
Diagnosed and Possible Undiagnosed Asthma: A Wisconsin Research Network (WReN) Study

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Background. Adult-onset asthma is frequently encountered in primary care and is responsible for a large proportion of asthma morbidity and mortality. The primary goal of this survey was to describe the epidemiology of diagnosed and possible undiagnosed asthma in Wisconsin Research Network (WReN) practices.

Methods. Physicians from 59 practices interviewed a systematic sample of their clinical population, which included all patients encountered during office visits one day each week for 3 or 12 months, to obtain a history of physician-diagnosed asthma or symptoms suggesting undiagnosed asthma (wheezing and shortness of breath). Age at diagnosis or at onset of symptoms and current disease activity were also recorded.

Results. The 14,127 patients surveyed closely resembled the age-sex composition of the 1990 general and family practice component of the National Ambulatory Medical Care Survey. Physician-diagnosed asthma that was active within the previous year was reported by

6.1% of WReN patients (5.8% of patients younger than 20 years of age and 6.2% of adults). Undiagnosed asthma that was active within the previous year was reported by 3.3% (2.9% of patients younger than 20 years of age and 3.4% of adults). Adult-onset asthma was reported by 46.3% of all patients with diagnosed asthma; and 56.7% of patients with undiagnosed asthma reported that their symptoms began in adulthood.

Conclusions. Adult-onset asthma accounts for approximately one half of all asthma cases. Since most patients with adult-onset asthma are managed by primary care physicians, practice-based research is necessary for the understanding, treatment, and possible prevention of this important disease.

Key words. Asthma; epidemiology; research; respiratory sounds; respiration disorders; respiratory tract diseases; dyspnea; primary care research network. (*J Fam Pract* 1994; 38:373-379)

The recent Expert Panel Report from the National Asthma Education Program has focused attention on the increasing prevalence, morbidity, and possible underdiagnosis and undertreatment of asthma.¹ However, the panel has been criticized for excluding the perspective of family physicians and for eschewing an evidence-based process in formulating its report.² From an etiologic perspective, the Expert Panel Report generally overem-

phasized the importance of allergy in asthma^{3,4} and failed to discuss the evidence associating adult-onset asthma with antecedent pulmonary infection.⁵⁻⁷

Adult-onset asthma is frequently encountered in primary care, is responsible for more morbidity^{8,9} and mortality¹⁰⁻¹³ than childhood asthma, and is also more likely to persist and recur.^{14,15} More resources should be invested in research on the underlying cause, prevention, and treatment of this disease.

Studies on the initiation and prevention of adult-onset asthma must include patients with the earliest manifestations of reactive airway disease because, in the later stages of disease pathogenesis, initiating factors may be unrecognizable or no longer present. However, most

Submitted, revised, February 7, 1994.

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adults with early symptomatic asthma are cared for in primary care settings, and few are referred to tertiary care settings where most asthma research is currently performed.

With the conviction that adult-onset asthma is a "primary care disease," the Wisconsin Research Network (WReN) conducted a survey of physician-diagnosed asthma and possible undiagnosed asthma (wheezing and dyspnea) to determine the prevalence of asthma and to obtain an estimate of the age and sex composition of the patient population in participating WReN practices.

Methods

WReN is a collaborative association of over 550 primary care providers interested in primary care clinical research. About 90% of WReN members are family physicians. All WReN members who were active practitioners were invited to participate in this study. Fifty-nine physicians (57 located throughout Wisconsin and 1 each in Minnesota and Illinois) agreed to submit data for 3 months, and 18 of these physicians submitted additional data for 1 year, for a total of 14,127 patient interviews. All but three physicians completed their entire 3-month or 1-year obligation.

Participants were instructed to administer a brief verbal questionnaire to all office patients encountered during 1 day each week, to obtain information from parents of infants and children, and to avoid reinterviewing returning patients. A nurse or medical assistant usually performed the survey while obtaining vital signs. Completed survey cards were mailed weekly to a central office and entered into a computerized database. A telephone survey of a sample of participating nurses and medical assistants revealed no systematic difficulties with the interview process, which usually took less than 1 minute per patient.

