

# WISCONSIN AIDS/HIV PROGRAM NOTES

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## Regional Distribution, Demographics, and Hepatitis C Genotype Trends in Wisconsin, 2007-2011.

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### Introduction

Hepatitis C virus (HCV) infection is an increasing health problem in the United States. HCV is a blood-borne pathogen that is transmitted through contaminated blood via routes such as blood transfusion, contaminated needles/syringes, and occasionally sexual activity. Infection is often asymptomatic and chronic, leading to constant inflammation of the liver. Consequently, serious health complications such as cirrhosis of the liver, chronic liver disease and hepatocellular carcinoma can occur. This has resulted in HCV-infection being the leading cause of liver transplants in the United States and accounts for the rise in HCV-related mortality. To address this growing public health problem, early detection and effective treatment of HCV is necessary.

Successful treatment of HCV is dependent on the genotype of the virus. HCV has six known genotypes and various subtypes that are identified based on different regions of its genome. These differences can account for slight variances in metabolism, pathogenicity, and response to treatment among the genotypes. For example, genotypes 1 and 4 are less likely to respond to treatment and require a treatment period twice as long as genotypes 2 and 3. The sustained virologic response (SVR), or the length of time at which the virus remains undetected also varies. Treatment outcomes show that the chance for patients with genotype 1 keeping the virus below a detectable limit is roughly 40%, while it is closer to 80% for patients with genotypes 2 and 3.<sup>1</sup> More recently, advancements in combination antiviral therapies have boosted SVR levels for genotype 1 closer to 70%.<sup>2</sup>

Understanding the prevalence of HCV genotypes is important for public health and in planning successful treatment outcomes. In the United States, genotype 1 accounts for 70-73% of the HCV-infected population, followed by genotypes 2 (13-16%) and 3 (8-12%), while genotypes 4-6 account for very little of HCV infection (1-3%). Within the United States, studies also show that genotype 3 accounts for a greater percentage of cases today than 10-15 years ago.

Epidemiologic characteristics among those with certain genotypes have also been investigated. Blacks or African-Americans are at significantly greater risk (9 out of 10 cases) for being infected with genotype 1.<sup>3,5</sup>

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<sup>1</sup> Manns MN et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: A randomised trial. *Lancet* 2001;358:958-965.

<sup>2</sup> Jacobson IM et al. Telaprevir for previously untreated chronic hepatitis C virus infection. *New England Journal of Medicine* 2011;364:2405-16.

<sup>3</sup> Blatt LM et al. Assessment of hepatitis C virus RNA and genotype from 6807 patients with chronic hepatitis C in the United States. *Journal of Viral Hepatitis* 2000;7:196-202.

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While no major differences are typically found by sex, some differences can be seen among different age groups. Those aged 45 years or older are often diagnosed with type 1 or 2, while type 3 more commonly infects younger populations (ages 0-44).<sup>4,5</sup>

### **Investigation**

HCV has been a reportable disease in Wisconsin since 2000. The Wisconsin Department of Health Services (DHS) receives results of any HCV reactive test, including the HCV genotype when performed. This information is stored and updated in the Wisconsin Electronic Disease Surveillance System (WEDSS).

Genotyping is a major consideration in planning treatment. As part of this investigation, it was assumed that reports with genotypes identified were cases being assessed for treatment, while reports without genotypes were not. This assumption may have had a small impact when determining cases without genotype information in cases of individuals who cleared the virus on their own.

A total of 11,470 past or present cases (excluding acute and Department of Corrections cases) with an episode date between January 1, 2007, and December 31, 2011, were analyzed. A total of 1,571 cases (13.7%) reported genotypes. These data were used to investigate:

- whether or not there is a bias in those receiving genotype testing by demographic characteristic and DHS region;
- how Wisconsin's patterns compare to those nationally by genotype distribution and by demographic characteristics of those with certain genotypes; and
- what genotypic data can suggest about HCV infection and treatment in Wisconsin.

### *Patients receiving genotype testing*

Using information from WEDSS, demographic characteristics including race, ethnicity, sex, age, and region were analyzed. Highlights are summarized below.

