



The Voice of the Patient: Living with Chronic Hepatitis B

Report of an Externally-Led Patient-Focused
Drug Development Meeting

Hosted by the Hepatitis B Foundation



Public Meeting: June 9, 2020

Report Date: October 2020



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This report has been prepared by the Hepatitis B Foundation (HBF) as a summary of the input shared by patients living with chronic hepatitis B during an externally-led Patient-Focused Drug Development (PFDD) meeting hosted by HBF on June 9, 2020. This report presents perspectives shared by individuals who participated in the meeting and/or the associated pre-meeting engagement activities. Participant input has been summarized by the authors to faithfully represent the comments and themes that emerged. This report does not represent any consensus among participants or the broader population of those living with chronic hepatitis B, and does not include all possible perspectives.

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Introduction

On June 9, 2020, the Hepatitis B Foundation hosted a public meeting to hear directly from patients about their experiences living with chronic hepatitis B infection. Patients shared their perspectives on how the disease impacts them, their experiences with existing treatments, and their hopes for future clinical trials, treatments, and, ultimately, a cure. The Hepatitis B Foundation designed this meeting to complement the work of the U.S. Food and Drug Administration (FDA) Patient-Focused Drug Development (PFDD) initiative. The patient and family member input collected at this externally-led PFDD meeting will inform the development and regulatory review of new drugs for hepatitis B that will have a meaningful impact on patients' lives.

Overview of Chronic Hepatitis B and Current Treatments¹

A Persistent Global Public Health Threat

Hepatitis B is a serious and potentially life-threatening infection of the liver that is caused by the hepatitis B virus (HBV). It is the most common serious liver infection worldwide and around 2 billion people have been infected with HBV at some point in their life. Most infections are acute and generally resolve within six months. However, it is estimated that nearly 300 million people worldwide have chronic hepatitis B infections that persist beyond six months, and more than 880,000 die annually due to HBV-related complications including liver cancer, liver failure, and cirrhosis that can result from long-term infection.^{2,3} In the U.S., estimates suggest that as many as 2 million people are living with chronic hepatitis B.⁴ Widespread uptake of the safe and highly effective hepatitis B vaccine has resulted in a significant decrease in the incidence of new HBV infections worldwide. Nevertheless, hepatitis B remains an urgent global public health threat and an important cause of morbidity and mortality worldwide.

Hepatitis B is a “silent disease.” Most of those who become infected are unaware because they do not experience any symptoms, but they can still unknowingly spread the infection to others. Chronic hepatitis B can remain undetected for decades, often until an individual begins experiencing symptoms of liver damage. Only about one-third of persons with chronic hepatitis B in the U.S. are aware they are

¹ Content in this section is adapted from the opening remarks provided by Poonam Mishra of FDA and Anna Lok of the University of Michigan Medical School. For more detail see:

Lok AS, Zoulim F, Dusheiko G, Ghany MG. 2017. Hepatitis B cure: From discovery to regulatory approval. *Hepatology* 66(4):1296-1313; and

Cornberg M, Lok AS, Terrault NA, Zoulim F, and the 2019 EASL-AASLD HBV Treatment Endpoints Conference Faculty. 2020. Guidance for design and endpoints of clinical trials in chronic hepatitis B - Report from the 2019 EASL-AASLD HBV Treatment Endpoints Conference. *Journal of Hepatology* 72(3):539-557.

² Razavi-Shearer D, Gamkrelidze I, Nguyen MH, et al. 2018. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: A modelling study. *Lancet Gastroenterology and Hepatology* 3(6):383-403.

³ WHO (World Health Organization). Hepatitis B Fact Sheet. 18 July 2019. <https://www.who.int/news-room/fact-sheets/detail/hepatitis-b> (accessed July 17, 2020).

⁴ For more information about hepatitis B see the HBF website: <https://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/> (accessed July 17, 2020).

infected. A simple blood test panel is used to detect the presence of the hepatitis B surface antigen (HBsAg) in serum, which indicates that someone is currently infected and able to transmit the virus to others. The panel can also detect the presence of hepatitis B surface antibodies (HBsAb) that indicate a person is immune to HBV as a result of recovery from a prior infection, or from vaccination.

There is no cure for hepatitis B. Treatments are available that can suppress the replication of the virus in the body and slow the progression of the long-term complications of chronic hepatitis B. Reducing the amount of virus circulating in the blood can also help to reduce the likelihood of transmitting the infection to others. But these treatments have limitations and are not without risk. Although many patients remain asymptomatic and do not require treatment, those who do generally face long-term or lifelong treatment to manage their infection. There is the potential for adverse reactions to the treatments, and long-term use can lead to the emergence of drug-resistant strains of the virus, though not typically with current first-line treatments (tenofovir or entecavir). Even with treatment, these patients are still at risk for liver damage and liver cancer.

Treatments are Available

Treatments for chronic hepatitis B that are approved for use in the U.S. fall into two main categories:

- **Interferons** are drugs that modulate the immune response. The most commonly used interferon for the treatment of chronic hepatitis B is pegylated interferon, a long-acting form that is given by injection, once per week, for about one year. Interferons have many side effects, and only about 20% of those treated experience a sustained benefit.
- **Oral antiviral drugs** are nucleos(t)ide analogs that reduce the level of virus circulating in the blood by interfering with the viral replication process. Commonly used antiviral drugs include tenofovir disoproxil fumarate, entecavir, and lamivudine, which are taken by mouth, once per day. Oral antiviral drugs have few side effects and are very effective in suppressing the virus. These treatments do not eliminate the virus, however, and most patients require long-term, often lifelong treatment. Stopping treatment can result in a resurgence of circulating virus and disease flare.

Current Treatments Suppress, but Do Not Eliminate Chronic Hepatitis B

In assessing the success of a treatment, the first approach is to measure the amount of virus circulating in the blood, referred to as the “viral load.” This is done by quantifying viral DNA. If treatment is working, the level of circulating virus decreases, ideally to levels low enough that the HBV DNA is not detectable by laboratory testing. Liver function tests are another measure, and the return of elevated liver enzymes in the blood to normal levels indicates improvement of liver disease.

The treatments currently available are generally effective in suppressing the virus and normalizing liver enzyme levels. They can prevent progression of disease to cirrhosis and liver failure in many cases, and also reduce the risk of liver cancer. Current treatments are less effective, however, in reducing the surface antigen that is the marker of HBV infection (HBsAg). Ideally, new successful treatments will result in HBsAg becoming undetectable in blood. Additional measures of success for an ideal chronic

hepatitis B treatment are complete eradication of the virus from the body, and prevention of hepatitis B-related cirrhosis, liver failure, and liver cancer.

Barriers to Eradicating Chronic Hepatitis B

It is very difficult to completely eliminate HBV from the body because the virus has a complex life cycle which is not yet fully understood. Once inside the nucleus of the human liver cell, the viral DNA forms a very stable covalently closed circle (cccDNA) that directs the production of new virus. This cccDNA persists in the liver cell nucleus as new virus is churned out. HBV cccDNA is also able to integrate into the DNA of the human liver cell, which compounds the challenge of eradicating the virus. Current antiviral treatments are not able to suppress cccDNA, which is the key to finding a complete cure for chronic hepatitis B.

People who are chronically infected with HBV also have an impaired ability to mount a strong immune response to the virus. They are not immunosuppressed, and they can fight off other infections, but they do not seem to fight HBV successfully.

An Added Treatment Challenge: Co-infection with Hepatitis Delta Virus

It is estimated that 5% to 30% of people who have chronic hepatitis B are also infected with the hepatitis Delta virus (HDV). HDV infection only occurs in conjunction with HBV infection, and coinfection with HBV and HDV leads to increased risk of cirrhosis and liver cancer. There are no approved treatments for HDV infection. Interferon has been shown to provide some benefit for a small proportion of patients, however the oral antiviral drugs, entecavir and tenofovir, are not effective. There are new drugs in development and clinical trials that might prove effective in controlling HDV, alone or in combination with interferon or antivirals.

Pursuing a “Functional Cure”

Because HBV hides in the liver cell nucleus as cccDNA and can integrate into the DNA of the human liver cell, developing a complete cure for chronic hepatitis B (i.e., elimination of HBV cccDNA and sustained, undetectable HBsAg after a finite duration of treatment) will be extremely difficult, and might not be possible. A more feasible approach is to pursue a functional cure for chronic hepatitis B, in other words, a treatment that can silence the virus even if it is not completely eliminated. A functional cure is defined as sustained, undetectable HBsAg and HBV DNA after completion of a finite course of treatment (without the elimination of cccDNA).

A very small proportion of patients are able to achieve a functional cure with currently available treatments (5-10% of patients after one year of treatment with interferon; 1-8% of patients after 5 years of oral antiviral treatments). Even without treatment, around 1% of patients who are not treated will demonstrate undetectable levels of HBV DNA and HBsAg each year. The initial goal for a new treatment would be to achieve a functional cure in at least 30% of patients after a finite duration of treatment. Achieving a functional cure likely involves blocking multiple steps in the hepatitis B virus lifecycle, blocking HBsAg production, and boosting the immune response.

The benefits of a functional cure include not only the potential for reversal of liver damage and reduced risk of cirrhosis and liver cancer, but also reduction of symptoms, improved quality of life, and elimination of the stigma of living with chronic hepatitis B.

Developing the Next Generation of Hepatitis B Treatments

At the time of this externally-led PFDD meeting there were 27 new products in clinical development for the treatment of chronic hepatitis B, and it was expected that additional clinical trials would be initiated in the near future. Although this is exciting, it is important to keep several issues in mind when developing new treatments. Current oral antiviral drugs are safe and very effective, and new products should be comparable or better. Current oral drugs are also convenient, and some are available as lower-cost generic products. As such, new products need to also be convenient and accessible to patients. New products should also be broadly applicable across the spectrum of disease, whether patients have mild symptoms or advanced cirrhosis. In this regard, FDA released a draft guidance, *Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment*, to help facilitate the efficient clinical development of the next generation of treatments for hepatitis B, addressing issues such as study design and trial population.⁵ Also essential to the development of successful new products is input from those who will ultimately use them, including the patients who have shared their perspectives during this PFDD meeting.

Meeting Design and Data Collection

The Hepatitis B Foundation designed this meeting to complement the work of the FDA's PFDD initiative. PFDD meetings give FDA, medical product researchers and developers, and other stakeholders an important opportunity to hear directly from patients and family members about the symptoms that matter most to them, the impact of the disease on patients' daily lives, and patients' experiences with currently available treatments. This externally-led PFDD was convened to help inform the development and regulatory review of products for the treatment of chronic hepatitis B.⁶

Hepatitis B research is at a critical juncture, with many investigational products in the development pipeline. These new products are leveraging the expanding understanding of the HBV lifecycle, and many are targeting different mechanisms than currently available drugs. Input from the people who will be using these products is more important than ever to ensure that their experiences, perspectives, needs, and priorities are factored into in hepatitis B programming, product development, and clinical trial design.

⁵ *Chronic Hepatitis B Virus Infection: Developing Drugs for Treatment, Guidance for Industry* is available at <https://www.fda.gov/media/117977/download> (accessed July 17, 2020).

⁶ More information on FDA's PFDD initiative is available at <https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development> (accessed July 17, 2020).

Planning for this externally-led PFDD began in July of 2019. The goals of the meeting were: (1) to document the physical, psychosocial, and professional impacts of living with chronic hepatitis B, and (2) to hear perspectives on current and future treatment needs and priorities from those who are living with chronic hepatitis B. To inform the development of the meeting agenda (Appendix 1), and to obtain broader input from individuals living with chronic hepatitis B than would be possible from a half-day meeting, the Hepatitis B Foundation also conducted 24 in-depth phone interviews and launched an online survey that garnered over 2,100 responses from people in 102 countries (Appendix 2).

More than 30 externally-led PFDD meetings have been convened, addressing a broad range of diseases.⁷ However, due to the ongoing COVID-19 pandemic, this was the first fully virtual PFDD meeting. The meeting format was very interactive, with more than 650 online participants including not only individuals and families impacted by chronic hepatitis B, but also professionals working in drug development and patient care. Live polling of individuals living with hepatitis B and family member participants during the meeting suggested that about two-thirds of participants were themselves living with chronic hepatitis B and one third were family members. Most responded that they were diagnosed more than ten years ago, and their reasons for being tested for hepatitis B varied widely. Half of the demographic polling respondents identified as female and half as male; 15% were age 18-30, about one third were 31-50 years of age, and one half were over the age of 51. Although the majority of demographic polling respondents (over 80%) indicated they were from the U.S., meeting registrations and email comment submissions suggest that there were many international participants.⁸

Following introductory remarks by experts in hepatitis B disease and treatment, the two main panel sessions addressed the topics of symptoms and disease impact, and current and future treatments. Each session began with pre-recorded testimony from four individuals living with chronic hepatitis B (Appendixes 3 and 4), followed by a live, moderated discussion among six patient/family member panelists (participating remotely). The discussion was guided by preestablished discussion questions and augmented by live polling of participants during each panel session (Appendix 5). Online attendees had the opportunity to call in and speak live, or submit an email comment, some of which were read live by the moderator. In total, more than 300 comments were submitted by email during the meeting and throughout the open comment period that ran from June 1st through 30th (Appendix 6).

The Hepatitis B Foundation hopes that this summary report will be of use to regulatory and other federal agencies, medical product developers, researchers, and healthcare professionals who will develop, evaluate, and deploy the next generation of treatments for chronic hepatitis B.⁹

⁷ Externally-led PFDD meeting reports are available at <https://www.fda.gov/drugs/development-approval-process-drugs/external-resources-and-information-related-patients-experience> (accessed July 17, 2020).

⁸ The response rate to both the demographic and disease experience polling was low, perhaps due to the challenges of the virtual format of the event. The results are not considered scientific data but provide a snapshot of who participated in the PFDD meeting and complement the live and emailed input on disease experience.

⁹ The archived webcast of the meeting is available at: <https://www.hepb.org/news-and-events/patient-focused-drug-development-meeting-virtual/> (accessed July 17, 2020).

Overview of Key Themes

This report summarizes the input provided by individual panelists and participants during the meeting, as well as the findings from pre-meeting engagement activities undertaken by the Hepatitis B Foundation.¹⁰ The themes that emerged from the externally-led PFDD meeting are consistent with the sentiments expressed by those interviewed during the meeting planning phase and the feedback obtained from the survey instrument and emailed comments (see Appendices 2 and 6).

A number of themes emerged throughout the meeting as participants shared their perspectives on how living with chronic hepatitis B impacts them, their experiences with existing treatments, and their hopes for the development of future treatments (highlighted below and discussed further in the report that follows).

The health effects of living with chronic hepatitis B span the range from asymptomatic to end-stage liver disease and liver cancer.

- Unrelenting chronic fatigue was repeatedly mentioned as a hallmark feature of living with chronic hepatitis B. For many, fatigue was debilitating and limited their ability to attend to necessary tasks in their life.
- Joint pain, muscle pain, and body aches were also discussed as having significant impact on patients' daily lives.

The personal and social impact of living with chronic hepatitis B can be significant.

- The stigma around hepatitis B persists and participants reported experiencing harassment, discrimination, social isolation and ostracization, and shame. It was discussed that stigmatization takes different forms in different cultures and regions of the world. The need for greater public awareness about hepatitis B was emphasized by participants.
- Fear, anxiety, and stress are pervasive as patients worry about issues such as the long-term health impacts of their disease (e.g., drug-resistance, cirrhosis and liver cancer, premature death); transmitting the disease to others (especially one's children); the need for life-long treatment; not being able to afford or access care and treatment; and the social ramifications of disclosing their disease status or having it discovered (such as job loss, strain on relationships with partners and family).

