possible causes for the observed ethnic/race disparities in prescription medication use among Hispanic people.

We also found risk factors such as obesity and smoking history were significant predictors of prescription medication use. Use of at least 5 medications increased substantially with increase in BMI. Participants with BMI ≥ 30 were more likely to use at least 5 medications compared to participants who were not overweight (BMI < 25). This is consistent with previous studies, including cross-sectional analysis among 9787 adults in NHANES that also found that obese adults had greater use of all common medication classes, except sex hormones,[9] and may be explained by the high prevalence of comorbid conditions among obese subjects. A high percentage of adverse drug events has already been reported among obese patients due to inappropriate medication dosing.[16,17] Thus, obese adults in Wisconsin on multiple medications are likely subject to an even greater risk of adverse drug events. The high prevalence of medication use in former smokers also is likely associated with a high level of comorbidities (eg, chronic obstructive pulmonary disease) in this group.

According to the NSHAP, medication use was more likely among those with greater formal education.[8] However, in this survey, college education was inversely related to medication use. The possible explanation is that NSHAP included only adults aged 57-84, while SHOW participants varied in age from 21 to 74. Older adults may have less education. Sixty-seven percent of the SHOW participants aged 60-74 have at least some college education compared to 71% among those aged 40-59 and 78% among those aged 21-39. On the other hand, age is a strong predictor of medication use. Age differences in the sample population may have led to different findings.

Similar to the most recent NHANES data,[1] SHOW determined that people without health insurance, prescription drug coverage, and a regular source of care were less likely to use prescription medications. Consequently, lack of access to health care may lead to suboptimal treatment of diseases among these adults.

One of the strengths of this study is that it is based on a probability sample of the population of the entire state of Wisconsin, regardless of access and patterns of health care use. A recent 2013 study using electronic medical record (EMR) data from the University of Wisconsin Department of Family Medicine (UW-DFM) primary care clinics reported that in patients aged 18-24 years, 25-34 years, 35-44 years, and 45-54 years, the percentage using at least 5 medications was 20%, 29%, 40%, and 55%, respectively.[18] These numbers are much higher than those found in our study. This difference is likely due to the EMR and clinical-based nature of the UW-DFM study, which will tend to result in an over-representation of heavy health care users and sicker individuals when compared to the strictly population-based nature of our SHOW sample. In any event, it is important to note that the UW-DFM study also found that, consistent with our findings, increasing age, female gender, and overweight, were associated with higher prevalence of medication use in this EMR-based study.[18] Furthermore, as was seen in our study, the UW-DFM study also found Medicaid beneficiaries were significantly more likely to use medications than patients with employer-based insurance.

Another strength of our study compared to telephone surveys and other surveys relying on self-report, is the accuracy of the prescription drug-use data since the interviewers recorded the medication names directly from the medication containers. Telephone surveys also have declining response rates, and our response rates relative to these studies are greater.

One limitation of this study is that it is unknown if the partic-

ipants showed all medications to the interviewers. However, there is little way of knowing how much this affects results. It is likely that this would pose little bias to this particular study because under-reporting for certain conditions would likely be uniform across the entire population. Therefore, relative comparisons across subpopulations regarding prescription drug use should be accurate. It is important to note that the prescription medications inventoried for SHOW included some over-the-counter medications (eg, aspirin, NSAIDs), but only if they had been prescribed by a health care provider.[5] Finally, sample sizes are relatively small for some subgroups, which have led to limited power to detect significant differences in some cases.

CONCLUSION

Similar to national trends, there was a high prevalence of prescription medication use in a general population sample in Wisconsin. A number of factors, including increasing age, female gender, obesity, and lower family incomes were associated with higher levels of multiple medication use (≥5 medications). Polypharmacy has been linked to numerous adverse outcomes and is an area of growing public health concern, particularly among the elderly. Concurrent use of multiple medications, and efforts to support appropriate prescription and medication use should be carefully monitored for vulnerable populations such as the elderly and the obese.

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CME

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Quiz: Overall Prescription Medication Use Among Wisconsin Adults: Findings from the Survey of the Health of Wisconsin

EDUCATIONAL OBJECTIVES

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

1. Describe the patterns of prescription medication use among Wisconsin adults.
2. Identify the types of patients where prescription misuse or drug-related adverse events may be more probable.

PUBLICATION DATE: December 15, 2014

EXPIRATION DATE: December 15, 2015

QUESTIONS

In this survey of overall prescription medication use among a representative statewide sample of Wisconsin adults age 21-74 years:

1. Nearly 55% of the participants took at least 1 prescription medication in the past month, and 30% took at least 5 prescription medications.
   - ❑ True
   - ❑ False
2. Hydrochlorothiazide (HCTZ), levothyroxine, lisinopril, metoprolol, and simvastatin were the top 5 prescription medications used by sample participants.
   - ❑ True
   - ❑ False

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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. You will receive an e-mail from wmj@wismed.org with instructions to complete an online evaluation. Your certificate will be delivered electronically.

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3. When age, gender, and race were controlled for, prescription medication use increased consistently with age in both categories (≥ 1 medication and ≥ 5 medications).
   - ❑ True
   - ❑ False
4. Female gender, a greater BMI (≥30 vs <25), a higher educational level, a higher family income, and former smokers (as compared to those who never smoked) were correlated with prescription medication use of ≥5 medications.
   - ❑ True
   - ❑ False
5. When age, gender, and race were controlled for, the prevalence of using ≥5 medications for those with health insurance doubled compared to those without health insurance for the previous 12 months.
   - ❑ True
   - ❑ False
6. Type of insurance and usual source of care appeared to affect medication use. Less than 10% of people on private insurance or Medicare coverage used ≥5 medications in the last month. In comparison, almost 28% of Medicaid beneficiaries used ≥5 medications.
   - ❑ True
   - ❑ False
7. More than a quarter of all participants ages 60-74 used 5 or more medications in the previous month. It is common for older adults to use prescription medications along with over-the-counter medications or dietary supplements; these factors pose an increased risk of inappropriate prescribing, misuse, drug-related adverse events, and drug-drug interactions among older adults.
   - ❑ True
   - ❑ False

Large Epidermal Inclusion Cyst Presenting as a Pelvic Mass

Paul D. Silva, MD; Rachael Summers, BS; Modupe Omole, MD; Scott Chapman, MD

ABSTRACT

Introduction: Epidermal inclusion cysts are common discrete nodules often formed in areas of previous trauma or surgery. A literature review indicated that large epidermal inclusion cysts of the pelvis are extremely rare. Accordingly, we present a case of a woman with a large pelvic epidermal inclusion cyst of the vaginal cuff, along with imaging studies and a review of the literature.

