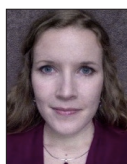


ADVANCES IN HCV

Current Developments in the Management of Hepatitis C Virus Infection

Cost-Effectiveness and Access to Care in the Treatment of Hepatitis C Virus Infection



Liesl Hagan, MPH candidate
Department of Epidemiology
Rollins School of Public Health
Emory University
Atlanta, Georgia

G&H Why is the economic burden of hepatitis C virus infection expected to increase while the rate of new infections is thought to be decreasing?

LH Hepatitis C virus (HCV) infection is estimated to more than double all-cause mortality and increase liver-related mortality up to 27 times. Non-liver-related mortality and medical complications are also increased in persons with HCV infection. Further, there are the indirect costs of loss of productivity when infected persons can no longer work and go on disability.

Medical costs and also indirect costs associated with HCV infection are increasing because very many infected persons became so 20 or 30 years ago. The prevalence of HCV infection in the United States is highest among persons aged 50 to 59 years, with rates of 4.3% compared with 1.8% in the general population. Most persons do not know that they are infected until complications, such as cirrhosis, emerge. We are in a situation now in which a lot of people with untreated chronic HCV infection are just finding out that they are infected.

It is also important to note that, although it has been reported that the incidence of new infections is decreasing, infection rates in some age groups are increasing. Several clusters and outbreaks of HCV infection have been reported in *Morbidity and Mortality Weekly Report* among young (younger than 30 years), white injection drug users in rural and suburban areas. Although much of the public health response is focused on the 1945 to 1965 birth cohort, the US Centers for Disease Control and Prevention and other organizations are also addressing other populations that are experiencing higher-than-expected incidence.

G&H Who should be primarily responsible for conducting HCV screening, and how can screening be optimized?

LH I do not think the responsibility for screening should fall on one type of practitioner. Collaboration among different members of the medical and public health communities is needed. General practitioners might be the first-line screeners, but if screening in any medical encounter becomes standard practice, more infected persons will be identified.

G&H What are the main challenges to access to care and getting newer therapies to patients who may benefit from them?

LH Getting affordable care to those who most need it is a challenge, and issues about access are being debated. There are a lot of parallels between HCV and HIV infection in terms of medications and access. The cost of HIV infection medications worldwide has gone way down in recent years because of competition, availability of generics, and, occasionally, because of compulsory licensing. There are places in the world in which the cost of antiretroviral therapy is \$60 per person per year, which is incredible considering that the cost of these agents was once very high.

I think that lessons can be learned from the history of HIV medicine and access to care. For example, bulk purchasing discounts of HIV drugs have been set up for large institutions such as the Veterans Health Administration. Internationally speaking, the Republic of Georgia, having received a grant from an international organization to treat its HIV/HCV-coinfected population, made a bulk purchase of interferon and paid about half of what

neighboring countries paid for it. A similar program providing public access to HCV medications does not exist in the United States except through The Ryan White HIV/AIDS Program (<http://www.hab.hrsa.gov>), which provides funding for treatment of HIV/HCV coinfection.

As more agents enter the market and more people are screened, perhaps there will be more activism, leading patients to demand access to better drugs. HCV drugs may also fall in line with pay-for-performance pricing in which insurance companies or other payors negotiate pricing deals for drugs based on their effectiveness.

G&H What have we learned from cost-effectiveness studies?

LH Many of the cost-effectiveness studies that look at screening focus on treatment rates. For example, a study conducted by Phil McEwan, PhD, of the Centre for Health Economics at Swansea University in Wales, United Kingdom and colleagues found that one-time, universal screening in the 1945 to 1965 birth cohort is cost-effective, provided that enough of the patients screened actually accept treatment. Other studies have arrived at the same conclusion.

Cost-effectiveness in relation to new therapies also depends on treatment uptake. The more patients receiving treatment and getting cured, the more downstream medical costs and indirect costs are being avoided, and the more life-years are being gained on a population level. A lot of variables are in play that may change with greater availability of new agents. Consider that, after a diagnosis of HCV infection is made, the diagnosing physician may or may not refer the patient to a specialist, and then the patient may or may not follow through with visiting the specialist. If he or she does present to the specialist, the specialist may or may not advise treatment depending on the patient's disease status and various comorbidities. If treatment is advised, the patient may or may not accept treatment and, if accepting treatment, may or may not adhere to treatment and may or may not achieve a sustained response.

As for the interferon-free regimens, once the word is out that a cure exists for most cases of HCV infection and that the adverse effects with the new treatments are so much less severe than they once were, I think more patients will follow through with attending the specialist visit. More will choose to accept treatment and adhere to treatment. Also, it is possible that patients with cirrhosis, including decompensated cirrhosis, can now be able to be treated, so more patients will be referred to specialists, and more specialists will advise treatment. As treatment regimens become less complicated with all-oral therapy, general practice physicians may also be able to treat infected persons directly, decreasing the need to see another doctor and removing one possibility for loss to follow-up.