Current treatments are effective in suppressing the virus, but they don't eliminate the virus, and there are other risks.

¹⁰ This report presents perspectives shared by patients and family members who participated in the meeting and/or associated engagement activities. Participant input has been summarized by the rapporteurs to faithfully represent the comments and themes that emerged. This report does not represent any consensus among participants or the broader population of those living with chronic hepatitis B, and does not include all possible perspectives.

- Currently available medications for chronic hepatitis B have improved the quality of life for many patients.
- Currently available oral antiviral medications are easy to take with few side effects, however, some treatment regimens include interferon, which many patients do not tolerate well.
- Treatment with oral antiviral medications can be long-term or lifelong, and there is the potential for the development of drug-resistant viral strains.
- Even while being treated, some still fear the possibility of disease progression and premature death.
- Some patients experience bothersome physical and cognitive side effects of treatments, which can negatively impact quality of life.
- Some of those living with chronic hepatitis B do not meet the current criteria for treatment, which some said made them feel nervous and uncertain about the future, and concern was raised about gaps in disease monitoring.
- Many have adopted healthy lifestyles to stay strong in the hope of preventing a disease flare.

Above all, patients want a functional cure for chronic hepatitis B.

- The ultimate goal is to develop a functional cure, a finite-duration therapy that can eliminate the hepatitis B surface antigen such that long-term/lifelong treatment is not needed to prevent disease progression.
- Patients want treatments that:
 - Achieve and sustain undetectable levels of HBsAg in blood
 - Achieve and sustain undetectable levels of HBV DNA in blood
 - Significantly reduce the risk of cirrhosis, liver failure, and liver cancer
 - Improve quality of life and reduce stigma and discrimination
- Patients favor convenience and prefer oral treatments over those that require injections or intravenous infusions. Injectable medications were acceptable to many if they were of limited frequency and duration. Some said they would be willing to tolerate a greater level of inconvenience (e.g., longer course of treatment, side effects) if there was a greater chance for achieving a functional cure.

Patients might participate in clinical trials of products that have a low risk of serious side effects and a high potential to provide a functional cure.

- For many meeting participants, the risk of serious side effects, such as a liver enzyme flare (significantly elevated ALT), was a key consideration in deciding whether to participate in a clinical trial. Concern was expressed about the potential for serious or permanent liver damage or other adverse effect from trial participation.
- The hope that the treatment under investigation could provide a functional cure was noted to be a compelling factor for trial participation.
- The burden of participation was also mentioned as a key factor, such as the time needed to participate or the travel distance, the route of treatment administration (e.g., oral vs. IV), and the potential for side effects that might impact daily life.

Topic 1: Living with Chronic Hepatitis B - Symptoms and Disease Impacts

To open the discussion of the first topic, participants watched pre-recorded video statements by four panelists, Bright, David, Alice, and Randy, who graciously shared their personal stories of living with chronic hepatitis B. These individuals were selected to help represent a range of different perspectives on how the physical symptoms of chronic hepatitis B have impacted their daily lives, what worries them most about living with chronic hepatitis B, and their experiences of stigma and discrimination. (Brief summaries of their statements are presented here. The full transcript of each video is available in Appendix 3. The questions used to guide the testimonies and subsequent panel discussion can be found in Appendix 5).

Patient Testimony on Living with Chronic Hepatitis B

The Physical Effects of Living with Chronic Hepatitis B – Bright’s Experience

Bright was born and raised in Ghana and immigrated to the U.S. in 2007. ***“For me the physical impact of hepatitis B has been debilitating and huge.”*** In early 2014, Bright began to experience fatigue, but he attributed it to working full time at a physically demanding job while also taking college classes and serving in the Army reserves. Soon the frequency of the fatigue increased and began to impact his daily life. He consulted his doctor and was diagnosed with chronic hepatitis B. ***“I wake up every morning tired, even before I try doing anything. Nothing helps, not even 12 hours of sleep.”*** Bright added that he also gets sudden bouts of fatigue during the day and needs to find a place to lie down. Another physical symptom he experiences is unexplained chronic muscle pain. The pain and the fatigue usually occur together and impact Bright’s ability to drive, cook, clean, or accomplish other tasks. His ability to take pain medication is limited due to the impact of these medications on the liver. As a result of his physical symptoms, Bright has been unable to work since 2016 and has been living with a friend because he can no longer afford an apartment. He has been told his condition “is not serious enough,” and that he “should learn to adjust.” The fatigue and pain have also forced Bright to become sedentary and isolated. He often does ***“not have the energy to get out of bed.”*** Bright must complete an eight-month field assignment for his degree in social work and is not sure how he will be able to accomplish this, as the accommodations he has been provided at the college might not be possible at his fieldwork location. A particular challenge, Bright said, is that ***“it is difficult not knowing and not having control over which days will be good or bad.”*** A recent asthma diagnosis has added to his challenges. ***“It is an exhausting life,”*** he said, and ***“some people ... in positions of authority, like school instructors, doctors, government officials, or work supervisors think that it is all in your head and you are just being lazy. It robs you of the little dignity you have left.”***

The Fear and Anxiety Associated with Having Chronic Hepatitis B – David’s Experience

David is 31 years old and lives in Michigan. He was born in South Korea and was infected with hepatitis B during birth as his biological mother was chronically infected. David’s adoptive parents were aware of

his hepatitis B status when they brought him into their family at five months old. ***“When I was 13 years old,... I was given a crash course on hepatitis B and what it meant to be a chronic carrier. My body shivered in fear and confusion.”*** As a teenager becoming interested dating and parties, he was suddenly faced with the reality that alcohol and sex would always present significant risks to himself and others. ***“The possibility of transmission and fear of others' reactions to my hepatitis B is what has been the most impactful in my life.”*** He is very selective about who he shares his status with, when, and in what context, and said he has avoided potential friendships because of fear of rejection. ***“The dating world was especially daunting for someone with a transmittable disease.”*** David’s approach has been one of “clear and honest communication.” He noted, however, that there are few if any positive depictions of hepatitis B in media, and negative public sentiment is compounded by “a glaring lack of empathy and sex education in the U.S.” He emphasized the need for increased public awareness. ***“If someone only relates the word ‘hepatitis’ with dirty, filthy, and disgusting, it's hard to reeducate from there.”*** Another source of anxiety is not knowing if he will ever be able to stop taking antiviral medication. He said he feels some relief that side effects have been minimal, and his viral load has been reduced to undetectable levels. But that could change over time, and he has a long life ahead of him. ***“Talking about concerns with my doctors and loved ones make me feel empowered but I don't always have that strength every day.”***

Social Stigma Associated with Chronic Hepatitis B – Alice’s Experience

Alice was born and raised in Hong Kong and now lives in California. Although she had jaundice as a teenager, it went away, and she was shocked when she was diagnosed with hepatitis B during her first pregnancy in the 1980s. Alice then learned her mother also had the virus, and that the virus was probably transmitted to her during birth. Alice explained that talking about illness was taboo in her traditional Chinese family. ***“My family tends to feel shame for having a chronic illness.”*** There was a fear of being isolated from friends and relatives if they knew, and health conditions were kept secret. Because those with hepatitis B have been stigmatized throughout history, Alice’s mother had been ashamed to disclose her status, which put Alice and her siblings at risk from mother to child transmission and serious complications in life due to chronic hepatitis B. Alice’s own children were protected from hepatitis B infection because her obstetrician adhered to protocols that prevent mother-to-child transmission, including vaccination and administration of hepatitis B immune globulin at birth. ***“As a parent, I chose to be open with my family and my children on health-related matters. I became involved in raising awareness in the local Asian communities. I believe knowledge is power.”*** Alice is now actively educating other parents about hepatitis B facts and myths, and promoting hepatitis B testing and vaccination in her community. She shared that doing this has helped her overcome her fear of isolation and focus on the positive. Still, she did not disclose her status openly until 2018, when she joined the #justB Storytelling Campaign sponsored by the Hepatitis B foundation. ***“I was empowered by the experience of engaging with other people living with HBV and family members impacted by the disease and seeing how everyone was able to share their stories without hesitation or feelings of shame. ... I was full of hope that living with hepatitis B is not disgraceful.”***

Discrimination Associated with Chronic Hepatitis B – Randy’s Experience

Randy and his wife live in Washington State. They were married while he was stationed at Camp Humphreys in South Korea and they have two grown sons. Randy’s wife and younger son are living with chronic hepatitis B. His wife was infected at birth, as were all of her siblings. Although both sons were vaccinated for hepatitis B at birth, the older son tested positive for hepatitis B and the younger son tested negative when they were tested in middle school. Around that time, the younger son decided he wanted to attend the U.S. Naval Academy. As a result of his exceptional grades, strong leadership qualities, and participation in the Navy Junior Reserve Officer Training Corps (ROTC) program, he secured a nomination and headed off to the Academy in Annapolis for basic training after high school. As the family was getting ready to attend his graduation from boot camp, their son called to let them know he had tested positive for hepatitis B. ***“We were in complete disbelief. ... We later found out that you can't serve in any branch of the military, officer or enlisted, if you have hepatitis B.”*** Randy’s said his wife was inconsolable and blames herself for ending her son's dream. ***“The disappointment is devastating, and we continually live with it.”*** Randy said they constantly think about what could have been. After the younger son’s diagnosis, the entire family was retested, and the older son tested negative. Randy feels that the only explanation is a mix up in the samples when the boys were first tested in middle school. The younger son has now completed his Associate’s degree and is living with friends and working at a local hospital. The family is very proud of how hard this son has worked to overcome this major setback in his life. ***“How amazing would it have been to have a pill, an injection, or some other kind of treatment that my son could have gotten at the Naval Academy? He could've continued on and he would have been a Naval officer today. Please put more effort, more resources into curing hepatitis B. So many lives depend upon it.”***

Perspectives on Living with Chronic Hepatitis B – Moderated Participant Discussion

Following the presentation of the pre-recorded testimony, the four panelists were joined by two other individuals, Joan and Maureen, for a live, moderated panel discussion. Joan, a nurse and one of the co-founders of the Hepatitis B Foundation in Pennsylvania, did not go public with her own hepatitis B diagnosis until she retired. Maureen is the adoptive parent of a (now adult) daughter who they did not know was very ill with hepatitis B at the time of her adoption from China. Panelists and participants expanded the conversation on how the physical symptoms of chronic hepatitis B have impacted their daily lives, and how living with hepatitis B has impacted their personal, social, and professional lives including what worries them most about living with chronic hepatitis B and their experiences of stigma and discrimination. Online participants also provided input by calling in, emailing comments, and responding to live polling questions. (Excerpts of the discussion are included below to help illustrate participants’ experiences. Additional highlights from comments submitted via email are provided in Appendix 6).

Physical Symptoms of Chronic Hepatitis B that Most Impact Patients' Daily Lives

- **Fatigue** – A primary concern expressed by most participants was unrelenting chronic fatigue. Some said that tiredness is the defining characteristic of their disease experience. Others described the fatigue as debilitating, impacting their productivity and their ability to care for their children. Some expressed regret about missing out on life due to fatigue, especially not being able to be more involved in their children's lives. One patient described suffering from insomnia on a regular basis, which contributes to her fatigue.
- **Muscle Pain, Joint Pain, and Body Aches** – Many participants described the impact of pain in their daily life, emphasizing joint pain, muscle pain, and body aches. Like fatigue, participants said that pain impacts their ability to work, socialize, and attend to necessary tasks in their life. Managing pain is a challenge as many pain medications impact the liver.
- **Digestive and Excretory Issues** – Participants also described experiencing a range of digestive issues, including bloating of the abdomen and weight loss. Jaundice was also noted as a concern.
- **Other Symptoms** –
 - Anxiety was mentioned as a symptom that patients might not recognize as being associated with hepatitis B. Concerns were raised that those living with hepatitis B and dealing with anxiety are not being properly managed by a provider.
 - Bone loss and osteopenia/osteoporosis were also mentioned as concerning symptoms, especially when taking certain antiviral medications long-term.

Patient Voices: Physical Symptoms

"As a child, my mother always said I was lazy because I needed to sleep a lot. As a young woman, I thought it was the stress of having children, working full time, that I was just a rather low energy person. And now as a 60 year old, I feel like, well it's my age. But in reality, having spoken to literally thousands of patients, I realized fatigue is probably the defining characteristic of living with chronic hepatitis B."

–Joan from Pennsylvania

"I have terrible pain, mainly in my abdomen. It impacts my work, and I have a very physical job."

– James from Hawaii

"The main symptom was fatigue, weight loss, and body aches. I was tired the majority of the time. My social life was on a halt."

– Neha from Kenya

"I happen to also deal with pain in addition to the chronic fatigue ... most of the time I spend my day in the house and it's just unbearable. I've tried everything from pain pills to pain creams and other stuff, but it's just impossible to get anything really to help.... I think it makes life much more unbearable than anything I can compare to."

– Bright from Maryland

The Impact of Living with Chronic Hepatitis B on Participants' Personal, Social, and Professional Lives

Living with chronic hepatitis B impacts individuals in many ways beyond the daily impact of the physical symptoms and limitations. The personal and social toll the disease takes in an individual's life can be significant. During the moderated discussion and online polling, participants described a range of personal, social, and professional implications of having hepatitis B, which are often interrelated.

- **Decreased Social Interactions and Isolation**— Many participants shared that living with chronic hepatitis B has led them to limit social interactions, both as a way to avoid potential harassment, discrimination, and stigmatization, and for fear of spreading the disease to others. Several participants pointed out that social gatherings often involve alcohol, and it can be difficult to explain, or make excuses for, why they are not drinking, so they avoid socializing. Dating and finding a life partner is a particular challenge for young people living with hepatitis B. Others shared that they have been rejected by family, friends, or coworkers which, for some, has led to isolation, loneliness, anxiety, and depression. Several participants emphasized the importance of making connections with others living with hepatitis B in helping to overcome the feelings of isolation.
- **Fears, Anxiety, and Stress** – Participants expressed health-related worries, such as a fear of transmitting hepatitis B to others, of contracting another disease, of not being able to afford or access treatment, of developing resistance to antiviral treatments, and of having inactive disease become reactivated. Many expressed fears of dying prematurely from liver cancer. For some, these health concerns lead to fears of being unable to date or marry, of being unable care for one's family, and of dying and leaving behind young children. Participants also expressed fears of having their disease status discovered or about how others will react if they choose to disclose their status, especially with regard to the potential social rejection, stigma, and discrimination that those with chronic hepatitis B often experience.
- **Harassment and Discrimination** –Some participants described experiencing discrimination based on their hepatitis B status. They shared stories of losing their jobs, being prohibited from getting jobs in certain sectors or countries, being discharged from military service, and having their children expelled from daycare. One participant said she has not experienced discrimination because she has chosen to not share her status beyond close family members.
- **Stigmatization** – It was emphasized that the stigma associated with hepatitis B persists, and there is a need to raise public awareness about the disease and counter the fear-based misinformation that leads to harassment, discrimination, and shame. It was observed that hepatitis B-related stigma is particularly prevalent in certain cultures and in some parts of the world. Some participants noted being ridiculed by relatives, others shared how stigma has impacted not just themselves but their families.
- **Shame** – Participants expressed having felt ashamed of their diagnosis, having felt “dirty,” and feeling they were somehow at fault for getting the disease. Some blame themselves for transmitting the disease to loved ones (especially women who unknowingly transmitted the virus to their children during birth). It was stated that there is a need for more disease education and support for those who have hepatitis B, so they can move beyond the stigma and shame and ask for help. Many

participants noted how hearing the stories of others who are living with hepatitis B has given them hope and reassured them that they are not alone.