Case Presentation: A 49-year-old woman, 13 years after vaginal hysterectomy, was found to have a 7-cm soft tissue pelvic mass, discovered on a computed tomography (CT) scan performed for abdominal pain. The transvaginal ultrasound showed typical findings of an unruptured epidermal inclusion cyst with a hypoechoic background with diffuse small variable echodensities (some intense echogenic reflectors), a thin wall, and no internal Doppler flow. A 7-cm epidermal inclusion cyst was removed laparoscopically from her vaginal cuff without complication.

Discussion: Epidermal inclusion cysts of clinical significance are rarely formed at the vaginal cuff or elsewhere in the pelvis. Increased utilization of abdominal/pelvic CT imaging is increasing the frequency in which benign pelvic cysts are encountered. The trauma of surgery may sequester portions of vaginal epithelium, which may form epidermal inclusion cysts. As the cyst increases in size, the cyst may be viewed as an incidental pelvic mass requiring clinical decision making.

INTRODUCTION

Epidermal inclusions cysts are discrete nodules with the wall composed of mature squamous epithelium.[1] They may be formed from areas of previous trauma,[1] which may cause the epidermis to sequester in the dermis allowing for slow growth of the lesion through sloughing of dead cells centrally.

Epidermal inclusion cysts commonly have been found on the vulva and clitoris from trauma from birth, episiotomies, or female genital mutilation.[2] A literature review indicated that large cysts of this type are rarely located in the upper vagina or pelvis,[2] although it is possible that with the increased use of imaging for diagnostics, they may occur more commonly.[3] Only 1 previous case report has described a large pelvic epidermal inclusion cyst located on the vaginal cuff status post hysterectomy.[2] That case report describes a 3.3-cm cyst that was found incidentally on a transvaginal ultrasound exam. Accordingly, we report a 7-cm vaginal cuff epidermal inclusion cyst that presented on a contrast-enhanced computed tomography (CT) scan performed for upper quadrant abdominal pain.

CASE REPORT

A 49-year-old woman, gravida 3 para 3, presented with back pain and pressure-like abdominal pain, mainly located in her upper abdomen. The patient had a vaginal hysterectomy 13 years prior because of vaginal prolapse. She had a history of elevated liver enzymes in the past, which remained mildly elevated. The patient had a previous diagnosis of non-alcoholic fatty liver disease with a prior ultrasound showing diffuse fatty infiltration of the liver. Significant other past medical history included chronic low back pain with right-sided radicular symptoms; a recent magnetic resonance imaging (MRI) of the lumbar spine was negative. The patient's height was 168 cm, weight 100 kg, and BMI of 36 kg/m^2. She was afebrile and had mild right upper quadrant tenderness on exam. Her white blood cell count was normal.

A right upper quadrant ultrasound showed no new findings. A CT scan noted a 7 x 4.5 x 4.5-cm smooth soft tissue mass in the midline in the posterior inferior pelvis that appeared to be separate from the ovaries (Figure 1). The mass was further characterized by transvaginal ultrasound as a 6.5 x 4.8 x 5-cm posterior inferior cystic pelvic mass with a hypoechoic background and multiple small punctate echodensities (some of these were quite intense echogenic reflectors), and no internal Doppler flow that

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Figure 1. Computed Tomography Scan with IV Contrast

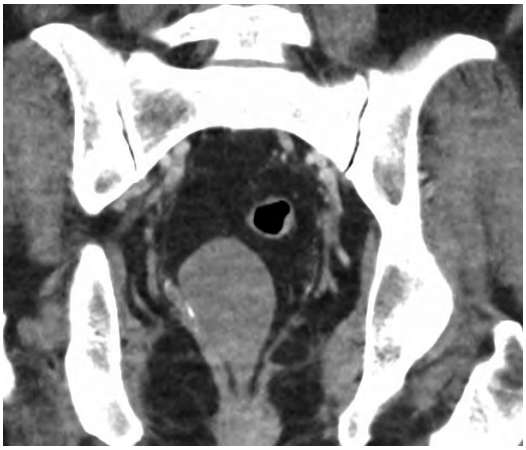

Image shows a 7 x 4.5 x 4.5-cm smooth nonenhancing posterior midline pelvic soft tissue mass.

Figure 2. Transvaginal Ultrasound

Image shows a 6.5 x 4.8 x 5.0-cm posterior inferior cystic pelvic mass with multiple variable small echodensities and a thin wall.

appeared to be separate from the ovaries (Figure 2). A bimanual exam palpated a cystic mass at the apex of the vagina, mildly tender to touch. Due to the pelvic location of the mass, a CA-125 was evaluated, which came back within normal limits. A colonoscopy also was performed in which 3 benign polyps were removed. There was no evidence of diverticulosis.

The patient continued to have symptoms of bloating and fullness, which extended throughout the abdomen. Also, because of the large size of the mass, it was decided to proceed to surgery. Since the mass had benign features (thin wall, no internal Doppler flow, normal CA-125), a laparoscopic approach was used. An 8-cm retroperitoneal mass was encountered in the area of the pouch of Douglas. The mass appeared cystic and closely connected to the posterior vaginal wall and vaginal cuff. The mass could not be removed without entering the vaginal cuff, and therefore the surgeon felt the mass arose from the vaginal wall.

Gross examination of the mass showed a tan-gray smooth walled 7.4 x 5.1 x 4.4-cm cyst filled with tenacious tan-yellow debris. Final pathology was reported as a benign squamous inclusion cyst (epidermal inclusion cyst).

DISCUSSION

Epidermal inclusion cysts can be found wherever there is squamous epithelium, presumably from sites of trauma including surgery.[1,2] Trauma is thought to result in sequester of the epithelium in the subepithelial tissue with subsequent slow growth through central accumulation of sloughed dead cells. In 1 review of epidermal inclusions cysts undergoing sonography for characterization, locations included 4 cases from the head or neck, 4 from the upper extremities, 2 from the chest wall, 1 abdominal, 3 from the buttocks, 2 from the inguinal or scrotal area, 2 from the sacrococcygeal area, and 6 from the lower extremities.[4] The largest cyst noted in this review[4] was 6 cm. The mass found on our patient was unusual with regard to size, having a largest diameter of 7.4 cm. In the pelvic area, epidermal inclusion cysts commonly form at an episiotomy scar or female genital mutilation sites. These cysts can continue to grow and cause mass-like effects or become infected and cause pain.[2] Although epidermal inclusion cysts are generally benign, squamous cell carcinomas have been reported.[2] On an ultrasound, epidermal inclusion cysts typically image as hypoechoic masses with variable echogenic foci without color Doppler signals;[4] this was the case in our patient (Figure 2).

