

10-Year Trends in the Diagnosis and Treatment of Hepatitis C and Concomitant Mental Health Disorders: 1995 to 2005

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Objective: To evaluate trends in the rate and timing of treatment for hepatitis C in those with and without mental health comorbidities.

Method: Data from the population-based Olmsted County Hepatitis C Registry in Minnesota were linked to patients' medical records to identify the dates and duration of any hepatitis C-specific therapy as well as all diagnoses of mental health comorbid conditions prior to initiation of therapy. The most common mental health conditions, major depressive disorder, alcohol dependence, and intravenous drug use, were assessed separately. The registry includes all Olmsted County residents with a physician diagnosis of hepatitis C or non-A/non-B hepatitis (ICD-9 criteria) from January 1, 1990, through December 31, 2005.

Results: The age-adjusted prevalence of diagnosed hepatitis C increased markedly between 1995 and 2000 (15.5/10,000 persons to 27.0/10,000 persons) but changed little between 2000 and 2005 (27.0 to 27.9/10,000 persons). The number of people with comorbid hepatitis C and depressive disorder (including minor depression) increased significantly between 1995 and 2005 from 18% to over 35% of all people with diagnosed hepatitis C. Treatment rates more than doubled between 1995 and 2005, while the time from diagnosis to treatment decreased during that same period. By 2005, major depressive disorders were associated with a high rate of reasonably prompt treatment. There were no gender differences in treatment rates or time to treatment when other comorbidities and age were included in the analyses.

Conclusions: From 1995 to 2005, rates of treatment for hepatitis C among people with and without comorbid mental health problems increased. Rates of increase were higher among those with depression and hepatitis C than among those with hepatitis C and drug abuse or other mental health diagnoses. Even with this progress in treating those with multiple diagnoses, over 75% of people with hepatitis C remain untreated.

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With the advent of broad community education, safe needle programs, and testing of all blood donors for hepatitis C, new infections of hepatitis C have been reported to have declined from 242,000 in 1990 to only 26,000 in 2004.¹ The declining incident rates plus deaths among prevalent cases have resulted in a leveling off of the number of hepatitis C cases in the United States with an estimated 4.1 million Americans infected, of whom about 3.2 million have chronic hepatitis C.^{2,3} While the decline in new cases and the stabilization of the prevalence of hepatitis C are very encouraging, the treatment of those with existing disease remains incomplete and inadequate.

Previously, treatment provided only fair results,^{4,5} but new medications and new regimens for hepatitis C treatment are reported to be efficacious for 42% to 80% of those treated.⁵⁻⁹ However, fewer than 1 in 4 people with hepatitis C are offered or receive treatment.^{10,11} Many among the 75% who are not treated or not offered treatment have mental health comorbid conditions. While untreated and uncontrolled major depressive disorder, alcoholism, or drug abuse may be considered contraindications to hepatitis C treatment, they may be amenable to identification and therapy, allowing hepatitis C treatment to occur.¹⁰⁻¹⁴

In response to this concern, several articles have appeared in the psychiatric literature that discuss appropriate monitoring and treatment for previously diagnosed major depressive disorders in those who are either candidates for hepatitis C treatment or who develop depression symptoms during treatment.¹⁵⁻¹⁷ A few studies have been completed demonstrating the ability to provide and complete hepatitis C treatment among drug users who are receiving methadone therapy.¹⁸⁻²⁰ To date, it is not clear if

these advances in awareness and treatment of mental health comorbidities resulted in increases in the overall proportion of patients with hepatitis C who were offered therapy or who initiated therapy.

This study provides an updated look at the rates of diagnosis, treatment, and failure to treat people with hepatitis C with special attention to those with hepatitis C who have mental health and chemical dependency comorbid conditions.^{10,11,14} Such information should help assess the impact of increasing awareness and educating a broad range of physicians regarding management of hepatitis C in the face of comorbid mental health conditions.^{9,18,21–23}

In this study, we used the hepatitis C registry data from Olmsted County, Minn., to evaluate the trends in diagnosis and treatment for all cases of diagnosed hepatitis C in Olmsted County residents.²⁴ This community population-based study provides data on those patients not usually included in hepatitis C treatment studies—the patients who are not referred to hepatologists or gastroenterologists as well as patients who are referred but choose not to complete visits to the specialists. In addition to assessing current awareness activities, these data could help tailor and target future efforts to increase access to treatment for more patients with known hepatitis C, including those with mental health comorbid conditions.