- While the statewide average of 13.7% of HCV-infected persons had genotype testing between 2007 and 2011, only 8% of cases among Blacks or African Americans were genotyped (Figure 1).
- No significant differences were found between Hispanics and non-Hispanics or males and females (Figure 1).

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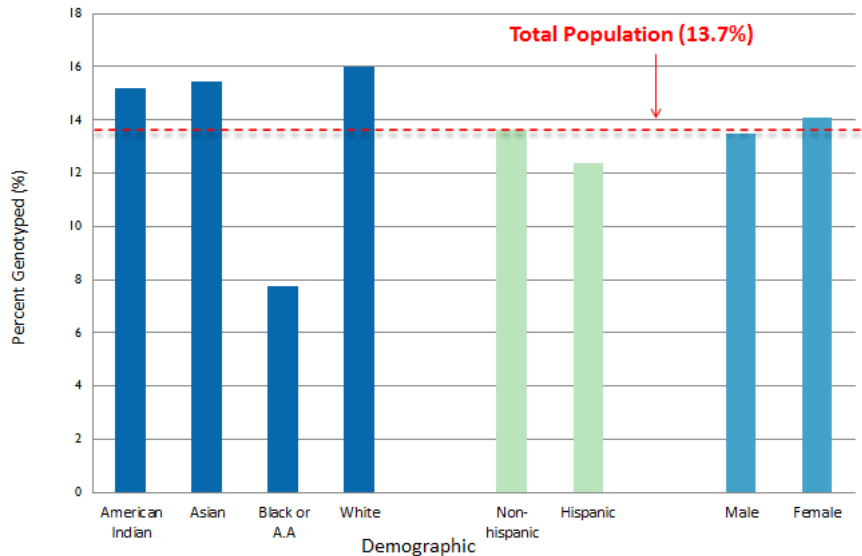
<sup>4</sup> Germer JJ et al. Hepatitis C virus genotypes in clinical specimens tested at a national reference testing laboratory in the United States. *Journal of Clinical Microbiology* 2001;49:3040-3043.

<sup>5</sup> Manos M et al. Distribution of hepatitis C virus genotypes in a diverse US integrated health care population. *Journal of Medical Virology* 2012;84:1744-1750.

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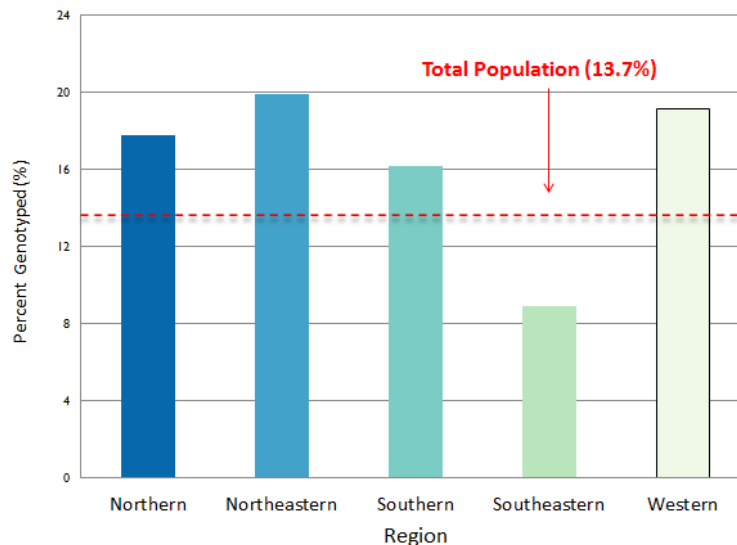
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Figure 1: Percent of HCV-infected individuals who were genotyped by demographic characteristic, 2007-2011.



- All age categories (0-30; 31-50; and 51+) were equally likely to be genotyped.
- Nine percent of those living with HCV in the southeastern region were genotyped. Genotype rates in all other regions of Wisconsin were above the 13.7% average and even higher in the northeastern and western regions, where nearly 1 in 5 people with HCV received genotype testing (Figure 2).
- In the southeastern region, Blacks or African Americans were genotyped only 6% of the time, compared to 12% of Whites.