In the preoperative differential diagnosis, benign cystic teratoma (dermoid cyst) initially was considered. However, benign cystic teratomas almost always are ovarian, and the ovaries appeared separate on the CT scan and sonogram, making this diagnosis unlikely. Benign cystic teratomas often are predominated by skin elements, so part or all of the tumor may have an ultrasound appearance similar to an epidermoid inclusion cyst (echogenic lines and dots).[5,6,7] A CT scan of a benign cystic teratoma often will identify calcifications or areas of fat components. These were not present in our case.[7]

Pelvic abscess also was considered initially in the preoperative differential diagnosis. Abscesses may contain variable echodensities with some strong echoflectors, possibly due to gas-forming organisms. The enhanced CT scan features for an abscess are characterized as thick-walled and rim enhancing.[8] The patient's mass was thin-walled and not rim enhancing (Figure 1), making this diagnosis unlikely. Also, clinically there was no fever or elevated white blood cell count, and there was little tenderness on pelvic exam.

Vaginal cysts are almost always benign and can be categorized into Müllerian duct cysts, epidermal inclusion cysts, Gartner duct

cysts, Bartholin cysts, and endometriotic cysts.[9] In one review of vaginal cysts, it was reported that Müllerian cysts occurred in 19 patients (44%), Bartholin cysts in 3 (7%), epidermal inclusions cysts in 10 (23%), Gartner cysts in 5 (11%), endometroid in 3 (7%), and unclassified in 3 (7%).[9] In this review, 3 out of the 10 epidermal inclusion cysts were located at sites of episiotomies or lacerations.[9] Müllerian cysts are derived from the paramesonephric duct remnants.[10] Müllerian cysts have been located throughout the vagina.[10] Gartner duct cysts, derived from Wolffian/mesonephric duct remnants, usually are located on the anterolateral wall of the vagina.[10] Bartholin glands are derived from urogenital sinus; Bartholin cysts are found in the caudal, inferior, and posterior portion of the vagina[10] and also can be considered as vulvar cysts.

A literature review revealed the only other report of an epidermal inclusion cyst appearing as a noticeable pelvic mass on imaging. The lesion measured 3.3 cm as compared to the 7.5-cm mass found in our patient. The previous case report indicated the patient's status also was post hysterectomy (6 years), with an asymptomatic mass found incidentally on transvaginal ultrasound imaging.[2] Our patient's mass also was found incidentally, when an enhanced CT scan was performed for upper abdominal pain. With advances in imaging and increased utilization, many incidental findings are being reported.[3]

With the increasing rates of using imaging to aid in diagnosis of abdominal pain, epidermal inclusions cysts may more commonly be found to enter the clinical decision-making process. In a retrospective chart review of abdominal/pelvic CT scan findings, it was reported that 56.3% patients had incidental findings.[3] In determining the significance of pelvic cysts found on CT scan, based on current literature it is thought that adnexal cysts with no complex features <3.5 cm do not require follow-up or intervention.[11] Our patient's mass was larger and was not characterized as a cyst on CT scan, but rather a soft tissue mass. Ultrasound was helpful to redefine it as a cystic mass with benign features (a thin wall and no internal Doppler flow). However, due to its large size and unclear preoperative diagnosis, the patient was offered removal. The benign ultrasound findings led to using a laparoscopic approach with some confidence. Perhaps this report may help in better defining preoperatively the diagnosis of large pelvic epithelial inclusion cysts in the future.

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Mirtazapine and Mefloquine Therapy for Non–AIDS-Related Progressive Multifocal Leukoencephalopathy

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ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is an opportunistic infection of the human nervous system caused by the JC virus. We report what is, to the best of our knowledge, the second reported case using a combination of mefloquine and mirtazapine in a patient with non–AIDS-related PML with a good clinical outcome. Conversely, the recent trial of mefloquine in 21 patients with AIDS and 3 without AIDS failed to show a reduction of JC viral DNA levels in the cerebral spinal fluid. However, the positive clinical response seen in our patient after the initiation of this combination therapy suggests that further studies in the form of randomized controlled trials for the treatment of non–AIDS-related PML are warranted.

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system caused by reactivation of the dormant JC virus (JCV) in an immunosuppressed host. The use of antiretroviral therapy in patients with HIV/AIDS has reduced the mortality of patients with PML.[1] There are no approved therapies in non–HIV-associated PML, although in some cases cytarabine, cidofovir, mirtazapine, or mefloquine have been used successfully (Table 1). Here we report a case of non–AIDS-related (B cell chronic lymphocytic leukemia) PML successfully treated with mirtazapine and mefloquine.

CASE REPORT

A 77-year-old man with chronic lymphocytic leukemia (CLL) (CD28 positive, 11q deletion, nonspecific 1:8 translocation, and isolated 13q deletion on bone marrow biopsy) and hypogammaglobulinemia was hospitalized for generalized seizures. Ten months prior to admission he underwent splenectomy for CLL-related splenomegaly. Three weeks before this admission, he was found to have progressive psychomotor slowing and decline in cognitive function. Laboratory studies on admission were significant for a white blood cell count of 18.8 x 10^3 uL with differential cell count of 63% lymphocytes, and human immunodeficiency virus (HIV) was nonreactive. A computerized tomography (CT) scan of the head revealed an area of low attenuation involving the frontal lobe with effacement of the cortical sulci and anterior horn of the lateral ventricle along with vasogenic edema. Magnetic resonance imaging (MRI) showed an abnormal signal in the left frontal lesion with edema and feathered enhancement pattern on post-contrast imaging suggestive of inflammatory or infectious processes (Figure 1A). The patient was started on empiric antibiotics of ceftriaxone intravenously (IV) (2 g every 12 hours) and metronidazole (500 mg IV every 8 hours) for treatment of presumed brain abscess, fosphenytoin for seizures, and dexamethasone for vasogenic edema.

A stereotactic brain biopsy of the left frontal lobe lesion was obtained for definitive diagnosis. Histopathologic evaluation of the tissue sample showed prominent reactive gliosis and frequent bizarre astrocytes (Figure 2). There were florid perivascular lymphocytic infiltrates spreading into the brain parenchyma. The lymphocytes were mostly small sized, along with many large macrophages in the adjacent brain tissue. Immunohistochemical stains and flow cytometry confirmed this is to be exclusively a T-cell lymphocytic infiltrate around vessels and within the parenchyma. Very few B-cells were present. JCV in situ hybridization study was positive (Figure 3). Antibiotics were discontinued when aerobic, anaerobic, and fungal cultures from the left frontal biopsy sample showed no growth.

