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What motivates patients to remain in longitudinal observational studies?

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What Motivates Patients to Remain in Longitudinal Observational Studies?

by

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Dedication

This thesis is dedicated to my parents, Ravichandran Kaza and Padmavathi Kaza for their constant encouragement; to my very supportive husband, Vamsidhar Yelavarthi; to my most precious child, Yuktha; and to my amazing mentor, Anna Lok.

Acknowledgements

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Abstract

Background: Low retention rates threaten the validity of clinical research studies and generalizability of the results.

Aims: To survey Hepatitis B Research Network (HBRN) Cohort Study participants to evaluate University of Michigan retention strategies, to develop best practices, and to identify other strategies that will improve retention.

Methods: 90 patients that are currently participating in the HBRN Cohort study at the University of Michigan were surveyed.

Results: Participants were a good mix of male (51.2%) and female (46.5%), mostly non-Hispanic, between the age of 40 and 60 years (50%). Roughly half were Asian Chinese (50.2%), had some graduate school education or a professional degree (54.7%), and an annual income of more than $100,000 (45.4%). All the participants had medical insurance (private 87.2% vs. government 12.8%). Average participation in the study was 3.95 years. 22.1% of the participants reported they had missed at least one study visit and the main reason was they forgot the appointment. Participants reported that no co-pay to see the specialists is a better motivating factor than receiving financial compensation for staying in the study (38.4% vs. 18.6%). Participants reported that the overall experience at the visit was the main motivating factor for them to stay in the study. Eighty-nine % of participants responded they are likely to stay in the study that is currently projected to end in late 2019 and moving away from the study site is the main reason why they would discontinue participation in the study.

Conclusion: Overall, participants in the HBRN study seem to be satisfied with how the study is being conducted at our site and willing to stay in the study until 2019, but the results did help us identify a few areas for improvement.

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Chapter 1: Introduction

A longitudinal observational study is a study that involves repeated observations of the same subjects over long periods of time and in which the investigators do not seek to intervene, only observe the course of events. Longitudinal studies are designed to examine associations between exposure to known or suspected causes of disease and subsequent morbidity or mortality (Coggon, Rose, & Barker, 2003). Since the first requirement of most longitudinal studies is the identification of the individuals forming the study group, longitudinal studies in epidemiology are usually referred to as cohort studies (Breslow et al., 1987).

Though cohort studies are complex to organize and expensive to conduct, longitudinal cohort studies remain important as many outcome variables can be examined in a single study and sometimes they are the only methods available (Mann, 2003). Well-characterized cohorts permit calculation of the effect of each variable on the probability of developing the outcome of interest. However, the validity of results from cohort studies can be severely compromised if the recruitment is low, if there is systematic bias in enrollment, or if there is a significant loss to follow-up of study participants with time.

Low retention rates in a study threaten the internal and external validity of a study (Amico, 2009). The study results may be biased by differential dropout between comparison groups or by differences in characteristics or outcomes between those participants who drop out and those that continue to participate. Low retention rates also threaten the generalizability of the results of a study and its statistical power (Friedman, Furberg, & DeMets, 2010; Szklo & Nieto, 2014).

Loss of patients over time is a common occurrence in prospective cohort studies due to subject relocation, loss of interest in the study, inconvenience of having to travel to study site for visits, lack of transportation, interference with work or family responsibilities, financial burden (transportation

for study visits, cost for standard of care evaluations and tests, lost wages due to time off work, child care), and poor rapport with study team (McSweeney, Pettey, Fischer, & Spellman, 2009; Nicholson et al., 2011; Tupasi et al., 2016; Walker et al., 2011).

Recruitment and retention are the cornerstones for research and often retention is less emphasized than recruitment. Literature review of retention strategies used in studies (Booker, Harding, & Benzeval, 2011; Bower et al., 2014; Butler et al., 2013; Hunt & White, 1998; Nicholson et al., 2011; Steinhauser et al., 2006; Tansey, Matte, Needham, & Herridge, 2007; Wijk, 2014) can mainly be categorized into 1) incentives to participants (Monetary and non-monetary), 2) frequent communications with participants which include sending reminder appointment letters, conveying research findings to participants and establishing trusting relationship with participants, 3) participant convenience, e.g. flexibility in scheduling appointments, and 4) participant contact, which includes frequent updating of participant contact information.

