The Impact of Living With Chronic Hepatitis B on Quality of Life: Implications for Clinical Management

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Abstract

Living with chronic hepatitis B (CHB) has physical, social, and emotional impacts that often negatively affect patients' quality of life. These impacts are not usually captured during routine care. This article presents information on the impact of living with CHB and the importance of integrating health-related quality-of-life assessment into CHB care. Using a global online survey, people ages ≥ 18 living with CHB were asked about physical, social, and worry impacts. Of 1707 respondents, most were male (67%), < 45 years of age (81%); and 52% identified as Black. Of all participants, 66% reported physical impact, 55% reported social impact, and 49% reported worry impact of living with CHB. Those from Africa and the Western Pacific were most likely to report physical impact. Younger participants (18-45) and those not on treatment were significantly more likely to report physical and social impact. People living with CHB are impacted physically, socially, and emotionally, varied by demographic factors and disease experience. These impacts should be captured and addressed as part of routine CHB care.

Keywords

physical impact, social impact, worry impact, health-related quality of life, patient-reported outcomes (PROs), chronic hepatitis B

Background

Chronic hepatitis B (CHB) infection affects 296 million people globally.¹ CHB continues to be the leading risk factor for primary liver cancer worldwide,^{2,3} even with effective vaccines and antiviral treatments that suppress viral replication and can prevent cirrhosis and liver cancer.⁴ Medical management of CHB focuses on specific clinical endpoints, such as normalization of liver enzymes (transaminases), Hepatitis B virus (HBV) viral load, and evidence of liver cirrhosis.^{2,5} However, these endpoints fail to document the health-related quality of life (HRQOL) impact of the disease on the daily lives of patients, leading to an unmet need for care that addresses the nonclinical aspects of hepatitis B, such as fatigue, stigma, and concerns about disease progression.^{6,7} CHB is often viewed as a "silent disease," but studies have shown there is often ongoing liver inflammation even when liver enzymes are normal or mildly elevated.⁸ In addition, people living with CHB have greater symptomatology than previously realized.⁶ The lack of focus on disease impact on patients' daily lives has the potential of making regular follow-ups less meaningful and effective for them.⁹

HRQOL is defined by the Centers for Disease Control and Prevention (CDC) as the "perception of an individual or group's physical and mental health over time."¹⁰ Studies have documented decreased HRQOL among those living with CHB in domains related to psychological well-being, physical health, and social functioning.^{6,11–13} As a growing field, there is still much to be understood about how extensive these impacts are, and how they might differ across groups. With a global push for hepatitis B elimination, and new treatments on the horizon, this research should be prioritized and HRQOL should become an integral component of clinical trials and clinical management of CHB. One way to incorporate HRQOL with a standardized and patient-centered approach is with Patient Reported Outcomes (PROs).¹⁴

There have been few published studies on the use of PROs in CHB management, and while their individual results vary,

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they consistently recommend comprehensively assessing the impact of the infection on patients' lives, to measure treatment effects that are meaningful to patients, to evaluate treatment plans, and to help manage the psycho-social impact of CHB.^{15–18} Despite the growing evidence on the value of integrating HRQOL assessment into CHB care, it is not addressed by society guidelines for CHB management, including those from the European Association for the Study of the Liver (EASL), the American Association for the Study of Liver Disease (AASLD), or the World Health Organization (WHO).^{19–21} However, improving quality of life is mentioned as one of the treatment goals by the Asian Pacific Association for the Study of the Liver (APASL).²²

In this study, we sought to (1) identify the physical, social, and emotional quality of life constructs that are most relevant to and reported by people living with CHB and (2) understand the patient characteristics that are associated with these constructs, hoping that these insights will enrich the discussion around the future use of PROs to assess HRQOL in CHB care.

Methods

Study Design

An online survey was used to assess the impact of living with hepatitis B as reported by people living with the disease. The survey was part of a larger study, however, this article reports only on results obtained from the online survey part of the study.

Study Instrument (Survey)

Data were collected via an anonymous online survey, which was developed by a panel of liver experts consisting of patients, providers and public health researchers. Before developing the survey, the panel did an extensive literature review to gauge the important constructs to include in the survey and the most acceptable way to ask those questions. After an initial draft, the survey was further reviewed by a hepatologist, public health and patient partners, and FDA staff who are knowledgeable about the topic. Before launching the survey, it was pilot-tested for clarity and consistency with a small subset of people living with CHB. Feedback was then incorporated to create the final form of the survey.

