

Freedom to Be Cured:

Who is driving the decisions on which groups of patients should be eligible for hepatitis C treatments?

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Is the freedom to make decisions about hepatitis C management and treatment being taken out of the hands of patients in collaboration with their doctors and handed over to the government?

For many patients, it certainly may have seemed that way since 1997, when the first National Institutes of Health (NIH) consensus statement on Management of Hepatitis C was written. Unfortunately, the impact of the 1997 consensus statement has been far-reaching, even after its contents became antiquated.

One area where this impact has been very apparent is the NIH guidelines concerning who should be treated. The 1997 statement included recommendations against treating people with normal ALT (liver enzyme) levels, children, elderly patients, people with psychiatric illness, and alcohol or drug users who had not been “clean and sober” for a minimum of six months. Even though the guidelines did not spell out specific recommendations regarding recovering injection drug users (IDUs) receiving methadone maintenance therapy, most healthcare providers and insurance companies have lumped this population in with the active alcohol and drug users who were not recommended for hepatitis C treatment. At the time the recommendations were written, there was not much room for debate in these areas because these patient groups had not been studied and the guidelines were written with little knowledge and few resources.

Now, five years later, a great deal has changed regarding our knowledge of the hepatitis C virus, the natural history of the disease, and how to treat hepatitis C in many different patient populations. In June the NIH consensus statement on **Management of Hepatitis C** was revisited. While the preliminary revised guidelines appear to have opened some doors to allow treatment for certain populations that have not had access in the past, will hepatitis C management and treatment really change as a result of the new consensus statement?

For example, I think few would argue that a person with normal ALT levels should be denied treatment now that we know that approximately 25% of patients with persistently normal ALT will go on to develop more advanced liver disease despite the absence of elevated liver enzymes. Who would say “no” to treatment for children now that it has been shown that not only do children achieve sustained virological response (SVR) rates similar to those of adults, but also that children suffer fewer side effects and tend to tolerate therapy better? Likewise, it has been shown that patients with psychiatric conditions can, with appropriate management and use of antidepressants, achieve favorable treatment outcomes.

So we can now add people with normal ALT, children, and people with psychiatric illness to the list of patients having endorsement for access to treatment. But a gray area remains. What about people who have not stopped drinking alcohol, patients that are still injecting drugs, and those on methadone maintenance therapy (MMT)?

Active injection drug users comprise the largest pool of new HCV infections, but have mostly been excluded

from receiving treatment on the basis of the 1997 consensus guidelines. Is this likely to change with the new recommendations? Why has this population been excluded from treatment? Has the decision been based on moral considerations, or has it been based on scientific evidence?

In my opinion, active injection drug users are the segment of our society facing the most widespread discrimination. Views about injection drug users vary, but the predominant opinion I hear is that people who inject drugs deserve whatever happens to them as a result of their lifestyle. One could argue that injection drug use is an addiction that requires substance abuse treatment, but even patients on methadone maintenance have pretty much been excluded from hepatitis C therapy. One also could argue that hepatitis C is a public health issue and should be addressed as such, regardless of a patient's behavior. After all, isn't stopping the spread of an infectious disease the ultimate goal of public health? Shouldn't this be a question of science over emotions? Fortunately, some recent small studies have shed some light these difficult questions.

Methadone Maintenance

Discovered by a German pharmacologist prior to World War II, methadone (brand name Dolophine, after the Latin for "dolor," or pain) is a synthetic narcotic with actions similar to heroin. Methadone works by blocking the euphoric effect of opiates and relieving the craving associated with opiate withdrawal. It is used for the treatment of addiction for a short-term period or over many years. Methadone can be dispensed only by hospital pharmacies and federally regulated drug treatment programs.

The perception that methadone is a substitute for heroin—rather than a treatment for addiction—accounts for the widespread discrimination against those on methadone maintenance therapy. However, scientific evidence has shown that methadone maintenance is an effective treatment for heroin addiction, and its use is best described as "dependence" on methadone maintenance therapy rather than "addiction" to methadone. Addiction implies compulsive drug use or loss of control over one's drug use. Methadone maintenance therapy stabilizes heroin addicts so that they can lead relatively normal and productive lives. Even former "Drug Czar" General Barry McCaffrey compares methadone maintenance therapy to the use of insulin to treat diabetes.