Most of the literature on participant retention is based on “lessons learned” and “what we used” and is mostly focused on “clinical trials” and not observational studies (Booker et al., 2011; Bower et al., 2014; Butler et al., 2013; Hunt & White, 1998; Steinhauser et al., 2006; Tansey et al., 2007; Wijk, 2014). Clinical trials differ from observational studies in that most trials offer potential direct benefit to the participant, e.g., free drugs, laboratory and other tests, clinical evaluations, and possibly a cure. Observational studies generally do not offer these benefits, instead, they often involve lengthy office visits, questionnaires to be answered, and blood draws.

Though there are many published studies that discussed the strategies that were employed to retain participants in a study, few studies actually asked the participants if the adopted strategies facilitated their continued participation in the study and what factors motivated them to remain in a longitudinal study.

Chapter 2: Background

University of Michigan has been participating in a National Institutes of Health (NIH) funded prospective observational study–the Hepatitis B Research Network (HBRN) Cohort Study since 2010. This study includes 21 adult clinical sites across the United States and in Toronto, Canada.[1] The investigators developed the study protocols and the Data Coordinating Center developed the electronic database and Manual of Procedures. Study coordinators were trained on the conduct of the study.

The HBRN Cohort study enrolls patients who meet the following criteria:

Inclusion criteria.

1. At least 18 years of age
2. Hepatitis B infection as determined by presence of hepatitis B surface antigen in the serum

Exclusion criteria.

1. History of hepatic decompensation based on clinical or laboratory criteria
2. Hepatocellular carcinoma (HCC)
3. History of solid organ transplantation or bone marrow transplantation
4. Current hepatitis B antiviral treatment
5. Chronic immunosuppression therapy
6. Known HIV co-infection
7. Medical or social condition which, in the opinion of the investigator, would make the patient unsuitable for the study or interfere with or prevent follow up per protocol.

[1] Information regarding the HBRN Cohort study and the study design information was directly extracted from HBRN Cohort study protocol. The official Study website is http://www.hepbnet.org/ . Anna SF Lok, MD, is the consortium chair and principal investigator for the study at University of Michigan; she can be contacted at aslok@med.umich.edu .

8. Unable or unwilling to return for follow-up visits

The Objectives of the Study:

Primary Aim.

- To describe participants with hepatitis B virus (HBV) infection in a prospective cohort in the United States (US) and Canada and identify predictors of disease activation and progression

Secondary Aims.

- To describe clinical, virological, and immunological characteristics of participants with HBV in the U.S. and Canada
- To evaluate changes in HBV infection status and quantitative HBsAg levels and factors associated with those changes
- To develop a bank of bio specimens (e.g., serum, plasma, DNA, lymphocytes, liver tissue) obtained from participants with HBV infection
- To identify participants with HBV infection who are potential candidates in one of the treatment studies to be conducted by HBRN
- To describe the natural history of hepatitis B infection in pregnancy

The HBRN Cohort Study is a prospective observational study in which participants receive standard of care that is billed to their health care insurance and clinical data (including laboratory, radiology, and histology results) are collected for the research. Participants are required to undergo a baseline evaluation and follow-up visits at Week 12, 24, 48, and every 24 weeks thereafter.

Baseline visit takes about two hours for

- reviewing the consent with the patient and consenting the patient;

- questionnaires on health behavior, symptoms, and quality of life (SF-36) to be completed by the participant;
- collection of information on family history, past medical history, antiviral therapy for HBV, and medication history; most likely source of the HBV infection, and the HBV phenotype that best describes the participant;
- brief physical examination;
- blood drawn for laboratory tests related to hepatitis B and liver disease (10–16 ml);
- blood drawn (with consent) to prepare and obtain serum or plasma for research testing including genetic testing (about 45 ml).