The patient was treated with mirtazapine (30 mg daily) and mefloquine (250 mg daily for 3 days followed by 250 mg once weekly), as well as tapering the dose of dexamethasone (2 mg twice daily for 7 days, then 2 mg once daily for 7 days). Post

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treatment follow-up in 18 months showed persistent mild improvement in cognitive function and resolution of diffusion abnormality and mass effect on the MRI of the head (Figure 1B). There was persistent, although markedly improved, increased T2 signal at the most posterior and inferior aspects of the left frontal lobe mass effect. The patient improved clinically and remains stable cognitively nearly 24 months on this combination therapy without relapse.

Table 1. Literature Summary–Experimental Therapy Used in Non-HIV/AIDS-Related Progressive Multifocal Leukoencephalopathy (PML)

Study	Regimen used	Condition
Aksamit et al, 2001[2]	5 day course IV cytarabine (2 mg/kg/d)	Non-AIDS related PML
Vulliemoz et al, 2006[3]	5 day course IV cytarabine (2 mg/kg/d) and ongoing treatement with Mirtazapine (30 mg/d)	Dermatomyositis and PML
Verma et al, 2007[4]	Mirtazapine	Polycythemia vera and PML
Owczarczyk et al, 2007[5]	Cidofovir (6 infusions) and Mirtazapine (15 mg/d)	Sarcoidosis and PML
Terrier et al, 2007[6]	Cytarabine and Cidofovir	Systemic Lupus Erythematosus and PML
Raedt et al, 2008[7]	Cidofovir	Sarcoidosis and PML
Yagi et al, 2010[8]	Cidofovir	Heerfordt syndrome and PML
Schroder et al, 2010[9]	Mirtazapine (60 mg/d) and Mefloquine (250 mg daily for 3 days followed by 250 mg once weekly)	Natalizumab and PML

DISCUSSION

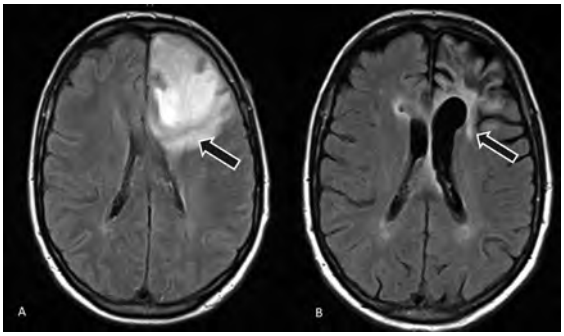
JCV is a double-stranded DNA human polyomavirus that invades oligodendrocytes in the central nervous system white matter, causing demyelination and neurologic deficits. The mechanism of infection is not clearly established, but it is believed to occur through inhalation. Once within the host, the virus remains dormant within the kidney and bone marrow, only to reemerge during periods of immunosuppression when there is impairment of immune surveillance. Once reactivated, the virus is believed to spread by B-lymphocytes to infect astrocytes and oligodendrocytes within the central nervous system by binding to 5-HT_{2A}, 5-HT_{2c}, and dopamine receptors.

In recent years, AIDS has been the underlying immunosuppressive illness most commonly associated with PML.[10] However, a variety of non-HIV immunosuppressive illnesses have been described in patients with PML, including lymphoreticular malignancies of the B-cell type (most commonly chronic lymphocytic leukemia or non-Hodgkin's lymphoma), organ transplantation and immunosuppression associated with rheumatoid arthritis, sarcoidosis, systemic lupus erythematosus, or dermatomyositis.[11,12] In general, PML is found in patients who have prolonged immunosuppression for at least 6 months.

In most non-AIDS patients, neurologic abnormalities are focal, predominately in the cerebral hemispheres. The ratio of cerebral to brainstem involvement is estimated to be 10:1 in these patients, but for reasons that are unclear, brainstem involvement is more common in AIDS patients, whose ratio of cerebral to brainstem involvement is approximately 4:1.[13] Symptoms include motor weakness, progressive decline in cognition, and visual disturbances. Thus, the diagnosis of PML should be suspected in immunosuppressed patients who present with subacute, focal, progressive neurologic symptoms. Although PML has been regarded as a "slow virus" infection, it is really a subacute illness with focal neurologic symptoms evolving over days to weeks.

MRI scanning is far superior to CT in visualizing abnormalities of PML in the brain.[14] Unifocal abnormalities on MRI scan

Figure 1. Magnetic Resonance Image (MRI)



MRI T2 fluid attenuated inversion recovery (FLAIR) image at time of presentation (A), and MRI T2 FLAIR image at 12 months post-treatment (B).

Figure 2. Histopathologic Evaluation of Tissue Biopsy

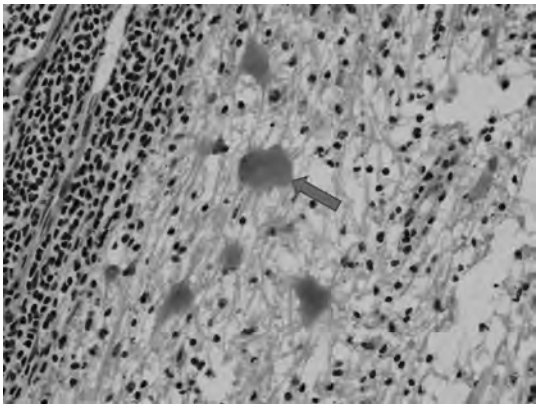
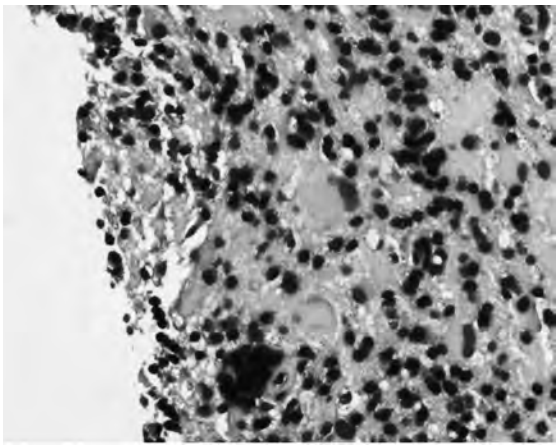


Image shows bizarre astrocytes with large atypical and eccentric nuclei (arrow). Hematoxylin and eosin stain, 40x magnification.