Patients were asked if they had ever had a physician diagnosis of asthma or if they had ever experienced wheezing with shortness of breath. These questions were chosen because patient report of a physician diagnosis of asthma appears to be as valid and reliable as any other measure of this condition,^{5,15-17} and because wheezing with dyspnea without a physician diagnosis of asthma has been identified as a marker for undiagnosed asthma.⁵ The strength of agreement between patient report and patient medical record information is substantial ($\kappa > 0.6$) for asthma.¹⁸

The age and sex distribution of the WReN sample was compared with that of the 1990 Wisconsin population¹⁹ and with the 1990 general and family practice (GP/FP) component of the National Ambulatory Medi-

cal Care Survey (NAMCS), which is a representative nationwide sample of primary care patients encountered by general and family practice physicians in 1990.²⁰

Fisher's exact test and a chi-square test were used to analyze contingency tables, and an analysis of variance (ANOVA) was used to analyze age differences of subgroups. *P* values of less than .05 were considered significant.

This study was approved by human subject committees representing the University of Wisconsin Hospitals and Clinics and the Dean Foundation for Health, Research and Education, Madison, Wisconsin.

Results

Between August 1992 and July 1993, 14,127 patients (0.3% of the Wisconsin population) were interviewed. When compared with the population of Wisconsin, the WReN patient population was older (WReN median age, 37.0 years; Wisconsin, 32.9 years) and contained proportionately more women (WReN, 61.3%; Wisconsin 51.1%). However, the WReN sample closely resembled the age and sex composition of the 1990 GP/FP component of the NAMCS²⁰ (Figure). Comparisons revealed no statistically significant differences between the WReN sample and the NAMCS sample in proportional age distributions for men (*P* = .08), women (*P* = .06), or for both sexes combined (*P* = 0.15).

Of the 14,127 cards submitted, 13,542 (95.9%) contained sufficient information about the presence or absence of a history of asthma or wheeze to classify the patient with physician-diagnosed asthma, undiagnosed asthma, or no asthma. Inability to classify (4.1%) was a result of patient refusal to answer questions (3.6%) or missing data (0.5%). Refusers were similar to nonrefusers in sex composition but were older (refusers' mean age, 42.4 years; nonrefusers, 39.1 years, *P* = .005).

Based on the denominator of 13,542 classifiable patients, 10.3% reported having had a physician diagnosis of asthma at any time, and 6.1% stated that their asthma had been active within the previous year. Results for reported wheeze without a diagnosis of asthma were 6.5% (at any time) and 4.0% (active in the previous year). For the combination of wheezing and dyspnea (undiagnosed asthma), comparable figures were 4.9% (at any time) and 3.3% (active within the previous year). The combined prevalence of diagnosed asthma and undiagnosed asthma (wheeze and dyspnea) were 15.2% (at any time) and 9.4% (active within the previous year).

The cumulative prevalence of diagnosed asthma and the combination of diagnosed asthma and undiagnosed asthma were significantly greater (*P* < .001) in women

