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RESEARCH ARTICLE

Factors affecting willingness to participate in hepatitis B clinical trials among diverse U.S. populations: mitigating missed opportunities

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Abstract

Objective: Including diverse participants in hepatitis B clinical trials is important for accurately evaluating the safety and effectiveness of new therapies. However, certain populations are underrepresented in clinical trials. Lack of trial awareness and use of inappropriate communication channels are barriers to participation among people living with hepatitis B (PLWHB). This study aimed to identify factors influencing willingness to participate in clinical trials among PLWHB of Asian, African, and Pacific Islander descent.

Methods: This qualitative study involved 10 ethnically and racially diverse U.S. communities, representing populations impacted by the disease. In total, 36 individuals (PLWHB, ≥18 years old) participated in this study, with 30 participating in focus groups and six participating in interviews. Communities included Somali, West African, Black, White, Chinese, Filipino, Korean, Vietnamese, Chuukese and Marshallese. Focus groups and semi-structured interviews were conducted in participants' preferred language. Data were analyzed using inductive content analysis.

Results: Barriers were identified and categorized into the Socio-Ecological Model of Health's institutional, cultural, interpersonal, and individual-level themes. Institutional factors included researchers' qualifications, physician trust, and access to supportive services. Cultural factors surrounded the roles of respect, distrust, and community involvement. Altruism and familial influences constituted the interpersonal level. Individual factors included anticipated treatment outcomes, knowledge gaps, and time constraints.

Conclusion: Challenges to clinical trial participation faced by PLWHB are multifaceted but can be effectively addressed through coordinated, multilevel approaches. Intersectional strategies can improve patient-centricity in clinical trials, enhancing participant diversity.

Keywords

Hepatitis B virus; clinical trial barriers and awareness; racial and ethnic minority populations; qualitative analysis

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1. Introduction

Chronic hepatitis B (CHB) is a global public health concern, as people living with hepatitis B (PLWHB) are at increased risk of liver cancer, cirrhosis, and premature death.[1]Approximately 296 million people globally are affected, with the highest burden of CHB found in the Western Pacific, African, Eastern Mediterranean and South-East Asian World Health Organization's regions.[2] Due to various factors, such as limited access to care, low awareness, and the lack of visible CHB symptoms,[3–5] the majority of PLWHB remain unaware of their status.[2,6]

This is a critical time for advancing CHB management, with several promising treatment-related clinical research studies underway, which are augmented by the World Health Organization's goals to reduce hepatitis B-related deaths by 65% and to treat more eligible people.[7] However, clinical trials (hereinafter referred to as "trials") focusing on CHB treatments exhibit a notable underrepresentation of diverse participants, impeding thorough assessments of treatment efficacy and safety among different racial and ethnic populations.[8,9] This is particularly evident among individuals of Asian and African descent, who are disproportionately impacted by CHB.[10–12]

There is an incomplete understanding of trial perceptions among PLWHB in the U.S. Previous studies show approximately 34% of PLWHB in the U.S. remain undecided about participation.[13] While recruitment and enrollment rates for these groups remain low,[8] there is an opportunity to increase PLWHB willingness.

Existing studies on trial participation barriers mainly focus on conditions like cancer and cardiovascular diseases.[14] Overall, there is a wide array of reasons behind underrepresentation of diverse groups, including medical mistrust, limited healthcare access, lack of trial availability in many African and Asian countries, and insurance barriers.[15] However, few studies have explored trial participation barriers for PLWHB, particularly for those who belong to ethnic and racial minority groups in the U.S. Underrepresentation of these groups may be due to structural and contextual barriers such as trial accessibility, non-tailored recruitment practices, eligibility criteria, and socio-cultural factors.[14] Addressing socioeconomic, cultural, or informational obstacles may contribute to improved trial diversity

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and may also lead to more equitable access to treatments. This is especially important for hepatitis B trials conducted in the U.S., as foreign-born people account for 69% of the estimated 2.4 million PLWHB.[1,12]

This paper reports on a qualitative component of a larger mixed-methods study that aimed to explore the perceptions, challenges, and barriers to trial participation among PLWHB who belong to diverse racial/ethnic populations in the U.S.[16] This paper investigates the factors related to one's willingness to participate and incorporates their suggestions to enhance the participation of diverse racial and ethnic minority populations in future hepatitis B trials.