The survey was offered only in English and was designed as a decision tree, consisting of 29 to 39 questions. The number of questions a respondent encountered depended upon their responses to previous questions, such as whether they had experience with hepatitis B medication. Questions included ranking options, multiple-choice questions, and open-ended items. Some of the questions included several statements where respondents expressed the emotional, psychosocial, and physical impact of living with CHB on a 5-point Likert scale. The survey also included questions about demographic characteristics, diagnosis and medication experiences, challenges living with CHB, and perspectives on current/future hepatitis B medications and clinical trials (the survey is attached as Appendix 1). The survey methodology was described in a previously published paper.²³

Participant Recruitment

The survey was open for 6 months (12/23/2019-06/30/2020). Potential participants were recruited by posting the link to the survey on the social media pages of the Hepatitis B Foundation (Facebook page and Twitter accounts). Additionally, the survey was promoted through our monthly e-newsletter subscriber list (n = 12,000). Finally, we used Facebook ads for 6 weeks to promote the survey to individuals who searched for the term "hepatitis B" on Facebook. Throughout the recruitment and data collection phases, no identifying information was collected from survey participants.

Survey participants were screened for eligibility at the start of the online survey with the following screening questions: (1) are you 18 years old or older? and (2) have you been diagnosed as living with CHB? If the survey taker answered no to either of these questions, they were directed to the disqualifier page with a thank you note, explaining that they needed to be at least 18 years old and be living with CHB.

Ethical Approval (IRB, No Identifying Information Have Been Collected)

Data for this study were obtained after obtaining the approval of an Institutional Review Board (IRB) (HIRB Project No. 191221-270). Survey responses were anonymous and no personal identifying information was collected.

Data Processing

Creating the Three Indices. We used a portion of related survey items to compose three indices to answer the stated research questions (Table 1). All survey questions used to compose the indices were 5-point Likert scale items, with response options ranging from 1 to 5, with 1 indicating the lowest score and 5 indicating the highest score possible (Table 1). We defined the indices as Physical Impact (PI), Social Impact (SI), and Worry Impact (WI). Each index was calculated using the average of the 5-point score on the scale for the variables included in each index. Indices were further transformed into a binary variable (yes/no) by calculating the sum score of each index and using the mean value of each index score as a cutoff value. All values above the cutoff value were labeled as "yes" (experiencing PI, SI, or WI), and values below the mean were labeled as "no" (not experiencing PI, SI, or WI).²⁴

Missing Data. The survey completion rate was 71%, as not all participants answered all questions. A complete survey

Index	Alpha (α)	Items included	Scale
Physical impact (PI)	0.712	 Managing fatigue Worrying about their ability to do their job Feeling tired more than others Feeling less productive 	 Not at all challenging = I A little challenging = 2 Somewhat challenging = 3 Very challenging = 4 Extremely challenging = 5
Social impact (SI)	0.847	 I feel shame I fear that I will face discrimination I feel life is less enjoyable I feel like avoiding others I feel that others avoid me I worry that my relationships with family and friends are negatively affected 	 Not at all challenging = 3 A little challenging = 2 Somewhat challenging = 3 Very challenging = 4 Extremely challenging = 5
Worry impact (WI)	0.748	 I worry that I will transmit the virus to someone else I fear that I could develop liver cancer I fear that I will live a shorter life 	 Not at all challenging = I A little challenging = 2 Somewhat challenging = 3 Very challenging = 4 Extremely challenging = 5

Table 1. The Survey Items Included in the Computation of Three Indices: PI, EI and SI.

submission was defined as reaching the end of the survey and clicking the "submit survey" button. Among those who submitted their survey, some respondents left some questions unanswered (not all questions were mandatory). This could have been caused by having the survey only in English, with some participants leaving out questions that they could not fully comprehend in English. Additionally, the survey was conducted online, and respondents may have experienced internet interruptions. Mean imputations were used to replace missing values, and the analysis was repeated, yielding similar results.^{25,26} Additionally, only participants who indicated having experience with CHB medications were offered a set of questions specific to their medication experience, which was not considered as missing values.