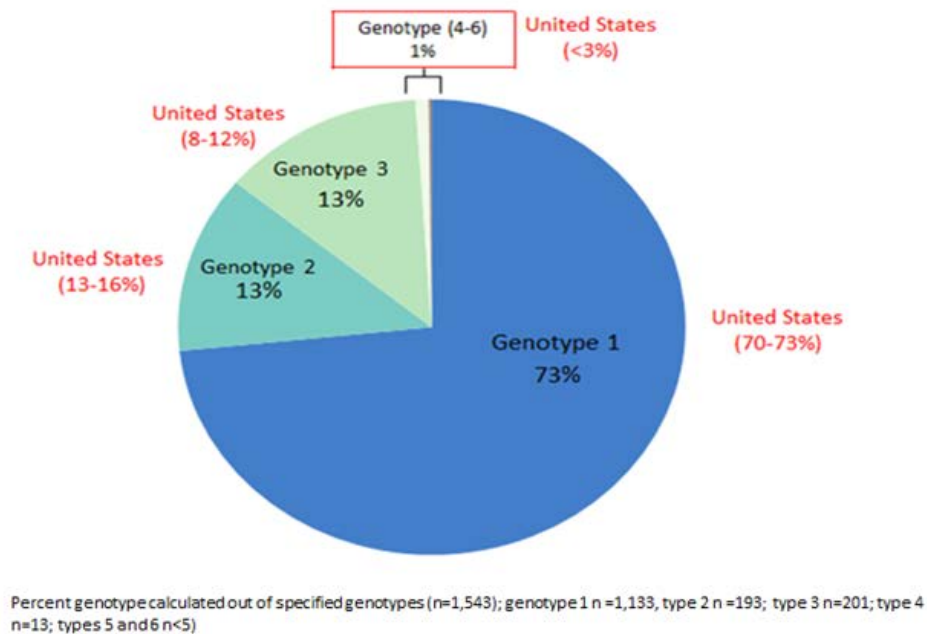
Figure 2: Percent of HCV-infected individuals who were genotyped by region, 2007-2011.



*Genotype comparison to the United States*

Of all specified HCV genotypes in Wisconsin over the last five years, genotype 1 comprised the majority (1,133 or 73%) of cases. Genotype 3 comprised 201 cases (13%) and type 2, 193 (13%) cases. Genotypes 4, 5, and 6 (<1%) were the rarest (Figure 3). As seen below, these rates closely resemble those reported in the United States. In Wisconsin, these prevalence rates have stayed relatively constant over the last five years.

Figure 3: Reported HCV genotypes in Wisconsin, 2007-2011.



*Regional distribution*

The southeastern region accounted for nearly half of all HCV infections in Wisconsin and the majority of genotype 1 and 2 infections. The northeastern region, location to only 16% of infections statewide, had the majority of genotype 3 cases. Active surveillance of HCV between 2010 and 2011 in Manitowoc County in the northeastern region did not affect the distribution of genotype 3 in the region.

*Demographic characteristics*

Similar to the United States, no major differences between genotypes by sex was found. Distribution among races also followed United States patterns, where Blacks or African Americans were more commonly diagnosed with type 1 than Whites (93% and 71%, respectively). Although there was not a significant difference in median ages between the genotypes (median age for genotype 1, 2 and 3 were 50, 50, and 48 years respectively), a larger percentage of genotype 3 cases were younger than age 45 when compared to genotypes 1 and 2 (%<45 years: type 1 = 32%; type 2 = 26%; type 3 = 40%).

This shift towards younger populations was further evaluated by comparing the ages of those with genotype 3 to those with genotypes 1 and 2 over a five year span (2007 vs. 2011).

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Although a switch from a unimodal age distribution to a bimodal age distribution was seen in all genotypes, genotype 3 represented a more pronounced shift (Figures 4 and 5).

Figure 4: Age Distribution of Genotypes in 2007.

