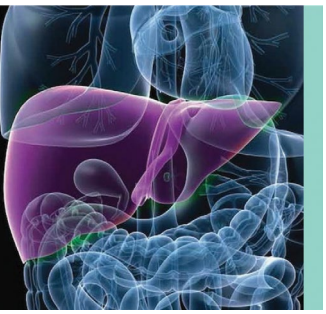

The Current Status of US and Global Access to Direct-Acting Antiviral Regimens for Hepatitis C Virus Infection

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The introduction of all-oral, direct-acting antivirals (DAAs) for hepatitis C virus (HCV) infection led to a number of global initiatives to allow access to these regimens. However, there are still significant barriers to access, and currently less than 10% of the world's population living with HCV infection has been treated and cured.[1] These market access experiences hold lessons for the future introduction of novel regimens against hepatitis B virus (HBV) infection, and some initiatives need to start now to avoid the same barriers that currently exist for access to HCV treatment.

SCREENING AND DIAGNOSIS

What Went Well. Many countries have moved away from targeted "risk-based" screening to more universal HCV testing initiatives.

Ongoing Barriers. In many low- and middle-income countries, there is limited access to nucleic acid testing or other tests that directly detect the presence of current HCV infection. True, affordable point-of-care assays that detect HCV RNA or HCV core antigen are needed.[2]

Implications for Hepatitis B. Treatments in development for HBV may also require detecting the presence of, or quantification of, serum HBV DNA levels. These nucleic acids tests are also prohibitively expensive and/or require technical expertise that may not be available in more remote locations. True point-of-care tests for quantitative or semiquantitative HBV DNA or assays, such as ones that detect hepatitis B core-related antigens, are needed.[3] Unlike with HCV, highly effective vaccines to prevent HBV infection and broader access to birth dose vaccine and vaccination of groups at high risk for infection, such as people who inject drugs, are needed.

Abbreviations: DAA, direct-acting antiviral; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; HCV, hepatitis C virus.

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ANTIVIRAL TREATMENT (BY COUNTRY-LEVEL INCOME CLASSIFICATION)

Low-Income Countries

What Went Well. Gilead agreed to voluntary licenses with companies that manufacture generic medications, and issued a list of more than 100 countries that would be allowed to access generic DAA regimens.[4] Bristol-Meyers Squibb worked with the Medicines Patent Pool to allow a similar spectrum of countries access to generic daclatasvir.[5] These approved generic regimens cost several hundred to $1,000. Countries such as Egypt and Pakistan allowed companies to manufacture unlicensed generic DAAs, and the prices of DAAs in these countries are close to the price predicted by Hill.[6]

Ongoing Barriers. Many countries that theoretically could access generic DAAs have not registered these drugs for country-level approval. Individual patients may be able to import generic DAAs for personal use, but these patients have to pay out of pocket (up to $1,000) because there is no government support.[7] Manufacturers need to be convinced that the volume of business warrants efforts at registration, which means each country needs to establish screening and care management services to demonstrate the volume of people who need HCV treatment. The global experience in HIV demonstrated that capacity-building investments, such as those provided by PEPFAR (US President's Emergency Plan For AIDS Relief) or the Global Fund, help break this logjam.[8] There is no equivalent global funding for HCV.

Implications for Hepatitis B. Companies that develop novel treatments for HBV will need to provide similar licenses to allow the manufacturing of generic drugs for low-income countries. These regimens need to be registered in every country. Global funding needs to be expanded to cover the diagnosis and treatment of HCV and HBV.

Middle-Income Countries

What Went Well. Nongovernmental organizations, such as Drugs for Neglected Diseases (DND*i*) and Initiative for Medicines, Access & Knowledge (I-MAK), have helped countries such as China analyze patents for sofosbuvir and overturn elements that were determined to be unmerited.[9] Novel regimens such as ravidasvir plus generic sofosbuvir are being developed as affordable alternatives.[10]

Ongoing Barriers. Middle-income countries that lie in close proximity to high-income countries have restricted access to regimens that are affordable because of the branded manufacturers' fears of unsanctioned exportation to high-income countries.

Implications for Hepatitis B. Tiered pricing of novel regimens needs to be implemented immediately on approval by a stringent regulatory authority.

High-Income Countries

What Went Well. Competition brought down prices of DAAs faster than with any previous launch of branded drugs in a new class. The "spread" between listed prices and actual prices paid after discounts and rebates became so great for certain regimens in the United States that Gilead spun off a generic company to provide generic alternatives whose prices better reflected actual prices being paid.[11] Louisiana negotiated a novel "Netflix"-style subscription to access DAAs for publicly funded programs such as Medicaid.[12] Washington state developed a similar program. Prices in Europe and Japan have also decreased compared with when DAAs were initially introduced.

Ongoing Barriers. Initial HCV treatment guidelines in many countries, intended to help providers prioritize patients waiting for treatment, were used by payers to ration access to treatment. In the United States, some Medicaid programs still restrict access, including rationing based on severity of liver fibrosis or length of sobriety.[13] State prisons and jails are still in the pool of payer entities used to calculate "best price," which determines prices for drugs in state Medicaid programs.[14] State prisons and jails do not belong in best price calculations and need to be removed to allow them to negotiate drug prices that better reflect constrained state Corrections health budgets. Indian Health Services receive about 25% of the per-capita funding spent for health care outside Tribal Nations in the United States, yet prices are not congruent with these "middle-income" countries located within the country that pays the highest price for drugs in the world. Prices in Eastern and Central Europe are still too high for universal access to DAAs.

Implications for Hepatitis B. Uneven access to novel HBV treatments will be at risk if current barriers present for

HCV regimens are not addressed. Guidelines will need to reflect, at a minimum, the populations of patients who are included in product labels.

Monitoring During and After DAA Treatment

What Went Well. Large cohort studies demonstrated that rates of hepatocellular carcinoma (HCC) declined after cure of HCV, although the risk for development of HCC is not eliminated. Advocates used these data to improve screening and insist on earlier treatment. Egypt embarked on a massive national HCV elimination effort that demonstrated to the world that monitoring during treatment could be simplified.

Ongoing Barriers. Laboratory monitoring for cure (and potentially future reinfection) requires the same access to affordable diagnostics that detect the presence of HCV that are required for screening programs. Access to ultrasound to monitor for HCC is not universal. Data to support how often to test specific populations for HCV reinfection are needed.

Implications for Hepatitis B. Ongoing monitoring for response to novel HBV therapies will likely be required, so efforts to develop affordable diagnostics need to start now. Certain people living with chronic HBV infection will likely also need long-term monitoring for HCC and affordable therapies for HCC if detected. Comprehensive elimination programs, such as the HBV, HCV, hepatitis D virus, and HCC elimination programs in Mongolia, need to be supported to generate data on cost-effective strategies in resource-limited settings.[15]

CONCLUSION

The World Health Organization has laid out a goal to eliminate viral hepatitis as a major public health threat by 2030, and specifically calls for "targets that seek to reduce the incidence of chronic hepatitis infection from the current 6–10 million cases of chronic infection to 0.9 million infections by 2030, and to reduce the annual deaths from chronic hepatitis from 1.4 million to less than 0.5 million by 2030."[16] Many countries, including the United States, are far from meeting these prevention, diagnosis, and treatment goals. The global experience with HIV has shown us that access to treatment drives sustainable programs, and universal access to HCV and HBV treatment will be required to eliminate new infections and premature death.

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