- **Other Issues –**

- Insurance coverage – One participant said she has been unable to obtain long-term care insurance, and the challenges of obtaining adequate health insurance led her to decide not to change jobs. Another participant said she lacked insurance coverage for her hepatitis B medications. The high cost of treatment even for those with insurance coverage was also noted.
- Access to care – A participant from Kenya noted the difficulty of getting access to care and treatment. He said some turn to traditional medicine, and many in rural villages die without being diagnosed.
- The impacts of aging on managing chronic hepatitis B – One participant pointed out that, as people age, they tend to develop comorbidities (e.g., breast cancer) or painful conditions that often require treatments that impact the liver.

Patient Voices: Disease Impacts

"I worry about dying prematurely. I worry about transmitting it to my loved ones. I worry about my increased bone loss on my osteopenia."

– Espi from Florida

"[S]ometimes when you feel a little bit of pain, you just start worrying is it cancer or what is it?... you just know sometime it might happen that you will have the liver cancer."

– Daniel from Illinois

"Emotionally, I was subject to prejudice ... harassment from my coworkers, my roommates, I was rejected. I was telling them to get vaccinated. And I told them about the disease, but gradually they rejected me, and I feel alone."

– Gooksa from Minnesota

"Often, I feel shame in sharing my diagnosis to friends, family, or coworkers, even though I understand that this disease is no fault of my own, as I've had it since birth.... Socializing can often be difficult also, as I often must explain why I'm not drinking alcohol."

– Raj from California

"I didn't attend any kind of big social gathering where I knew that there would be a lot of drinking involved because I succumbed to peer pressure when I was younger and drank alcohol.... And if someone asks you why you're not drinking, it's sometimes very difficult to know what to do in that situation.... I've skipped invites to birthdays or invites to weddings ... just because of massive amount of fear that that generated."

– David from Michigan

"The health community group emphasizes public awareness, vaccination, and prevention, but they do little for people living with the disease. There's no dedicated support group for hepatitis B."

– WL from California

"In Africa, the stigma is very high and that's why people don't come out to speak about it."

– Victor from Nigeria

"I decided against making a job change partly because of the increased challenge in obtaining adequate health insurance, especially with HBV, at a reasonable cost in the private sector compared to my government employment.

"[A]s you get older, you start getting all sorts of other conditions ... that you're going to need to take medications for, and how to juggle that with having a compromised liver.... [Y]ou start suffering more pain, and pain medications are not good for the liver.... I'm 65 now and when I look at the future, it's a bit daunting to think about how to manage all of this."

– Karin from California

"[W]hen I found that I had hepatitis B, first I lost my job and my child was kicked out of daycare.... I felt really ashamed ... it's most likely I got it from my birth mother, but at the time you just think 'I'm a dirty person'.... [F]or almost 30 years, I really didn't talk about it because it just became one of those things that just opens up too many boxes of questions.... [I]f you can't tell people, it's a part of yourself that becomes secret and you don't feel authentic.... There is this feeling when I tell a new person, I feel anxiety about how are they going to react.... [W]hen I finally came out of the closet two years ago, it was such a huge relief.... [F]or the first time, I feel like I'm whole, because now that everybody knows I don't have to keep it secret anymore. If I'm tired, I can say I'm tired because it's hepatitis B."

– Joan from Pennsylvania

Topic 2 – Perspectives on Current and Future Approaches to Treatment

The second panel discussion also began with pre-recorded video statements by four panelists, Jacki, Peter, Wendy, and Joe, who kindly shared their experiences with treatment and their hopes for the future. These individuals were selected to help represent a range of different perspectives on current and future approaches to the management of chronic hepatitis B, including medications and medical procedures, as well as diet, exercise, and other lifestyle modifications. Panelists were also asked to reflect on what is most important to them in considering whether to participate in a clinical trial. (Brief summaries of their statements are presented here. The full transcript of each video is available in Appendix 4. The questions used to guide the testimonies and subsequent panel discussion can be found in Appendix 5).

Patient Testimony on Current and Future Approaches to Treatment

Current Treatment Experiences – Jacki's Perspective

Jacki was born in Taiwan and now lives in New Jersey. He was first tested for hepatitis B in 1998, after his brother was diagnosed with cirrhosis and liver cancer due to chronic hepatitis B. At that time, the only available treatments were interferon, which has many side effects, and lamivudine, which was known to lead to drug resistance. Because Jacki had few symptoms other than elevated liver enzymes and occasional fatigue, he did not start treatment. In 2008, after developing severe fibrosis, he began antiviral treatment. His viral load dropped to undetectable levels, his liver enzymes gradually returned to normal and he felt less fatigued. However, he said, ***"it was not easy to take the medication every day***

for many years. Many times, I forgot or purposely ignored the medication.” As a result, his virus level intermittently became detectable and his liver enzyme levels increased. Currently, Jacki is taking a new oral drug, which has a very low incidence of drug resistance and a better safety profile for bones and kidneys. *“[E]ven though this treatment might have lowered my risks of developing cirrhosis and liver cancer, [it has] not reduced the discomforts I experienced frequently, which might be a result of liver fibrosis ... caused by the virus, or accumulated toxicity due to long-term use of the drug.”* Jacki added that treatment does not eliminate his constant worries that he might develop liver cirrhosis or liver cancer, or develop resistance to the antiviral drug. *“With the advent of new technologies and greater support for basic and translational research, I hope that one day soon, we can all take a simple pill for a short period of time, and finally be able to get rid of this virus from all of us.”* Jacki pointed to the intense drug development efforts for HIV, hepatitis C, and now for the new coronavirus and said *“...it is clear that hepatitis B has been ignored for too long. We need a cure for hepatitis B now, and we need to stop the spread of this deadly virus.”*

Current Treatment Challenges – Peter’s Experience

Peter is 51 years old and lives in Arizona. After being treated with an antiviral for 12 years, his viral load was reduced to an undetectable level. His doctor decided to stop treatment and monitor him with blood testing every six months. About a year and a half later, however, Peter said he was feeling very fatigued. His skin and eyes became yellow, his urine was very dark, and his stool was light in color. *“[My wife] immediately took me to the emergency room.... [T]hey placed me in a coma to keep me alive. But, after 10 days, I woke up and my wife told me the hepatitis B virus had completely destroyed my liver and that I had a liver transplant.”* Peter is nearing the close of the three-year post-transplant recovery phase and is being closely monitored by his providers. *“My greatest health risk right now is organ rejection, bacterial and viral infections, and hepatitis B reactivation.* Because he has stage three chronic kidney disease as a result of the acute liver failure, Peter is currently being treated with a new antiviral that has less renal toxicity. He is monitored with blood testing every three months, and receives an intravenous hepatitis B immunoglobulin (HBIG) treatment every six months. Peter suffers from extreme fatigue, and he also noted there are side effects from the transplant anti-rejection medications. Another challenge of hepatitis B treatment is that it can be very costly. *“Even with insurance, the cost of [my antiviral] is about \$1,100 each month. HBIG is also very expensive, and with my insurance, costs about \$6,000. Because I have a very good insurance, the financial impact to me for hepatitis B is minimal, but I realize that that isn't necessarily true for everyone else.”* He added that, without this level of coverage, decisions of the costs versus the health benefit would have to be made very carefully. *“[A] cure for hepatitis B would be wonderful so others don't have to experience the trauma that I went through before, during, and after my liver transplant.”*

Future Ideal Treatments – Wendy’s Perspective

Wendy is 57 years old and lives in Vancouver, British Columbia. She was diagnosed with hepatitis B in college in the 1980s, which she acquired at birth from her mother. In 1998, her mother died within 6 months of being diagnosed with advanced liver cancer. At this point, Wendy said she began to take her

condition more seriously and to be monitored regularly with blood tests and abdominal ultrasounds. Since her blood tests showed no signs of active liver disease, she was not started on antiviral treatment. ***“My only treatment thus far has been to try to eat healthy foods, exercise regularly, and of course, to not drink alcohol. Due to fatigue caused by this disease, I also tried to get at least eight hours of sleep.”*** Wendy mentioned only being able to work part-time due to her fatigue and, prior to retirement, she was could only manage to work two days a week. Although she is grateful that antiviral treatments are available, she is very concerned about the development of antiviral resistance, and about the potential long-term side effects of being on a lifelong medication. ***“I would hope that the future treatment of this disease would be viral suppression without having to take antivirals for a lifetime. I would also prefer though that there would be a treatment that leads to the loss of the hepatitis B surface antigen. My ultimate wish of course, would be the elimination of the cccDNA.”*** She added that new treatments should have minimal side effects, finite treatment length, and be orally administered. With regard to participating in a clinical trial, Wendy said that the safety and lack of adverse side effects of the drug being tested are her top concerns. She also noted the importance of still begin able to function and carry out regular daily activities while participating in any trial. ***“There is so much uncertainty when living with hepatitis B, it's an exhausting disease. And at times I feel like I have a ticking time bomb in my body. But having a cure would be so wonderful ... I wouldn't have to have the fear of dying of liver cancer, as my mom did, or developing life-threatening liver cirrhosis.”***

Clinical Trial Participation – Joe’s Experience

Joe is 67 years old and lives in California. He was tested for hepatitis B in 1977, after a friend noticed he looked jaundiced. ***“I was not told I could be infectious, or that it could lead to cancer. So I just forgot about it.”*** In 1997, Joe was diagnosed with a hepatitis D co-infection, and by 2003 his liver was becoming cirrhotic. Antiviral treatment suppressed the hepatitis B virus, but not much was known about hepatitis D at the time. In 2013, after his specialist informed him that the hepatitis D infection was more virulent than the hepatitis B infection, and that there was no good treatment, Joe joined a three-part NIH clinical trial. For Joe, enrolling meant numerous cross-country trips, lost work and income, separation from loved ones, and having to endure medical procedures alone. He said, however, ***“My fear of doing nothing was stronger. I made 70 round trips from California to the NIH. Most were overnight marathons of travel and procedures.”*** Joe said he experienced some very difficult symptoms of hepatitis during the trial. However, five years into the trial, in 2018, his hepatitis D virus levels became undetectable. ***“I may have been the first patient for whom a Delta infection became undetectable through treatment.”*** Unfortunately, in early 2019, during the third phase of the trial, he was unable to tolerate the interferon lambda that was added to his treatment regimen. His reaction was so severe that his doctors stopped all study drugs two months early. His blood tests were abnormal, he had ascites, acid reflux, hernias, depression, loss of appetite, and weight loss. Still, he said ***“I wanted to finish the Delta study follow ups because quitting early meant incomplete wasted data and continued monitoring by the NIH was vital for my health.”*** After stopping the study drugs, the adverse symptoms abated, but Joe’s hepatitis D viral load is slowly increasing. He is striving to eat healthy and exercise, he avoids alcohol and pain medications, and takes his treatments and supplements as prescribed. In a recent series of tests, many of his blood tests had values close to normal, and both his hepatitis B and D

viral levels were low. *“As for future treatments ... The next step would be a hepatitis B cure. It would be a twofer since hepatitis Delta can't survive without hepatitis B.... Finally, for the huge numbers of hepatitis patients, like myself, who can't tolerate it, we really need treatments free of interferon.”*

Perspectives on Current and Future Approaches to Treatment – Moderated Participant Discussion

Following the presentation of the pre-recorded testimony, the four panelists were joined by two other individuals, Su and Thomas, for a live, moderated panel discussion. Su is a primary care physician who treats many patients with hepatitis B, and who is herself living with chronic hepatitis B. Thomas is a researcher studying the molecular structure of the hepatitis B virus, and was diagnosed with hepatitis B in his teens. Panelists and participants discussed their current approaches to managing their hepatitis B disease; how current treatments impact daily life; the most important benefits they would like to have from new therapies; and their thoughts on participating in clinical trials of new treatments. Online participants also provided input by calling in, emailing comments, and responding to live polling questions. (Excerpts of the discussion are included below to help illustrate participants' experiences. Additional highlights from comments submitted via email are provided in Appendix 6).

Hepatitis B Disease Management and Treatment Impact

Benefits of Currently Available Medications – Many participants expressed that taking currently available medications for hepatitis B has helped improve their quality of life. Some felt a sense of gratitude, with one participant expressing that hepatitis B medication had saved her life. One participant noted a great sense of relief that he was now unlikely to pass the infection on to loved ones. Some participants felt hopeful that being on medication lowered their chance of getting liver cancer. It was observed that the currently available oral antiviral medications are easy to take with very few side effects.

Negative Impacts of Medications – Another participant, however, said that even on treatment, she still fears the possibility of disease progression and premature death. Some patients mentioned a range of bothersome physical and cognitive side effects of treatments which, in some cases, had significant negative impacts on the patient's quality of life. A participant said he understood that his treatment was necessary, but the side effects were detrimental physically, mentally, and emotionally. One participant described developing resistance to the first antiviral drug she was treated with and developing osteoporosis as a result of the second drug. Now on her third hepatitis B antiviral drug, she is worried that she may run out of options. Lifestyle impacts were also mentioned, such as the inconvenience of needing to fast before and after taking certain oral medications. Several participants expressed that they did not feel that medication was having the desired effect as they were, for example, still experiencing symptoms, and had fluctuating liver enzyme levels. One participant felt his symptoms had become worse while on treatment. Concern was also expressed about the implications of lifelong treatment for

patients who already have impaired liver function, such as cirrhosis, including the possibility of developing lactic acidosis.

Other Approaches to Disease Management– Participants who do not meet current guidelines for treatment based on their disease status shared how they are managing their disease in other ways. Some described taking a “whole person approach” to maintaining health and wellness as a way to manage their hepatitis B disease and protect their liver. Several mentioned managing their disease by eating healthy foods. Some said that, although they understood they were not being treated because they showed no sign of active liver disease, thus, their risk for disease progression was considered low, not being treated made them feel nervous and uncertain about the future.

Patient Voices: Disease Management and Treatment Impact

“[W]hat I often tell my patients, and kind of my belief too, is just to keep the rest of your body healthy, just the whole person approach. Protecting the liver obviously is important, so I make sure I’ve had all my vaccinations, like hepatitis A.... Fatty liver is a big issue ... [and] is impacted by having diabetes, being overweight, exercising. ... I don't take any herbals or supplements. ... I generally just try to have a healthy lifestyle.

“I think many of us who are not on any medication sometimes feel anxious that we're kind of sitting on a ticking time bomb.”

– Su from New Jersey

“[O]n the physical front, I don't know if the medication has helped at all, but on the mental front of not feeling like I'm infectious to family, and closer contacts, and particularly children, has been such a weight off of my mind after taking this. Just the act of being able to do something against the virus has been sort of empowering. And I think that's a huge part of treatment and the benefits you do get from treatment.”

– Thomas from Australia

“I think that anyone with hepatitis B that is not on treatment, does feel a level of uncertainty as to what their future holds, because they feel like they're not able to take a proactive course other than healthy lifestyle.

“[Treatment is] inconvenient because I have to fast two hours before and two hours after. I do not like going four hours without eating because I'm a very active person and I'm always hungry. ... And I have to go to bed very hungry because I have to fast before.”

– Wendy from Canada

The Most Important Benefits that New Hepatitis B Treatments Could Provide

During the moderated discussion and online polling, participants highlighted the key outcomes and aspects they hoped an ideal new treatment for hepatitis B would offer.

Desired Outcomes of Treatment:

- **A Functional Cure for HBV infection** – A “complete cure” or complete elimination of HBV (HBV cccDNA) from the body is the ideal outcome. As this might not be possible, most participants agreed

that a “functional cure” -- that is, a finite course of treatment leading to a sustained loss of HBsAg and undetectable HBV DNA in the blood -- would be acceptable. Some noted they would be willing to endure a longer course of treatment or side effects to achieve a functional cure.