2. Materials and methods

2.1 Community-engaged research

Individuals with lived experience of CHB, either from living with the disease, or caring for others living with it, have a form of expertise. The researchers of this study ensured that those with lived experience informed the entire research process from study inception to conclusion by organizing a panel of experts, including PLWHB, public health researchers, and an epidemiologist. The researchers also partnered with six community-based organizations (CBOs) with whom they had long-standing relationships, to ensure the study's cultural appropriateness. The six partner CBOs were located across the U.S. and served diverse Asian, Pacific Islander, and African communities. These CBOs were knowledgeable about the communities they serve, as well as how CHB impacts their communities. Partner CBOs helped develop all study materials, reviewed survey translations to ensure cultural appropriateness, assisted with recruitment efforts for the survey, led focus group recruitment, facilitated focus group discussions, and were offered co-authorship on all manuscripts to ensure the presented findings are appropriate and relevant to their respective communities.

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2.2. Data collection tool

The aforementioned panel of experts developed and reviewed a qualitative, semi-structured interview/focus group guide.[16] The tool development was described in detail in a previously published paper from this study.[16] The guide was developed using a directed qualitative content analysis approach, informed by existing evidence. It was designed to examine perceptions of trial participation, barriers to participation, and factors PLWHB may consider when deciding whether to participate. This approach ensured that key domains identified in prior research were explored.

2.3 Recruitment

Qualitative data for this paper were collected via in-depth interviews and focus group discussions. Inclusion criteria for participation included having a self-reported CHB diagnosis, being 18 years old or older, and living in the U.S. Exclusion criteria included being under 18 years of age and not living with CHB. Participants were recruited via purposive sampling between January and August 2023. Partner CBOs played a central role in recruitment of minority populations with a focus on Asian, African, and Pacific Islander participants. Recruitment materials for the study were sent by partner CBOs to potential participants via organizational e-newsletters and social media posts (reaching approximately 45,000). Trusted community navigators from partner CBOs, who were known and respected within their communities and often fluent in participants' native languages, were instrumental to this study's success.

Navigators served as cultural and linguistic bridges between the study team and community members. Their familiarity with the communities' cultural dynamics and lived experiences fostered trust, which was essential given the stigma surrounding CHB. Once the community navigator reached at least 5 potential participants, they contacted those who had agreed to confirm their participation. Navigators accommodated participants' schedules, particularly for those working long or irregular hours, and ensured that focus groups were scheduled at convenient times for participants, often outside of typical business hours.

Despite their effectiveness, the navigators faced notable challenges, including managing the stigma associated with CHB and the logistical complexities of coordinating discussions around participants' demanding work schedules. Nevertheless, their involvement was a key strength of this study, contributing to higher levels of participation, richer data collection, and a more inclusive and respectful research process. Further details on the methods can be found in previously published work.[16]

2.4 Data collection

Community navigators were trained to conduct the focus groups. Between February and August 2023, a total of five semi-structured focus groups were conducted virtually via Zoom, and one was conducted in person. A few participants expressed they would be more comfortable participating in a one-on-one interview rather than in a group setting, due to fear of stigma. Therefore, six in-depth interviews were held to accommodate participants' confidentiality preferences. Sessions lasted between 60 and 90 minutes. Participants received remuneration of USD 75 as a token of appreciation.

Focus groups were intentionally selected because they enabled participants to engage in shared reflections and collective perspectives on participation in clinical trials, engagement in care, and experiences of stigma. This strengthened discussions, since these views are often shaped by community norms and social contexts. The decision to use focus groups was further supported by CBO partners who emphasized that group discussions facilitated by trusted community members would help reduce fear and create a supportive environment for participants to share their perspectives. Most focus groups were conducted virtually, which reduced barriers to participation and enhanced privacy. Participants were given the option to remain anonymous, including using pseudonyms and keeping cameras turned off, allowing them to control their level of visibility and disclosure. These measures supported participant comfort and safety while preserving the benefits of group-based discussion.

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Most sessions were conducted in participants' native language, unless participants preferred English. Other languages included Somali, French, Vietnamese, Chuukese and Korean. Interviews and focus groups were recorded and transcribed, then translated to English, when needed, by a minority-owned transcription company with expertise in social science qualitative research. Translated transcripts were then sent to the respective moderators, who were native-language speakers, for review to ensure that all nuances of the discussion were appropriately captured, thus enhancing clarity and cultural accuracy. All data were stored on a password-protected computer.