Follow-up visits take about 45 minutes to complete and include

- physical examination;
- blood drawn for laboratory tests related to hepatitis B and liver disease (10–16ml);
- interim history;
- assessment for possible interim occurrence of any events related to disease progression (e.g., cirrhosis, hepatic decompensation, HCC, or liver transplantation);
- interim antiviral treatment and any changes in medications;
- liver biopsy data (if one was performed for clinical indication);
- for participants who consented, serum/plasma samples for research testing (24 ml at annual visits and 20 ml at semiannual visits).

The study began enrolling in January 2011. Initially, the study was to continue for 6 years, but NIH recently extended the funding period and maximum follow-up may be up to 10 years. While a longer follow-up period will increase the number of events and the power of the data analysis, a

major concern of the NIH, the Data and Safety Monitoring Board, and the investigators is the validity of the data due to participant attrition over time.

The current retention rate in this cohort at University of Michigan is 86.6 % while the overall retention rate is 75.7%. The major reasons for disenrollment are shown in Table 1 and University of Michigan retention strategies are shown in Table 2.

Table 1

Reasons for Disenrollment

	University of Michigan	**Overall HBRN Cohort**
No. of participants consented (as of 5/2/16)	119	2015
No. of participants disenrolled (as of 5/2/16)	16 (13.4%)	490 (24.3%)
Reasons for disenrollment:		
Withdrew Consent	2 (12.5%)	152 (31.0%)
Relocation to cities/states outside HBRN study sites	6 (37.5%)	87 (17.8%)
Lost to follow-up	4 (25%)	149 (30.4%)
Non-compliant with the protocol	0	48 (9.8%)
Ineligible patient enrolled	0	4 (0.8%)
Screen failures (HBsAg negative at baseline)	4 (25%)	21 (4.3%)
Other	0	29 (5.9%)

Table 2

Retention Strategies Employed at University Of Michigan

Category	Strategies used since inception of study
Incentive	Provide $25 subject fee at each visit on same day of visit
	Eliminate Co-pay for the visit (Clinic visit and research visit are combined) [NB co-pay for tests not eliminated]
	Use patient care dollars to cover co-pays of tests when the participant has a lapse between health insurance coverage or high co-pays for tests
Patient convenience	Combining clinic visits with research visits to avoid multiple visits to the hospital
	Flexibility in scheduling appointments (more options of days and times) and options to reschedule with less hassles
	Scheduling next appointment at their current visit and giving participants time to plan ahead
	Scheduling multiple appointments on the same day (e.g., ultrasound and study visit)
	Access to specialists with no wait or minimal wait as a part of the study
	If participant cannot make it to the clinic within the protocol window, they were encouraged to get local labs drawn and to complete the questionnaire at home and sent back to study site.
Overall experience for the visit	Visits are shorter and more efficient when compared to clinic (e.g., on site blood draw with no wait time)
	Same staff at each visit helps build relationship
	Complimentary refreshments at each visit, especially after a fasting blood draw
Participant contact	Updating participant information (Addresses, phone numbers & insurances) at least yearly
	Collecting participant alternative contact information
	Asking what is the best mode of contact (email, phone, regular mail) and noting participant preferences
	Sending reminder appointment letters at least 2 weeks ahead of time with date, time and location of visit.
Communication	Encouraging participants to communicate and ask questions and to alert study staff with any changes to medications, health conditions, etc.
	Bi-yearly newsletters are sent to participants on what's happening in the study, what we have learned so far from the information collected and some educational articles with regard to the disease and brief overview of published papers from the study
	Providing a direct phone number and email for participants to contact study team and prompt response to questions and requests for changes in appointment
	Follow-up email or phone call is made to communicate results to the participant after each visit.

The HBRN study has a Recruitment and Retention committee that oversees recruitment and retention and develops policies to improve these processes. Recently, the committee was charged to examine the practices for participant retention adopted at each site with the goal of identifying best practices that can be shared across the network.

I have been involved in the HBRN Adult Cohort Study since the beginning of the study and have been the primary study coordinator at the University of Michigan site since August 2010. Although our retention rate is higher than the overall retention rate for the entire network, I decided to conduct a survey of our participants to understand what motivates them to stay in the study and what more can we do to facilitate their continued participation in the study.

