

Epidemiologic Trends in Infection, Mortality, and Transplants Related to Hepatitis C in Wisconsin

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ABSTRACT

Hepatitis C virus (HCV) infection is the most common chronic bloodborne infection in the United States. An estimated 3.9 million persons nationally and 85,000 persons in Wisconsin are currently infected. The disease is responsible for approximately 8000 to 10,000 deaths nationally each year.

This article summarizes epidemiologic trends in infection, mortality and transplants related to HCV in Wisconsin. It presents surveillance data collected during 1997-2004; HCV-related deaths during 1995-2002, with HCV as an underlying or contributing cause of death; and data for liver transplants related to HCV between 1993 and 2004. During the time periods reviewed, there were 16,668 cases of HCV infection reported, 1186 HCV-related deaths, and 356 HCV-related liver transplants involving HCV in Wisconsin.

Infection rates and related adverse health outcomes related to HCV are highest in males, persons ages 35-64, Milwaukee residents, and inmates in the state correctional system. African Americans have high rates of morbidity (24% of cases) and mortality (16% of decedents), but are under-represented among recipients of HCV-related transplants (6% of recipients).

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Between the first and second half of the periods reviewed, there was an increase in the number of reported infections (112%), a result of improved detection and reporting. Increases in the number of deaths (70%) and transplants (118%) are a consequence of aging and disease progression in a population infected in previous decades.

BACKGROUND

Hepatitis C virus (HCV) infection is the most common chronic bloodborne infection in the United States: an estimated 3.9 million Americans (1.6%) are HCV antibody positive.^{1,2} If the prevalence of HCV infection in Wisconsin is the same as that of the nation, it is possible that 85,000 Wisconsin residents have current or past HCV infection. This is roughly equivalent to the number of persons who reported ever having had a stroke.³ HCV accounts for approximately 8000-10,000 deaths nationally each year.⁴

Prospective studies have shown that 60%-80% of persons with HCV infection fail to resolve the infection,⁵ and that 15%-20% of persons with chronic HCV infection have progressive liver fibrosis leading to cirrhosis, end-stage liver disease, and hepatocellular carcinoma. Nationally, HCV-associated end-stage liver disease is the most frequent indication for transplantation among adults,⁶ accounting for 40%-50% of liver transplants.⁷ There was a 5-fold increase in the annual number of patients with HCV who underwent liver transplantation in the United States between 1990 and 2000.⁸

This article summarizes the epidemiologic trends of HCV infection in Wisconsin using surveillance data collected during 1997-2004, HCV-related mortality for the period 1995-2002, and HCV-related liver transplants during 1993-2004.

METHODS

Hepatitis C Infection

This summary includes all confirmed cases of hepatitis C infection reported between January 1, 1997 and

December 31, 2004. A confirmed case is anti-HCV-positive by enzyme immunoassay with a signal-to-cut-off ratio ≥ 3.8 ; or anti-HCV-positive by recombinant immunoblot assay; or HCV ribonucleic acid-positive by polymerase chain reaction, or has a detectable viral load, or an identified HCV genotype.^{9,10} To be included, cases must have been reported to the Department of Health and Family Services (DHFS), as required by law; be confirmed; and subjects should be presumed to be living. The Wisconsin Hepatitis C Program conducts surveillance for HCV infection under the authority of Wisconsin State Statute 252.05, Stats. and Wisconsin Administrative Code HFS 145.04, which require hospitals, laboratories, and health care professionals to report cases of HCV infection to the local health officer. Year 2000 census data were used to calculate prevalence rates.

Hepatitis C Mortality

The article also reports on Wisconsin death certificate data for 1995-2002 with mention of an International Classification of Diseases (ICD) code related to HCV as either an underlying or contributing cause of death. Deaths for the years 1995-1998 use ICD-9 codes (070), those for 1999-2002 use ICD-10 codes (b171 and b182).

Hepatitis C-Related Liver Transplants

Finally, transplant data were obtained from the United Network for Organ Sharing (UNOS) Organ Procurement and Transplantation Network (OPTN) Web site.¹¹ UNOS administers the nation's only network for organ procurement and transplantation and collects and manages data about every transplant event occurring in the United States.