Data Analysis

Statistical analysis was performed using SPSS Statistics 27.²⁷ For this article, 13 items related to the challenges of living with CHB were used, in addition to demographic and disease experience items. In addition to descriptive analysis of demographic characteristics, disease experience, and impact indices, we ran a chi-square (chi²) test of independence to explore relationships between each index and respondents' demographic characteristics and disease experiences. For each chi² test, Cramer's V,²⁸ odds ratio (OR), and *p*-value were reported to show the strength of relationships and significance levels ($p \le .05$, $p \le .01$, $p \le .001$).

Results

Reliability and Fitness of Indices

The PI index was developed by computing a 5-point scale average of four 5-point Likert scale items. A reliability test was performed, and it showed that this index was fit for use (Cronbach's alpha is 0.712).²⁹ In the same way, SI index was computed using six items (Cronbach's alpha is 0.847), and the WI was computed using three items (Cronbach's alpha is 0.748).

Respondents' Characteristics

Of all eligible individuals who clicked on the survey link, 71% (n = 1707) successfully submitted a complete survey. The majority of respondents identified as male (67%). Most respondents were <45 years of age. A vast majority identified as persons of color, as 52% selected African/African American and 30% selected Asian/Asian American/Pacific Islander (AAPI). Native Hawaiian (NH) ethnicity was offered in the survey, however, no survey respondent identified as NH. Pacific Islanders were grouped with Asians as the number of respondents who self-identified as such was too small for meaningful analysis (1%). The number of Latino/Latina participants was small (0.3%), and they were grouped with other race/ethnicity groups. 42% of respondents were college graduates, and 36% had postgraduate degrees. The majority of respondents were from Africa (47%), followed by North America (18%) and Southeast Asia (13%). Respondents were offered a drop-down menu to select their country of residence, and countries were grouped into 7 regions for analysis, using the WHO as guidance.³⁰ Table 2 shows the demographic characteristics of survey respondents.

Regarding disease experience, most respondents (52.8%) received their hepatitis B diagnosis in the last 5 years. A combined 57% had experience with hepatitis B medication, either currently or in the past. Of those taking medication, 80% began treatment within the last 5 years. Table 3 summarizes disease experiences living with CHB (in terms of diagnosis and experiences with hepatitis B medications).

A majority (66%) of respondents indicated that the PI of living with CHB is a challenge; 55% indicated that the SI

 Table 2. Demographic Characteristics of Respondents.

Respondents*	
Age group (n = 1707)	
18–30	32% (546)
31–45	49% (836)
46–60	14% (237)
60+	5% (88)
Gender (n = 1707)	
Female	26% (445)
Male	67% (1140)
Preferred not to answer	7% (122)
Race/ethnicity $(n = 1433)$	
African/African American	52% (740)
AAPI**	30% (435)
White	14% (202)
Others	4% (56)
Education $(n = 1431)$	
High school or less	13.5% (194)
Technical/ some school	9% (130)
College	42% (599)
Postgraduate	35.5% (508)
Region (n = 1492)	
Africa	47% (707)
Southeast Asia	13% (188)
Western Pacific	9% (131)
Europe	7% (106)
Middle East	5% (71)
North America	18% (275)
Latin America***	1% (14)

*Some respondents did not answer all questions, the number of those who answered each question is between parentheses.

**AAPI: Asian, Asian American, or Pacific Islander.

*** respondents who identified to be from countries in Central and South America.

of living with CHB is a challenge; and 49% of respondents indicated that the WI of living with CHB is a challenge.

Physical Impact

Table 4 shows the results of chi² test between PI and patient demographic and disease experience. Age, race, geographic location, treatment status, and years since diagnosis were all independently significantly associated with a high PI index. Notably, younger groups (18-30 and 31-45) were more likely to report high PI than older groups (46-60 and >60) ($p \le .001$), and those who identified as Black were most likely to report high PI ($p \le .05$). Neither gender nor education were significantly associated with PI.

Social Impact

As seen in Table 4, geographic location, age, race, treatment experience, and years since diagnosis were all found to be significantly associated with a higher likelihood to report SI as a challenge ($p \le .001$). Younger age groups (18-30 and 31-45), and those identifying as Black or AAPI were most

 Table 3.
 Respondents' Disease Experiences Living With CHB (in Terms of Diagnosis and Experiences With Hepatitis B Medications).