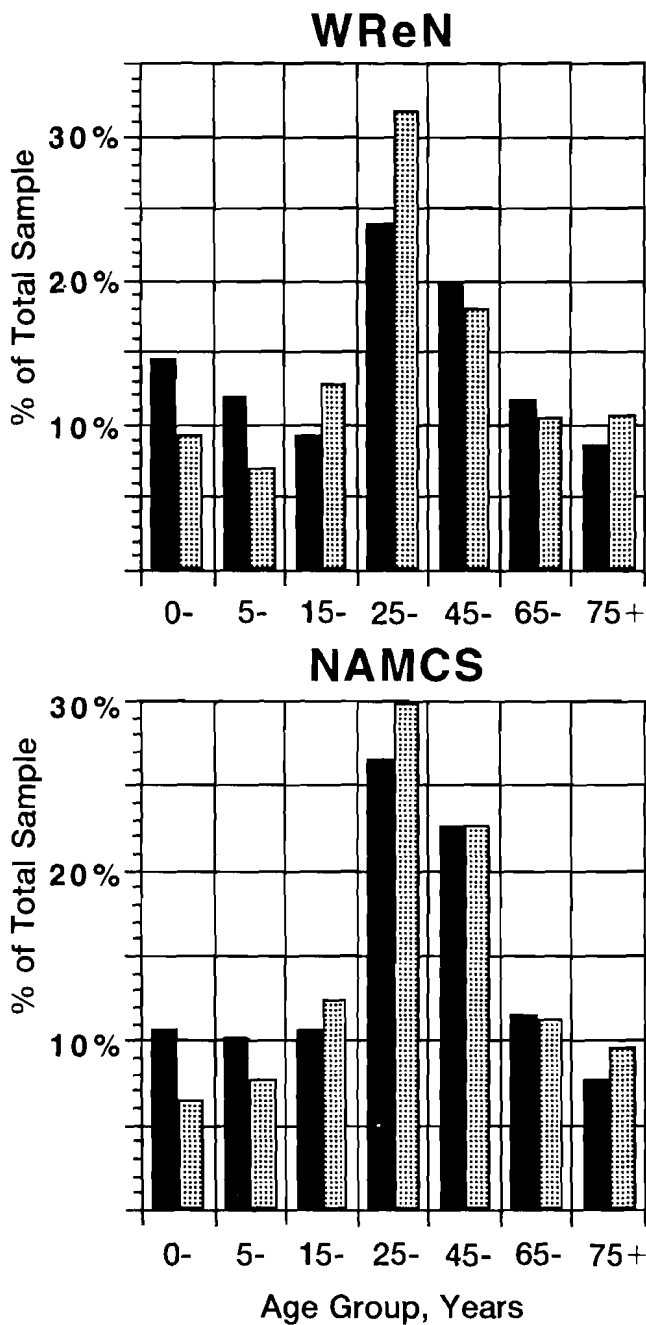


Figure. Age and sex composition of the patient populations in 59 participating practices of the Wisconsin Research Network (WReN) and of the general and family practice component of the 1990 National Ambulatory Medical Care Survey (NAMCS), a randomly selected group of primary care sites located throughout the US. The proportional age distributions of the two clinical populations were not significantly different for men ($P = .08$), women ($P = .06$), or for the group as a whole ($P = .15$). Solid bars denote men, stippled bars, women.

between 20 and 39 years of age than in younger or older female age groups but did not vary significantly by age for men (Table 1). Therefore, cumulative prevalence was

greater in young men than in young women, greater in middle-aged women than in middle-aged men, and greater in elderly men than in elderly women. Similar patterns of sex ratios were present when the analysis was restricted to disease activity within the previous year (Table 2).

Adults 20 years of age or older reported having had a physician diagnosis of asthma some time in their lives more frequently than did patients younger than 20 (10.7% vs 9.0%, $P < .005$), but the frequencies of currently active asthma were similar (5.9% vs 5.6%, $P = NS$). Currently active but undiagnosed asthma was present in 3.3% of adults and 2.8% of patients younger than 20 years of age ($P = NS$).

Of those reporting age at diagnosis or symptoms of possible asthma, 46.1% stated that their diagnosis was made after age 20, and 57.3% of undiagnosed patients reported not having symptoms until adulthood (Table 3).

Discussion

This large WReN sample of family practice outpatients representing a patient population served by 59 physicians was similar in age and sex composition to the GP/FP component of NAMCS, a large random national sample of primary care outpatients.²⁰ Resemblance between the WReN and NAMCS samples suggests that simple systematic sampling in a busy clinical setting may effectively capture a generalizable patient population, provided the sample is large.

The survey revealed that asthma is prevalent in primary care outpatients. Over 10% of patients reported a physician diagnosis of asthma some time in their lives, 5% reported experiencing wheezing and shortness of breath (our criteria for undiagnosed asthma) at some time, and an additional 1% to 2% reported some wheezing without shortness of breath. Overall, nearly 17% of patients in this study reported a history that could have represented asthma at some point in their lives. Because other asthmatic symptoms, such as persistent nocturnal cough or exercise-induced dyspnea, were not pursued, it is possible that the cumulative prevalence of asthma in this clinical sample may have been underestimated.