The 1997 hepatitis C treatment guidelines state, "Treatment for addiction should be provided prior to treatment for hepatitis C." However, patients on methadone maintenance therapy have for the most part been excluded from HCV treatment and lumped together with active drug users. In some studies the prevalence of HCV among those on methadone maintenance therapy approaches 90%, but there have been very few clinical trials to address the benefits and costs of treating this population with current HCV medications. However, some small trials have been conducted that can shed light on some basic questions.

Dr. Diana Sylvestre of the Organization to Achieve Solutions in Substance Abuse (OASIS) is a pioneer in the field of treating HCV positive patients on methadone maintenance therapy. In an ongoing clinical trial Dr. Sylvestre has treated 59 patients on methadone with interferon plus ribavirin combination therapy. An important aspect of this trial is the scope of services offered by OASIS, which combines medical and psychological services based on a peer-support model. Compared to average participants in HCV clinical trials, the patients on methadone maintenance in this trial were older, were infected for a longer period of time, had more advanced disease progression, reported higher rates of psychiatric illness, and were more racially and sexually balanced than in most studies. In other words, this group was more representative of the population with hepatitis C. In spite of these negative predictors of successful treatment outcomes, a carefully selected group of patients on methadone maintenance achieved an average SVR rate of 28%, compared with an average SVR rate of 41% in large trials of people with HCV that excluded patients on methadone maintenance therapy and active drug users.

Injection Drug Users

I think most prejudice-free people who closely examine the scientific data to date would agree that methadone maintenance patients should and can be successfully treated for hepatitis C. However, treating

active drug users poses a more difficult problem due to a lack of scientific data, compounded by even greater prejudice than that experienced by people on methadone maintenance therapy. Critics argue that active drug users are a difficult group to treat, and that treatment would not be effective in this population.

However, some small clinical trials with limited data refute these claims. Markus Backmund and colleagues from Munich, Germany, studied 50 hepatitis C patients enrolled in a trial while undergoing drug detoxification. Participants were treated with interferon or with interferon plus ribavirin by liver specialists and physicians who specialize in addiction medicine. The average SVR in this group was 36% at 24 weeks after the end of treatment. The authors concluded that the sustained response rate was not significantly different than that of non-drug-using patients.

Another compelling argument against treating active drug users concerns the potential for HCV reinfection. In other words, why spend money, time, and effort treating patients if they are likely to reinfect themselves with HCV? In the study described above, Backmund's team instructed participants about prevention measures to avoid HCV reinfection if they resumed injecting drugs. The ten patients that continued to inject heroin during the 24-week post-treatment period did not become reinfected. In another study, Olav Dalgard and colleagues from Oslo, Norway, reported that of the 27 IDUs they treated, only one reinfection was observed during a follow-up period of 13-82 weeks. The researchers concluded that the long-term outcome of HCV treatment in IDUs was excellent, despite reinitiation of drug injection.

Cost is another argument critics use to discourage treatment of active injection drug users. The cost of HCV medications range from \$20,000 to more than \$30,000 annually, which does not include the costs associated with office visits, lab tests, and adjunct therapies. It has been proven that HCV treatment is cost-effective in comparison with the burden of long-term medical care and loss of work productivity. But is the same true for active drug users? The answer is yes, since the majority of new HCV infections occur in injection drug users, and successful treatment of this population would prevent new infections and would lower future medical costs associated with disease progression.

Clearly, more studies are needed to address these complex issues, but the limited evidence available to date indicates that people on methadone maintenance therapy and former and active injection drug users can be effectively treated, and that the majority will not become reinfected. It is also evident that treating these populations is a complicated process that is best carried out using an interdisciplinary approach that combines the expertise of addiction medicine and liver disease specialists. But isn't this what medicine is about—an integrative approach to the prevention and treatment of disease?

Hopefully, the 2002 NIH consensus guidelines for Management of Hepatitis C will open the door and researchers and doctors will step in to answer these complicated questions, rather than outright denying treatment to any segment of the population out of prejudice. The ultimate goal should be to put medical care into the hands of patients in collaboration with their healthcare providers.