	Respondents*
Years since diagnosis (n = 1280)	
5 years or less	53% (676)
6-10 years	17% (223)
More than 10 years	27% (34I)
Don't remember	3% (40)
Medication status (n = 1176)	· · · ·
Currently on treatment	36% (419)
Previously on treatment	21% (252)
Never been on treatment	43% (505)
Medication duration** (n = 642)	· · · ·
5 years or less	80% (510)
6-10 years	8% (53)
More than 10 years	9% (S7)
Don't remember	3% (22)
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*Some respondents did not answer all questions, the number of those who answered each question is between parentheses.

**This question has been offered only to those who reported having any experience with CHB medications (current or previous = 671).

likely to report SI as a challenge. Those who had past experience with hepatitis B medications (but were no longer on treatment) were the most likely to report SI as a challenge, whereas those who are currently taking medication for hepatitis B were the least likely to report SI as a challenge. Those diagnosed within the past 10 years were more likely to report SI as a challenge.

Worry Impact

As seen in Table 4, the WI was found to be independently significantly associated with a variety of factors, including geographic location, age, race, gender, education, and years since diagnosis. Respondents from North America, those who identified as White, those who were 46 or older, and those with less than a college degree were more likely to report high WI ($p \le .001$). Females and those who were diagnosed for >10 years were also more likely to report a high WI index ($p \le .05$). Comparing WI with SI for the same racial categories shows that although those who identified as Black were more likely to report the social impact of CHB, they were least likely to report worries and fears of disease progression.

Discussion

Physical Impact

Physical symptoms in the form of fatigue, pain, and lack of energy to complete work tasks were reported as a daily challenge by survey participants. A study about the symptomatology of CHB in the United States found that it may feature symptoms more often than recognized by the medical and scientific communities, and that these symptoms differ by

	Physical impact index	Social impact index	Worry impact index
	Yes	Yes	Yes
Region	strong association (Cramer's V > 0.15) OR: 56 ($p \le 0.001$)****	strong association (Cramer's V > 0.15) OR: 47.5 $(p \le 0.001)^{***}$	very strong association (Cramer's $V > 0.25$) OR: 153.5 ($p \le 0.001$)****
Africa	67%	63%	38%
Southeast Asia	59%	64%	39%
Western Pacific	77%	71%	57%
Europe	63%	52%	39%
Middle East	63%	67%	39%
North America	42%	41%	82%
Americas	73%	75%	25%
, mericas	(N = 1264)	(N = 1177)	(N = 1169)
Age group	strong association (Cramer's $V > 0.15$) OR:43 ($p \le 0.001$)***	very strong association (Cramer's $V > 0.25$) OR: 80.8 ($p \le 0.001$)***	moderate association (Cramer's V > 0.10) OR: 24.2 (p ≤ 0.001)***
18-30	69%	70%	51%
31-45	63%	62%	42%
46-60	51%	39%	59%
60+	39%	24%	63%
	(N = 1278)	(N = 190)	(N = 1182)
Gender	No association (0 < Cramer's V < 0.05) OR: 0.3 (p > 0.6)	No association (0 < Cramer's V < 0.05) OR:2 (p > 0.15)	weak association (Cramer's V > 0.05) OR: 5.8 ($p \le 0.05$)*
Female	62.5%	55%	55%
Male	61%	60%	47%
	(N = 1250)	(N = 163)	(N = 63)
Race	weak association (Cramer's $V > 0.05$) OR:10.4 ($p \le 0.05$)*	strong association (Cramer's V > 0.15) OR: 29.8 $(p \le 0.001)^{***}$	strong association (Cramer's $V > 0.15$) OR: 34.4 (p ≤ 0.001)****
Black (African or	65%	63%	41%
African American)			
Asian/Pacific Islander (AAPI)	57%	60%	55%
White	56%	40%	62%
	(N = 1278)	(N = 190)	(N = 90)
Education	weak association (Cramer's V > 0.05) OR: 5.6 (p > 0.2)	weak association (Cramer's $V > 0.05$) OR: 4 ($p > 0.3$)	moderate association (Cramer's $V > 0.10$) OR: 26.7 ($p \le 0.001$)***
High school or less	58%	56%	61%
Technical/some school	69%	56%	63%
College	61%	61%	48%
Postgraduate	61% (N = 1278)	58% (N = 1188)	42% (N = 1180)
Treatment experience	weak association (Cramer's $V > 0.05$) OR: 9.3 (p ≤ 0.05)*	moderate association (Cramer's $V > 0.10$) OR: 23.2 ($p \le 0.001$)***	weak association (Cramer's V > 0.05) OR: 0.9 (p > 0.6)
Currently on treatment		50%	46.5%
Previously on treatment	72%	68%	49%
Never been on	67%	62%	50%
treatment	(N = 1176)	(N = 1176)	(N = 1168)
Years since diagnosis	weak association (Cramer's $V > 0.05$) OR:6.1 ($p \le 0.05$)*	weak association (Cramer's $V > 0.05$) OR:11.9 ($p \le 0.001$)****	weak association (Cramer's V > 0.05) OR:9.4 $(p \le 0.01)^*$
10 years or less	64%	62%	46%
More than 10 years	56%	51%	56%
-	(N = 1239)	(N = 1156)	(N = 1148)