2.5 Data analysis

An inductive content analysis approach was used to allow codes, categories, and themes to emerge directly from the collected data.[16] Each week, the coding team met to review and discuss a specific community transcript, focusing on emerging codes and themes. This iterative process allowed the team to assess thematic saturation across all study groups and within individual communities, ensuring that themes unique to particular groups were also identified. Once no new themes emerged in either cross-community or community-specific analyses, the coding team agreed that thematic saturation was achieved and finalized the codebook.[16] Each code was clearly defined to improve coding accuracy and inter-coder reliability. To ensure coding accuracy, two trained researchers independently coded all transcripts using the qualitative analysis software NVivo (version 13). Both coders met weekly with a third senior researcher and reviewed coding discrepancies through discussion until consensus was achieved. Inter-coder reliability (Kappa) was assessed using the NVivo Kappa calculation tool, resulting in a final Kappa coefficient of 0.81.[16]

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2.6 Ethics approval and consent to participate

This study received ethical approval from Heartland Institutional Review Board (HIRB Project No. 081122-407). Personal identifying information was not collected to ensure participant confidentiality. Prior to participation, focus group and interview participants (herein referred to as "participants") received details on the study's confidentiality and signed an informed consent form. If participants were not comfortable reading or understanding English, a trained community navigator read the forms to them in their native language during the focus group or interview. Participants then provided verbal consent that was recorded.[16]

3. Results

The study involved a total of 36 participants, divided into two groups: 30 participants took part in six community focus groups, representing Vietnamese, West African (Senegalese, Burkinabé, Cameroonian), Somali, Korean, Chinese, and White (Caucasian) communities. Six individual interviews were conducted with participants from Filipino, Black, Marshallese, and Chuukese backgrounds. Further demographic details are provided in Table 1.[16] Table 2 provides information on participants' hepatitis B-related characteristics.[16]

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Table 1. Focus group and interview participant demographic details, 2023 [*n* (%)].[16]

Categories	Results
Gender	
Male	16 (44.4)
Female	20 (55.6)
Race/Ethnicity	
Black or African American*	13 (36.1)
Somali	6 (16.7)
West African	5 (13.9)
Black	2 (5.6)
White (Caucasian)	3 (8.3)
Asian	17 (47.2)
Chinese	5 (13.9)
Filipino	1 (2.8)
Korean	3 (8.3)
Vietnamese	8 (22.2)
Native Hawaiian or other Pacific Islander	3 (8.3)
Chuukese (Micronesia)	2 (5.6)
Marshallese	1 (2.8)
Age	
18–< 31 years	2 (5.6)
31–< 46 years	9 (25)
46–< 60 years	15 (41.7)
≥ 61 years	10 (27.8)
Previous clinical trial participation	

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Yes	4 (11.1)
No	32 (88.9)

*None of the study participants self-identified as African American.

Table 2. Focus group and interview participants' hepatitis B-related data, 2023 [*n* (%)].[16]

Categories	Results
Time since hepatitis diagnosis	
0–< 6 years	11 (30.6)
6–10 years	1 (2.8)
> 10 years	20 (55.6)
I don't remember	4 (11.1)
Diagnosed before arriving in the United States	
Yes	15 (41.7)
No	19 (52.8)
Prefer not to answer	2 (5.6)
Currently or previously on prescribed antiviral medication	
Yes, I'm currently taking medication	17 (47.2)
No, but I used to take medication	3 (8.3)
No, I have never taken medication for hepatitis B virus	16 (44.4)
Healthcare provider for hepatitis B	
Long-term liver specialist	12 (33.3)
Long-term primary care physician	21 (58.3)
Do not have a regular provider	1 (2.8)
Prefer not to answer	2 (5.6)
Frequency of visiting provider for hepatitis B*	

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Every 6–12 months	26 (74.3)
Every 1–2 years	3 (8.6)
When I have a new symptom	1 (2.9)
I don't have access to a medical provider	2 (5.7)
Consult with a natural healer or an herbalist	2 (5.7)
Other	1 (2.9)
*One participant did not answer the question about their frequency of visiting a provider for hepatitis B, so the sample size for this question is 35 instead of 36.	

Themes describing factors affecting the willingness of racial and ethnic minority populations to participate in trials at institutional, community, interpersonal, and individual levels were identified (Table 3). The themes were organized into a modified version of the Socio-Ecological Model of Health.[17]

Table 3. Factors affecting willingness to participate in HBV clinical trials.

Socioecological model	Themes
Institutional	• Role of trusting the research team • Role of treating physicians in recruitment and retention • Suggested support services
Community and culture	• Impact of culture on willingness to participate • Culture and wariness
Interpersonal	• Familial influence on participation • Altruism
Individual	• Anticipated treatment outcomes • Knowledge gaps • Time

HBV: hepatitis B virus.

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3.1 Institutional-level factors

3.1.1 Role of trusting the research team

Participants had varied opinions on the importance of racial or ethnic concordance between themselves and the research team. Some, like a Marshallese participant, felt that the race of the researchers did not impact their willingness to participate, stating, "For me, it doesn't really matter whether [the researchers are] from the same race."