- **Decreased Risk of Developing Liver Cancer** – Participants expressed the need for treatments that normalize liver enzyme levels, reverse fibrosis, and reduce the risks of cirrhosis and liver cancer.
- **Improved Quality of Life** – Participants highlighted the need for new treatments that can address their fatigue and pain without further damaging the liver. It was also noted that new treatments should have minimal side effects.
- **Elimination of Transmission to Others** – The risk of passing hepatitis B on to others is of great concern to many participants and elimination of this risk was a key desired outcome of any new treatment.

Desired Aspects of Treatment:

- **Finite Course of Treatment** – As noted above, participants discussed their desire for a finite course of treatment, perhaps 6 months to a year, that resulted in sustained outcomes after stopping treatment. It was also mentioned that a finite duration treatment would have a better chance of practical success in resource-poor regions than a long-term, indefinite-length intervention.
- **Convenient Administration** – It was observed that taking medications is burdensome. Current oral antiviral treatments are easy to take and have few side effects, and participants noted concerns about the route of administration of new medications, especially if they required injections or IV infusions. Participants favored oral medications that can be taken once per day, ideally for a short time period.
- **Elimination of the Need for Interferon as Part of Treatment** – Although treatment with interferon is of finite duration and can be very successful, for many patients, interferon is not well tolerated, side effects are common, and administration by injection is undesirable.

Patient Voices: Key Treatment Benefits

“[F]or me, an ideal treatment would be one that gives me a functional cure... [S]omething that could lower the probability of liver cancer. So something that would lower our viral load to undetectable levels, something that would protect my liver from inflammation, scarring, fibrosis... [N]ot necessarily clearing it out of my body, but essentially having a functional cure where I could have confidence of living a full life.”

– Raj from California

“I would be willing to endure longer treatments if there's some chance that I would be able to achieve that functional cure.”

– Su from New Jersey

“I got interferon for hepatitis D in the clinical trial, and I reacted very, very badly.... And speaking as someone who really went to a frightening place with interferon, I just am hoping that research will go into treatments that don't include interferon.”

– Joe from California

Deciding to Participate in Clinical Trials of New Treatments

Patient participation in clinical trials is essential for the development of new treatments. During the moderated discussion and online polling, participants shared their perspectives on the type of clinical trial they would be willing to participate in.

Key Factors in the Decision to Participate in a Clinical Trial:

- **The risk of rare, more serious side effects** – Many participants felt that the risk of serious side effects, such as a liver enzyme flare (significantly elevated ALT), would be a key consideration in deciding to participate in a clinical trial. One participant said that, as she ages, she is becoming less willing to tolerate the risk of serious side effects in a clinical trial.
- **Quality of Monitoring** – The same participant also expressed concern about how thoroughly she would be monitored for serious adverse effects during a trial, and the impact of any side effects on her longer-term health. She suggested that the distance one must travel to participate can impact appropriate monitoring, and that better tools for monitoring are needed.
- **Potential for the treatment to provide a functional cure or improve physical wellbeing** – The need for a functional cure was again emphasized, and the hope that the treatment under investigation could provide a functional cure was noted to be a compelling factor for trial participation.
- **Burden of participation** – The decision to participate in a clinical trial might also take into account the impact it would have on one's daily life, such as the amount of time it would take to participate, and the distance and time it would take to travel to the study site.
- **Route of treatment administration** – Most participants favored orally administered treatments, and many were willing to take several pills per day for about a year. Some participants were also amenable to weekly or monthly subcutaneous injections for a year or two. Few were interested in treatments that required IV infusion, alone or in combination with another therapy.
- **The risk of common or less severe side effects** – Based on polling, less common side effects, such as headache or nausea, were less of a concern for most participants.

Other Concerns Related to Clinical Trials

During the moderated discussion, it was also raised that there is “widespread and persistent underrepresentation” of minority populations in clinical trials conducted in the U.S., and that the data suggest that different populations might respond differently to a given treatment. One participant pointed out that most people living with chronic hepatitis B in the U.S. are immigrants or people in minority communities, and she emphasized that clinical trials for hepatitis B treatments need to actively reach out and engage historically underrepresented communities who are at high risk of hepatitis B.

A participant emphasized the need for thorough and accurate monitoring of all people living with chronic hepatitis B, whether on treatment, not currently being treated, or participating in a clinical trial. She expressed concern that gaps in monitoring persist, and that those taking antiviral treatments can develop a false sense of security that monitoring is less necessary.

Patient Voices: Clinical Trial Participation

"[W]hat I would be willing to tolerate in the way of trial and treatments during a trial is probably a little bit different now than it might've been when I was younger. I would have been willing to put up with more, maybe higher ALT flares or less comfortable side effects than I would now that I'm older."

– Karin from California

"[Y]ou want a clinical trial that sort of gives you a high hope of a cure, a functional cure or real cure, which I think is the most important. We are looking for a cure.... I don't want to take the medication for the rest of my life."

– Jacki from New Jersey

Closing Remarks

The Hepatitis B Foundation is grateful to the more than 600 individuals around the world living with chronic hepatitis B, and their family members and advocates, who participated in this first fully virtual externally-led PFDD meeting, and without whom this meeting could not have been a success. HBF is also grateful for the participation of staff from FDA who are committed to serving patients and advancing safe and effective treatments for hepatitis B. The voices of the patients and family members heard at this meeting provide a window into the challenges and triumphs they face daily in living with chronic hepatitis B and highlight their unmet treatment needs. It is hoped that the experiences shared by these individuals will help to guide the development and oversight of the next generation of treatments, and hopefully a functional cure, with ultimately a complete cure, for chronic hepatitis B.

Appendices

Appendix 1: Meeting Materials

- Agenda
- Demographic Polling Questions

Appendix 2: Pre-Meeting Patient Engagement

- Highlights from In-Depth Interviews
- Summary of Pre-Meeting Survey Results

Appendix 3: Full Transcript of Patient and Family Member Testimonies on Symptoms and Disease Impacts of Living with Chronic Hepatitis B

Appendix 4: Full Transcript of Patient and Family Member Testimonies on Current and Future Approaches to Treatment

Appendix 5: Meeting Discussion and Polling Questions

Appendix 6: Selected Comments Submitted via Email (June 1-30, 2020)

Appendix 1: Meeting Agenda and Demographic Polling Questions

Externally-Led Patient Focused Drug Development Meeting on Chronic Hepatitis B

June 9, 2020 – 12:30 pm-4:30 pm ET

Virtual Meeting

12:30 pm	<p>Welcome Chari Cohen, DrPH, MPH, Senior Vice President, Hepatitis B Foundation Timothy Block, PhD, President and Co-Founder, Hepatitis B Foundation</p>
12:40 – 12:50 pm	<p>Opening Remarks Poonam Mishra, MD, MPH, Deputy Director for Safety, Division of Antivirals, Center for Drug Evaluation and Research, U.S. Food and Drug Administration</p>
12:50 – 1:00 pm	<p>Background on Hepatitis B and Current Treatment Landscape Anna SF Lok, MD, Professor and Director of Clinical Hepatology, University of Michigan Medical School</p>
1:00 – 1:15 pm	<p>Overview of Discussion Format James Valentine, JD, MHS, Moderator</p>
1:15-1:20 pm	<p>Demographic Polling questions</p>
1:20 – 1:40 pm	<p>TOPIC 1 – Living with CHB: Symptoms and Disease Impacts Four Panelists Living with Chronic Hepatitis B Infection</p>
1:40 – 2:40 pm	<p>Group facilitated discussion and polling questions on Topic 1 <i>Facilitator asks questions with patient/family member responses via audience response system.</i></p>
2:40 – 2:50 pm	<p>BREAK</p>
2:50 – 3:15 pm	<p>TOPIC 2 – Perspectives on Current and Future Approaches to Treatment Four Panelists Living with Chronic Hepatitis B Infection</p>
3:15 – 4:15 pm	<p>Group facilitated discussion and polling questions on Topic 2 <i>Facilitator asks questions with patient/ family member responses via audience response system.</i></p>
4:15 – 4:20 pm	<p>Meeting Summary Larry Bauer, RN, MA, Senior Regulatory Drug Expert, Hyman, Phelps & McNamara</p>
4:20 – 4:25 pm	<p>Wrap Up and Thank You Robert Gish, MD, Medical Director, Hepatitis B Foundation</p>
4:25 – 4:30 pm	<p>Evaluation Forms and Concluding Remarks Chari Cohen</p>

Demographic Polling Questions

1. Are you a person living with hepatitis B or a family member of someone with Hepatitis B?
 - A. Person living with hepatitis B
 - B. Family member of someone with hepatitis B

2. Where do you currently reside?
 - A. United States
 - B. Europe
 - C. Middle East
 - D. Africa
 - E. Asia (includes India)
 - F. Australia
 - G. Canada
 - H. South or Central America
 - I. Other

3. How do you identify?
 - A. Male
 - B. Female
 - C. Gender variant/non-conforming
 - D. Prefer not to answer

4. How old are you?
 - A. Younger than 18 years
 - B. 18-30 years
 - C. 31-50 years
 - D. 51-60 years
 - E. >60 years

5. When were you diagnosed with chronic hepatitis B?
 - A. Less than 1 year
 - B. 1-5 years
 - C. 6-10 years
 - D. I don't remember

6. What was your primary reason for being tested for hepatitis B?
 - A. There was a free community hepatitis B screening event
 - B. I was tested during pregnancy
 - C. A family member was diagnosed with hepatitis B, so I was worried
 - D. I was having symptoms
 - E. My doctor recommended that I get tested
 - F. I donated blood and received a letter that I had tested positive
 - G. It was a pre-work requirement
 - H. Other

Appendix 2: Pre-Meeting Patient Engagement

To obtain broader input from individuals living with hepatitis B than would be possible from a half-day externally-led Patient-Focused Drug Development (PFDD) meeting, the Hepatitis B Foundation conducted 25 in-depth phone interviews and launched an online survey that garnered over 2,100 responses from people in 102 countries.

Highlights from In-Depth Interviews

Experience Living with Chronic Hepatitis B

- Relationships with partners were impacted. Some mentioned losing their partners because of their diagnosis, and some mentioned that they were unable to start a new relationship because they were afraid to tell potential partners about their status.
 - Most of the time, family support played an important role in coping with the disease. However, very few noted that family relationships had some tension because of chronic hepatitis B.
- There was significant emotional impact for people living with chronic hepatitis B that included:
 - Stigma (either sensed by the patient or experienced by them in their community)
 - Isolation (mainly self-isolation – to avoid telling others about their status)
 - Fear of developing liver cancer and facing premature death (especially among those who have young children and want to be part of their lives)
 - Feelings of anger because they “did nothing wrong” that led to being infected (this is particularly mentioned more often among patients who were infected at birth)
- Career choices were somewhat affected in terms of finding a job with health insurance or avoiding jobs that are not physically taxing.
- There was stress around social pressure of social gatherings with drinking (more often), or peer-pressure to donate blood during a blood drive.
- Lack of public awareness about hepatitis B appeared to cause stressful situations for some of the interviewees.

Current Treatment Experience

- Interviewees frequently cited that finding the right doctor who is knowledgeable about chronic hepatitis B and willing to spend the time to educate the patient about their disease is one of the biggest hurdles to getting good care.
- Many interviewees expressed feeling stressed that they had to take a daily pill for life to manage their disease.
- Few interviewees reported side effects, but the cost of treatment was a major issue even for those with health insurance.
- Many of the interviewees who were on treatment acknowledged that they felt that the treatment was helping them manage their disease.
- Many interviewees reported adopting healthy lifestyles to manage their disease, like practicing mild-moderate exercise, eating healthy food, and abstaining from alcohol.

Thoughts on an Ideal Treatment

- Almost all interviewees expressed a strong desire and hope for a cure (like for Hepatitis C).
- A treatment that reduces the risk of developing liver cancer was the most hoped-for feature of an ideal treatment.
- A treatment that is taken for a limited duration of time was a commonly cited feature.
- Route of administration:
 - Most interviewees had a preference for oral treatment.
 - Many stated that they would be OK with injectable routes of administration if it would be for a short duration, and if it would not interrupt their life routine (e.g. require a long commute to a medical facility).
- Mild symptoms like mild nausea or mild headache were mostly acceptable by interviewees.

Clinical Trials Participation

- Many interviewees were willing to participate in clinical trials, but with some requirements:
 - Clear safety information about the investigational treatment in the trial.
 - Side effects should not interrupt their daily life/daily routine.
 - Assurance no severe or permanent damage to body organs (liver and kidneys) would result from the trial.
- Those with children were particularly cautious about participating in clinical trials. They were afraid of dying prematurely and leaving behind their children. They hesitated to take part in clinical trials because they didn't want to jeopardize their chance to be there for their children's lifetime milestones.
- Many interviewees required a success rate between 50%-70% to participate in a clinical trial.

Summary of Pre-Meeting Survey Results

A total of 1,707 respondents completed the Hepatitis B Foundation survey. The average age was 37 years old (range 19-75). Almost 83% of survey participants indicated that they live outside the United States, representing 99 countries. The top five countries represented were Nigeria, U.S., Ghana, India and Philippines (29%, 17%, 10%, 9% and 7%, respectively). About 67% of participants identified as male and 26% identified as female, while 7% preferred not to answer the gender identity question.

Topic 1: Living with Chronic Hepatitis B – Symptoms and Disease Impacts

Fatigue: The most notable physical symptom

When asked about their physical symptoms of chronic hepatitis B, 78% of respondents indicated that they feel tired a lot (more than people they know). About 42% of respondents indicated that managing fatigue is a challenge they face in their daily life.

Additionally, 42% of respondents said that they worry that their ability to do their job is negatively affected by their chronic hepatitis B condition.

Social and family relationships

When asked about reasons for not disclosing their chronic hepatitis B diagnosis to their social circle (either a family member, spouse, or friend), 37% said they feared they would be treated differently, and 24% said they feared worrying their loved ones.

In a related question, 48% indicated they worry that their relationship with their family and friends are negatively affected by their chronic hepatitis B: 47% said they feel shame, 43% said they feel like avoiding others, while 60% said they feel others avoid them because of their chronic hepatitis B.

Additionally, 40% worried they might transmit the virus to others.

Overall, 62% of respondents felt that their life was less enjoyable because of their chronic hepatitis B.

Worrying about developing liver cancer or dying prematurely

When asked about their concerns for their disease prognosis, fear of developing liver cancer was the number one concern: 55% of respondents said they fear that they could develop liver cancer, and 48% said they fear living a shorter life because of their chronic hepatitis B.

Stigma and discrimination

A total of 58% indicated that because of their chronic hepatitis B, they fear facing discrimination, such as losing a job or being denied school admission.

When asked about reasons for not disclosing their chronic hepatitis B diagnosis to their social circle (either a family member, spouse, or friend), 33% said they feared being discriminated against.

Additionally, 25% of respondents cited more than one reason for not disclosing their diagnosis with people in their close circle.

Topic 2: Perspective on Current and Future Approaches to Treatment

Current treatment experience and challenges with medications

Treatment is not required for all patients with chronic hepatitis B; however, those who are on treatment face several challenges when it comes to managing their disease. The top challenges cited by survey respondents were treatment side effects, cost of medication, and the burden of taking a daily pill for a long time, possibly for a lifetime.

A total of 56% of respondents were either taking hepatitis B medication at the time they completed the survey or have taken medication in the past. Of those who indicated current or previous experience with hepatitis B medication, 79% said that they have been on (or have taken) medication for 5 years or less. About 30% of those who indicated being currently on medication also indicated using herbal and supplemental vitamins for their liver to help manage their disease.