Table 4. Relationship Between PI, SI, and El and Respondents' Demographic Characteristics and Disease Experiences.

ethnicity and are impacted by disease perceptions.⁶ Our study showed similar results, with more participants from the Western Pacific and African regions experiencing the physical impact of CHB. Additionally, younger participants were more likely to experience physical impact, compared to those 46–60 years old, which could be related to the physiological age-related evolution of perceiving pain.³¹ It could also be related to the longevity effect of living with the disease and the acceptability of pain as a symptom. Our study shows that those who have been diagnosed for more than 10 years were less likely to experience physical impact than those who have been diagnosed more recently. The longevity of experiencing pain has shown to impact the acceptance and perception of pain by the patient.^{32–34}

The physical impact of living with CHB influences daily living and overall quality of life. Results of the 2020 Hepatitis B Externally Led Patient Focused Drug Development (PFDD) Meeting found that physical symptoms were common, and interrupted family schedules, social gatherings, and professional pursuits. Particularly noted were pain and fatigue, which were debilitating for some.⁷ Together, these findings call for more attention to the physical impact of living with CHB by the scientific and medical community.

Social Impact

The social impact also varied by location, age, and years since diagnosis. Participants in North America were least likely to report social impact as a challenge, where there are legal protections for people living with CHB, and social support is offered by active patient advocacy organizations in this region. The social impact also varied by race, as Blacks had the highest rate of reporting social impact as a challenge, followed by Asians, compared to Whites. This may be related to the considerable cultural and social stigma surrounding hepatitis B in many communities, which has been well documented in several studies showing that such stigma has social, familial, and professional ramifications.35-40 People with CHB often avoid being in intimate relationships or engaging with social groups, they lose relationships or are shunned from families. The PFDD revealed that decisions to pursue professional careers can be limited by a fear of stigma and that some avoid professions where they fear they will be asked to disclose their hepatitis B infection status.^{7,40} These social experiences can lead to chronic stress, and sometimes to depression. Noteworthy, those who were currently taking medication to manage their CHB were less likely to report social impact as a challenge. This is consistent with previous studies that found that patients who are not receiving antiviral medications may experience lower quality of life,⁴¹ and that viral suppression was shown to improve general health perception.¹⁷

Worry Impact

Our study found a significant worry impact among participants, primarily focused on worry and fear about long-term disease progression. These findings align with other studies.^{7,9,11} A primary concern was developing hepatocellular carcinoma (HCC). The data obtained in this study show that the fear of disease progression was significant across all participants, with a significantly higher proportion of those living in North America worried about disease progression, compared to those in other world regions. This may be the result of more frequent use of liver cancer screening in North America, and increased messaging about the link between hepatitis B and liver cancer. However, this highlights how screening and health messaging, when not reinforced by psychosocial support services, can cause stress and apprehension. This also emphasizes the importance of capturing the impact of living with CHB and integrating these impacts into the care cascade.