Table 2. Mortality Rates in AIDS-related Progressive Multifocal Leukoencephalopathy (PML) and Natalizumab-associated PML

Category	Mortality	Comments
AIDS-related PML	1-year mortality ranges from 30.5%[18] to 37.6%[19]	The improvement in 1-year mortality associated with HAART was independent of HIV RNA load and the total CD4+ T cell count at diagnosis however JC virus-specific cytotoxic CD8+ T cell responses are important.[20]
Natalizumab-associated PML	66% mortality within 2 years of initiating natalizumab	Of the 3 case reports of natalizumab-associated PML, 1 PML patient survived, indicating that withdrawal of natalizumab, possibly in combination with antiviral therapy, may permit survival.[21]
Non-AIDS/non–natalizumab-associated PML	High	Heterogeneous category and hence the exact mortality rates unknown.

Figure 3. Positive Chromogenic In Situ Hybridization (CISH) for JC Virus (JCV) under 40x Magnification



with little mass effect and contrast enhancement in the brainstem suggest PML. Polymerase chain reaction (PCR) analysis of cerebral spinal fluid (CSF) is used for confirming the diagnosis by detecting the viral particles.[15] Brain biopsy at the advancing edges of suspected PML lesions is confirmatory in patients with PCR-negative CSF. In situ hybridization or immunohistochemistry are the confirmatory techniques for identifying JCV in an affected brain.[11,16]

To date, there is no satisfactory treatment for PML. The disease is almost always progressive, barring very rare cases where spontaneous partial recovery and prolonged survival have been reported.[12] Mortality rates for PML in both AIDS-associated and non-AIDS associated patients remain high (Table 2). Reduction or withdrawal of immunosuppressants in patients with non-AIDS PML, and the use of highly active antiretroviral therapy (HAART) in AIDS-related PML, are the only known previous interventions that allowed immune reconstitution and control of pathological viral activity.

Since the 5-HT2A serotonin receptor has been found to act as a receptor for JCV in glial cells,[21] the use of medications selective for these receptors, such as the antidepressant mirtazapine and antipsychotic risperidone, appears warranted.[13] These classes of medications have been shown to inhibit viral entry into unaffected glial cells. The antimalarial drug mefloquine recently has been recognized to have anti-JCV activity at nontoxic concentrations with in vitro culture and passes the blood-brain barrier to achieve concentrations in the brain above the level inhibiting JCV replications in vitro.[22] Mefloquine works through a different mechanism, inhibiting JCV replication in cells after viral entry.[22] Experience with these medications has come from case reports and case series. The use of either of these agents has not been shown to improve outcomes in large prospective studies.

There have been several case reports on the successful use of mefloquine alone or in combination with mirtazapine in treatment of non-HIV PML.[9,23-25] Schroder et al[9] described a 41-year-old woman in whom JCV (1387 copies/mL) was recovered from CSF samples during the treatment for multiple sclerosis with natalizumab. She was placed on mirtazapine 60 mg daily and mefloquine 250 mg daily for 3 days followed by 250 mg weekly. The patient began to improve, and 1 month after initiation of the combination therapy, her CSF JCV load decreased to 169 copies/mL.[9] In our case, mirtazapine (30 mg daily) was selected to block infection of oligodendrocytes with JCV, preventing further demyelination, and mefloquine (250 mg daily for 3 days followed by 250 mg once weekly) was added to prevent viral replication. The patient responded well with both clinical and radiological improvement and is into his 24th month of treatment.

CONCLUSIONS

In the recent trial involving PML patients, the antimalarial drug mefloquine was investigated to determine its efficacy in reducing JCV DNA levels in the CSF. It was noted that mefloquine failed to reduce JCV DNA levels in the CSF.[26] However, of the 24 patients who were analyzed, 21 patients were HIV-positive (all of them were on HAART) and 3 patients were HIV negative. The sample size for non–AIDS-related PML (secondary to either cancer or rheumatoid arthritis) patients was small and therefore difficult to draw definitive conclusions. Additionally, this clinical trial used monotherapy, unlike our case where combination therapy with mefloquine and mirtazapine was administered. The clinical

response (functional and cognitive) seen in our patient after the initiation of combination therapy (mirtazapine and mefloquine) suggests additional studies in the form of randomized controlled trials in non–AIDS-related PML are needed to validate this therapeutic approach.

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Mastocytosis as an Unusual Cause of Hip Fracture in an Elderly Woman

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ABSTRACT

Mastocytosis is a type of myeloproliferative neoplasm characterized by accumulation and proliferation of morphologically and immunophenotypically abnormal mast cells in 1 or more organ systems. Clinical manifestations vary depending upon the organ involved and chemical mediators released by mast cells along with constitutional symptoms and musculoskeletal complaints. We report a case of isolated bone marrow mastocytosis in an 87-year-old woman who presented with a fall resulting in proximal femur fracture. Bone marrow biopsy revealed mastocytosis, and no evidence of systemic involvement or peripheral mastocytosis was found. Physicians should be aware of this entity, especially in patients with osteoporosis.

CASE PRESENTATION

An 87-year-old woman with significant medical history for osteopenia presented with a mechanical fall. She had been diagnosed with osteopenia 1 year previously and was treated with alendronate. Upon presentation, her physical examination was remarkable for limited painful motion in her left hip with superficial bruising. The initial workup was remarkable for anemia hemoglobin (Hgb 9.5 ng/dL). An x-ray of the left hip showed osteoporosis and a femur neck fracture with suspicion of a pathologic fracture. The patient underwent open reduction and internal fixation where a bone marrow biopsy was taken for pathologic fracture workup that showed hypercellular marrow (40%) with sheets of mast cells (Figure 1A). Granulocyte, erythroid, and megakaryocyte precursors were normal with normal maturation. An increase in mononuclear cells with round nuclei and numerous distinct metachromatic granules were noted. These cells had cytological and cytochemical features of mast cells. The Giemsa stain showed aggregates and diffuse infiltration of these mast cells. Immunohistochemical analysis was positive for leukocyte common antigen and CD15 and negative for pancytokeratin and S–100 stains. These cells also were positive for CD117 (Figure 1B), CD2 and CD25 expressions, tryptase, and aberrant mast cell phenotype by flow cytometry. The patient did not follow up after discharge, but presented to the emergency department a month later after another fall, where she was found to have right intertrochanteric and left tibial fractures. The patient was lost to follow-up after consultation with oncology (outpatient setting) when she opted for comfort care. Upon our review, we found that she later died.