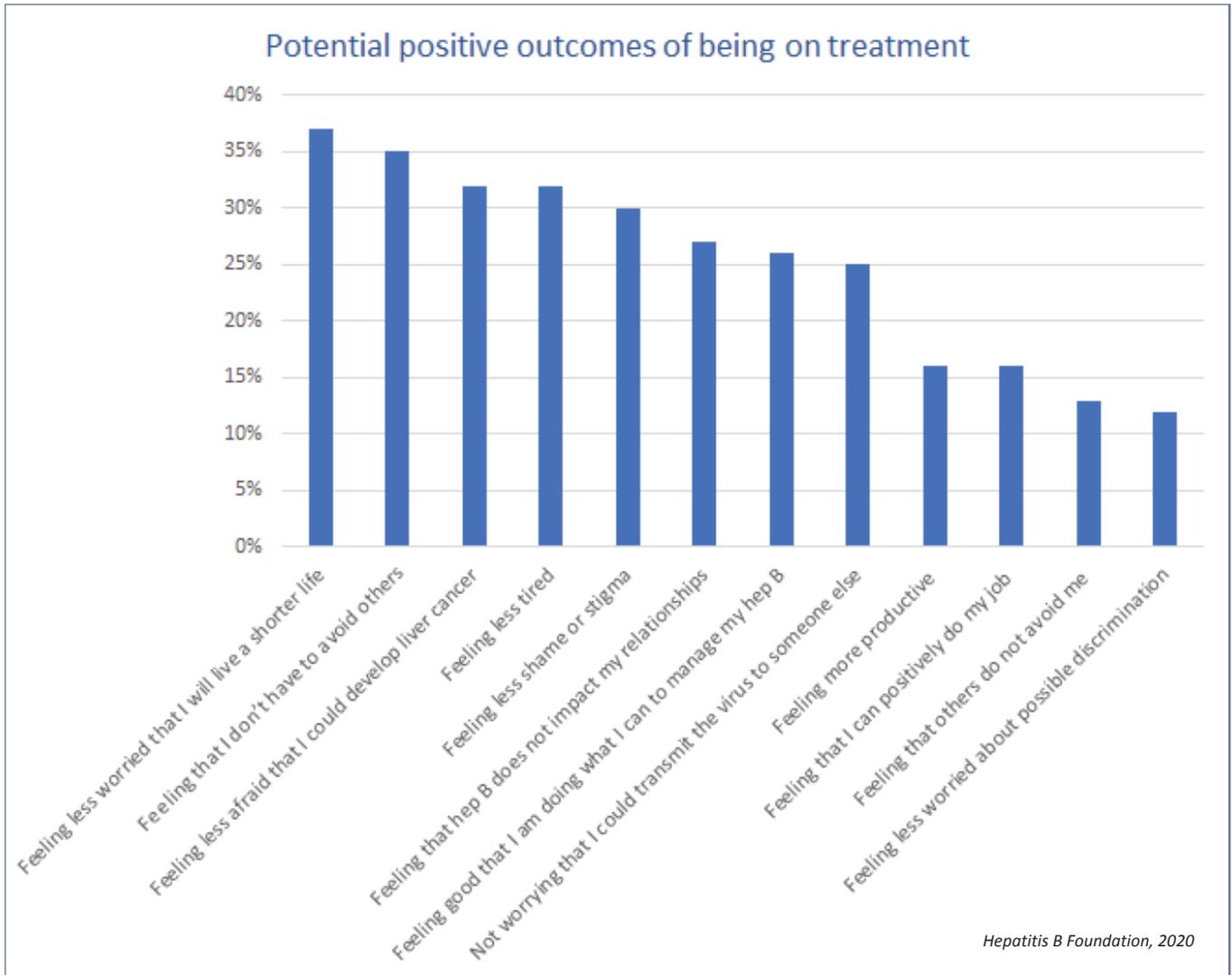
About 49% of those who indicated current experience with hepatitis B medication reported treatment side effects as one of the challenges they face. The top three cited side effects (among those who reported any) were fatigue (32%), pain (25%), and gastrointestinal side effects (20%).

When asked about reasons for not being on medication, of those who had previous experience with hepatitis B medication, 51% said that they primarily stopped their medication because they couldn't afford it. Of those who had never been on hepatitis B treatment, 20% indicated that the primary reason was affordability. Overall, cost was cited as a challenge for those currently taking medications: 61% said that cost of the medication is a challenge for them.

Another challenge faced by those who are currently taking medication is taking a daily pill; 30% said that taking a daily pill is one the challenges they face.

Potential positive outcomes of being on treatment

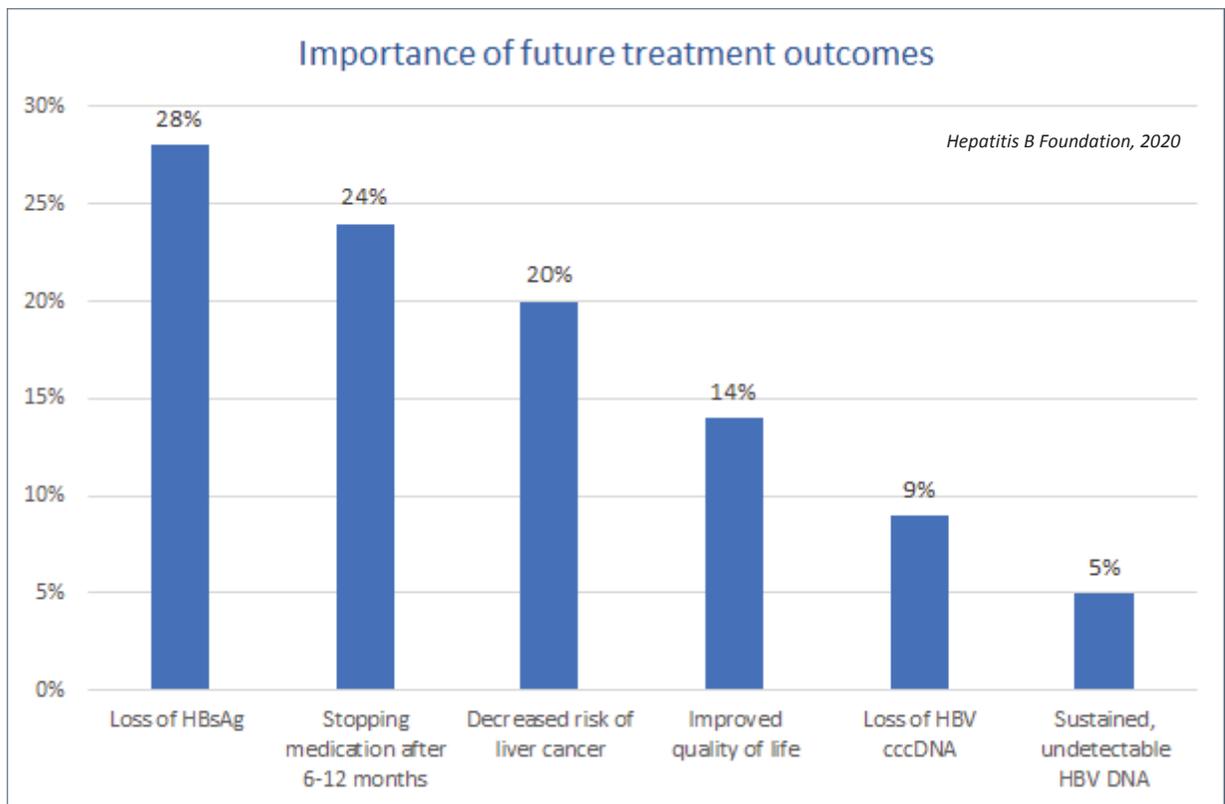
Those who responded that they currently take medications cited several positive outcomes for being on treatment:



Ideal treatment outcomes and thoughts on future medications

Overall, 73% of respondents indicated they would be willing to potentially participate in a clinical trial for a new treatment for chronic hepatitis B, while 21% remained undecided about their participation, and 6% said that they would not be willing to participate in one. Respondents were asked about how the success rate of losing the hepatitis B surface antigen (HBsAg) would impact the likelihood of their participation in a new hepatitis B clinical trial. The likelihood for participation correlated with the success rate of losing HBsAg: as the success rate increased from 25% to 90%, the likelihood of participation also increased from 43% to 88%.

When asked about ideal future treatment outcomes, respondents ranked the importance of the following outcomes from most important to least important:

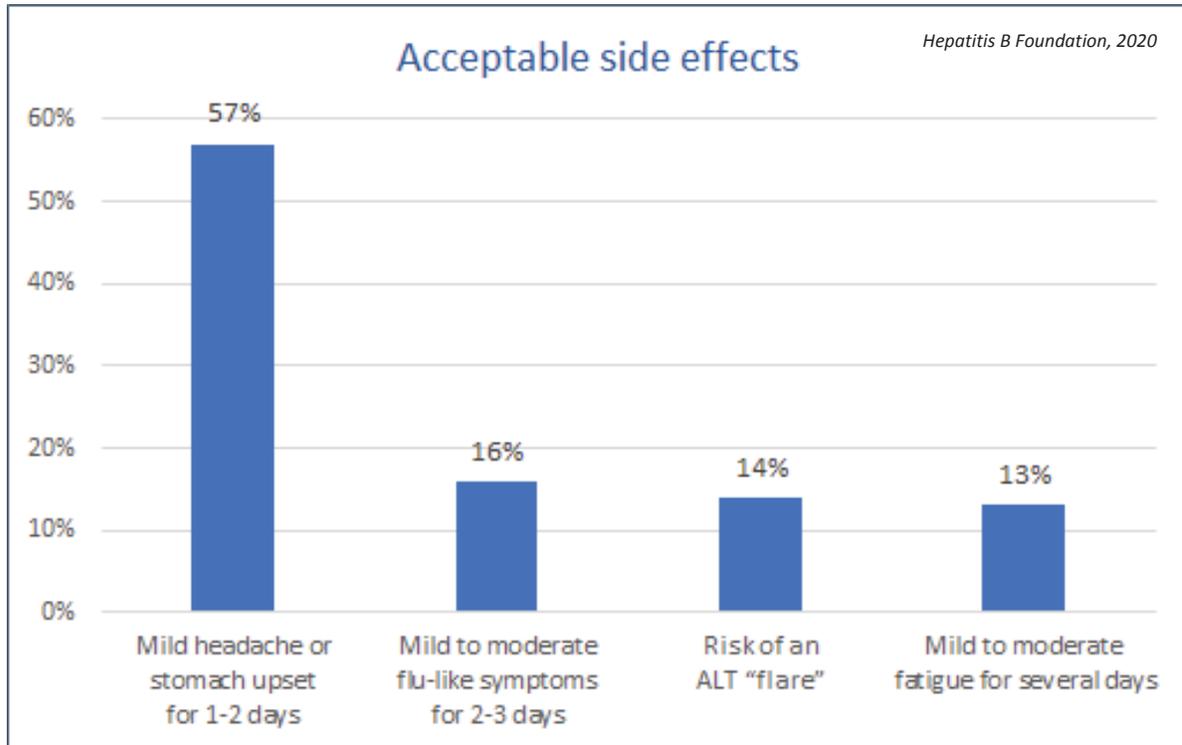


Accepted routes of administration

When asked about acceptable routes of administration for new hepatitis B treatments, 69% of survey respondents were willing to tolerate intravenous infusions when the duration of treatment was less than 6 months, but the response decreased to 36% when the duration of treatment increased to one year. A similar pattern was noted with subcutaneous injectable medications. The frequency of injections was another important factor to assess acceptability by respondents. As the frequency increased from a monthly injection to weekly, acceptability decreased from 82% to 47%.

Acceptable side effects

Acceptable side effects of potential new hepatitis B treatments were ranked by respondents as follows:



Cure terminology

In the survey, we described a hypothetical clinical situation where a potential new treatment resulted in sustained, undetectable HBsAg and HBV DNA after completion of a finite course of therapy. When asked about the terminology for this situation, 61% of respondents felt that “functional cure” was the most appropriate and meaningful term. Respondents understood that a “complete cure” for chronic hepatitis B would ultimately mean the elimination of HBV cccDNA as well.

U.S. versus international responses:

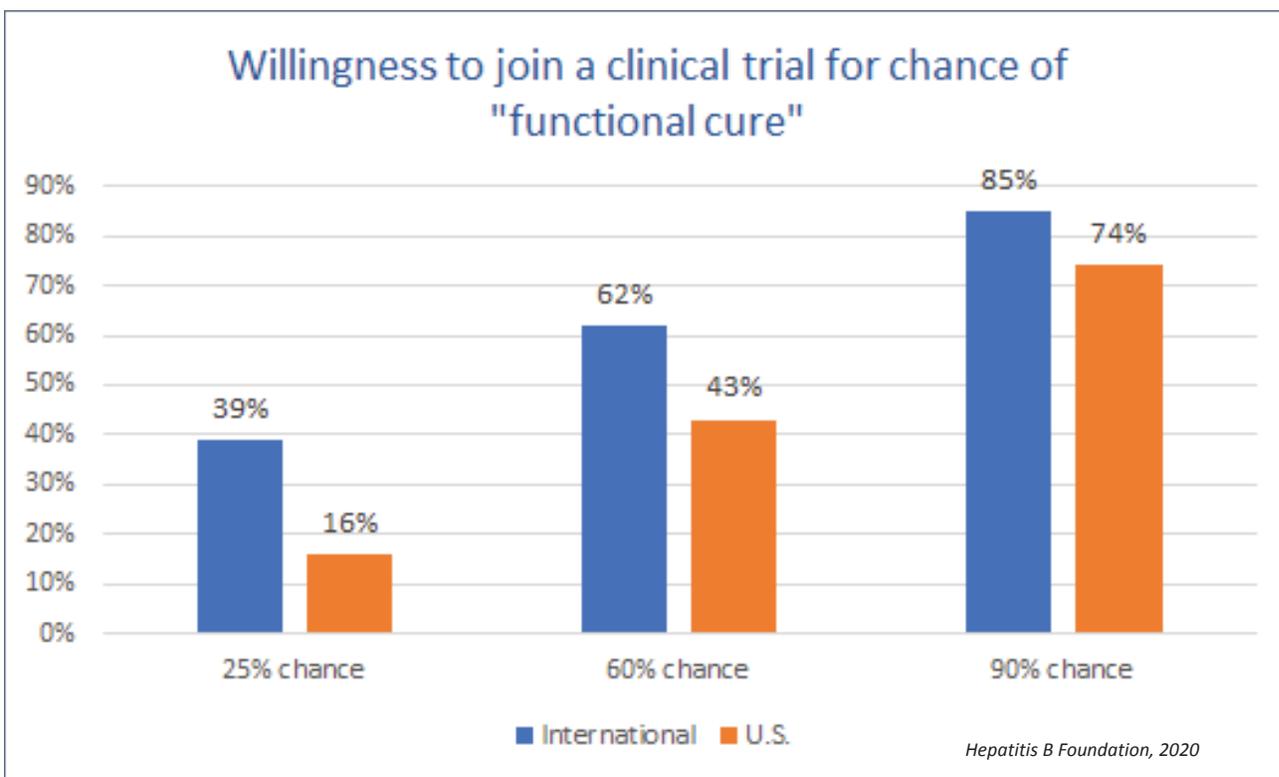
International respondents stated that they faced multiple challenges with the care and treatment of their chronic hepatitis B. About half (53%) of international respondents said they are not under the care of a medical provider. Many of those not under care (41%) stated that they could not find a medical provider to manage their hepatitis B, and 51% stated that they could not afford to see a medical provider.