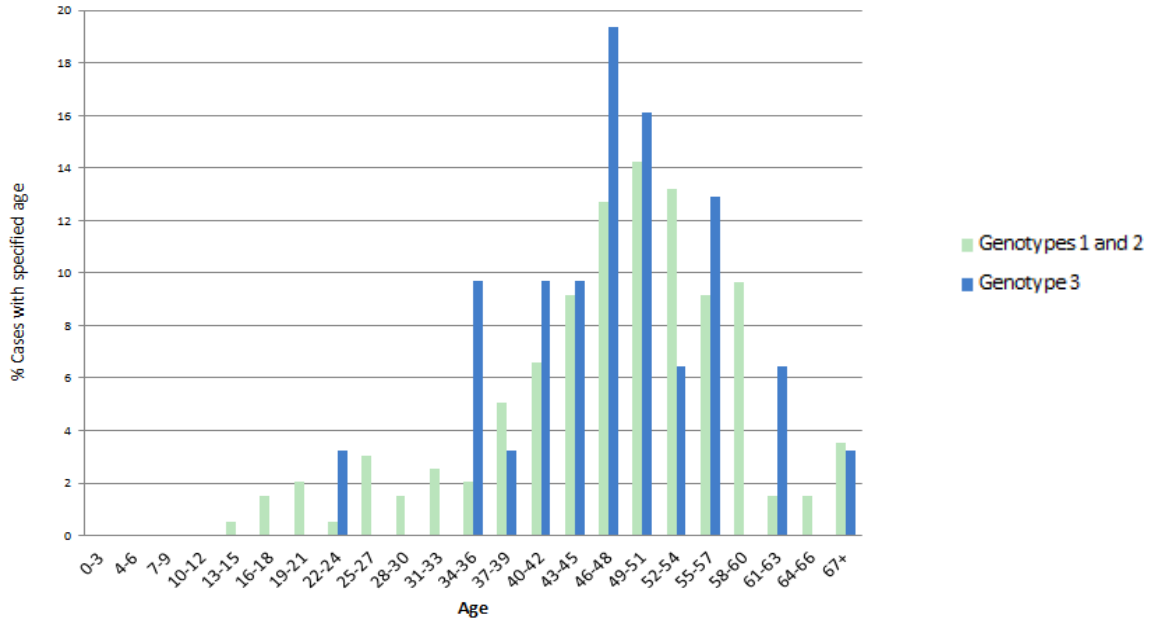
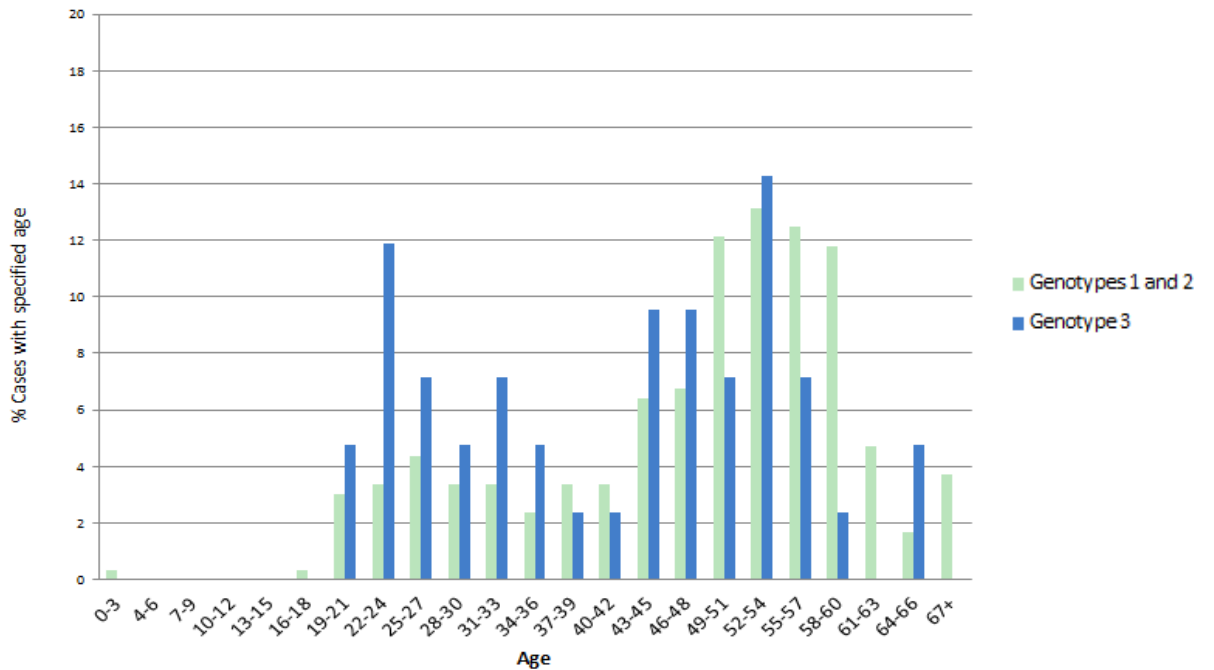