Another concern among participants was transmitting hepatitis B to others. This infectability is also a source of stigma (internalized and societal) and discrimination.^{11,42} The concept of U = U (undetectable viral load = untransmittable) is a message in human immune deficiency virus (HIV) that has had a tremendous impact by assuring people who have undetectable viral load that they cannot transmit HIV to people they love, 43,44 but this message does not exist for CHB. This may help explain why participantsregardless of their treatment status-reported experiencing lingering worry about transmitting the virus to others. As a communication strategy, U=U could improve HBV treatment uptake and adherence and it could also reduce stigma associated with the fear of transmission. This, along with the idea of "treatment as prevention,"44 can help combat the stigma that patients face surrounding infectability. However, at this time, these concepts have not been incorporated into treatment guidelines from AASLD, EASL, APASL, or WHO.¹⁹⁻²²

Future Implications

This study suggests that there is considerable physical, emotional, and social impact among those living with CHB. Chronic hepatitis B infection has been characterized as a silent and largely asymptomatic condition.^{6,7} The term hepatitis B "carrier" has often been used to describe people with CHB. This has had the effect of minimizing the disease to healthcare providers and staff, the wider community and even those living with CHB. It has projected a belief that the infection is latent and stagnant even though the natural course of hepatitis B infection is dynamic, with many phases, and people can go in and out of inactive and active states throughout their lifetime. Thus, it is thought that many with CHB experience little impact from living with the disease.^{6,7} However, research is revealing that hepatitis B is not as silent as medical professionals have traditionally described it. By focusing only on diagnostics and biochemical markers rather than the patient experience, physicians and researchers are missing an important aspect of the impact of hepatitis B and overlooking methods of assessment which may relieve patient suffering.

One way to incorporate the physical, emotional, and social impact into the clinical management of CHB is through the use of PRO tools. The use of PROs in clinical care settings in liver disease has been evaluated, and the overall findings confirm that using PROs is an effective method to assess HRQOL impact on people with CHB, cirrhosis, and even HCC.^{45–47} These studies consistently recommend the use of PROs for integrating patients into the process of managing their disease, helping with patient adherence to treatment and follow-up visits, and creating an opportunity for physicians to assess treatment outcomes. Incorporating patients' values

and emotional impact into treatment initiation and having a model of shared decision-making could lead to medical care that is more meaningful to patients, and patient preferences should be considered in making treatment decisions. The currently communicated message that clinical endpoints are the only important parameters to assess CHB progress outside of clinical trials may lead patients to forgo or abandon care if they feel their quality-of-life needs are not being met. Enhancing patient engagement is critical to improve outcomes, reduce loss to follow-up of patients,^{48–50} and overcome linkage-to-care challenges in hepatitis B care.

Study Limitations

Our survey was offered in English only and was only available online, thus it is not representative of all those living with hepatitis B. We promoted the survey through Hepatitis B Foundation (HBF) social media platforms, which are not available in all countries and would not reach individuals who do not utilize social media (or are not part of HBF's outreach).

As with all surveys, response bias is possible. People who felt physical, social, or worry impacts of CHB might have been more likely to respond to the survey than those who did not. We did not assess liver disease status, comorbidities, or common co-infections that may contribute to disease experience. The survey did not assess socioeconomic characteristics of participants, however, our results conform with other studies that investigated the physical, social, and emotional impacts of living with CHB.^{12,13,16–18}

Our survey tool was not assessed through psychometric validation; however, the purpose of this survey was to explore and document the lived experiences of people living with hepatitis B around the globe, rather than creating a tool to measure HRQOL for people living with hepatitis B.

Conclusion

This study adds to the growing body of evidence that there is physical, social and emotional impact of hepatitis B on a person's life. Additional studies should explore this impact, how it affects quality of life among people living with CHB, and how it can be measured and incorporated into clinical management of CHB in the future.

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Authors' Contributions

YI: writing—concept development, original draft, data collection and formal analysis. CC: writing—concept development, original draft (has access to the data). MU: writing, data cleaning. SW: writing—review and editing. All authors contributed to the interpretation of the results and critically revised the paper. All authors read and approved the final manuscript.

Ethical Approval and Consent to Participate

The study that included collecting this data was IRB approved by Heartland Institutional Review Board LLC (HIRB Project No. 191221-270). Participation in the survey was voluntary and anonymous.

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Availability of Data and Materials

Please contact the corresponding author for data requests. Data is available upon reasonable request.

Consent for Publication

Not applicable. No individual identifying data have been collected. Survey responses were all anonymous.

Competing Interests

The authors declare that they have no competing interests.

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Supplemental Material

Supplemental material for this article is available online.

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