Fewer international respondents were treated for hepatitis B compared to U.S. residents (32% international vs. 54% U.S.). The most stated reason for non-treatment was cost: 67% of international respondents said cost was a challenge vs. 52% of U.S. respondents. Additionally, international respondents described missing medication doses more often than U.S. respondents: 9% missed a dose

every other day compared to less than 3% of U.S. respondents. When asked for the reason that they missed a dose, 46% of international respondents stated they missed doses due to running out of medication before they were able to get a refill (compared to 22% of U.S. respondents who listed this as a reason).

International respondents more often stated that life was less enjoyable (60% international vs. 46% U.S.), and more often stated that they avoided others (42% international vs. 34% U.S.) because of their hepatitis B. International respondents were also more worried about: transmitting hepatitis B to others (67% international vs. 51% U.S.), facing discrimination (66% international vs. 51% U.S.), that their relationships were negatively impacted (47% international vs. 41% U.S.), and that their ability to do their job was negatively impacted by hepatitis B (45% international vs 40% U.S.).

A total of 79% of international respondents would be willing to join a clinical trial for a possible “functional cure” (sustained loss of hepatitis B surface antigen or HBsAg) vs. 59% of U.S. respondents. While a decreased risk of liver cancer was the most important outcome for U.S. respondents, the most important outcome for international respondents was loss of HBsAg.



Appendix 3: Full Transcript of Patient and Family Member Testimonies on Symptoms and Disease Impacts of Living with Chronic Hepatitis B

Bright' Story

The physical impact of hepatitis B, my experience. My name is Bright. I was born and raised in Ghana, West Africa for most of my life. I immigrated to the US in 2007. I currently live in Maryland. My journey with hepatitis B started in 2014. One of the first symptoms I experienced was fatigue, which is still impacting me today. In January of 2014, I noticed that I was feeling more tired than usual. I did not take it seriously because I was taking some college classes, working full time at a physically demanding job, and serving in the Army reserves at the same time, but the fatigue continued, and the frequency began to affect most of my days. I consulted with my doctor about my concern, and that is when I was diagnosed with chronic hepatitis B. I wake up every morning tired, even before I try doing anything. Nothing helps, not even 12 hours of sleep. I would still wake up feeling even more tired. Some days I wake up feeling a little better thinking I can get something accomplished, but guess what? I crash only an hour or two later. So, occasionally it feels as if something zaps or sucks the energy out of me. I immediately feel drained and have to find a bed to lie down or somewhere to sit.

In addition to the chronic fatigue, I also have unexplained chronic muscular pain. I experienced this pain in my lower back, neck and on top of my shoulders to my upper back. No one medically really knows what is causing this pain. Many medical tests have been done, but the results have all been negative except for hepatitis B. The pain and the fatigue usually happen in tandem and make it extremely hard to get anything accomplished. On days that I experienced this pain, the muscles around my neck, shoulders, and back will tighten up, ache and feel as if I have a hard rod running along my spine. It is hard to drive some days, cook, or even to help with cleaning in and around the house. Because most pain medications can be tough on the liver, I'm limited to what I can safely take.

For me the physical impact of hepatitis B has been debilitating and huge. I've been unable to work since 2016 because of the fatigue and muscular pains. Yet I've been told that my condition is not serious enough, that I'm too young and should learn to adjust. I've been denied social security disability multiple times. I have been living at a friend's place for the last three plus years as I could not afford to keep my apartment since I was unable to work. I love playing sports but, unfortunately, I have not been able to do that anymore. In the process, I've also been diagnosed with asthma. With all this combined, I have not been able to play tennis, run, hike, or ride a bicycle for a while. My fatigue and pain have forced me to live a sedentary lifestyle, which is not like me at all. It is hard to tell how it is going to be from one day to another. So, I live by the moment.

I have been struggling a lot these last two years because of my symptoms. They seem to have become worse and are affecting my daily life more now than they did in the past years. I love cooking, but it takes time and my body just does not cooperate well. I'm not able to hang out with friends as much as I wish. So many times I make appointments to meet up with friends, but then I have to call and cancel because I do not have the energy to get out of bed, let alone to drive. I do not participate in any school extracurricular activities mostly because of chronic fatigue and pains. On my best days, I can drive to my

medical appointments in Baltimore alone, or cook a complete meal at home. On my worst days, I can barely do simple tasks, such as getting out of bed and walk into the bathroom or kitchen to get something to eat or drink. I'm currently studying for a degree in social work. And as part of the program, I'm required to do an eight-month field placement starting in September of this year. I've been worried and concerned as to whether I can do it. At school, I've relied heavily on accommodations to get to this point. But my field place accommodations may be limited. I will need to complete 16 hours each week and I worry that even with any accommodations, this is going to be a tough eight months for me. Currently, it is more difficult not knowing and not having control over which days will be good or bad. It just happens. This has become a new headache and stress.

It is an exhausting life when you are experiencing something this difficult. Feeling like you are the only person that fully understands what is going on, while some people around you or even those in position of authority like school instructors, doctors, government officials, or work supervisors think that it is all in your head and you are just being lazy. It robs you of the little dignity you have left. A million times, I've wished I had never had this virus, that it will leave my body and never return again.

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David's Story

Hello. My name is David. I'm 31 years old and live in Ann Arbor, Michigan. I was adopted from Seoul, South Korea when I was five months old. I've lived with hepatitis B for most of my life, as my biological mother transmitted the virus to me when I was born. My adoptive parents knew about my hepatitis B status when they were given my adoption file, and in a huge show of unconditional love, they adopted me regardless and educated themselves as best they could about the disease. Throughout my childhood, I was raised like most other children. The main difference was that I was taken to the doctor's office more often than most kids were and received blood draws on a semiannual basis. Not knowing any better, I never questioned these blood draws and I didn't talk about hepatitis B until years later. Thinking back on those times, it's extremely difficult to imagine my life without actively knowing about my hep B.

When I was 13 years old, I remember being taken to the doctor by my parents one day after school. I cannot remember much specifically from this day. It seems like a series of blurry images with muffled audio. What I do remember is that I was given a crash course on hepatitis B and what it meant to be a chronic carrier. My body shivered in fear and confusion. My arms and legs went numb and I started to sweat while the doctor explained that it could be transmitted through blood. I remember feeling very disappointed when I was told to stay away from alcohol. I was in eighth grade at the time. I had a pretty diverse friend group and was becoming interested in dating. Drinking, sex, and parties were starting to come up in conversation and I was excited about the prospects of my teenage years. I felt fairly comfortable in my skin, especially for being a teenager. That all changed after that day.

When I got home from the doctor's office, I couldn't help but feel extreme dread about returning to school. How would I keep this secret and what if someone found out and told everyone? Would I be

ostracized? How in the world would I tell any of my friends about this? The possibility of transmission and fear of others' reactions to my hepatitis B, was the most impactful in my life. Having a chronic transmittable disease has led me to be very selective about who I tell my status and in what context I tell them. I waited until I was 18 years old to talk about my status with any of my friends. And it wasn't until my twenties, that I could talk openly with therapists about fears and worries related to hep B. You can never know exactly how someone else will react to you and that is painful to think about sometimes.

I've made new friendships throughout my life where I've felt completely lost as to how to talk about hep B or even whether to talk about it at all. I've avoided potential friendships because of fear of rejection. Even with old friendships, it's been very difficult sometimes to explain the basics of this illness without making people very anxious. Toeing the line between managing who knows about my status and how much I tell them is been very difficult for me. Dating has been a turbulent practice most of my life. I'm so grateful to have met a wonderful partner and best friend last year. But before that, the dating world was especially daunting for someone with a transmittable disease. When and how do I tell them about my status? How will they react? These are questions that don't have the same answers depending on who you are talking about.

People have different expectations for things, and I've learned throughout my experiences with dating that it's different for different people. Clear and honest communication from my end seemed to work out the best overall. Positive depictions of hepatitis B in the media are few and far between. I've never seen anyone positively talk about hepatitis B in any commercial, movie or TV show I've ever watched. Hep A, B and C might as well be the same disease. Some people look at others with these diseases and think of them as less than human. I blame this on a glaring lack of empathy and sex education in the United States. If someone only relates the word hepatitis with dirty, filthy, and disgusting, it's hard to reeducate from there.

Being on medication and not knowing if I'll be able to stop taking it is also a cause of worry for me. I've been taking tenofovir alafenamide or TAF since June of last year. I had gotten a liver biopsy done a few months earlier and was taking another drug until switching. TAF is working very well in my body so far. My viral load has been reduced to undetectable levels, which gives me some relief knowing I'm potentially less contagious. While I do take medication, it does cause me anxiety from time to time. I don't know if I'll ever be able to stop. For now, the side effects have been minimal, but what if that changes? I still have a lot of good years ahead of me and thinking about taking this pill for the rest of my life doesn't exactly make me happy.

I hope someday I can think of stopping the medication as a real possibility. Physically, my chronic hepatitis B has gotten better over time. The fear and anxiety I feel do vary quite a bit. Talking about concerns with my doctors and loved ones make me feel empowered but I don't always have that strength every day. Since I've gotten involved with the Hepatitis B Foundation, I can see a glaring lack of funding and need for more awareness. I can only hope that someday I can look and not see.

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Alice's Story

My name is Alice. I live in Sacramento, California, and was born and raised in Hong Kong. I grew up in a traditional Chinese family where talking about illness is taboo. My parents always remind us not to talk about illness because it can change your wellbeing. When we were not feeling well, home and herbal remedies always came first. We could only visit a doctor if the illness got worse. As I recall, my family tends to feel shame for having a chronic illness. And we were afraid of being isolated from friends and relatives around us if they knew. So we usually did not disclose our health condition, always keeping it a secret among ourselves.

I was first diagnosed with hepatitis B during my first pregnancy in the 1980s. I was shocked that I have been living with hep B and didn't know. I recall an incident that my friends had noticed jaundice in my eyes when I was a teenager, but my parents did not express any concern and told me the jaundice will go away in a few days and it did. I then learned my mom also had the virus and that it was probably transmitted to me at birth. My mother expressed that she was ashamed to tell me because hep B has been stigmatized throughout history. Her lack of knowledge about hep B put all of her children at risk from mother to child transmission and serious complications in life due to chronic hepatitis B. I also learned that some of my siblings have chronic hep B.

My two children were protected from hep B infections because I was cared for by a dedicated OBGYN to provide full protocols to prevent mother-to-child transmission. My children received the first dose of hep B vaccine and immune globulin shot at birth. Then they completed the three-shot series. They tested negative for hep B at one year of age. As my oldest brother died of liver cancer in his middle age, I did not want to suffer the same fate as my brother. When my family doctor informed me that I have a 25% chance of getting liver cancer, I felt very distressed and depressed about the unknown in my future. I pursued if there's anything that I can do to slow the liver damage, to live a normal life without being discriminated against or isolated. Medications can help and stop the disease to progress so that I would be able to raise my children to adulthood. My doctor, however, did not recommend any treatment or use of medications. I was monitored by blood tests every six months and ultrasound of the liver annually.

So far, I have not taken any medications for hep B treatment. I have opted to adjust my lifestyle in the hope to build a strong body to fight against the chronic infection. I have been thinking positively that I can overcome the burden of a chronic hepatitis B infection by doing the right thing for myself. I believe all the activities have worked to improve my liver health because I feel stronger and less fatigue. I am happy to know that my viral load has remained low. And my liver ultrasound continues to be normal.

As a parent, I chose to be open with my family and my children on health-related matters. I became involved in raising awareness in the local Asian communities. I believe knowledge is power. As my children attended Chinese language school during weekends, it gave me the opportunity to educate some parents about hep B facts, myths, vaccination, and testing. To this end, it helped me to overcome the fear of isolation and focus on the positive because I wanted everyone to know that hep B can be prevented by testing and vaccination. Although we continue to do outreach to promote hepatitis B

prevention in the community, I had not disclosed my liver status openly until 2018. At that time, I participated in a training to become a hep B storyteller in the #justB Campaign sponsored by the Hep B Foundation. During the three-day storytelling workshop, I was empowered by the experience of engaging with other people living with HBV and family members impacted by the disease and seeing how everyone was able to share their stories without hesitation or feeling of shame. The #justB workshop sparked amazing changes in me to openly discuss my chronic hep B. I was full of hope that living with hep B is not disgraceful and that I am grateful to be part of the hep B community working to find a cure and end the virus.

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Randy's Story

Hello. My name is Randy. I live in Port Orchard, Washington with my wife of 26 years. I met her while I was stationed in Anjeong-ri, South Korea in Camp Humphreys, from 1993 through 94. We met, fell in love, and got married there. Then we moved on to England where we had two sons. I don't have hepatitis B, but my wife does and my youngest son does. My deepest hope is that someday there will be a cure for hepatitis B. Thank you for this opportunity to share our family story. Both of our sons were vaccinated for hepatitis B. I wish I'd known that it wasn't necessarily foolproof. We just thought it was going to be okay. My wife contracted hepatitis B through the birthing process. All of her siblings have hepatitis B. In 2006, my wife's mom passed away. It was shortly after that that she took testing very seriously and found out that she needed to take both entecavir and adefovir to keep her levels in check. She's doing good right now with her levels and the doctor says her levels are almost nonexistent, but she still takes the medicine today.

Then in sixth grade, we had both sons tested for hepatitis B. Our oldest son showed signs of hepatitis B virus but was not sick and did not require medication. Our sons entered eighth grade and upon that timeframe, our youngest son showed signs that he was interested in attending the Naval Academy. This is an extremely difficult task to get into the Naval Academy. It requires exceptional grades and strong leadership qualities, but he started his journey at that time. His dream started. And at that point, he really was working hard on his grades and he showed signs of interest in the local high school's Navy Junior ROTC program. They allowed him to start attending in ninth grade even though he still was in junior high. Our son excelled at the Navy Junior ROTC program. And then in his junior year, he was one of only three cadets who were selected to attend the Northwest Navy Junior ROTC Academy. Later, he eventually secured his nomination and we accompanied him to Maryland, where we saw him swearing in a grand ceremony. It was amazing. And then he was off for eight weeks of an extreme intense bootcamp.

Phone calls were few and far between. We were already making plans to return to Maryland to see the graduation from basic training and as excited as they were to see him swear in, we were about to experience the absolute opposite feeling and have our lives irrevocably changed. He called one day, we were so excited to talk to him. We were telling him of all our plans to come see him and bring his grandfather to see him. We were going to be so excited to be there for him. And he said, "Dad, don't get

too excited about that." He says, "I pop solid for hepatitis B." We were in complete disbelief. We reminded him that he had tested negative for hepatitis B back in sixth grade. Later, that week, he had some more tests taken at Bethesda Naval hospital and they confirmed that result. He did in fact have hepatitis B. We later found out that you can't serve in any branch of the military, officer or enlisted, if you have hepatitis B.

At this point, my wife was beside herself. There's been nothing I can say to take the pain away. She blames herself for killing her son's dream. I tell her that's not true and it's not for you to pick up. I hope no one ever has to go through what we did. The disappointment is devastating, and we continually live with it. I believe that time does heal all wounds, but for us, it's just hard to move on. The other last year would have been our son's graduation from the Naval Academy. I just happened to be channel flipping that year, come across the graduation ceremony, where the guys were throwing their hats in the air, I just hung my head and cried. To think what could have been, is a constant thought that we have a difficult time letting go of. When others speak about their kids as accomplishments, we just find it difficult to participate in that kind of conversation or even be around others who would like to brag about their kids. Not necessarily because that's wrong, but if we share our story, it would be like pouring cold water on the conversation. We don't have very many friends and we don't go out very much. My wife doesn't even speak to her family all that much back in Korea. Although that has changed recently due to the coronavirus and I have been excited about that prospect. Not only for her, but for I as well. That's one positive thing that's happened as a result of this pandemic.