Figure 5: Age Distribution of Genotypes in 2011.



**Summary and Implications**

*Black or African American population*

From the data presented, Blacks or African Americans experienced the greatest disparity for

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genotypic testing and possible treatment, suggesting the need for increased access to genotyping and treatment in this population.

- Only 8% of infected Blacks or Africans Americans were genotyped; 6% in the southeastern region.
- 93% of Blacks or African Americans living in Wisconsin with HCV infection have type 1, the most difficult genotype to treat.
- 60% of all Blacks or African Americans infected with HCV were reported as living in the southeastern region, the region with the most HCV infections but where persons receive the least HCV genotyping.

### *Genotype 3 shift*

A previous investigation into the HCV cluster in North Central Wisconsin showed that HCV infection is becoming more prevalent in the younger, drug injecting population.<sup>6</sup> It also established a shift in infection from the densely populated southeastern region to the north and west. These data correlate with the findings of genotype 3 in this study, where infection occurred in younger populations (ages 0-44), and increasingly was found away from the centralized southeastern region. In addition, there was a significant shift to a bimodal age distribution between 2007 and 2011.

An explanation for this shift may lie in the transmission routes of HCV. Since the screening of blood in 1992, the primary route of transmission has changed from blood transfusion to injection drug use and needle sharing. Consequently, studies have reported a possible shift in genotypes because of this changing route of transmission.<sup>3,7</sup> Although risk was not assessed in the current analysis, genotype 3 has been associated with injection drug use (IDU) more than any other genotype and has been found to be the leading source of risk for young adults.<sup>8,9</sup>

### *Need for more genotype testing*

Genotype 1 continues to be the most prevalent in HCV infection. Despite being the hardest type to treat, new effective therapies are available, making the need for genotypic testing and targeted treatment critical. Unfortunately however, less than 14% of the infected Wisconsin population is being genotyped and presumably assessed for these treatments. This suggests a gap in care that needs to be filled. Access to genotypic testing and improved therapy will lead to greater success rates in treatment. More successful treatments will ultimately result in a decline of HCV-related mortality and help decrease the public health burden of HCV infection in Wisconsin.



<sup>6</sup> Notes from the Field : Hepatitis C Virus Infections Among Young Adults — Rural Wisconsin, 2010. MMWR Morb Mortal Wkly Rep 2012; 61:358.

<sup>7</sup> Nainan, Omana V., et al. "Hepatitis C virus genotypes and viral concentrations in participants of a general population survey in the United States." *Gastroenterology* 131.2 (2006): 478-484.

<sup>8</sup> Gigi E et al. Epidemiology, clinical data, and treatment of viral hepatitis in a large cohort of intravenous drug users. *Journal of Addiction Medicine* 2013;7: 52-57.

<sup>9</sup> CDC. Hepatitis C Virus Infection Among Adolescents and Young Adults - - Massachusetts, 2000-2009, 2011. MMWR Morb Mortal Wkly Rep 2011; 60:537-41.