DISCUSSION

Systemic mastocytosis (SM) is classified as a myeloproliferative neoplasm according to revised World Health Organization (WHO) classification 2008 for myeloid neoplasms.[1] SM is characterized by mast cell infiltration of extracutaneous organs like bone marrow, the gastrointestinal tract, liver, and spleen.[1,2] Cutaneous mastocytosis (CM) frequently presents in children under 2 years and regresses spontaneously in most of the cases.[3] Incidence of SM is about 5 to 10 per million,[4] and it typically manifests in the 5th to 8th decades of life.[5] Indolent systemic mastocytosis (ISM)—the most common form of SM—is slowly progressive, whereas aggressive systemic mastocytosis (ASM) is rare and typically presents with constitutional symptoms, organ dysfunction such as hepatic fibrosis and portal hypertension, malabsorption, cytopenias, or pathological fractures.[6] Smoldering systemic mastocytosis (SSM) is a type of ISM, characterized by high mast cell burden (> 30% of the bone marrow), high tryptase levels (> 200 ng/mL), liver or spleen enlargement without signs of hypersplenism or functional liver impairment, and subtle signs of myelodysplasia or myeloproliferation. Isolated bone marrow

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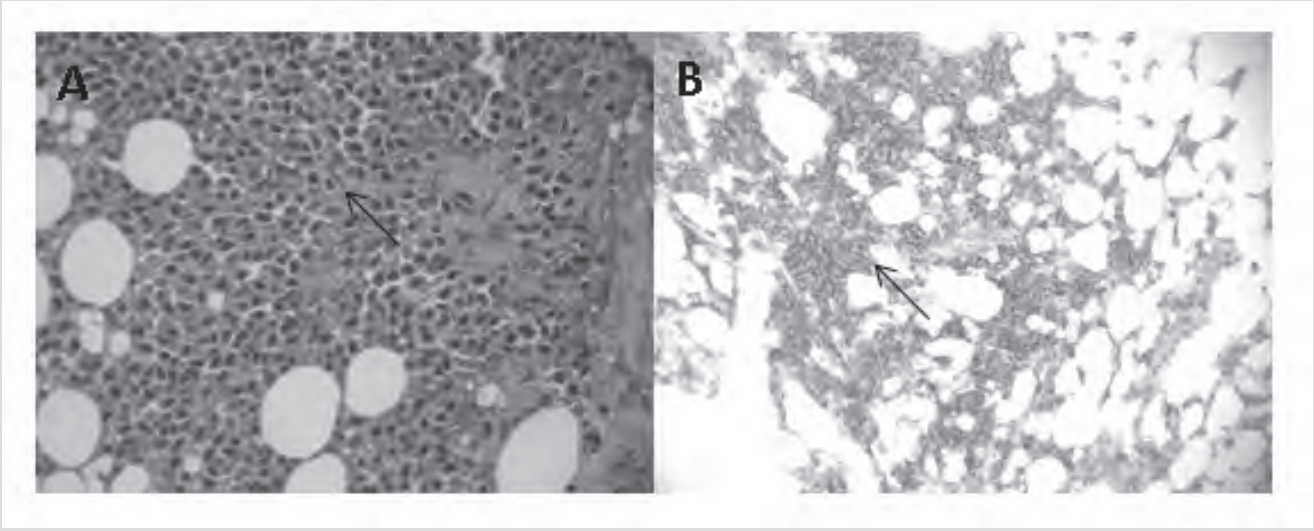
Figure 1. Hematoxylin and Eosin Stain of Bone Marrow Biopsy



mastocytosis (BMM) is also a type of ISM that involves the bone marrow without skin involvement and serum tryptase level is usually less than 30 ng/mL. Patients with BMM appear to be at increased risk of osteopenia and osteoporosis regardless of the age group.[7] The long bones and vertebrae are commonly affected in patients with SM, causing back pain, diffuse musculoskeletal pain, or a pain syndrome resembling fibromyalgia. Osteoporosis is thought to be due to effects of mast cell mediators such as histamine, heparin, and cytokines on bone.[8] Presentation of SM can be confused with metastatic lesions and require a bone marrow biopsy for diagnosis.

The diagnosis of SM is made by either presence of the major criterion and 1 minor criterion; or 3 minor criteria. The major criterion is detection of multifocal, dense infiltrates of mast cells (≥ 15 mast cells in aggregates) in sections of bone marrow and/or other extracutaneous organs. Minor criteria are more than 25% morphologically immature or atypical mast cells in the bone marrow, presence of KIT codon 816 mutation, expression of CD2 and/or CD25 by mast cells in addition to normal mast cell markers, and serum total tryptase more than 20 ng/mL.[7]

A bone densitometry is recommended for evaluation of osteoporosis, whereas skeletal scintigraphy is used to characterize the extent of disease.[9,10] Advanced imaging like multidetector computed tomography and magnetic resonance can be helpful when bone scintigraphy and densitometry are inconclusive.[5]

Prognosis and survival for SM are variable and depend upon the subtypes. ISM has better survival than other types, whereas ASM carries poor prognosis with 41 months median survival and 5% leukemic transformation.[2,7] Other poor prognostic factors include old age at onset, weight loss, high lactate dehydrogenase, high alkaline phosphatase, low hemoglobin levels, low albumin, low platelet count, hepatosplenomegaly, and ascites.[5,7]

Patients with ISM and stable SSM are treated with symptomatic management including histamine receptor blockers, glucocorticoids, epinephrine or immunotherapy, and bisphosphonates.[11] Cytoreductive therapy is used to inhibit mast cell proliferation in high grade SM variants,[6] whereas interferon α-2b plus prednisone is used as first-line therapy for ASM. Cardiotoxicity, thrombocytopenia, and depression are known adverse effects of interferon α-2b.[12] Cladribine, a purine analog chemotherapeutic agent has transient response and hence is used as a second-line treatment.[13] Tyrosine kinase inhibitors like imatinib, dasatinib, nilotinib, and midostaurin are used in patients with C findings where there is organ dysfunction; however, currently imatinib is the only Food and Drug Administration approved treatment specifically for ASM without KIT mutation. Other tyrosine kinase inhibitors currently are under investigation and their use is not recommended outside the clinical trials.[14] In young patients with suitable donor, hematopoietic stem cell transplantation (SCT) induces remission in advanced SM but has not been shown to improve survival.[15] Hydroxyurea is used for cytoreduction in resistant cases although data on efficacy of hydroxyurea in SM is limited.[16]

Our case of isolated bone marrow involvement was unusual due to old age at presentation, however, the case met major criterion (multifocal mast cells) and 2 minor criteria (positive for surface markers CD2, CD25 and greater than 25% of the tissue cells) confirming the diagnosis of systemic mastocytosis.

