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Data to Guide the "Test and Treat Era" of Hepatitis C

See "Predicted effects of treatment for HCV infection vary among European countries," by Deuffic–Burban S, Deltenre P, Buti M, et al, on page 974.

Health leaders around the world are facing critical questions regarding how to combat a rising tide of hepatitis C virus (HCV)-associated liver disease. Worldwide, an estimated 130–170 million persons are living with chronic HCV infection, and HCV causes 1 in 4 cases of cirrhosis and 170,000 deaths per year.[1] Persons living with HCV are often unaware they are infected, reflecting the relatively asymptomatic nature of HCV infection until late in the course of disease and the often decades-long latency between acquisition of HCV and the development of end-stage liver disease and death. Many HCV-infected persons were infected decades ago, before the discovery of the virus in the late 1980s and the advent of blood bank screening and other prevention measures. As time passes and HCV has a longer opportunity to cause progressive liver damage, the number of HCV-infected persons developing end-stage liver disease (hepatocellular carcinoma and liver cirrhosis) is increasing at an accelerating rate.[2] For example, in the United States, the number of persons dying from HCV-associated conditions recently surpassed the number of deaths from HIV/AIDS. The US Centers for Disease Control and Prevention (CDC) estimate that HCV-related cirrhosis and morbidity will continue to increase year over year into the next decade and beyond.[3,4]

Fortunately, health officials are not empty handed in facing this looming crisis. A growing arsenal of direct-acting antiviral agents can clear HCV from the body (ie, achieve virologic cure). The addition of 1 of 2 commercially available protease inhibitors to treatment regimens can increase rates of sustained virologic response (ie, viral eradication after completion of treatment) to 63%–75%.[5,6] Other compounds under study in clinical trials may increase rates of viral eradication even further.[7] Achieving a sustained virologic response is important, because persons successfully clearing virus after HCV therapy have lower rates of hepatocellular carcinoma and all-cause mortality.[8,9]

The opportunity created by these new therapies is compromised by the lack of quality information that can be used to target case identification and treatment efforts. Insufficient public health surveillance systems that track HCV disease, mortality, and access to testing and medical care hinder health leaders from recognizing the growing threat of chronic hepatitis C and the potential benefits that accompany HCV testing, care, and treatment.[10] Seeking to fill this information gap, Deuffic–Burban et al

brings together data from 6 European countries to model trends in HCV-related cirrhosis and mortality and to identify the potential impact of new HCV therapies on these trends.[11]

To estimate the country-specific impact of treatment on the incidence of cirrhosis and mortality for the 6 European nations over the past 10 years and in the 10 years to follow, the authors make several assumptions and use a complex simulation model. Despite its complexity, at the core, this model forecasts a future of increasing HCV morbidity and mortality for these countries while demonstrating the promise of enhanced HCV screening and new therapies in limiting the impact of HCV infection. The model in the Deuffic–Burban et al paper mirrors the 4 most recently published models of HCV disease in the United States, each of which demonstrates how the implementation of new testing strategies and/or treatments can cost-effectively diminish the accelerating public health impact of HCV infections acquired decades in the past.[12–15]

Much of the complexity and assumptions of the Deuffic–Burban et al model were associated with the authors' objective to obtain country-specific estimates for each of the 6 nations. The authors found a range of possible impacts of HCV infection and new treatments over the coming decades, which varied based on differences in local epidemiology, HCV genotypes, and national health systems. Although the authors made a laudable effort to synthesize a wide range of data from a variety of sources, additional primary data on HCV are badly needed.

Several limitations are noted by the authors, including assumptions about past disease incidence, techniques to recreate treatment rates from pharmaceutical sales data, and the use of expert opinion in the place of observational data. These limitations point to a larger truth: When compared with other chronic, progressive diseases, there is much to be learned about HCV epidemiology, the rate of progression to end-stage liver disease, and the relative risk of liver cancer and liver failure depending on achievable sustained virologic response rates.