Many studies have documented that asthma is underdiagnosed in primary care.²¹ Our results, which show a 3% to 4% prevalence of active wheeze and shortness of breath, support this conclusion. It has been suggested that enhanced recognition of undiagnosed asthma will produce better patient outcomes,¹ but testing is needed to verify this hypothesis. Not all underdiagnosis is caused by physician misinterpretation of reported patient symp-

Table 1. Age and Sex Distribution of Patients with a History of Physician-Diagnosed Asthma, Undiagnosed Asthma (Wheezing with Shortness of Breath), or Either One of These

Age Group, y	Sex Distribution*		Diagnosed Asthma, %		Undiagnosed Asthma, %		Total, %	
	Men (n)	Women (n)	Men	Women†	Men	Women	Men	Women†
0-19	1840	1674	10.1	7.5	4.3	3.7	14.4	11.2
20-39	1083	2648	10.3	11.5	4.4	5.0	14.7	16.5
40+	2466	3800	9.3	9.6	5.7	4.5	15.0	14.1

*Fewer than the 13,542 patients classified with diagnosed asthma or undiagnosed asthma because of missing data concerning disease activity.

†Prevalence varies significantly ($P < .001$) among age groups for women with diagnosed asthma and for women with diagnosed asthma and undiagnosed asthma combined.

toms, since patients with significant respiratory symptoms and pulmonary function abnormalities may not consult physicians for these problems.

Between-study comparisons of asthma prevalence are difficult to interpret because of differences in study populations and the lack of standard epidemiologic definitions of asthma.^{22,23} Nevertheless, our findings concerning active asthma and possible asthma resemble those of other studies. Between 5% and 6% of children in our study had active physician-diagnosed asthma, and an additional 2% to 3% reported active symptoms of wheeze and dyspnea, which we classified as undiagnosed asthma. These results are comparable to those of a review of studies of asthma prevalence in Europe and North America: asthma occurs in about 5% of children, rising to 10% if other wheeze is included in the definition.²⁴ Our study found that among adults, the prevalence of active asthma is almost 6% and the prevalence of active undiagnosed asthma is more than 3%. Summary estimates for adult asthma prevalence in Europe and North America are 3% to 5%, and around 9% if other wheeze is included.²⁴

In contrast to most other studies,²⁴ asthma prevalence was slightly greater for adults than for children in the WReN sample. Some children with asthma, who are seen exclusively by pediatricians or pediatric subspecial-

ists such as allergists or pulmonologists, were not identified in our survey. This may explain the difference, since it is likely that a greater proportion of children than adults with asthma are seen exclusively outside primary care offices.

The age of onset of asthma is an important epidemiologic variable relating to possible underlying cause.^{25,26} Therefore, we analyzed patient self-reports of age at diagnosis or symptom onset and found that approximately one half of patients with asthma or possible asthma reported adult-onset disease (Table 3). However, these reports require cautious interpretation. The validity of patient report of age at which diagnosis was made or symptoms of asthma began is uncertain because of recall bias, the likelihood that asthma was present long before the diagnosis was made, and the possibility that asthma was present long before the patient noticed symptoms.^{27,28} The age-specific pattern for reported onset of diagnosis or symptoms in the WReN study closely resembles the age-incidence pattern reported by Dodge and Burrows⁵ in their prospective, longitudinal study of asthma.⁵

The WReN age-at-onset pattern is distinctly different from that of another clinical population in our region reported by Yunginger and associates²⁹ who concluded that most asthma begins in childhood. This conclusion

Table 2. Age and Sex Distribution of Patients with a History of Active (Within the Previous Year) Physician-Diagnosed Asthma, Undiagnosed Asthma (Wheezing with Shortness of Breath) or Either One of These

Age Group, y	Sex Distribution*		Diagnosed Asthma, %		Undiagnosed Asthma, %		Total, %	
	Men (n)	Women (n)	Men	Women†	Men†	Women	Men	Women†
0-19	1840	1674	6.4	4.8	2.7	2.6	9.1	7.4
20-39	1083	2648	4.6	6.9	2.8	3.3	7.4	10.2
40+	2466	3800	5.4	5.7	4.0	3.0	9.4	8.7

*Fewer than the 13,542 patients classified with diagnosed asthma or undiagnosed asthma because of missing data concerning disease activity.

†Prevalence varies significantly ($P \leq .01$) among age groups for women with diagnosed asthma and for women with diagnosed asthma and undiagnosed asthma combined. For men with undiagnosed asthma, prevalence also varied significantly ($P = .04$) among age groups.