However, others discussed how they would feel more comfortable if someone on the research team looked like them. Members of the Marshallese, Vietnamese and Korean communities expressed their appreciation for researchers who speak their languages. Additionally, a Chuukese participant stated, "I'd be very happy to partake if (the researcher) came from Chuuk."

Interestingly, one Korean participant discussed how, since hepatitis is more prevalent in different Asian ethnicities, they believe it "would be good to have (researchers of) a race where the disease occurs a lot" though it is not necessary to precisely be Korean.

Overwhelmingly, communities agreed that the teams' academic and professional qualifications to conduct research were important motivating factors, alongside information about their success in previous similar work. A Chinese participant shared how their trust depended on the institute's reputation: "Well, it doesn't necessarily (have) to be my doctor, but if the whole facility is a famous, well-known facility that will definitely make me more willing to participate." A Black participant shared the importance of researchers' qualifications, "for me, it's not very important, because I know that they are medical professionals."

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Many communities also expressed greater trust in research teams based in the U.S., versus those in their native countries, as they possess these qualifications and must follow strict federal safety guidelines. One Vietnamese participant explained, “if the research team is (in) the U.S. and they have a degree... But if I was invited to a clinical trial in Vietnam, I don’t think I can trust them.” Hence, participants suggested researchers provide trusted CBOs with information about their teams’ qualifications and their institution’s accreditations to present to potential participants.

3.1.2 Role of treating physicians in referral for clinical trials recruitment: a missed opportunity

Across communities, people expressed greater willingness to participate in a trial if their treating physician suggested it. For example, one Chinese participant explained that while they had never previously wanted to participate in a trial, if their doctor offered it to them, they would “be willing to learn more”, highlighting the importance of leveraging established physician-patient relationships in recruitment strategies.

While physicians are often the primary and most trusted source of health-related information, most participants discussed how they have not learned about trials from their treating physicians. Only some West African, Chinese, and Black participants reported learning about trials from their doctors, with one Chinese participant stating, “sometimes the doctors do mention them.” While White, Korean, and Filipino participants had never been asked to participate in a trial by their physicians. A Vietnamese participant mentioned: “I once asked a specialist, but the doctor said there was no trial at that time, and then I stopped asking.” One Chinese participant posited that while they have been informed by one doctor about research opportunities, it is possible that “not every doctor knows or has the resources to tell the patients”.

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3.1.3 Role of treating physicians in retention

While most communities agreed that they did not necessarily require their treating physician to serve as their trial provider, they felt that their motivation to participate in a trial would increase if their regular physician was part of the experience. One West African participant stated, “It gives more motivation to continue with your treating doctor.”

Across all communities, participants expressed that if they were to participate, they would want to consult with their treating physician about the trial, especially about their participation status. They indicated that they would feel more comfortable participating if their treating physician was regularly involved in the research process, as summarized by a White participant’s sentiments: “whoever was conducting the trial would have to be open with my current doctor pretty much all steps of the trial.”

3.1.4 Suggested support services

Participants across communities emphasized the benefits of having trial support groups. A White participant said, “the offer of a support group would influence my decision.” Participants also felt that trial developers should consider incorporating transportation services and/or reimbursements. One Marshallese participant explained: “Taking medication can seriously affect your thinking ability and your mobility... providing transportation will be one solution for that problem, and when I miss my work, you need to pay me and compensate me for my (missed) work hours.” Other suggested support services included peer navigators from participants’ local communities, childcare facilitation and flexible participation modalities.

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3.2 Community- and cultural-level factors

3.2.1 Impact of culture on willingness to participate

Many communities felt differently about the role culture plays in peoples' willingness to participate in research. Most agreed that their culture does not negatively influence their willingness to participate in trials. In the words of one Vietnamese participant, "... my cultural background is not a main factor, it's an unreasonable factor to refuse or participate in a treatment or study." Additionally, a Chuukese participant explained that since researchers are professionals, "Whatever their knowledge is on how things should be done, it's up to them. Whatever they want to do, they should do it" rather than "be limited unnecessarily by our cultures".

Other communities, however, wanted the freedom to practice their cultural activities without judgment or restrictions from the research team. For example, one White participant discussed how, while the cultural makeup of the research team does not bother them, they would value the ability to "practice my culture in the study... (like) if I wanted to pray".