The aims of this retention survey study are as follows:

1) To determine HBRN Cohort Study participants' evaluation of the University of Michigan retention strategies
2) To identify other strategies that will improve retention rate among HBRN Cohort Study participants at the University of Michigan
3) To develop best practices for retention in the HBRN Cohort Study that can be shared with other sites

Clinical Significance:

Results of this study will provide us an insight on what motivates participants to stay in a long-term observational study and what can be done to further improve participants' experience in observational studies and thereby their retention in these studies. Our findings will help us retain HBRN participants in the remaining 4 years of this study and will be shared with other sites in HBRN such that overall retention can be improved.

Chapter 3: Methodology

The study was designed to ask our participants in HBRN cohort study to evaluate the strategies we at University of Michigan employ for participant retention and to identify other strategies that may improve retention rates in the HBRN Cohort study at University of Michigan. To meet these research goals, a questionnaire was developed drawing on surveys used in similar studies previously published.

Study Population

University of Michigan HBRN cohort study enrolled 119 participants between January 2011 and Nov 2015. Over a period of 6 years, 2 participants have transferred to a different site within the network, 2 participants have died, and 16 participants were disenrolled from the study for various reasons as noted in table 1. Thus, we are actively following 99 participants in the study.

Exclusion Criteria

Non-English speaking participants.Of the 99 participants actively followed, four are non-English speaking, and the survey was administered to 95 participants.

Research Design

Pre-Study Phase.

- Reviewed literature on patient recruitment and retention.
- Designed study, questionnaire, informed consent, and intervention plan.
- Obtained approval from thesis committee.
- Obtained approval of the study from University of Michigan IRBMED & EMU's University Human Subjects Review Committee (UHSRC)

Study Phase.

Survey. The survey included demographic information and questions to capture patient's affinity to participate in research, their motivation and demotivation to participate in the HBRN Cohort study, and the likelihood they will stay in the study, which is expected to continue until late 2019.

***Conduct of survey*.** Permission to conduct this survey was obtained from University of Michigan IRB (Appendix A) and EMU's UHSRC (Appendix B). The study was deemed exempt by both IRB under **EXEMPTION #2 of the 45 CFR 46.101.(b):**Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

While waiting for the study approval, the survey questionnaire was created in Qualtrics and tested for compatibility to complete the survey on tablet, smart phone, and computer (laptop or desktop).

Following IRB approval from both University Of Michigan and EMU, eligible participants were identified from our HBRN database, and I called all the actively followed participants to determine if they are interested to participate in the study. Survey was rolled out on June 23, rd 2016 and was open for a month. Participants who provided verbal consent over the phone were provided the option of either completing the survey online or by regular mail. Participants who had scheduled visits during the survey period and who consented completed the survey during the study visit. For participants who preferred to complete the written (paper and pencil) survey, survey questionnaire was sent via

mail and pre-addressed stamped envelope was provided to return the survey. For participants who preferred to answer the questions online, a link to the survey was sent to the participant via an email.

The UHSRC and IRBMED approved Appendices C, D & E to be used as introductions to the survey questionnaire as appropriate. The survey introductions briefly described the purpose of the study, study procedures, patients' rights, and study team contact information and invitation to participate.

Survey

Survey questionnaire (Appendix F) was used as the main and primary data gathering source for this study. The survey included seven demographic questions, seven questions on patient's affinity to participate in research studies, 13 questions on motivation to continue participation, four questions on demotivators to continue participation, and four questions to capture participants' response whether they would stay in the study untill the end, main reason they would discontinue participation, other suggestions, and comments for the study team. Most of the questions were multiple choice questions with some being open ended.

Motivation to participate. Participants were asked to rate retention strategies employed at the University Of Michigan for the HBRN cohort study as motivators to continue participation in the study using a 5- point Likert scale with a score of 1 being "completely disagree" to 5 being "completely agree". One additional question was asked to elicit the most important motivating factor to stay in the study.

Demotivators to continue participation. Four questions were asked what the participants think are major demotivators for staying in the study, and responses were recorded on a 5-point Likert scale with a score of 1 being "completely Disagree" to 5 being "completely agree".