METHOD

Overview

This retrospective medical record study reviewed all medical care provided to all people listed in the Olmsted County Hepatitis C Registry^{25,26} to identify documentation of hepatitis C–specific therapy, mental health diagnoses, and mental health treatment among individuals in the registry. The registry includes all Olmsted County residents with a physician diagnosis of hepatitis C from January 1, 1990, through December 31, 2005.

Subjects

All individuals with confirmed hepatitis C who were residents of Olmsted County, Minn., and who provided research authorization of their medical records data were the subjects of this study. Olmsted County is a metropolitan statistical area of approximately 120,000 residents and includes the city of Rochester. The county is 90 miles south of Minneapolis and St. Paul, medically isolated, and surrounded by rural agricultural land. Olmsted County residents are served by 2 large integrated medical centers, the Olmsted Medical Center and its hospital and the Mayo Clinic and its 2 affiliated hospitals, which provide primary through tertiary outpatient and inpatient care. The population of Olmsted County is mainly white with a lower rate of uninsured residents than is common in most regions of the United States. Both inpatient and

outpatient mental health and chemical dependency programs are available locally.

The Olmsted County Hepatitis C Registry has been described previously.^{10,25,26} Briefly, the diagnostic index of the Rochester Epidemiology Project (REP) was used to identify all residents of Olmsted County who had diagnostic codes potentially consistent with a diagnosis of hepatitis C or non-A/non-B hepatitis (ICD-9 codes 070.51, 070.41, 070.42, V02.62, 070.54, 070.44, 571.40, 571.49, and 573.0). The REP is a database and linkage system funded continuously by the National Institutes of Health (NIH) for the past 40 years. The system includes a diagnostic index, all laboratory data, surgical index, and imaging index allowing complete ascertainment of diagnoses and positive testing for hepatitis C.^{25–28} The REP index links the diagnoses or test or surgery to the date and site of service. From this, all medical records for each date and service can then be accessed.

After receiving approval from the Olmsted Medical Center and the Mayo Clinic Institutional Review Boards, each potential registry subject who had provided general research authorization, as required by Minnesota statute, was linked to all sites where he or she received any medical care in Olmsted County from 1990 to the present using the REP.^{25,26} This system is reported to capture 98% of all health care for all Olmsted County residents. Only patients who did not refuse the general research authorization required by Minnesota statute were included.

Data

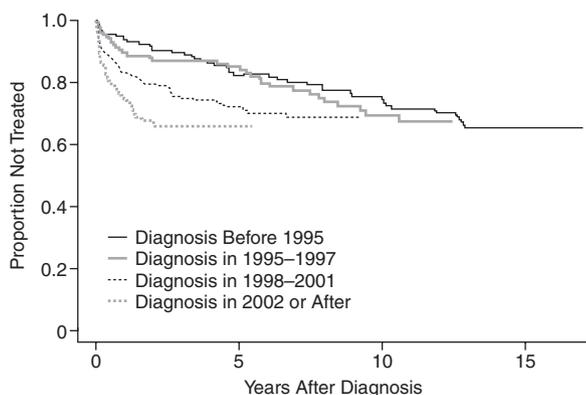
All medical records for each potential registry subject were reviewed, and the patient was entered into the registry if a diagnosis of hepatitis C could be confirmed. From 1990 to 2000, the criteria for including patients in the registry were updated as new tests became available, e.g., second-generation enzyme immunoassay and polymerase chain reaction (PCR) tests for the hepatitis C virus (HCV).^{10,29} Not all patients had a complete evaluation by the current standards. Overall, 8.5% had only a positive HCV plus risk factors or elevated liver function tests (LFT), 55.5% had a positive HCV and recombinant immunoblot assay (RIBA) test, and 36.0% had a positive HCV, RIBA, and PCR. People with positive HCV, negative RIBA, normal LFT, and no risk factors were considered false positives and were not included in the study. Patients originally diagnosed with non-A/non-B hepatitis were included only if they had positive hepatitis C–specific tests.