Later, we had our whole family tested again for hepatitis B. At that point, we found out that our oldest son who we thought had the hepatitis B no longer shows any signs of hepatitis B whatsoever. And our younger son still has hepatitis B. The only explanation for that is that the test that we had the kids take back in sixth grade was somehow mixed up. After this, our son showed an amazing degree of maturity and decided to go back to his Naval Academy Preparatory School to finish his associate degree. After graduation, he came back home, he looked for work around the area but found none.

He decided to move back to Alabama where he now has moved in with some other friends of his and he works at a local hospital where he's been handpicked to set up a surgical ward with supplies. He's working really hard to try to overcome the things that have happened to him and we're very proud of him. How amazing would it have been to have a pill, an injection, or some other kind of treatment that my son could have gotten at the Naval Academy? He could've continued on and he would have been a Naval officer today. Please put more effort, more resources into curing hepatitis B. So many lives depend upon it. Recently, we learned that my wife's brother had a portion of his liver removed due to hepatitis B and the effects of it. I thank you for this opportunity and I just hope that someday there will be a cure.

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Appendix 4: Full Transcript of Patient and Family Member Testimonies on Current and Future Approaches to Treatment

Jacki' Story

Hi, my name is Jacki. I'm from Princeton, New Jersey. I was born in Taiwan during the 1960s. In 1998 my elder brother was diagnosed with liver cirrhosis and liver cancer, due to chronic hepatitis B Infection. I decided to get tested at that time and found out that I also carry the virus. I didn't start treatment immediately. When I was first diagnosed, at that time, I didn't have many symptoms except for elevated liver enzymes and sometimes feeling fatigue. I was also busy with my career, but most importantly, there were no good treatments at that time for hepatitis B. The only available treatments were interferon, and the first-generation nucleotide analog, lamivudine. Interferon is an injectable drug that has a high tendency of side effects while lamivudine is known to cause drug resistance easily. However, due to a serious liver condition, my brother had no choice but to start lamivudine treatment. Later on, he was switched to entecavir when it became available. So, when my other family members with their encouragement, and the fact that I also had severe fibrosis, I decided to take on this potentially life-long journey for hepatitis B treatments and with entecavir in 2008.

After starting the antiviral therapy, my hepatitis B viral load dropped quickly. Within three months, the virus had dropped to undetectable level. My liver enzymes gradually returned to normal. Also, I feel less fatigue and was able to walk with small energy and to enjoy my free time. However, it was not easy to take the medication every day for many years. Many times I forgot, or purposely ignored the medication. My doctor gave me a warning and sometimes my hepatitis B virus became detectable. Fortunately, I was able to keep up with routine doctor's visit and had laboratory tests and ultrasound exam regularly to monitor the condition of my liver. My different enzyme level sometime exceeded normal range, which constantly reminded me of the importance of keeping up with the treatment. For now, I have continued my treatment with the most recent anti-hepatitis B drug, tenofovir alafenamide. The drug has a very low instance of drug resistance and a better safety profile for the bone and kidney.

Currently my hepatitis virus is undetectable and my liver enzymes are within normal range. However, even though this treatment might have lowered my risks of developing cirrhosis and liver cancer, they have not reduced the discomforts I experienced frequently, which might be a result of liver fibrosis as a damage caused by the virus, or accumulated toxicity due to long-term use of the drug. Also, this treatment did not redeem my constant worry that I might go on to develop liver cirrhosis or liver cancer eventually, or one day the virus might fight back and become resistance to the antiviral drug.

So, what's the ideal treatment I would like to see for hepatitis B. Ideally, there should be a combination of oral drugs that target different stages of the virus lifecycle. New candidates blocking different pathways of the viral replication cycle should be developed and tested quickly. With the advent of new technologies and greater support for basic and translational research, I hope that one day soon, we can all take a simple pill for a short period of time, and finally be able to get rid of this virus from all of us. We should aim to eliminate hepatitis B as early as possible. Hepatitis B is like a global pandemic that no one talks about or perhaps cares about. There are more than 250 million people affected by this deadly

disease. And it can easily spread from human to human. Compared with the vigorous research and development for therapeutic agents against HIV and hepatitis C and for the current coronavirus pandemic, it is clear that hepatitis B has been ignored for too long. We need a cure for hepatitis B now, and we need to stop the spread of this deadly virus. Thank you.

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Peter's Story

All right. My name is Peter and welcome to always sunny, Gilbert, Arizona. I promise you it's sunny outside. It's also 108 degrees. So that's why I'm inside. I'm currently 51 years old. I have hepatitis B and was on oral medication, tenofovir, for 12 years. The medicine had reduced my viral load to an undetectable level. And my GI doctor said at that time that I didn't need to take it anymore. He said he would just review my blood work results about every six months, so I stopped. About a year and a half later, shortly after new year, I was feeling very fatigued. My wife told me my skin and eyes like very yellow. I told her that my pee was very dark and my poop was very light in color. She immediately took me to the emergency room.

I don't remember much after this because they placed me in a coma to keep me alive. But after 10 days I woke up and my wife told me the hepatitis B virus had completely destroyed my liver and that I had a liver transplant. I remained in the hospital for another two weeks for follow ups and therapies to regain my strength and speech. It has now been close to two and a half years since my liver transplant. I'm still within the three-year recovery phase and being closely monitored by my post liver transplant team. My greatest health risk right now is organ rejection, bacterial and viral infections, and hepatitis B reactivation. The post liver transplant treatment regimen is very complicated, and I have suffered a great deal, but that is a story for another day.

Today I want to focus on the treatment challenges I face for hepatitis B virus condition. Immediately after my liver transplant I was given a treatments of tenofovir alafenamide, or TAF, and hepatitis B immunoglobulin or HBIG, which is done through IV infusion for seven days. I continued to take TAF daily, but the HBIG treatment is now only when my hepatitis B surface antibody is below 250 mIU per milliliter. Since I currently have stage three chronic kidney disease as a result of my acute liver failure, I was switched to TAF since it has less renal toxicity. My hepatitis B virus condition and treatments are monitored every three months with blood work results. My hepatologist believes the combination of TAF and HBIG is the best treatment to prevent reactivation of the hepatitis B. One drug suppresses the hepatitis B while the other prevents it from attacking my new liver. I suffer from extreme heat, or extreme fatigue, or exhaustion, especially around the 5:00 PM hour, slightly as a side effect from my anti-rejection medications that I'm taking. However, I personally have observed a higher energy level as a positive side effect lasting up to about one week immediately after taking the HBIG medication.

I do not notice any negative side effects while taking either the TAF or the HBIG medication, but this hepatitis B treatment combination is very costly, which I understood from the beginning as explained by my hepatologist. Even with the insurance, the cost of TAF is about \$1,100 each month. HBIG is also very

expensive, and with my insurance, they cost about \$6,000. Currently the interval between HBIG treatment is about every six months or so. Because I have a very good insurance, the financial impact to me for hepatitis B is minimal, but I realized that that isn't necessarily true for everyone else. I would have to agree I'm currently very fortunate and blessed to have an insurance plan that can offset the financial burden of taking a daily antiviral medication and undergoing an IV infusion of HBIG about every six months or so. Otherwise, the decisions of cost versus the weight and health benefit would have to be made very carefully.

Other treatment options, such as the at home injectable syringe, HBIG alternative, a lower cost alternative to TAF, or clinical trials where new hepatitis B medications may be available. But I opted for the treatment combinations that have been proven most effective to me. Yet, a cure for hepatitis B would be wonderful so others don't have to experience the trauma that I went through before, during and after my liver transplant.

Thank you for your audience and especially a big thank you to the Hepatitis B Foundation for being an anchor to all of us who have been affected by the hepatitis B. Thanks again.

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Wendy's Story

My name is Wendy, and I live in Vancouver, British Columbia. I found out I had hepatitis B while in university, in the 1980s, and I had acquired it at birth as my mom was positive for HPV. I didn't know much about the disease, but I did know it was infectious. So other than assuring that my fiancé at the time was protected from transmission, I did not make any major changes to my lifestyle.

Then in 1998, my mom was diagnosed with advanced liver cancer and died six months later. It was horrible watching my beloved mom die of such a terrible disease. After her death, I did start to take my condition more seriously and ask my doctor for regular blood tests and abdominal ultrasounds, which I did not have before my mom's diagnosis. Through these tests, I found out I was still in phase one of the disease, meaning I had a high viral load, no fibrosis, and my liver enzymes were within normal range. Hence, I did not receive antiviral treatment. My only treatment thus far has been to try to eat healthy foods, exercise regularly, and of course, to not drink alcohol. Due to fatigue caused by this disease, I also tried to get at least eight hours of sleep as well.

Because of my fatigue, I was only able to work part-time. When I graduated from university, I had ambitions to advance my career by found I was too tired to work full time. Since my profession was in high demand, I was often asked if I was willing to work more shifts, but physically I was unable to, even after my children had grown up. In fact, prior to retirement only work two days a week, which I found to be exhausting. My coworkers would often tease me about my part-time status as they did not know about my condition. Now, I am 57 years old. I'm still not on antivirals, but recently my liver enzymes have been elevated, so I may need to start treatment soon. Even though I am not on treatment, I have a close family member who is taking an HPV antiviral, so I'm familiar with how the medication suppresses viral replication, but unfortunately it does not cure the disease.

I am grateful that antivirals are available for Hep B and can prevent further liver damage. Nevertheless, every time my family member gets a blood test, I'm concerned that the virus will become resistant to the medication. And then what will be the treatment options? I'm also worried for my family member's overall health because of the possible long-term side effects of being on a lifelong medication. It is very stressful, as I'm often concerned more about my relative than myself, especially since this person needed to go on medication because of fibrosis of the liver that was diagnosed at an early age.

So, I would hope that the future treatment of this disease would be viral suppression without having to take antivirals for a lifetime. I would also prefer though that there would be a treatment that leads to the loss of the hepatitis B surface antigen. My ultimate wish of course, would be the elimination of the cccDNA, which I know is a lofty goal. If a treatment is discovered, my hope is that it has minimal side effects, has a finite treatment length, and can be taken orally. I don't like needles or IV administration.

I have not been in a clinical trial, but if I was to participate one, safety and lack of adverse side effects would be my top priorities. I would need to know that the potential benefits such as a high probability of curing this disease would outweigh the risk of receiving an experimental treatment. I, of course don't want my liver to be damaged by the clinical trial. And I also want to be able to function and carry out my regular activities while participating in the trial. There is so much uncertainty when living with hepatitis B, it's an exhausting disease. And at times I feel like I have a ticking time bomb in my body, but having a cure would be so wonderful that I wouldn't have to have the fear of dying of liver cancer as my mom did, or developing life-threatening liver cirrhosis.

I know there are no guarantees in life, especially during these uncertain times, but it would be wonderful to have not have to constantly worried about my health or the health of those I love. Thank you.

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Joe's Story

I'm Joe, 67, a landscaper living in Santa Rosa, California, with my husband Wayne. I've had hepatitis B since 1977. I never felt ill when I contracted it. A friend noticed I was jaundice and I got tested. With the positive result, I was not told I could be infectious, or that it could lead to cancer. So I just forgot about it. Around '97, I was diagnosed with a co-infection of hepatitis D or Delta, a virus that only affects those with chronic hep B. Around 2003, I was shocked to learn my liver was on the verge of cirrhosis. I remember crying. For years, I had kept myself safe from HIV while viral hepatitis was quietly damaging my liver. Fortunately, antivirals suppressed my hep B, the Delta infection remained a curiosity rarely spoken of.

In 2013, I was prescribed entecavir when my first hep B antivirals became ineffective. My specialist told me that the Delta infection was more virulent than B and that there was no good treatment. Well, I didn't want to wait 20 years for something to come along. So I got online and I found the only active trial to cure hep Delta in the Western hemisphere. Although hep B alone is very serious, Delta coinfections can speed up progression to fibrosis, cancer, and liver failure.

Joining the three-part NIH clinical trial from 2013 to 2018, brought huge changes. I hesitated because of the many cross-country trips I'd have to make with the NIH. I could lose lots of work and income, and it meant being separated from my loved ones during scary medical procedures. My fear of doing nothing was stronger. I made 70 round trips from California to the NIH. Most were overnight marathons of travel and procedures. I experienced very difficult symptoms for the first time since I'd contracted B. Sometimes I was so ill I couldn't face making another 4,000 mile round trip.

In December, 2018, I may have been the first patient for whom a Delta infection became undetectable through treatment. I wanted to kiss my doctor's feet, but by mid January, 2019, it was clear I couldn't tolerate interferon. I had tolerated different combos of lonafarnib and ritonavir in phase one and two, but with the addition of interferon lambda in phase three, I reacted so severely, my doctors stopped all study drugs two months early. At that time, my MELD was 17. MELD is a score that estimates a patient's chances of surviving their liver disease in the next three months. The higher the score, the more urgent the need for a liver transplant. My blood work was frightening to read. I had ascites, acid reflux, hernias, depression, loss of appetite. I lost 25 pounds in three weeks. I wanted to finish the Delta study follow ups because quitting early meant incomplete wasted data and continued monitoring by the NIH was vital for my health. As a result of stopping the study drugs, I'm over all the symptoms. At the same time, my Delta viral load is slowly increasing. I try my best to eat healthy, exercise, I avoid alcohol pain, meds, all recreational drugs. I take entecavir, furosemide, and the electrolyte supplements faithfully.

As of February, 2020, many of my blood tests are close to normal with a hep B viral load of 10, and a Delta viral load of 4,500, both considered quite low. In the past, my Delta viral load has been in the millions. My GI doctor believes the clinical trial may have had some good effect after all. Today, because my blood tests have improved, my MELD score is at eight and I don't qualify for a liver transplant. As for future treatments, entecavir is ideal for controlling my hep B. The next step would be a hep B cure. It would be a twofer, since hep Delta can't survive without hep B. And there's also the chance that my liver might reverse some of the cirrhosis. Finally, for the huge numbers of hepatitis patients, like myself, who can't tolerate it, we really need treatments free of interferon.

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Appendix 5: Meeting Discussion and Polling Questions

The discussions at this externally-led PFDD were guided by pre-established questions and augmented by live polling of participants during each panel session.

Topic 1: Living with Chronic Hepatitis B – Symptoms and Disease Impacts

Discussion Questions

1. How have physical symptoms or liver disease associated with chronic hepatitis B impacted your daily life, and what has had the most significant impact? (Examples may include cirrhosis or liver transplant, fatigue, joint pain, abdominal pain, etc.)
2. What impact has your diagnosis had on your personal, social and professional life? (Examples may include rejection by family and friends, fear and anxiety about dating, social isolation because fearful of disclosing status to others, discrimination or termination from work, etc.)
3. What worries you most about living with chronic hepatitis B? (Examples may include developing liver cancer and dying prematurely, not being able to date or get married, not being able to take care of my family, transmitting the virus to loved ones, etc.)
4. Have you ever felt stigma and/or discrimination because of your chronic hepatitis B diagnosis, and if so, could you share an experience with us? (Examples may include feeling “dirty” or shame for being diagnosed with CHB, not being allowed to share meals with others, facing rejection in the dating world, being asked for a divorce, being denied a job or educational opportunity, etc.)