OPTN data were queried regarding transplants of all organs and of livers for the period 1993-2004. Data were obtained for Wisconsin by diagnosis, by year, and by demographic characteristic. On the advice of medical staff at OPTN, the review of HCV-related liver transplants included diagnoses of Acute Hepatitis Necrosis: Type C; Cirrhosis Type C; Cirrhosis Types B and C; Cirrhosis: Chronic Active Hepatitis: Etiology Unknown; and Alcoholic Cirrhosis with Hepatitis C.¹²

RESULTS

Hepatitis C Infection

From 1997 through 2004, a total of 16,668 confirmed cases of HCV infection were reported. The number of cases reported annually doubled from an average of 1335 cases in 1997-2000 to an average of 2832 cases in 2001-2004 (Figure 1). The cumulative overall prevalence of reported cases was 311 per 100,000 population.

Table 1 shows the distribution of cases and rates per 100,000 population by gender, age group, race/ethnicity,

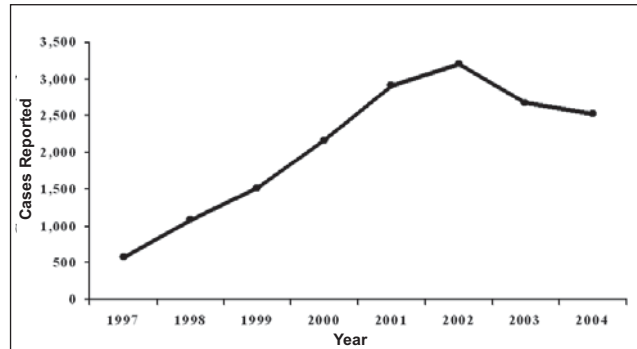


Figure 1. Reported cases of confirmed hepatitis C virus infections among Wisconsin residents, 1997-2004.

Table 1. Hepatitis C Virus Infections and Rates per 100,000 Population by Gender, Age, Race/Ethnicity, and Jurisdiction for Counties with 200 or More Cases, Wisconsin, 1997-2004

	% of Wis. Pop.	% of Cases*	No. of Cases	Rate†
Total	100%	100%	16,668	311
Gender				
Female	51%	32%	5272	193
Male	49%	68%	11,250	423
Age Group				
0-19	29%	1%	146	9
20-29	13%	4%	668	96
30-39	15%	21%	3550	439
40-49	16%	48%	7950	943
50+	28%	26%	4260	281
Race/Ethnicity				
Asian/Pacific Islander	2%	1%	53	52
African American	6%	24%	2328	713
Hispanic	4%	6%	534	278
Native American	1%	2%	152	219
White	85%	67%	6447	134
Other	2%	0%	45	43
Correctional System	—	16%	2732	—
County of Origin (counties with more than 200 cases)				
Milwaukee	18%	36%	4575	487
Dane	8%	8%	965	226
Racine	4%	5%	671	355
Waukesha	7%	4%	498	138
Kenosha	3%	4%	476	318
Rock	3%	4%	472	310
Brown	4%	3%	379	167
Winnebago	3%	3%	342	218
La Crosse	2%	2%	291	272
Walworth	2%	2%	236	257
Outagamie	3%	2%	225	140

* Percent of total cases where demographic characteristics are known.

† Rate is per 100,000 population.

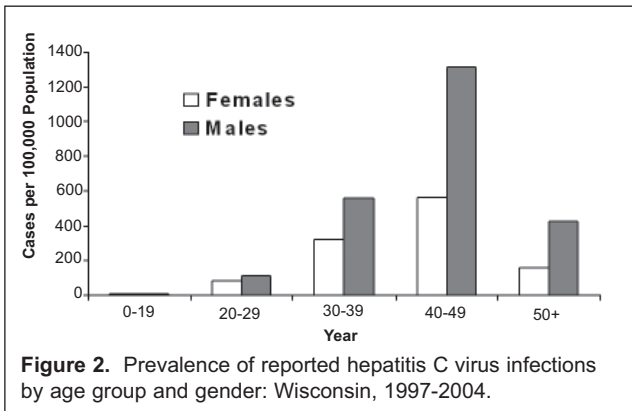


Figure 2. Prevalence of reported hepatitis C virus infections by age group and gender: Wisconsin, 1997-2004.