Likelihood of staying in the study. Participants answered one question on how likely they would stay in the study that is expected to end in late 2019 on a 5-point Likert scale with 1 being "extremely likely" to 5 being "extremely unlikely". They were also asked to answer multiple choice questions on what would be the major reasons for them to discontinue participation.

Lastly, two open-ended questions were asked to seek any recommendation to further improve the experience of the research visits and to address any concerns.

Data Management and Analysis

Four weeks after the survey was sent out, the study was closed and the study data analysis phase began. Responses of hard copy surveys were entered into Qualtrics so data from all participants can be combined for analysis. To preserve anonymity, the survey database did not collect any information or data (such as Internet protocol (IP) addresses) that might identify participants. Answers originally obtained on 5-point Likert scale were later condensed to three categories, i.e., from completely agree, agree, neutral, disagree, and completely disagree to agree, neutral and disagree. Similarly, the options extremely unlikely, unlikely, neutral, likely, and extremely likely were condensed to unlikely, neutral, and likely. Data were analyzed using Tableau Desktop version 9.3.

Chapter 4: Results and Discussion

A total of 90 participants out of 95 invited responded to the survey for a response rate of 94.7%. The response rate is much higher than usual survey studies as we were surveying a familiar population who has been under our care since 2011. Table 3 shows the response rates for each method of survey administration. The response rate ranged from 100% for participants approached in person in the clinic to 87.5% for those who chose to return hard copy (paper and pencil) survey by mail.

Table 3

Methods of survey administration and response rate

Method of Survey Administration	**Number sent**	**Number returned**	**Response Rate**
Mail survey	8	7	87.5%
In-person/At-visit Survey	10	10	100%
Electronic Survey via Qualtrics	77	73	94.8%

Four participants who completed less than 25% of the questions were excluded from data analysis. Thus, data from 86 participants were analyzed.

Demographics

The demographic characteristics of the participants are summarized in Table 04. Participants were a good mix of male (51.2%) and female (46.5%), and mostly non-Hispanic. Half of the participants were between the ages of 40–60 years, median age was 46±13 years and range was 20 to 79 years. Half (50.2%) of the participants were Asian Chinese followed by White (22.4%) and

Asian, non-Chinese (18%). Slightly over half (54.7%) of the participants had some graduate school or professional degree training, and only 10.5% participants had high school education or less. Almost half (45.4%) of the participants had annual income of more than $100,000 while 18.6% had annual income ≤ $50,000. All the participants had medical insurance with the majority (87.2%) having private medical insurance and the remainder had Government medical insurance (Medicare and Medicaid).

Table 4

Demographic characteristics of Survey participants

Characteristic	*Number (N=86)*	*Percent*
Gender		
Female	40	46.5%
Male	44	51.2%
Not Answered	2	2.3%
Age		
20-40 years	26	30.2%
40-60 years	43	50.0%
60-80 years	17	19.8%
Ethnicity		
Hispanic or Latino	3	3.5%
Not Hispanic or Latino	78	90.7%
Not Answered	5	5.8%
Race		
Asian, Chinese	38	50.2%
Asian, non-Chinese	17	18.0%
Black or African American	5	5.7%
White	22	22.4%
Other	4	3.7%
Education		
High school graduate or less	9	10.5%
Some college & College graduate	30	34.9%
Some graduate school & Graduate /professional Degree	47	54.7%
Income		
Less than $50,000	16	18.6%
$50,001- $100,000	23	26.7%
Greater than $100,000	39	45.4%
Not Answered/Unknown	8	9.3%
Insurance		
Government medical insurance (for example: Medicare, Medicaid)	11	12.8%
Private medical insurance (for example: HMO, PPO, Blue Cross)	75	87.2%

Affinity to Participate in Research Studies

Most (82.6%) of the participants reported they had not participated in any other research studies previously and HBRN cohort study was the first research study that they ever participated in.

Biggest Motivation to Sign up for the HBRN Study

Half (52.3%) of the participants reported that the biggest motivation to sign up for the study is to help future patients in their situation, followed by perception they would get better care by participating in the study (36.1%) as shown in Figure1.