Cost-effectiveness also depends on willingness-to-pay thresholds. This is where the perspective of the payor—be it Medicare, a private insurance company, a single-payor system, or a prison system—comes into play about how much it is willing to pay for each quality-adjusted life-year that a new treatment provides. For example, the willingness to pay may be lower in the prison setting than elsewhere because prisons have tighter budgets compared with other payors.

Cost-effectiveness research also heavily depends on the perspective taken. In general, it looks at whether the benefits of a treatment outweigh its costs compared with another option—in this case, interferon-free treatment compared with standard interferon-based regimens. The catch is that the specific stakeholder is taking on the burden of the costs of treatment up front. Those receiving the benefits later on may not be the same, making assessment of cost-effectiveness difficult. With HCV, a specific payor will cover the cost of treatment while individual persons and society receive the benefits of cure and avoid future infections.

Taking the prison system as an example again, although treating inmates for HCV infection benefits the inmate and society because downstream medical costs and additional infections have been avoided, the prison system itself does not see as many of those benefits because, by the time the benefit is accrued, the inmate has long been released from the prison system. Although the prison system will eventually see a reduction in HCV prevalence as a result of its investment in HCV treatment, that benefit is farther down the road.

G&H What model programs are in place that encourage treatment as well as screening?

LH The Veterans Health Administration currently has a system in which an electronic alert pops up in the medical charts of patients who are in the at-risk birth cohort or have any other identified risk factors for HCV infection, such as injection drug use or HIV infection. The alert prompts the examining physician to offer HCV screening to the patient. A similar program, which is the TILT-C (Internal Medicine Trainees Identifying and Linking to Treatment for Hepatitis C) study, conducted by researchers at the Grady Memorial Hospital, is happening in urban downtown Atlanta, Georgia. The study is funded by the US Centers for Disease Control and Prevention. In it, everyone who comes through the door for any reason who is in the 1945 to 1965 birth cohort is screened for HCV infection. If a patient tests positive, he or she is referred to the liver clinic at Grady Memorial Hospital, where not only is the patient treated but also educated about how HCV infection is transmitted and given support from staff and peers.

A program in Australia led by Jason Grebely, PhD, of the University of New South Wales focuses on HCV treatment within the injection drug use communities. He and

colleagues found that screening and treatment of HCV infection that are concurrent with drug treatment programs, especially when they are directly observed and involve peer counseling, have been very effective. Another program, conceived by Anne Spaulding, MD, MPH, of Emory University in Atlanta, Georgia, is a “warm line,” used to overcome barriers to care in settings such as prisons, where the rate of HCV infection is about 17%. The warm line is a triage resource for a general practitioner in which he or she can get guidance from an experienced specialist to help provide appropriate treatment for an HCV-infected inmate.

G&H What other insights, based on your research in cost-effectiveness of HCV regimens, can you share?

LH In my research, I have found that cost-effectiveness also depends on HCV genotype. Because the cost of standard interferon-based treatment is so much more expensive for genotype 1 infection (\$70,000-80,000 because of the need for protease inhibitors, compared with \$23,000 for genotypes 2 and 3), it is more similar to the cost of interferon-free drugs. If the cost of newer regimens is similar to that of the standard of care, efficacy is higher, and adverse effects are lower, curing a patient is ultimately more cost-effective than if the new treatment is more expensive than standard of care. Although interferon-free regimens lead to better outcomes for genotypes 1, 2, and 3, they are most cost-effective for genotype 1.

My research also found that it is more cost-effective to treat younger than older age groups, although this finding is controversial. It is more cost-effective because a younger person has more life-years to live after treatment, and, as a result, treatment curtails more downstream medical costs associated with disease progression.

G&H What take-home message do you have for our readership?

LH Of greatest importance is to get patients screened and to build the support system needed to treat them. It should be a multidisciplinary endeavor. In addition, advocacy for pricing that allows the best drugs to be available to everyone is needed. Public awareness is needed about the disease, treatment, and access to care.

Ms Hagan has no relevant conflicts of interest to disclose.

Suggested Reading

Hagan LM, Wolpe PR, Schinazi RF. Treatment as prevention and cure towards global eradication of hepatitis C virus. *Trends Microbiol.* 2013;21(12):625-633.

Hagan LM, Yang Z, Ehteshami M, Schinazi RF. All-oral, interferon-free treatment for chronic hepatitis C: cost-effectiveness analyses. *J Viral Hepat.* 2013;20(12):847-857.

McEwan P, Ward T, Yuan Y, Kim R, Litalien G. The impact of timing and prioritization on the cost-effectiveness of birth cohort testing and treatment for hepatitis C virus in the United States. *Hepatology.* 2013;58(1):54-64.

Miller L, Fluker SA, Osborn M, Liu X, Strawder A. Improving access to hepatitis C care for urban, underserved patients using a primary care-based hepatitis C clinic. *J Natl Med Assoc.* 2012;104(5-6):244-250.