Polling Questions

1. What has been the most significant physical impact of living with chronic hepatitis B on your daily life?
 - A. Disease severity such as cirrhosis, liver cancer, or post-liver transplant
 - B. Physical symptoms such as fatigue, joint pain, or abdominal pain
 - C. Both A and B
 - D. Other
2. How has living with chronic hepatitis B affected your daily quality of life? Select all that apply.
 - A. Physical impact of symptoms
 - B. Feel anxious/depressed
 - C. Feel stigma
 - D. Feel isolated
 - E. Feel discrimination
 - F. All of the above

- G. Other
3. What are your TOP three worries about living with chronic hepatitis B? Select 3.
- A. Being unable to date or get married
 - B. Transmitting hepatitis B to loved ones
 - C. Impact on school or work
 - D. Being unable to take care of my family
 - E. Dying prematurely from liver cancer
 - F. Other

Topic 2: Perspective on Current and Future Approaches to Treatment

Discussion Questions

1. What are you currently doing to help manage your symptoms and your condition? (Examples may include prescription medicines, over-the-counter products, herbal remedies such as milk thistle, physical exercise, and alternative therapies such as acupuncture.)
2. If you are currently taking a prescribed medication for hepatitis B, how do you feel it's affecting your daily life? (Examples may include side effects, cost of medication, eating restrictions related to the drug, visiting the doctor every 3-6 months, taking a drug for a lifetime, not a cure, etc.)
3. What do you consider the most important benefits of an ideal treatment? (Examples may include loss of surface antigen, a pill taken for less than a year, no stigma or discrimination, etc.)
4. If you were to enroll in a clinical trial for an experimental hepatitis B medication, what routes of administration and what length of treatment would you be willing to accept? What side effects, if any, would you be willing to tolerate? (For example, ALT flares, etc.)

Polling Questions

1. In general, how much do you think your hepatitis B medications have helped improve your quality of life?
 - A. No benefit at all
 - B. Helped somewhat
 - C. Helped a lot
 - D. Not sure
 - E. Other
2. What would be the TOP 2 most important benefits of a new "ideal treatment" for chronic hepatitis B? Select two options.
 - A. Being able to stop taking medication after 6 to 12 months

- B. Experiencing an improved quality of daily life (e.g. less fatigue, joint pain, more energy)
 - C. Loss of hepatitis B surface antigen (testing negative for HBsAg)
 - D. Decreased risk of developing liver cancer
 - E. Eliminate possibility of transmission to others
 - F. Other
3. What are the TOP 3 factors that would help you decide whether to participate in a clinical trial for an experimental hepatitis B treatment? Select 3 options.
- a. How the treatment might improve my physical well-being (e.g. fatigue, etc.)
 - b. How the treatment might improve my emotional well-being (e.g. stigma, anxiety)
 - c. Distance and time it takes to travel to the study site
 - d. The risk of common, less severe side effects (e.g., headache, nausea)
 - e. The risk of rare, more serious side effects (e.g., elevated liver enzymes or ALT flares)
 - f. The amount of time it would take to participate or impact my daily life
 - g. The way that treatments are administered (for example a pill or injection)
 - h. Other
4. If you decided to enroll in a clinical trial for an experimental hepatitis B medication, would you be willing to accept the following routes of administration? Please check all that apply.
- a. An intravenous (IV) infusion over 1 hour given weekly (for up to 6 -12 months)
 - b. A subcutaneous (SC) injection under the skin (not muscle) given weekly or monthly for up to 1 or 2 years
 - c. Two or three pills taken every day for up to 6-12 months
 - d. A combination of A & C only (IV infusion plus pills)
 - e. A combination of B & C only (SC injection plus pills)

Appendix 6: Selected Comments Submitted via Email

Online attendees had the opportunity to call in and speak live, or submit an email comment, some of which were read live by the moderator. In total, more than 300 comments were submitted by email during the meeting and throughout the open comment period that ran from June 1st through 30th. Selected comments are provided below.¹¹

Topic 1 Discussion Questions with Selected Comments

1. How have physical symptoms or liver disease associated with chronic hepatitis B impacted your daily life, and what has had the most significant impact? (Examples may include cirrhosis or liver transplant, fatigue, joint pain, abdominal pain, etc.)

“Symptoms for my daughter included extreme fatigue and joint pain due to her extensive fibrosis. From others living with chronic hepatitis B, I hear about everything from fatigue to digestive system issues and terrible anxiety related to living with a chronic Hepatitis B. What is heartbreaking is that many are not properly managed by a knowledgeable health care professional, so they have no idea if the symptoms they are experiencing are due to their hepatitis B or something unrelated.”

-Maureen from Maryland

“I have had 2 types of treatment. I have had antivirals, which were tenefovir and vemlidy, as well as interferon injections to manage my hepatitis B viral load.

“Living with the interferon therapy was a nightmare, and the side effects were a disaster. I was in bed the majority of the time due to the fatigue and body ache and got osteoporosis. I would like to mention that on the side I started taking milk thistle and had a great change in my diet. Loads of vegetables, fruits, and gluten-free food helped me with better blood work and viral load.

“I have been on treatment for 7 years. My treatment was done in India for 5 years because in my country (Kenya) medical services for hepatitis B are pathetic. But recently, I have been going to Thailand for my treatment which has finally made my viral load undetectable.”

-Neha from Kenya

“My father had diabetes, so we thought the signs and symptoms he had were due to that. It wasn't until he had tremors that we looked deeper, which lead us to a liver biopsy. It was at this point that he was diagnosed with hepatocellular carcinoma due to the hepatitis B virus.”

-Kim from Minnesota

¹¹ The full set of comments received by email is available on the Hepatitis B Foundation website at: <https://www.hepb.org/news-and-events/patient-focused-drug-development-meeting-virtual/> (accessed July 17, 2020).

2. What impact has your diagnosis had on your personal, social, and professional life? (Examples may include rejection by family and friends, fear and anxiety about dating, social isolation because fearful of disclosing status to others, discrimination, or termination from work, etc.)

“Living with hepatitis B has greatly affected my life. I am not allowed to work in some organizations like Uganda Wildlife Authority, I can't work in United Arab Emirates countries, some institutions segregate, and I had to lie to get a vacancy. I can't freely associate with people when they come to know I have it. I am even a laughingstock to some of my relatives. But however many the challenges, I have decided to continue with my medication no matter what people are saying about me. I wish those infected could be treated as normal human beings since we can't transmit the disease when we are on medication, especially on issue of close contact like shaking hands and hugging, among others.”

-Rukundo from Uganda

“Isolation. As someone living with hepatitis B for 26 years, I feel I'm going through it alone. The health community group emphasizes on public awareness, vaccination, and prevention but they do little for people living with the disease. There's no dedicated support group for hepatitis B. The ones I found are for hepatitis C and liver cancer, so I don't fit those "disease" categories. The American Liver Foundation has information about hepatitis C, cancer, and transplants, but little for hepatitis B. So having hepatitis B feels like a marginalized experience.”

-W.L. from San Francisco Bay Area, California

“I think we all put a stigma in our heads because of the virus. Feelings of being dirty and doing something wrong are hard to get rid of. It's stopped me applying for jobs over the years, and hiding it for 25 years in my current employment. I'd love to “come out” but people don't understand the disease, and then you are stigmatized.”

-Ian from the UK

“Living with hepatitis B as a poor person in a poor country with no adequate health care service is like living a life in hell, because even if the services and proper medication are available, I wouldn't have the financial strength to continue or buy my medication. I can't get into a relationship now with any woman because of this unexpected situation surrounded by poverty and poor health facilities.”

-Tamba from Liberia

3. What worries you most about living with chronic hepatitis B? (Examples may include developing liver cancer and dying prematurely, not being able to date or get married, not being able to take care of my family, transmitting the virus to loved ones, etc.)

“My biggest fear is passing on the hepatitis B virus to my children if I ever get pregnant. I am advised not to get pregnant at the moment, but it is heartbreaking for me hearing that as I love children. Every single day I have to worry.”

-Neha from Kenya

“To this day, it weighs on me to think about how many people I might have innocently and ignorantly infected, both as a child and as a young adult. Much later, after my chronic hepatitis B diagnosis, and learning more about the disease, I was very concerned about having transmitted the virus to my daughter, members of my family, and others, but fortunately I had not infected any of them and by that time the HBV vaccine had become available.

“My biggest concern now, is the elevated risk of liver cancer, especially after having also had breast cancer. Almost equally concerning is the osteoporosis I have developed, probably accelerated by taking tenofovir for 10 years and the likelihood of needing to restart antiviral treatment at some future point increases my concern that bone loss might become my most serious issue.”

-Karin from California

“After it was confirmed that I am hepatitis B positive, I took a couple of clinical tests, except one (viral load) — it cost 20,000 Nigerian naira. I have begged the doctors severally to work with the tests I was able to afford but they refused. I am a student and self-sponsored; I just fear I'm too close to my grave day after day. I sleep and wake up every day with so much fear.”

-Abdul from Nigeria

4. Have you ever felt stigma and/or discrimination because of your chronic hepatitis B diagnosis, and if so, could you share an experience with us? (Examples may include feeling “dirty” or shame for being diagnosed with CHB, not being allowed to share meals with others, facing rejection in the dating world, being asked for a divorce, being denied a job or educational opportunity, etc.)

“I'm losing hope because of stigmatization. My income is spent on laboratory investigation, medications, and inflated consultation fee. My job is not secure because of my status. I just need someone to tell me that everything is going to be okay.”

-Adeiza from Nigeria

“Yes, we have experienced stigma. We disclosed my daughter’s status for the early intervention program because she was undergoing treatment with interferon and she was in pain. We were refused services by some of the staff and were asked to change home schools. The principal resented that I involved a civil rights attorney to protect my daughter’s information from being shared with other staff. As a result, her IEP from Kennedy Krieger was denied, so she was refused services, and I felt she was assigned inferior teachers. More significantly, I felt that there were people that knew about her status, and that she dealt with a more quiet form of rejection or

discrimination – a fear of hugging her, having a mother rush up to ensure she did not touch the toe of her baby or breathe over his carriage. There were numerous, hushed experiences.”

-Maureen from Maryland

“I have felt stigma and discrimination all my life in every corner of China.”

-Dee Lee from China

Topic 2 Discussion Questions with Selected Comments

- 1. What are you currently doing to help manage your symptoms and your condition? (Examples may include prescription medicines, over-the-counter products, herbal remedies such as milk thistle, physical exercise, and alternative therapies such as acupuncture.)**

“I have had hepatitis B since birth - I am 27 - and recently gave birth to my first child. I have never required treatment, only monitoring, but as you know it is critical to make my OB/GYN aware of my infection to step up monitoring for ALT flares etc., and to ensure the immunization birth dose for my child. I found my OB/GYN quite unaware of hepatitis B, and monitoring requirements for women during pregnancy. I have been adamant in making sure my daughter has received her hep B immunizations - with or without COVID-19 barriers - but I want to underscore I made this happen because we know an unusual amount about hepatitis B. If English were my second language or if I were not aware that my hepatitis B status was not shared with my OB/GYN, my care would have been very different.”

-Jin from Maine

“I take my Viread medication daily. I exercise regularly and have recently stopped drinking alcohol. I get my blood work checked every 6 months along with a bi-annual ultrasound and yearly MRI. I try to recognize that each day is a gift, so I’m driven to extract the most out of the time that I’m here.”

-Raj from California

- 2. If you are currently taking a prescribed medication for hepatitis B, how do you feel it’s affecting your daily life? (Examples may include side effects, cost of medication, eating restrictions related to the drug, visiting the doctor every 3-6 months, taking a drug for a lifetime, not a cure, etc.)**

“Taking an antiviral has definitely improved my life - less fatigue, less worry about being ‘infectious,’ and more hopeful that I won’t get liver cancer. The only downside, however, is that I have to see my doctor every 6 months for blood tests and an ultrasound. When I was working fulltime, taking time off was a hassle and all the co-pays related to the visit, blood tests, and ultrasounds took its financial toll. In addition, every visit was anxiety-provoking because I always wondered if ‘this visit’ would be where I learned that I had liver cancer. Chronic hepatitis B is very much like living with a time bomb.”

-Joan from Pennsylvania

"I am currently on Vemlidy for treatment and numerous other medications for issues related to hepatitis B virus and cirrhosis. Although, I was told there would be little to no side effects with Vemlidy, I was sort of 'brain dead' for 3 months afterward. I could not think, process, remember, I was irrationally emotional, couldn't speak properly, etc. It took another 6 months after the initial first 3 months to start getting back memory and vocabulary. It also caused digestive issues. I still live with these issues on a little less scale with the help of more medications.

"My quality of life plummeted once I started treatment. I know treatment was necessary and inevitable but the issues and effects after the fact are just as detrimental; not just physically but mentally and emotionally."

-Paul from California

"Taking antiviral medication gives me peace of mind, reduces the risk for liver cancer, is a possible life saver, will increase my longevity. Unfortunately, it means a lifetime on drugs (not a cure), has side effects and has an exorbitant cost (I felt the need to mortgage my house to pay)."

-Espí from Florida

3. What do you consider the most important benefits of an ideal treatment? (Examples may include loss of surface antigen, a pill taken for less than a year, no stigma or discrimination, etc.)

"A cure would be ideal. But a 'functional' cure would be welcome too. Something that would make passing hepatitis B virus onto others no longer a risk and would also reduce the chance of cirrhosis and liver cancer - even if not completely removing the virus. And it would do so with limited side effects whether they are used long-term or short-term. Preferably short-term use, perhaps no longer than 6 months of treatment.

"Treatment should not cause financial stress and burden. Having a chronic and contagious illness can cause anxiety and stress which can lead to inflammation and disease progression. Having to pay high insurance rates and co-pay for the rest of your life is a true burden. Having private insurance does not guarantee affordable drug costs. No one should have to choose between paying for food/rent or a lifesaving drug."

-Lindsey from Kentucky

"I am the parent of a child with chronic hepatitis B. The ideal treatment for hepatitis B would act similarly to the current treatment for hepatitis C, completely eradicating the virus.

"Any treatment that would require ongoing/indefinite regimen of pills (similar to current HIV treatment) would be ineffective in resource-poor regions and countries without access to universal health coverage, including the United States.

“Many people living with hepatitis B would not qualify for Medicaid or SSI, as is the case with many people living with HIV. This leaves a large percentage of minority and marginalized Americans without access to or ability to afford long-term treatment.

“Also, many who live with hepatitis B in the United States are immigrants or second-generation individuals who face health equity issues, including a lack of health insurance, unemployment, language barriers that limit access to treatment, lack of paid sick leave, income disparities, and an immigration status that stops many from seeking care out of fear of deportation.”

-Chris from Maine

4. If you were to enroll in a clinical trial for an experimental hepatitis B medication, what routes of administration and what length of treatment would you be willing to accept? What side effects, if any, would you be willing to tolerate? (For example, ALT flares, etc.)

“I think if life insurance is given to patients with the hepatitis B virus for drug trials a lot of people will be willing to take trial drugs since most patients are adults who have dependents.”

-Victor from Nigeria

“Having spent much of the last 7 years in a clinical trial on the opposite side of the country from my home, it would be so much easier if some of the testing or some of the trial visits could be conducted at a cooperating research institution close to home rather than at the main research institute that requires 12 hours of travel one way.”

-Joe from California

“I would be willing to participate in a clinical trial if it will help me live longer, even if for one or two years. Because that is more time to spend with my child and wife. My goal is to see my child graduate and to be able to take care of himself.

“For this goal, I am willing to accept any route of administration and any side-effects, including mild side effects, like headache and mild nausea, or moderate – mild to moderate flu-like symptoms, or fatigue for a couple of days.

“This all depends on whether this is just another antiviral, or a new therapy that would achieve at least functional cure.

“I would do anything that can help prolong my life, and also help find a cure for this disease.”

-DeWayne from Georgia