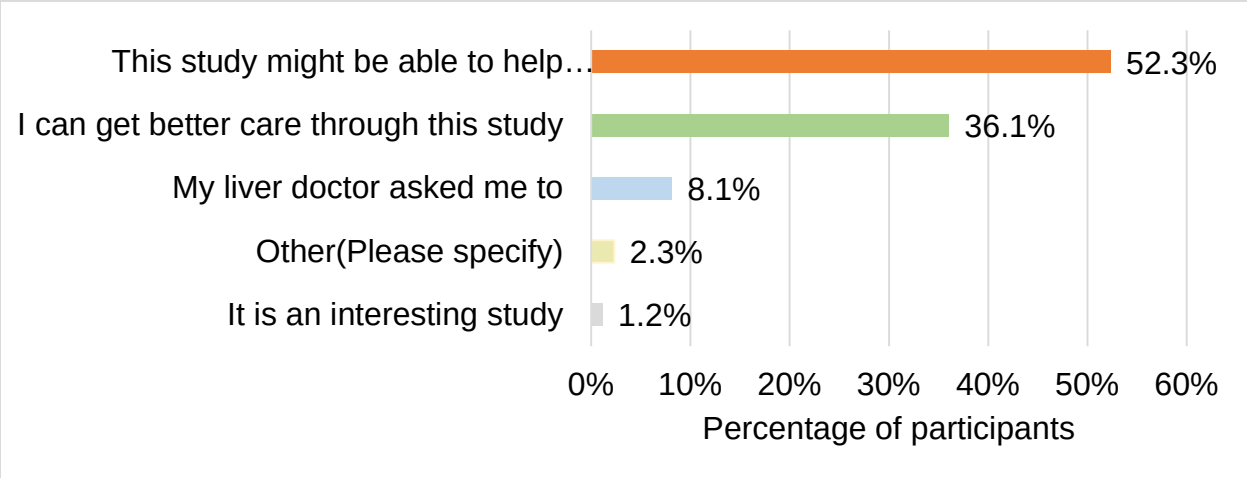

Figure 1.Motivation to sign up for HBRN study

Number of Years in HBRN study:

Participants had been followed in HBRN cohort study for a mean of 4.0±1.7 years with a range of 1–6 years as shown in Figure 2.