For this study, additional data were abstracted to enrich the registry information. In addition to the usual data on the content and date of the initial HCV diagnostic process, information was collected on any discussions of treatment, referrals for treatment consideration, and any treatment initiated as well as all comorbid chronic illness with special emphasis on chemical dependency and mental health diagnoses. The mental health diagnoses were further

Figure 1. Incidence Rates of Hepatitis C and Percentage of Patients Treated



Figure 2. Trends in Time From Diagnosis to Treatment of Hepatitis C in all Cases



divided into those with psychotic features (bipolar disorders, schizophrenia, schizoaffective disorders), personality disorders (borderline personality disorder), major depressive disorders, and anxiety/posttraumatic stress disorders. In addition, data were collected on all HCV-related laboratory data (i.e., LFT, HCV, RIBA, PCR, and viral load), which have been used in previous analyses.¹⁰

Data Analysis

Demographic and risk factor data were summarized with means and ranges. Frequencies were compared across subgroups using χ^2 or Mantel-Haenszel tests. Trends were assessed using Mantel-Haenszel analysis or Poisson regression. Time to treatment was estimated using Kaplan-Meier methods.

RESULTS

The Olmsted County Hepatitis C Registry includes data on 626 confirmed cases of hepatitis C: 373 (60%) in

Figure 3. Recent Trends in Time From Diagnosis to Treatment of Hepatitis C: 2000-2004

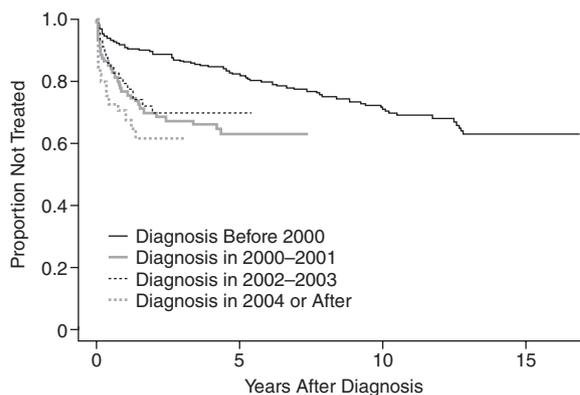


Table 1. Time Trends in Percentage of Hepatitis C Patients With Mental Health Codiagnoses^a

Variable, N (%)	1995 (N = 177)	2000 (N = 337)	2005 (N = 375)
No psychiatric conditions	140 (79)	231 (69)	245 (65)
Depressive/anxiety disorders	24 (14)	71 (21)	85 (23)
Posttraumatic stress disorder	2 (1)	3 (1)	4 (1)
Borderline personality disorders	1 (1)	3 (1)	3 (1)
Schizoaffective disorders	1 (1)	6 (2)	9 (2)
Schizophrenia	2 (1)	3 (1)	2 (1)
Bipolar disorders	7 (4)	20 (6)	27 (7)

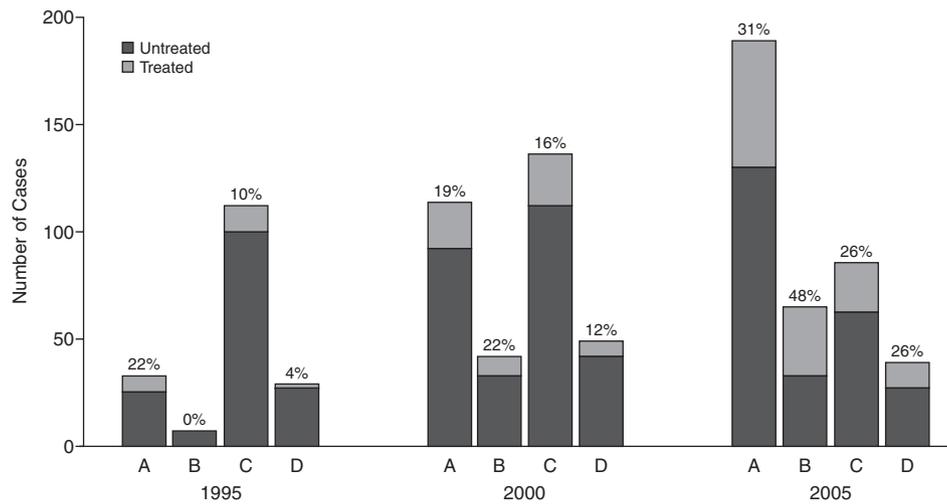
^aThe column percents may equal more than 100% due to rounding.

men and 253 (40%) in women. The mean age at diagnosis was 43 years with a range of 1 day to 87 years. Overall, 165 patients (26%) have received treatment, and 33 (6%) have died during the follow-up period.