Table 3. Reported Age at Diagnosis of Asthma or Age at Onset of Symptoms of Undiagnosed Asthma

Age at Diagnosis of Asthma or at Onset of Symptoms of Undiagnosed Asthma, y	Diagnosed Asthma, % of Total (No.)		Undiagnosed Asthma, % of Total (No.)	
	Men	Women	Men	Women
0-19	61.8 (296)	49.0 (380)	45.5 (107)	40.7 (136)
20-39	15.4 (74)	29.3 (227)	20.4 (48)	30.2 (101)
40+	22.8 (109)	21.8 (169)	34.0 (80)	29.0 (97)
All ages*	100.0 (479)	100.0 (776)	100.0 (235)	100.0 (334)

*Includes patients with diagnosed asthma or undiagnosed asthma for whom there were sufficient data to allow classification. Percentages may not add to 100 because of rounding off.

was based on a retrospective review of medical records; patients were not interviewed for a history of undiagnosed asthma. Our results, which show that more adults than children reported a history of undiagnosed asthma, suggest that conclusions based solely on medical record review may miss more adult than childhood asthma, as children seem more likely to be taken to a physician and to have the diagnosis recorded. The Yunginger study also excluded adults with significant airway obstruction, but, since fixed obstruction is associated with adult-onset asthma,³⁰ this exclusion would tend to underestimate the incidence of adult-onset asthma. Compared with patient interview, studies based solely on medical record review may underestimate asthma prevalence and incidence to a greater degree, particularly in adults.

The sex differences noted in our study are consistent with previous data but remain largely unexplained. Regarding asthma prevalence and age of onset, the patterns of male predominance in childhood and female predominance in early and middle adulthood reported here are the same as those found in other epidemiologic studies of asthma incidence,^{5,29} prevalence,^{31,32} morbidity and hospitalization,³³ and temporal increases in asthma.³⁴⁻³⁶ It has been noted that whereas adult women tend to be diagnosed with asthma, men with the same symptoms may be diagnosed with chronic obstructive pulmonary disease (COPD).⁵ This diagnostic bias probably explains some of the sex differences noted for asthma. It does not seem likely, however, that diagnostic bias could account for similarities in sex ratio patterns in the asthma measures documented from many countries with presumably different diagnostic habits. Furthermore, diagnostic bias cannot explain differences in sex ratio patterns found in the current study for undiagnosed asthma. Sex differences may be a clue to the underlying pathophysiology of asthma, but the role they play is not fully understood.

The cause of adult-onset asthma is unknown, but a growing body of evidence suggests a possible causal association with chronic atypical pulmonary infection.³⁷ Antecedent respiratory illness has been associated with

adult-onset asthma in a prospective, population-based study,⁵ and bronchitis has been associated with subsequent asthma in recent clinical studies.^{6,7} Adult-onset asthma is not associated with aeroallergen skin-test positivity,^{16,38-40} but is associated with IgE antibody and eosinophilia,^{16,38,39} suggesting that an unidentified antigen or antigens, perhaps produced by chronic pulmonary infection, play a causative role in adult-onset asthma.^{38,41}

Chlamydia pneumoniae is an atypical intracellular pathogen capable of causing acute respiratory illnesses including pneumonia, bronchitis, sinusitis, otitis, laryngitis, and pharyngitis.⁴²⁻⁴⁴ Several studies suggest that chronic *C pneumoniae* infection may be a causal factor in adult-onset asthma.^{41,45-47} Furthermore, *C pneumoniae* infection may be contributing to the increase in asthma prevalence noted in recent decades.^{46,48} Most patients with adult-onset asthma beginning after age 40 have been seropositive for *C pneumoniae*,^{37,41,45} and case reports^{45,46} and a case series⁴⁷ suggest that some patients with this type of asthma will respond to prolonged antichlamydial antibiotic therapy. These preliminary findings support the hypothesis that nonatopic adult-onset asthma may be related to chronic chlamydial infection.

Recognition that chronic inflammation plays an important role in asthma pathophysiology has led to important advances in the palliation of asthma symptoms.¹ Research on the initiating factors for asthma may lead to more effective treatments or even preventive strategies, but it will require further study of asthma in its earliest stages. Most current asthma research is performed on patients with long-standing, established disease and is focused "downstream" on the consequences of the inflammatory cascade in the asthmatic lung. WRcN and other primary care research consortia are a good resource for the study of earlier manifestations of asthma, focusing on the source rather than the consequences of asthma.