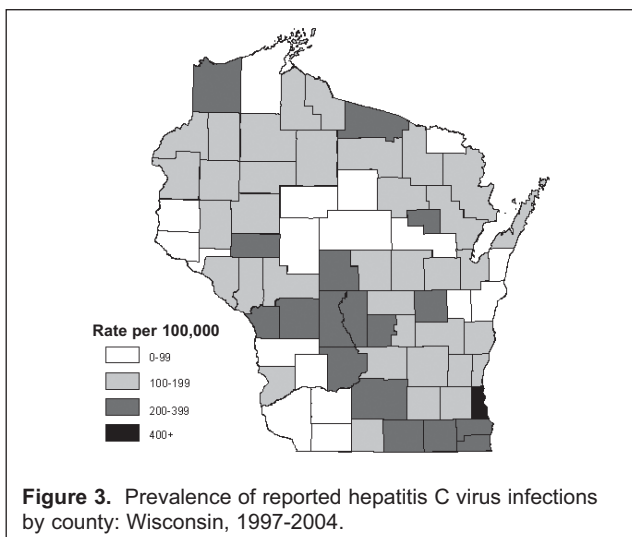


Figure 3. Prevalence of reported hepatitis C virus infections by county: Wisconsin, 1997-2004.

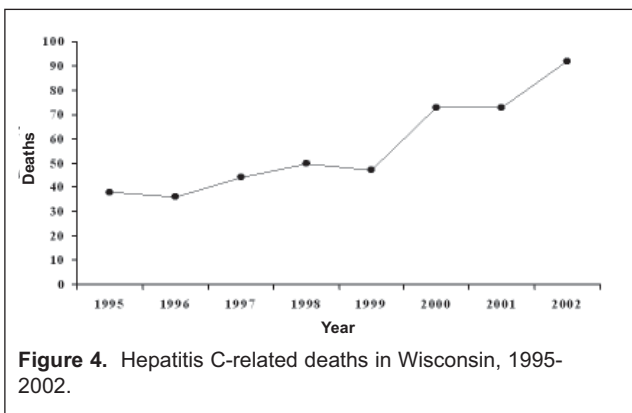


Figure 4. Hepatitis C-related deaths in Wisconsin, 1995-2002.

and jurisdiction for the state correctional system and counties with more than 200 cases.

The overall prevalence in rate of reported HCV infection per 100,000 population was twice as high among men (423) as among women (193) and peaked among persons in the 40-49 year age group (943). In this age group, the prevalence of reported HCV infection among men (1318) was 3 times higher than among men of all age groups (Figure 2).

The rate of HCV infection per 100,000 population was 5-fold higher among African Americans (713), 2-fold higher among Hispanics (278) and 1.6-fold higher among Native Americans (219) compared to whites (134) (Table 1).

The prevalence of reported HCV infection was highest in Milwaukee County (487 per 100,000), at 1.6 times the statewide rate; it exceeded by 28% the county with the next highest rate (Figure 3).

More than 16% (2732) of the reported cases of HCV infection occurred among persons residing in the state correctional system. The number of cases reported annually among persons living in the state correctional system increased 3.5-fold from an average of 161 cases from 1997-2000 to 570 cases 2001-2004.

Hepatitis C Mortality

During 1995-2002, there were 1186 HCV-related deaths in Wisconsin. HCV-related deaths increased by 70% between the first and second half of the 8-year period (Figure 4).

Decedents were predominantly male (72%) and had a mean age of 55.6. Whites accounted for the majority of decedents (82%), although the rate per 100,000 population for African Americans (3.7) was 3 times higher than for whites (1.2). Rates also increased much more sharply between the first and second half of the period among African Americans (165%) than among whites (59%). Hispanics comprised 2% of HCV-related decedents for 1999-2002, compared to 3.6% of the state's population. Data for other racial groups were not available.

Hepatitis C-Related Liver Transplants

There were 7949 organ transplants in Wisconsin from 1993 through 2004. Of these, 17% (1378) were liver transplants and 11% (150) of these were repeat transplants. One quarter (356) of the liver transplants were HCV-related. Of HCV-related transplants, 41% (145) were alcoholic cirrhosis with HCV. Reasons for liver transplant unrelated to HCV include alcoholic cirrhosis, cholestatic liver disease, biliary atresia, metabolic diseases, and malignant neoplasms.

Liver transplants increased steadily from 1993 to 2004, with a peak of 162 transplants in 2002, as shown in Figure 5.

To assess the role that hepatitis C infection played in the rate of increase in transplants, a comparison was made between causes of organs transplanted in each of 2 6-year periods: 1993-1998 and 1999-2004. Between the 2 time periods, liver transplants due to HCV increased by 118%, compared to much smaller increases in transplants of all organs (18%), and of livers, all causes excluding HCV (16%).

Table 2 shows the demographic characteristics of the 356 Wisconsin recipients of liver transplants from 1993 to 2004 where HCV was the cause of liver failure. HCV-related transplant recipients are predominantly male (74%); persons ages 35-64 account for 95% of transplants. Whites comprise the majority of recipients (80%), followed by Hispanics (11%), African Americans (6%), and persons of other races/ethnicities (3%).