Most participants agreed that researchers should be kind and respectful of every participant, without allowing cultural barriers to jeopardize the research process, as discussed by a West African participant: "The person should be able to understand your background and understand how uncomfortable you can be with certain things." To enhance participant comfort and improve research collaboration, many participants discussed the importance of potential participants informing the research team about their cultural norms and religious practices prior to participation.

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3.2.2 Culture and wariness

Despite many communities explaining how their culture does not reduce their willingness to participate in trials, some expressed how fear of the unknown, stemming from limited knowledge, misconceptions and unfamiliarity with trials can make people wary of participation. For example, one West African participant expressed how, despite their own willingness to participate in research, certain community misconceptions could result in their peers refusing to participate: "They will say it's for injecting things into their body, adding more diseases." A Marshallese participant explained their community's apprehension: "They may hesitate to participate because this is a new world, new knowledge to them." Additionally, a Somali participant discussed how fear of death reduces their community's willingness to participate in research, as people are "afraid to die if they test themselves with this medicine first". Having a peer navigator from the community explain the pros and cons of participation would allow for greater confidence in trials and increase the inclination to participate.

Conversely, two White participants expressed increased wariness toward research participation due to a general distrust rooted in historical experiences with government and pharmaceutical companies. One participant stated, "I know what pharmaceutical companies have done in the past and I also know what our government has done in the past to a certain extent on bans when it comes to trials and experimentation."

3.3 Interpersonal-level factors

3.3.1 Familial influence on participation

Participants with children or dependents in the Vietnamese and Korean communities reported hesitancy to participate due to the fear of the unknown risk of leaving loved ones behind, with one Korean participant stating, "I have children, and it is difficult for me to decide whether to participate or not." Black participants also shared hesitancies, stating that the decision to participate was a collective family decision, "I really need to talk it out with my family."

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3.3.2 Altruism

Participants expressed solidarity and a sense of duty towards others living with CHB around the world. Although altruism may not be their only motivation to participate, most participants noted that this was a primary motivation for trial participation. One Vietnamese participant posited, "there have to be people who sacrifice, so that the others can have the medicines to use," while a West African participant stated, "First, I want to contribute to getting a good medication for people. Also, I want to be the first person to be in good health."

3.4 Individual-level factors

3.4.1 Anticipated treatment outcomes

Many communities discussed treatment outcomes that would enhance people's willingness to participate in a trial. Particularly influential is the potential of a cure. As shared by a Filipino participant, "if there's a medication to cure that virus for you to feel better even sooner than one year, for me that's better to be involved with that trial." One West African participant explained how they would be willing to participate if the treatment ensured they would not "transmit the disease to anybody else". Other desired outcomes included the ability to discontinue CHB medication after 6–12 months, liver cancer prevention, enhanced quality of life, low viral load, and the loss of hepatitis B surface antigen. Interestingly, some Chinese participants exhibited a greater inclination to participate when confronted with a deteriorating disease condition: "If my disease (starts) deteriorating, I feel like I have more urge to participate." Conversely, some White participants expressed greater hesitancy if their condition was worsening: "I'm definitely hesitant because my situation has changed over the past five years."

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3.4.2 Time constraints

Time constraints, particularly the potential loss of work or paid time, were identified as barriers across all communities. This concern was expressed by a Filipino participant, "I could volunteer myself to be studied, but I need to work to pay my expenses. I don't have extra time to volunteer and that's my concern." However, the travel time to the study site was less concerning to participants if they were adequately supported through provision of transportation services or reimbursement.

Table 4 outlines participants' suggestions to boost CHB trial recruitment and enrollment among diverse communities affected by hepatitis B.

Table 4. Recommendations to enhance recruitment and enrollment among diverse communities in hepatitis B clinical trials, 2023.

Socioecological model	Recommendations
Institutional	• Employ translators and culturally sensitive staff • Leverage existing physician-patient relationships • Establish collaborative partnership with doctors, inform them of trial opportunities, provide training to discuss trials with patients and keep them informed of trial progress • Incorporate support groups, transportation services (rideshare services, mobile health vans), flexible participation options (weekend appointments), and reimbursements into trial protocol • Provide culturally appropriate communication and education • Inform potential participants of field expertise, qualifications, and institutional reputation
Community and culture	• Design trials with respect for participants' cultures: emphasize that participants have freedom to practice religion and cultural activities during trial (allow time to pray) • Employ culturally responsive team members, open to learning about cultural differences • Collaborate with community-based organizations, learn about

	communication styles and cultural nuances • Integrate peer navigators from community into recruitment and result dissemination process
Interpersonal	• Include families in conversations about clinical trial participation and the informed consent process
individual	• Involve people living with hepatitis B in the design of clinical trials, from implementation to dissemination • Incorporate treatment outcomes that are most important to people living with hepatitis B into trial protocol • Share research outcomes with previous participants

4. Discussion

This study identified a general willingness among diverse PLWHB to participate in trials for new CHB medications but identified various barriers which hindered their participation. Participants provided suggestions to overcome these barriers to enhance participation of diverse racial and ethnic populations in hepatitis B trials.