The identification of hepatitis C continued to increase through 2005 but at a much slower and not statistically significantly different rate from 2000 to 2005. In 1995, the age-adjusted prevalence of hepatitis C was 15.5/10,000 community residents (based on 177 cases). By 2000, the prevalence was 27.0/10,000 community residents (based on 337 cases) and by 2005 had increased only slightly ($p > .10$) to 27.9/10,000 community residents (based on 375 cases). The p value for trend is $< .05$, but the increase has clearly declined since 2000. Figure 1 demonstrates that the decline in incidence appeared to begin even before 2000 and was present in both men and women.

Figure 1 also shows the rate of treatment, which has increased from less than 18% in the early 1990s to over 35% of newly identified cases in 2003 to 2005. In addition to higher percentages of cases being treated in more recent years, the cases are being treated sooner after diagnosis. Figures 2 and 3 demonstrate the time to treatment by year of diagnosis. The more rapidly the line falls, the more quickly the identified cases are being treated. In figure 3, the top line (those diagnosed before 2000) is indicative

Figure 4. Treatment Rates Among Hepatitis C Patients With and Without Comorbid Mental Health Conditions^a



^aA = no depression, drug use, or alcohol dependence; B = major depressive disorders; C = intravenous drug use without depression; and D = alcohol dependence without drug use or depression.

of the low treatment rates that occurred prior to 2000 and indicates that most people diagnosed prior to 2000 remain untreated. Since 2000, people with newly diagnosed hepatitis C are more likely to receive treatment, especially in the first 3 years following diagnosis ($p < .01$). However, after the first 3 to 4 years following diagnosis, few additional cases are treated. Figure 3 shows the continuation of this trend, providing greater detail regarding treatment in the period from 2000 to 2004.

As we reported previously,¹⁰ many people with hepatitis C have mental health comorbidities. Table 1 shows the trend in diagnosed mental health conditions in those with known hepatitis C. In 1995, 22% of those with a diagnosis of hepatitis C had a mental health condition, increasing to 32% by 2000 and reaching 35% by 2005 ($p < .01$). Most of the increases in mental health comorbidities are from major depressive disorders. In fact, between 2000 and 2005, the majority of new cases of hepatitis C (28 of 45) identified were in people with mental health conditions, primarily major depressive disorders.

Figure 4 illustrates the increase in treatment for hepatitis C between 1995 and 2005 among people with no mental health diagnoses as well as those with alcohol dependence, intravenous (IV) drug use, and major depressive disorders. The greatest increase in treatment rates among those with all mental health conditions was in those with major depressive disorders. The numbers of hepatitis C patients with IV drug use and alcohol dependence actually fell from 2000 to 2005, probably due to the greater mortality rate among prevalent cases in those with these highly risky behaviors. Furthermore, treatment is even less likely to occur or to be more delayed in people with

comorbid hepatitis C and mental health diagnoses other than major depressive disorders.

DISCUSSION

Despite declining new diagnosis rates for hepatitis C in Olmsted County, Minn., the rate of people with comorbid hepatitis C and mental health diagnoses is rising, and, with the exception of those with major depressive disorders, these conditions appear to continue to be barriers to hepatitis C treatment. Overall, in our population, hepatitis C treatment rates are increasing, and treatment is being initiated more rapidly after the diagnosis is made.