Despite these limitations, the authors' estimations provide data in ≥3 key areas. First, as with forecasts for the United States, all of these countries (with the exception of Italy) can expect increases in HCV-related cirrhosis into the next decade and, for Spain and the United Kingdom, likely beyond. For some countries, these trends signal a need for immediate action. In Belgium, France, and Germany, the epidemics of HCV-related disease are expected to peak within 10 years, leaving little time to expand capacity for HCV testing, care, and treatment.

Second, the Deuffic–Burban et al model also demonstrates the potential impact of HCV therapy in curbing the expected increases in HCV-related cirrhosis and mortality. Assuming no changes in screening or treatment practices in the next 10 years, the authors estimate HCV treatment-related reductions in cirrhosis and mortality by 21% and 12%, respectively. However, the projected declines were not uniform. For example, the authors forecast the greatest impact of HCV therapy for France (39% reduction in cirrhosis, 26% decreases in mortality), where the authors estimate a larger proportion of HCV-infected persons are tested and receive treatment.

Finally, the model of Deuffic–Burban et al also suggests a greater payoff in disease averted and lives saved when improvements in HCV therapy are accompanied by expanded access to HCV testing, care, and treatment. Although the data are sparse, the author's estimate that with the exception of France, ≤50% of HCV-infected persons have been tested. The authors demonstrate that increases in HCV testing and treatment could result in an additional 26% reduction in cirrhosis cases and 20% reduction in deaths averted among persons living with hepatitis C.

With the availability of effective HCV therapies, countries can use data and models, like those employed by Deuffic–Burban et al, to reconsider and realign their prevention priorities. In the United States, where an estimated 45%–85% of HCV-infected persons are unaware of their infection,[16] national priorities for HCV prevention are being transformed to help identify HCV-infected persons and link them with care and treatment. Specifically, the CDC recently expanded its HCV testing guidelines to recommend a 1-time HCV test for all persons born in and between 1945 and 1965, reflecting the high HCV prevalence (5-fold greater than other adults in the United States), burden of HCV infection and mortality (approximately 75% of all HCV infections for both) among persons in this population.[16] With full implementation of this strategy, CDC estimates that 800,000 persons currently unaware of their HCV infection will be identified. Moreover, when persons found to be HCV infected are linked to appropriate care and direct-acting antiviral agents treatment, >120,000 HCV-related deaths will be averted. With forecasted estimates and additional primary data points, other countries can examine their existing HCV testing policies and design new approaches tailored for their own epidemiologic characteristics of infection, resulting in greater reductions in HCV morbidity and mortality trends.

The health impact of expanded HCV testing can only be achieved when persons found to be infected with HCV receive appropriate care and treatment. Thus, regardless of country, policies must be accompanied by resources for a comprehensive set of implementation activities (eg, community education, provider training, laboratory quality assurance, and antiviral therapy). National plans can bring together different health sectors to improve HCV prevention by ensuring that more persons receive testing

and recommended care and treatment services.[17] Recognizing the need for such policies, the US Department of Health and Human Services published a viral hepatitis action plan in 2011 that outlines explicit steps for improving HCV testing, care, and treatment.[18]

The limitations in the Deuffic–Burban et al model highlight the need for better primary data to inform decision making for health policies to prevent HCV and reduce HCV-associated morbidity and mortality. Despite these limitations, the trends identified by the authors underscore the powerful call to action needed to mitigate the harm of HCV infection: HCV morbidity and mortality are increasing, and these increases can be curbed by expanded access to HCV testing and a growing array of effective HCV therapies. This era of effective therapy for HCV creates opportunities for health leaders worldwide to identify and implement new strategies that increase the number of HCV-infected persons who are aware of their infection and who receive effective treatment. Further, with the collection of more robust primary data, countries can employ strategies reflective of their local epidemiology and feasible for their health systems. By implementing these changes, countries can achieve population-wide reductions in HCV-associated morbidity and mortality.

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