These findings present new insights into critical gaps in existing knowledge regarding hepatitis B clinical trials, including barriers to participation and areas where patient perspectives are insufficiently represented in the literature. They highlight the importance of adopting innovative, multi-faceted and intersectional strategies to address participation disparities in clinical research for CHB among diverse racial and ethnic populations in the U.S. These challenges should be addressed at the institutional, community, interpersonal, and individual levels. These levels are often intertwined and hence the solutions could be designed through system-wide policies and cross-cutting strategies, to effectively educate trial teams about patients' needs and expand the dialogue between drug sponsors and research teams to involve participants.

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4.1 Institutional

Institutional factors can significantly affect one's willingness to participate in a trial. This study described how trust can be built to increase PLWHB willingness to participate in research. Participants highlighted the preference for a well-qualified research team, rather than racial/ethnic concordance, and wanted to know of the teams' expertise in the field of the study, as previously shown.[18] Notably, this differs from prior literature suggesting Black participants showed less inclination to join trials due to limited trust in research.[15] In this study, trust was primarily linked to institutional credibility and reputation rather than racial concordance , an important distinction for trial recruitment strategies. Along with qualified researchers, trial teams should also employ translators and culturally sensitive staff to enhance communication and trust between the researchers and participants from diverse backgrounds.

Albeit different from previous literature,[15,19] the findings display a wide span of preferences within and across minority racial and ethnic groups in the U.S. Informing potential participants about trial opportunities with culturally appropriate communication and education about the risks and benefits of participation, and ensuring potential participants learn about the scientific and academic credentials of the research team could help reduce mistrust and enhance recruitment efforts within diverse groups who have reservations about trial participation. Also highlighted was the missed opportunity to effectively incorporate treating physicians into the trial process. Institutions conducting research must acknowledge the trusting relationships between treating physicians and their patients, and understand the pivotal role that physicians play in the referral to- and retention in- trials.[20] In this study, many participants requested that their treating physicians be informed of the trial's progress and the participants' health status throughout the trial so that they could consult with them. This corresponds with existing evidence.[14] Treating physicians can inform their patients about trial opportunities and address challenges related to communities' limited knowledge and trust. Lack of discussions and referrals from treating physicians are primary reasons many minority groups have limited knowledge about, and lower willingness to participate in trials.[21,22] Potential participants hope their treating physicians will inform them of the importance of

trials, the overall research process, duration, eligibility requirements, and how their research participation will help others.[23] Trial developers can establish collaborative relationships with minority-serving physicians and build trust with them by seeking out their expertise and learning what information they need to feel confident when referring their patients to future trials.[20]

Research institutions should engage treating physicians who serve minority populations by keeping them well-informed about current trials to effectively discuss these opportunities with their patients, providing regular updates during the trial's implementation to support participants' retention, and communicating trial results. This would significantly reinforce trust and enhance retention of diverse participants throughout the trial.[14,15,18,20–22] This study highlights how people living with the disease have the power to bring the discussion about trials to the table. It is crucial for treating physicians to be well-informed about trials, but it is equally important to create an environment where patients feel comfortable discussing and inquiring about trial opportunities without the fear of being dismissed.[14] This two-way communication may encourage physicians to find more information about trials that might benefit their patients, thus boosting recruitment and enrollment efforts.

There are solutions to various systemic challenges that impede racial and ethnic minority groups from participating in research. Specifically, this study presents several actionable recommendations to overcome the lack of support services during participation, which has been identified as a barrier previously.[14,22] One recommendation is going beyond reimbursement of travel costs toward travel facilitation, such as trial sites organizing transportation like rideshare services,[24] or mobile health vans from academic centers to facilitate convenient participation, which has been successful previously.[23]

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4.2 Culture and community

For many, one's community and cultural traditions represent their social safety net. This is particularly evident among immigrant and minority populations.[25] Therefore, designing trials that foster the role of the community and respect for participants' culture has proven to be more successful at recruitment and retention of participants.[26]

Limited knowledge about trials, skepticism of pharmaceutical companies and the government, and fear of research participation are additional challenges that must be addressed to increase the diversity of participation in trials.[14,22,26,27] Suggestions to reduce diverse communities' mistrust and skepticism of drug development included the need for researchers to collaborate with trusted CBOs to establish relationships with the community, and having research teams who are aware and respectful of the different communication styles and cultural nuances of their participants. These suggestions support existing literature.[14,22,28]