CONCLUSION

In summary, BBM represents a clinical challenge due to co-existence of osteoporosis and absence of cutaneous manifestations, especially in an elderly patient. SM should be considered in the

differential diagnosis of fracture of unknown origin in elderly patients with a high index of suspicion. Physicians should keep in mind mastocytosis as a plausible, but very rare cause of a long bone fracture, especially in patients with osteoporosis.

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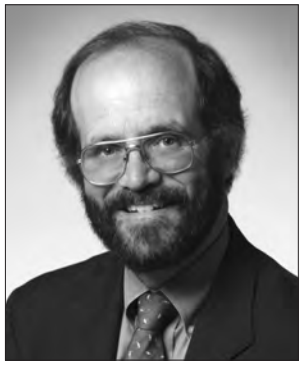
Richard Moss, PhD



Robert N. Golden, MD

Discovery, Education and Community Engagement—Foundations for Improving Public Health

Richard Moss, PhD; Robert N. Golden, MD

This is the second of two articles that describe the activities of the University of Wisconsin School of Medicine and Public Health's (SMPH) Wisconsin Partnership Program. The program represents a far-reaching commitment by the school to greatly improve the health of people in Wisconsin in the years to come. The Wisconsin Partnership Program—which is celebrating its 10th anniversary and recently released a plan for its next 5 years—includes two main, complementary committees: the Oversight and Advisory Committee (OAC) and the Partnership Education and Research Committee (PERC). SMPH faculty members chair the committees. Richard Moss, PhD, chairs the PERC; Patrick Remington, MD, MPH chairs the OAC. The first article was published in the August 2014 issue of WMJ *(volume 113, number 4).*

• • •

Richard Moss, PhD, is senior associate dean for basic research, biotechnology, and graduate stud-ies, University of Wisconsin School of Medicine and Public Health (SMPH); Robert N. Golden, MD, is dean of the SMPH and vice chancellor for medical affairs, UW-Madison.

In the decade since its 2004 inception, the Wisconsin Partnership Program (WPP) has allocated grant funds to research, education, and community partnerships designed to improve the health of state residents. In the August 2014 Dean's Corner, we summarized the impact of programs funded by the WPP's Oversight and Advisory Committee (OAC), which focuses on collaborative projects involving community and local government agencies and university faculty. This month, we describe the activities of the WPP's other arm, the Partnership Education and Research Committee (PERC), which focuses on research and education projects. This committee has awarded 137 grants totaling $99.3 million—a significant contribution to our vision of making Wisconsin a healthier state.

> Wisconsin faces substantive, entrenched public health challenges. The most effective responses require broad-based mobilization of stakeholders.

The PERC supports a remarkable breadth of meritorious programs, selecting those with the greatest potential impact on the health of people in Wisconsin. PERC grants aim to address issues of health and health care in a continuum that spans basic, clinical, translational, and applied public health research, as well as education and training and community interventions.

PERC Strategic Programs

The following strategic PERC programs are designed to launch new approaches to health and health care issues in response to emerging needs in the state.

The **Master of Public Health (MPH) Program,** which received start-up funding from the PERC, responds to the State Health Plan goal of developing a sufficient, competent, and diverse public health workforce. Two-thirds of its graduates have remained in Wisconsin and are working for local and government public health agencies, health care organizations, schools, and universities.

Transforming Medical Education (TME) is making significant progress toward more fully integrating public health into the educational experiences of our medical students and graduate medical trainees. Integrative cases comprise a particularly innovative component of

TME, which has developed 7 comprehensive case studies. With a cast of instructors from the SMPH and communities, students examine health issues from many perspectives, including public health, social and ethical issues, health care systems, clinical services, and basic science. The SMPH is widely considered to be among the nation's top programs for integrating public health into the curriculum.

The **Wisconsin Academy for Rural Medicine (WARM),** which received start-up funding from the PERC, is dedicated to increasing the number of physicians who will practice in rural Wisconsin. Fifty SMPH students have completed the WARM program, and more than 60% of them have entered Wisconsin residencies.

The Survey of the Health of Wisconsin (SHOW) collects data from healthy people across Wisconsin and makes the data available to researchers and public health officers to identify population health priorities and rigorously evaluate the effectiveness of state and community programs and policies in improv-ing population health. As examples, SHOW evaluated the effectiveness of the statewide smoking ban and partnered with the state of Wisconsin to obtain data and biological samples to measure mercury and polychlorinated biphenyl (PCB) levels in people who fish in the state. SHOW also is collaborating with community partners in Racine County on an application to the US Department of Housing and Urban Development for Promise Zone funding, a federal initiative focused on poverty-related challenges.

The **Health Innovations Program (HIP)** works to improve health care delivery and population health across Wisconsin through partnerships between UW faculty and Wisconsin health organizations. For example, together with the Wisconsin Collaborative for Healthcare Quality and the Wisconsin Institute for Healthy Aging, HIP hosts statewide educational events that focus on improving the quality of care for patients with diabetes and other high-priority chronic conditions.

Investigator-Initiated Research Projects

The PERC also features a robust portfolio of SMPH faculty-initiated research programs. The **New Investigator Program** provides opportunities for early-career faculty to initiate new, innovative pilot research projects that, if successful, can lead to more substantial extramural support from federal and other granting agencies.

The **Collaborative Health Sciences Program** supports established investigators in new programs of collaborative, interdisciplinary research focused on critical health problems that haven't yielded to traditional approaches. With PERC funding for initial feasibility studies, the best of these ultimately succeed in securing extramural funding and opening subfields of research such as antibiotic resistance in infectious diseases and early diagnosis of Alzheimer's disease.

Sustained Impact Through Leveraging

Much of the PERC grant funding is intended to support project initiation with the anticipation that sustainability will depend upon competitive extramural support for research or institutional support for educational initiatives. Overall, sustainability has been extraordinary: PERC-initiated projects have leveraged more than $220 million in extramural funding—more than double the total PERC grants that have been awarded.

OAC/PERC Joint Programs

Bringing the PERC and OAC resources together to support programs is a priority for both committees and reflects their shared purpose. For example, the OAC initiated the Lifecourse Initiative for Healthy Families (LIHF), which addresses the dramatic disparities in birth outcomes for African Americans in Beloit, Kenosha, Milwaukee, and Racine. In turn, the PERC became a partner in advancing this program and supported the appointment of a maternal and child health expert, Deborah Ehrenthal, MD, MPH. She provides faculty leadership in bringing together health care providers and public health leaders, and engaging community leaders and other stakeholders in a coordinated effort aimed at this concern through research, education, and community interventions.