DISCUSSION

Hepatitis C Infection

During the last 6 years, HCV infection has become one of the most frequently reported communicable diseases in Wisconsin. Recent increases in the number of reported cases of HCV infection are primarily due to increases in testing and changes in case reporting.

Requests for HCV tests from the State Laboratory of Hygiene have increased in recent years, a trend also detected in national data.⁴ Expanded testing appears to have resulted from greater awareness of HCV infection screening and testing recommendations among health care professionals and the public.⁴ Routine testing of incoming inmates, instituted in Wisconsin in 2000, is responsible for increases in reported cases among persons incarcerated in Wisconsin Department of Corrections facilities. Federal guidelines provide information regarding testing and treatment of hepatitis C infection in correctional facilities.¹³

Improved guidance from DHFS regarding HCV reporting also contributed to more complete disease reporting practices among health care organizations and professionals. DHFS intensified case surveillance in the late 1990s by publishing a case definition with specified laboratory criteria.⁹ The Department also facilitated reporting by including HCV serology results with checkbox options on the Acute and Communicable Disease Case Report form (HFS 4151) in 2001.

It is unlikely that the increase in the number of reported cases of HCV infection is due to an increase in the number of new HCV infections in the state. Many of the persons diagnosed in recent years were infected in the 1970s and 1980s. Because acute HCV infection is usually asymptomatic and rarely diagnosed, incidence data on HCV infection in Wisconsin are unavailable. Nationwide, however, the incidence of HCV infection has declined since 1990⁴ and there is no reason to believe that this trend differs in Wisconsin.

The prevalence of reported HCV infection by gender and age group in Wisconsin is consistent with national data on HCV infection. A recent analysis of data from the current National Health and Nutrition Examination

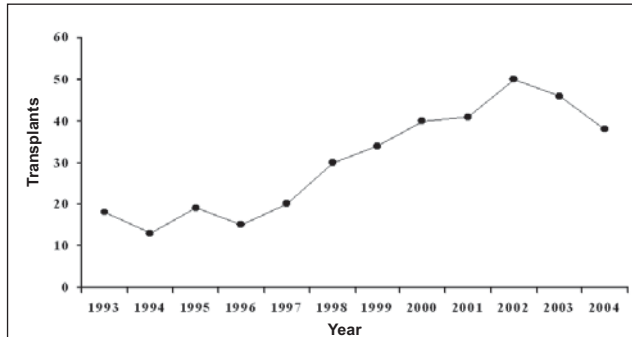


Figure 5. Hepatitis C-related transplants in Wisconsin, 1993-2004.

Table 2. Demographic Characteristics of Liver Transplants Recipients with Hepatitis C Diagnosis, Wisconsin, 1993-2004

	HCV-Related Transplants	
	No.	%
Total	356	100%
Sex		
Female	91	25.6%
Male	265	74.4%
Age		
0-17 Years	0	0.0%
18-34 Years	2	0.6%
35-49 Years	193	54.2%
50-64 Years	144	40.4%
65+	17	4.8%
Race		
Asian/Pacific Islander	5	1.4%
African American	21	5.9%
Hispanic	38	10.7%
Native American	6	1.7%
White	284	79.8%
Multiracial	2	0.6%

Survey conducted during 1999-2002 determined that the prevalence of HCV infection was higher among males (2.1%) than females (1.1%); higher among African Americans (3.0%) than whites (1.5%); and highest among those in the 45-49 year age group.²

Milwaukee County bears a disproportionate burden of HCV infection. The county accounts for 17% of the state's population but has 36% of HCV cases where jurisdiction is known and where cases from the correctional system are excluded. Milwaukee has the largest proportion of residents with a history of injection drug use, with an estimated 4700 injectors in the Milwaukee-Waukesha area.¹⁴ Five of the state's 12 methadone maintenance programs, and 60% of the state's 2000 clients reside in Milwaukee County. Milwaukee also has the largest African American population, 24.6%, compared

to 5.7% in the state as a whole. In addition, it is also possible that proportionally more private and public health care professionals in Milwaukee County have instituted HCV screening and testing activities, thus identifying a greater proportion of people with HCV.

The analysis of HCV surveillance data is limited by the extent of testing and completeness of reporting, which vary significantly among health care facilities. In addition, laboratories, which report the majority of cases of HCV infection, do not generally report demographic data such as region or race, so fully 43% of cases during the period were reported without an identified race. Finally, risk factors, such as shared injection equipment or blood transfusions prior to improvements in protecting the blood supply, are not routinely reported.