While having trial providers from the same race/ethnicity as patients may not be necessary, ensuring that healthcare staff are trained to understand, respect and accommodate cultural differences is crucial.[29] Another key finding is establishing community trust through peer navigators. Peer navigators, who share similar cultural, racial and ethnic backgrounds with participants, inherently command a higher degree of trust among prospective participants, thereby playing a pivotal role in facilitating trial enrollment, advocating for participation, and ensuring adherence among minority populations.[22,30,31] Integrating peer navigators into the recruitment and result dissemination processes serves to bridge knowledge gaps pertaining to trials and fosters community-based participatory research.

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4.3 Interpersonal

Close relationships, including those with family and friends, play an important role in an individual's health behaviors, and contribute to their life experiences. This study identified that family has great influence over one's willingness to participate; for example, people with family commitments and dependents were less likely to participate. This has also been seen in previous literature.[13] Contrary to what has been shown in previous literature, where family encouragement had little influence on non-Hispanic Black participants' odds of participation,[15] non-Hispanic Black participants in this study indicated their participation was a joint decision with their family. Further studies are needed to identify other factors like culture or tradition that affect participation willingness beyond race and ethnicity. Therefore, it is important to consider these relationships when exploring factors influencing one's decision to participate in trials.

4.4 Individual

Some of the factors that affect one's willingness are inherent, like age or gender, while others may involve individual treatment preferences and trial-related knowledge. Understanding these factors will inform strategies that promote attitudes, beliefs, and behaviors that may increase one's willingness to participate in trials.

To address individual-level factors that influence racial and ethnic minorities' participation, researchers must involve patients' input when designing trials, from implementation to dissemination. Patient engagement in the trial design and implementation phases has enhanced efforts to disseminate trial results, specifically those that are clinically meaningful to patients, and in an accessible format.[32–34] Incorporating relevant patient health outcomes into the trial design and employing peer navigators who speak the language of the communities to disseminate trial results can enhance racial and ethnic minorities' willingness to participate in future research endeavors, as they feel respected by the research team. When potential participants see how their peers were treated during participation and the trial's outcomes, they are more likely to participate in future trials. When participants receive trial results, they feel appreciated and more inclined to either continue participating or enroll in future research.[35] Sharing trial outcomes

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with those who participated, and with the greater community, is considered an ethical practice, as it allows those who helped generate the data to understand how it is being used, fostering transparency and trust between researchers and participants.[35]

4.5 White and minority populations: perception differences

This research highlighted distinct differences between minority and White communities concerning trusting the research team. White participants exhibited wariness due to government mistrust, while other communities' mistrust stemmed from misconceptions about trials. Furthermore, White participants were more cautious and less inclined to participate under worsening health conditions, whereas Chinese participants seemed more likely to participate if their CHB worsened.

White and minority communities shared similar attitudes towards prioritizing the academic and professional qualifications of research teams over the team's ethnicity, preference for their treating physicians' involvement throughout participation, and respecting each other's cultural practices. They unanimously recognized altruism as a primary participation motivator and acknowledged challenges related to having dependents and time constraints for working individuals.

These findings emphasize the importance for research teams to learn more about the communities they are trying to recruit from. One size does not fit all, rather it requires culturally appropriate recruitment strategies.

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4.6. Strengths and limitations

This study offers unique insights from individuals belonging to minority populations living in the U.S. who are disproportionately affected by hepatitis B. However, several limitations should be acknowledged.

All participants were recruited through CBO partners, meaning they had some level of connection to care or support services. Therefore, the findings may not fully represent the experiences of individuals who remain completely disconnected from healthcare or community support systems. While this may affect transferability of study findings, the results are highly relevant to similar groups and present useful recommendations for engaging similar groups in clinical trials, especially by leveraging partnerships with CBOs. Several focus groups and interviews were conducted in languages other than English. While this approach strengthened cultural and linguistic inclusivity, it introduced potential variability in facilitation and translation. Bilingual community navigators conducted sessions in participants' native languages. Recordings were then transcribed and translated back into English. This process may have introduced subtle differences in how questions were posed or how responses were interpreted, especially when words or phrases had no direct English equivalent. However, to safeguard data accuracy, translated transcripts were reviewed by the bilingual community navigators who confirmed that the translations accurately captured the participants' intended meaning.