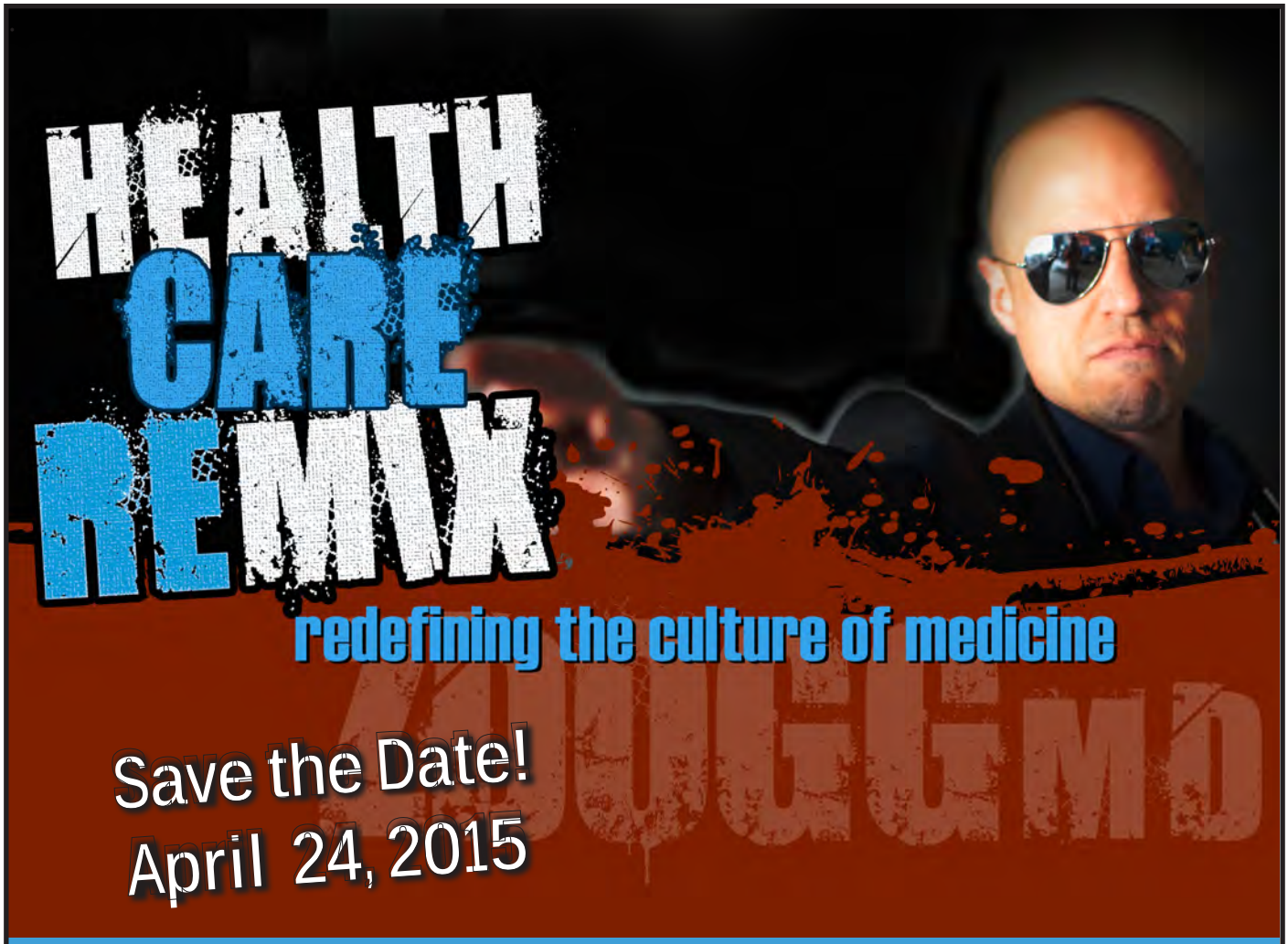
Another OAC/PERC collaboration—the Wisconsin Obesity Prevention Initiative—addresses one of the most challenging public health issues facing Wisconsin. The PERC established the program, and the OAC committed to support the development of community-level interventions to help prevent childhood obesity. This initiative brings together many organizations in the state that have been addressing obesity separately and provides an infrastructure to work together toward common solutions.

Other collaborations involve successful OAC community grants that then receive follow-up PERC support for research that tests and evaluates the generalizability of findings on a broad, statewide scale. An example of this approach is a fall-reduction intervention developed by Jane Mahoney, MD, professor of medicine, which received support for a larger scale study after a successful community pilot program.

Looking Ahead

Wisconsin faces substantive, entrenched public health challenges. The most effective responses require broad-based mobilization of stakeholders. Collaboration by the OAC and PERC on two of the most challenging public health issues—infant mortality among African Americans and the obesity epidemic—provide strong evidence of the SMPH's commitment through the Wisconsin Partnership Program to provide leadership in addressing difficult health problems.

The PERC also has devoted significant resources to innovative changes in education of the next generation of health care professionals. These innovations reflect our vision of integrating the fields of medicine and public health. At the same time, the PERC hopes to create an environment that nurtures close, collaborative partnerships between Wisconsin communities and our faculty. In this way, we hope to advance the health of the people of Wisconsin, and in doing so, serve as a national example that other states can emulate.



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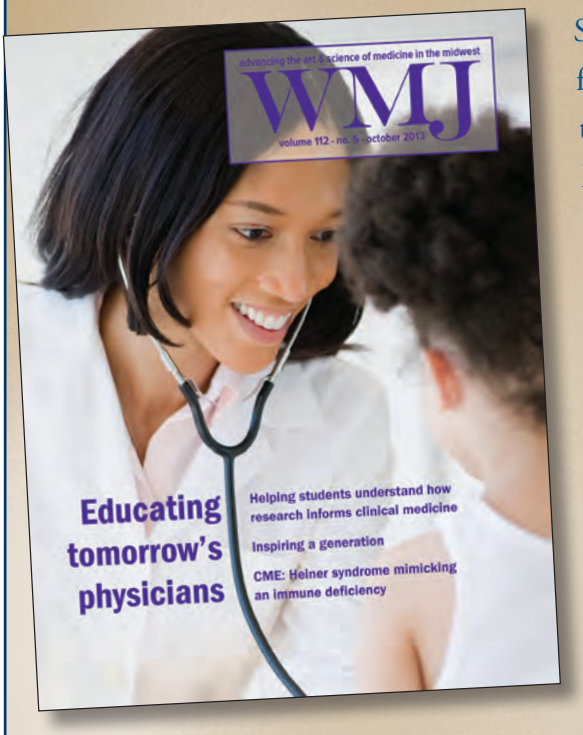

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