HCV-Related Deaths

Deaths related to HCV continue to increase, and in 2002, for the first time in Wisconsin, the number of deaths related to HCV (92) exceeded the number related to HIV (84).¹⁵ The increase in HCV-related deaths is primarily due to aging and disease progression in a population infected with HCV several decades ago. Although there is now effective treatment for patients with chronic HCV infection that achieves sustained virologic response in 54%-56% of treated cases, many patients are unaware of their infection, are not candidates for treatment, are unable to complete treatment, or fail to respond.¹⁶

When comparing deaths for the 2 time periods, 1995-1998 and 1999-2002, it is important to note that the earlier period used ICD-9 codes, whereas the later period used ICD-10 codes. Data on comparability of the 2 sets of codes are available for these and other causes of death¹⁷ but the comparability rates address the underlying cause of death, whereas our analysis included any mention of HCV on the death certificate.

Hepatitis C-Related Liver Transplants

The number of liver transplants related to HCV infection increased markedly (118%) between the period 1993-1998 and 1999-2004 compared to much smaller increases for transplants of all organs (18%) and of livers, all causes excluding HCV (16%). This indicates that the demand for livers due to HCV infection was far greater than for other conditions.

Liver transplants peaked in 2002 at Wisconsin's largest transplant center due to a record number of living donor liver transplants. However, aside from this 1-year jump, liver transplants have remained relatively stable since 2000.¹⁸

For gender and age, the characteristics of HCV-related transplant recipients are predictable based on case

surveillance data. Males account for 74% of transplant recipients, compared to 68% of HCV cases, and persons ages 35-64 account for more than 80% of both transplant recipients and cases.

However the data reveal an important racial disparity. African Americans account for 24% of reported HCV infections and 16% of HCV-related deaths, but receive only 6% of liver transplants for HCV-related liver failure. National data also show disparities between liver transplants and HCV prevalence rates; African Americans accounted for only 8.7% of liver transplant recipients during 1993-2004,¹¹ while estimated HCV prevalence rates are twice as high in African Americans (3%), as in whites (1.5%).²

The causes of this discrepancy are not known but may be due to a host of complex factors.¹⁹ Possible explanations include that African Americans may experience greater barriers than do other racial/ethnic groups, especially whites, to obtaining health care, including organ transplants.²⁰ African Americans are referred for organ transplants at lower rates,²¹ have lower rates of fibrosis and progression to cirrhosis necessitating transplant,²² have lower rates of survival after liver transplant,²³ and have different preferences regarding transplants.²⁴

Treatment options for HCV have improved in recent years. Nevertheless the magnitude and burden of undiagnosed or untreated viral hepatitis nationally and in Wisconsin remain substantial.

CONCLUSION

The number of cases of reported HCV and deaths and transplants resulting from HCV infection has increased in recent years. Reported cases have increased because of improved screening, testing, and reporting practices. More reports of HCV infection are expected in the future, since as of the end of 2004, <20% of the expected number of persons with HCV infection in Wisconsin had been identified and reported. The vast majority of infected persons have yet to be screened and tested. HCV-related deaths and transplants have increased because of aging and disease progression in a population infected in previous decades.

Males, persons 40-49 years of age, and persons living in Milwaukee County or the state correctional system are disproportionately affected by HCV infection. African Americans are over-represented among reported cases and decedents, but under-represented in the number of transplant recipients. Surveillance data suggest that clinicians should ask about history of injection drug use and other risk factors for HCV infection, particularly when providing care to persons with the demographic

characteristics indicated. Identification provides infected persons the opportunity to obtain referral for medical evaluation and management as well as information on preventing spread and on disease progression.

Increased testing in recent years has identified more cases of chronic and acute HCV. While there have been advances in treatment for HCV in recent years, only a small proportion of infected patients are able to access or successfully complete treatment.¹⁶ High levels of morbidity result in expanded needs for health care and liver transplants. Increased mortality results in increases in years of potential life lost. Incidence of HCV can be reduced through prevention and testing, specifically screening of donors of blood products, screening and testing of persons at risk, reductions in transmission risk behaviors among injectors, and alcohol and drug treatment for drug users. Given the magnitude and burden of viral hepatitis nationally and in Wisconsin, it will be important to continue to monitor trends in morbidity and mortality²⁵ and to continue to increase options for prevention, testing and treatment of hepatitis C infection.

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