Importantly, participants chose their mode of participation, either focus groups or individual interviews. While this may have introduced some differences in framing discussions, it also allowed flexibility for session timing, location, and one's ability to participate, especially among individuals who might have otherwise declined involvement due to scheduling or stigma-related concerns. Notably, there were no observed systematic differences in the content by data collection modality; core themes related to clinical trial awareness, perceived risks and benefits, and trust emerged consistently across modes. Additionally, virtual participants were able to turn off their cameras, which may have allowed more privacy and space to speak freely. Furthermore, all sessions were conducted by trusted community navigators, thereby reducing the risk of social desirability bias.

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Lastly, due to the virtual nature of some sessions, potential participants with low digital literacy and those without access to the required technology may have been missed during recruitment. While this introduced potential selection bias, the overall sample size, the participants' geographic and linguistic diversity and channeling recruitment through local CBOs strengthened the robustness and relevance of the findings.

Despite these limitations, this study has several notable strengths. First, it showcases a successful engagement model with trusted community partners, featuring linguistic and cultural inclusivity and a robust design. Community members with lived experience informed the entire research process from inception to conclusion. Their experiences served as a valuable form of expertise and meaningfully shaped the research process, from defining research questions to interpreting findings. This collaboration fostered trust, mutual learning, and shared ownership between researchers and communities. These features allowed for the collection of rich, contextually grounded data and underscore the importance of community involvement in public health research to address health disparities.

Second, this study adopted a comprehensive, multi-level perspective by examining individual, interpersonal, community, and institutional factors influencing engagement in hepatitis B–related research. This approach is particularly valuable in the context of hepatitis B, a disease that remains comparatively understudied despite its substantial global burden. Finally, the study highlights the central role of the physician–patient relationship within a highly stigmatized disease context, demonstrating how trust, communication, and perceived support can meaningfully influence patient engagement in research. These insights are especially actionable for informing strategies to enhance inclusive and equitable global participation in hepatitis B clinical trials.

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5. Conclusion

Meeting the varied needs and preferences of people living with hepatitis B across diverse racial and ethnic communities in the U.S. is challenging. However, intersectional strategies are essential to accurately assess treatment safety and efficacy, particularly within populations most affected by hepatitis B. By incorporating the insights and recommendations from this study, trial developers can address participation barriers across multiple levels and design inclusive and culturally appropriate clinical trials. These findings add to the understanding of why people join clinical trials, especially among diverse racial and ethnic groups in the U.S. for diseases like chronic hepatitis B. Future research should explore the complex mix of challenges that affect participation of diverse racial and ethnic groups to optimize clinical trial recruitment and retention efforts.

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6. **Ethics approval and consent to participate**

This study received ethical approval from Heartland Institutional Review Board (HIRB Project No. 081122-407). Personal identifying information was not collected to ensure participant confidentiality. Prior to participation, focus group and interview participants received details on the study's confidentiality and signed an informed consent form. If participants were not comfortable reading or understanding English, a trained community navigator read the forms to them in their native language during the focus group or interview. Participants then provided verbal consent that was recorded.

7. Consent for publication

Consent for publication was obtained from all study participants.

8. Funding

This research was supported by the Food and Drug Administration, grant number 75F40121C00096 and through general operating funds of the Hepatitis B Foundation. The funder had no involvement in the study's design, execution or interpretation.

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9. **Availability of data and materials**

Data supporting this study are included within the article and/or supporting materials. Additional data supporting this study cannot be made available due to privacy or ethical restrictions.

10. Conflicts of Interest

The Hepatitis B Foundation receives public health program and research grants from BMS, GSK, Gilead Sciences, Vir Biotechnology, and Dynavax Technologies. Chari Cohen serves on a patient/advocacy advisory committee for GSK and Gilead Sciences, with funds being distributed to the Hepatitis B Foundation. Yasmin Ibrahim serves on a patient/advocacy advisory committee for Roche/Genentech, with funds being distributed to the Hepatitis B Foundation. No corporate funds supported this research.

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CRediT authorship contribution statement

Yasmin Ibrahim: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Tanya Machado**: Formal Analysis, Investigation, Project Administration, Writing – original draft, Writing – review & editing. **Fiona Borondy-Jenkins**: Formal Analysis, Writing – original draft, Writing – review & editing. **Shreya Koirala**: Writing – original draft, Writing – review & editing. Mi Dong: Writing – review & editing. **Ellen Tham**: Writing – review & editing. Ibrahima Sankare: Writing – review & editing. **Mohamed Ali**: Writing – review & editing. Ashley Che: Writing – review & editing. Chari Cohen: Funding Acquisition, Supervision, Writing – review & editing.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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