Future WRcN asthma research will confirm clinical diagnoses of asthma in patients derived from a broad-based population, producing a combined methodology

of clinical assessment and epidemiology unique to primary care network research.

Acknowledgments

This study was supported by the Dean Foundation for Health, Research and Education, Madison, Wisconsin.

We wish to thank Mary Stone for her administrative assistance, and Barbara Tenor Livingston (posthumously) for study coordination.

Wisconsin Research Network (WRcN) participants in the Asthma Prevalence Study include:

Jerome Andres, MD, and Ivy Will, Mosinee; Jose Angoncillo, MD, and Joyce Jackson, West Allis; Roy Balder, MD, and Linda Chute, Elroy; Adam Balin, MD, Oregon; Elizabeth Barr, MD, Mosinee; Daniel Barry, MD, Madison; Dennis Baumgardner, MD, and Avis Christopherson, Milwaukee; John Beasley, MD, and Karen Armstrong, Verona; Lou Beltran, MD, and Sabrina Florzak, Elm Grove; William Benn, MD, and Joan Hoppe and Cindy Wizen, Rosholt; Tim Bjelland, MD, and Sally Von Ruden, Mauston; Rebecca Bull, MD, and Kay Schott, Madison; Robert Cape, MD, and Brenda Kluever, Madison; Bruce Carlson, MD, and Judy Senn and Susan Rogers, LaCrescent, Minnesota; Anthony Chen, MD, and Anita Foster, Hinsdale, Illinois; William Cooke, MD, and Jan Hooker and Brenda Hasburg, Richland Center; Barbara Crapster-Pregont, MD, and Patty Folta, Merrill; Doug DeLong, MD, and Debbie Stiner, Ladysmith; Dan Erickson, MD, Horicon; Michael Faudree, MD, and David Kohls, Black Creek; Beth Gillis, MD, and Debra Retzlaff, Tigerton; Kay Gruling, MD, and Heidi Borchardt, Marathon; Ted Haglund, MD, and Kathy Day, Madison; David Hahn, MD, and Carol Pribbenow, Madison; Terry Hankey, MD, and Kathy Bower, Waupaca; Cynthia Haq, MD, and Eloise Anderson, Belleville; Kay Heggestad, MD, and Judy Poellmann, Madison; Glen Heinzl, MD, and Virginia Jaeger, Wausau; David Hoffmann, MD, and Sandi Radcliffe, Mauston; William Hopkins, MD, and Diane Larson, Owen; David Kirby, MD, and Denise West, Madison; Geoff Kloster, MD, and Mary Klonecki, Galesville; Steven Kream, MD, and Tina Becherer, Milwaukee; Dean Kresge, MD, Stoughton; Robert Kriz, MD, and Pat Staven, Madison; David Kuter, MD, and Mary Noss, Baraboo; Gerry Larmor, MD, and Sue Raboine, Burlington; Donna Lawlor, MD, and Rosemary Martin, Harvard, Illinois; Margaret Leonhardt, MD, and Tammy Randa, Hales Corners; Rick Lewan, MD, and Barbara Murphy, Waukesha; Richard London, MD, and Theresa Osterman, Milwaukee; Thomas Looze, MD, and Barbara Heberer, West Bend; Dannen Mannschreck, MD, and Rita Frederick, Lancaster; Maureen Murphy-Greenwood, MD, and Merry Schultz, Wisconsin Dells; William Nietert, MD, and Nancy Stefoniak, Mosinee; Lori Neumann, MD, Darlington; David North, MD, and Sharon Aschbrenner, Wausau; Doug Olmanson, MD, and Marge Johns, Wausau; Cheri Olson, MD, and Sally Olson, LaCrosse; David Olson, MD, and Sharon Patterson, Elm Grove; David Onsrud, MD, and Pat Ebner, LaCrosse; Judith Pauwels, MD, and Sandy Moore, St. Croix Falls; Thomas Peterson, MD, and Virginia Jaeger, Wausau; Leon Radant, MD, and Julie Christenson, Mauston; Dan Sherry, MD, and Melanic Galle, Ellsworth; James Siepmann, MD, Oshkosh; Alan Strobusch, MD, and Karla Dobberstein, Waupaca; Rose Varona, MD, and Helga Hoffman, Milwaukee; Ren Whitaker, MD, and Joanne Ferguson, Prairie du Chien.

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