Among the common mental health diagnoses, major depressive disorders are the most typical and the most treatable. Several reviews in the medical literature have been addressed to psychiatrists to increase awareness of the common association of major depressive disorders and hepatitis C.^{12,13,16,17,30,31} The need for this awareness and collaboration between mental health care professionals and those treating people with hepatitis C undoubtedly arose due to the risk of new onset or recurrence of depressive symptoms during hepatitis C therapy, especially therapy including interferon.^{16,30,32} Our data suggest that this increased awareness may be resulting in increased rates of treatment in those with comorbid hepatitis C and major depressive disorders. Patients whose depressive symptoms are recognized and evaluated and whose major depressive disorders are treated may have more frequent visits to physicians, allowing increased attention to all of their medical problems including hepatitis C.

It is imperative that primary care physicians who often diagnose hepatitis C and then decide whether or not to send patients on for evaluation and possible therapy are also aware that major depressive disorders are not an absolute contraindication to hepatitis C therapy.^{29,33} In previous surveys, primary care physicians reported that referrals of people with hepatitis C and chronic or even resolved major depressive disorders were often refused by gastroenterologists, leaving referral to a much later time when cirrhosis is more likely to be the diagnosis.^{30,33} That barrier to treatment appears to be resolving, and primary care physicians need to know that they can expect people with hepatitis C and controlled major depressive disorders to be candidates for therapy. Continued improvement will likely depend upon broad and expanded collaboration across the medical community in the management of people with hepatitis C.

For those with mental health diagnoses other than major depressive disorder,^{10,11,16,17} the rate of hepatitis C therapy is less encouraging. A few creative and dedicated physicians have chosen to try to offer hepatitis C treatment to patients receiving methadone maintenance therapy.^{20,34,35} Such programs have the benefit of allowing clinicians the opportunity to see patients daily or almost daily and to administer both the methadone and the hepatitis C therapy on-site. In addition, seeing the patient daily allows for regular monitoring of the potential side effects as well as therapeutic effects of the medications. Drop-out rates from therapy are comparable to those among hepatitis C patients with no mental health problems (14% vs. 13%, respectively).³¹ However, among former drug addicts not receiving methadone maintenance therapy, the drop-out rate is as high as 43%, suggesting that either the underlying personal issues or the lack of daily supervision are important in completing therapy.³¹

Similar solutions might be possible in patients with other chronic conditions such as schizophrenia when those patients are in halfway houses or are seen regularly at home or at a center for medication maintenance. Implementing such dual programs would require additional training and support for existing staff but might help lower long-term costs for those with these codiagnoses.^{17,34}

People with alcohol dependency and hepatitis C are a special concern.^{1,17} The NIH guidelines recommend that a patient should abstain from alcohol for at least 3 to 6 months before beginning hepatitis C therapy, with heavy alcohol consumption an absolute contraindication to HCV therapy and moderate consumption a relative contraindication.^{6,9,23,36} Many specialists ask for even longer periods of abstinence.¹⁰ Further work needs to be completed to assess when it is safe to begin therapy for a person who either has recently stopped drinking or continues to drink in moderation. Perhaps newer treatments will allow continued alcohol consumption (moderate levels) with less concern about liver toxicity.³⁷⁻⁴⁰

Our study has limitations. Although we used all medical records in the community, it is possible that additional cases of hepatitis C are diagnosed outside the county and are never recorded in the community medical records. This is likely to be a small group of people since Olmsted County has all levels of care and several hepatitis specialists available locally with the next closest site of tertiary care more than 75 miles distant. Our study population was primarily white and may not reflect the experience among other racial and ethnic groups. Our community also has local access to mental health treatment facilities that may improve the ability to recognize and treat major depressive disorders, allowing higher rates of hepatitis C treatment among those with both conditions.

Hepatitis C continues to be a major health problem, and only about 1 in 4 people with hepatitis C are receiving hepatitis-specific treatment, with lower rates of therapy among people with comorbid mental health conditions. Since 2000, physicians appear to have become more adept in treating people with hepatitis C and major depressive disorders with increasing rates of therapy and more rapid onset of hepatitis C therapy after diagnosis, narrowing the disparity gap among those with hepatitis C with and without mental health diagnoses. This encouraging trend needs to continue for those with codiagnoses of major depressive disorders and hepatitis C and be extended to those with hepatitis C plus other mental health conditions. This extension will require collaborative care among primary care, specialists in hepatitis C, and those with expertise in mental health and chemical dependency management.

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