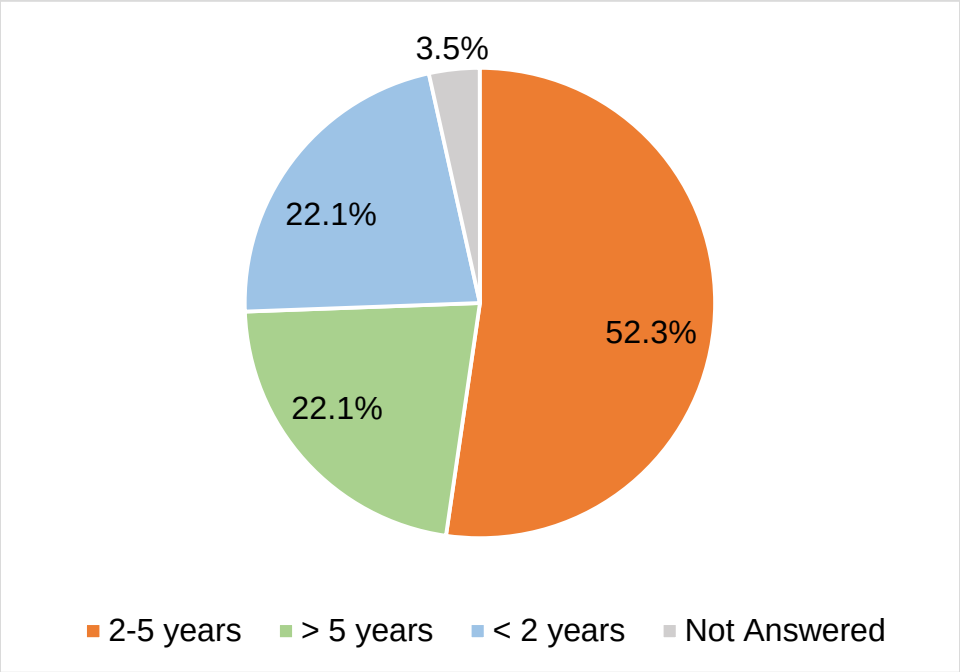

Figure 2. Distribution of duration of participation in the HBRN Cohort Study

Missed Visits and Reasons for Missed Visits

Nineteen (22.1%) participants reported, they had missed at least one visit during their participation in the HBRN cohort study; of these, 8 missed only one visit and 2 missed three or more visits.

The major reasons for missing visits were participants forgot their appointment (36.8%) and out of town/country at the time of the scheduled visit (15.8%). Other reasons included appointment was not at a convenient time, participant did not have a ride, and participant did not have time, or had conflicting family commitments as mentioned in Figure 3.

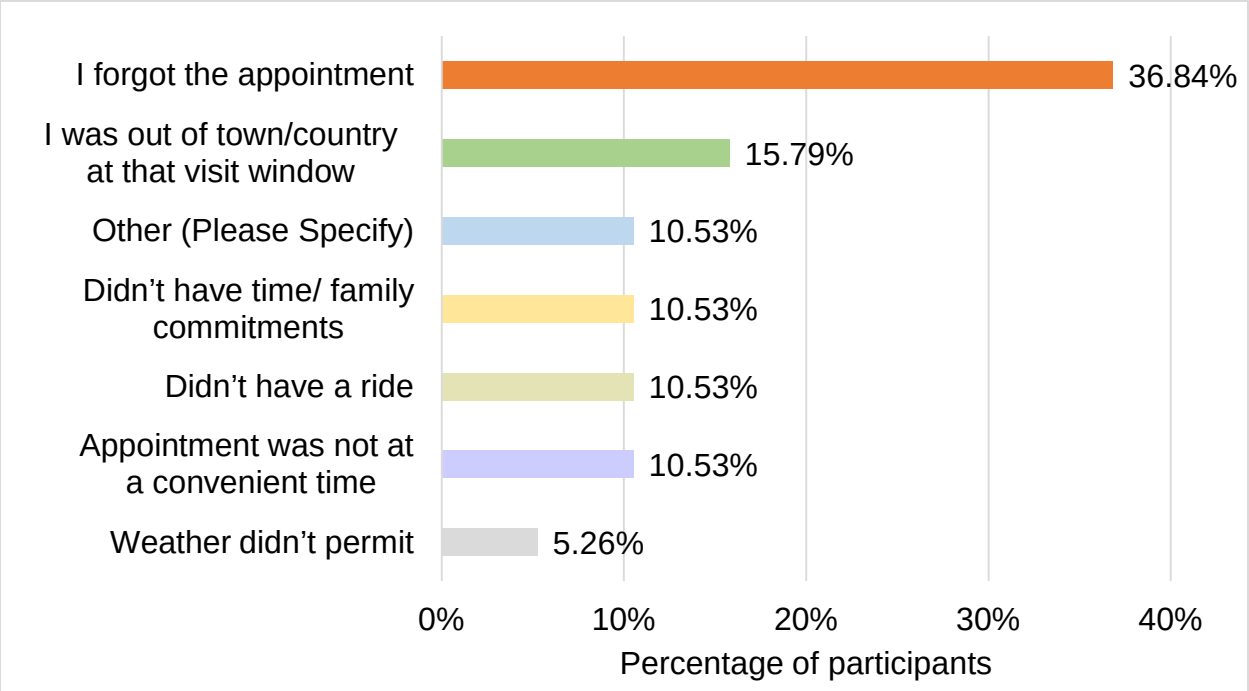

Figure 3.Reasons for missed visits

Co-pay at Each Visit

Thirty-six (41.9%) participants reported they had copay at each visit, with 20%(7)of those who responded to the question on amount of copay at each visit indicating that the amount per visit was $51–100 and 22% indicating that the amount was more than $100 per visit (as shown in Figure 4).

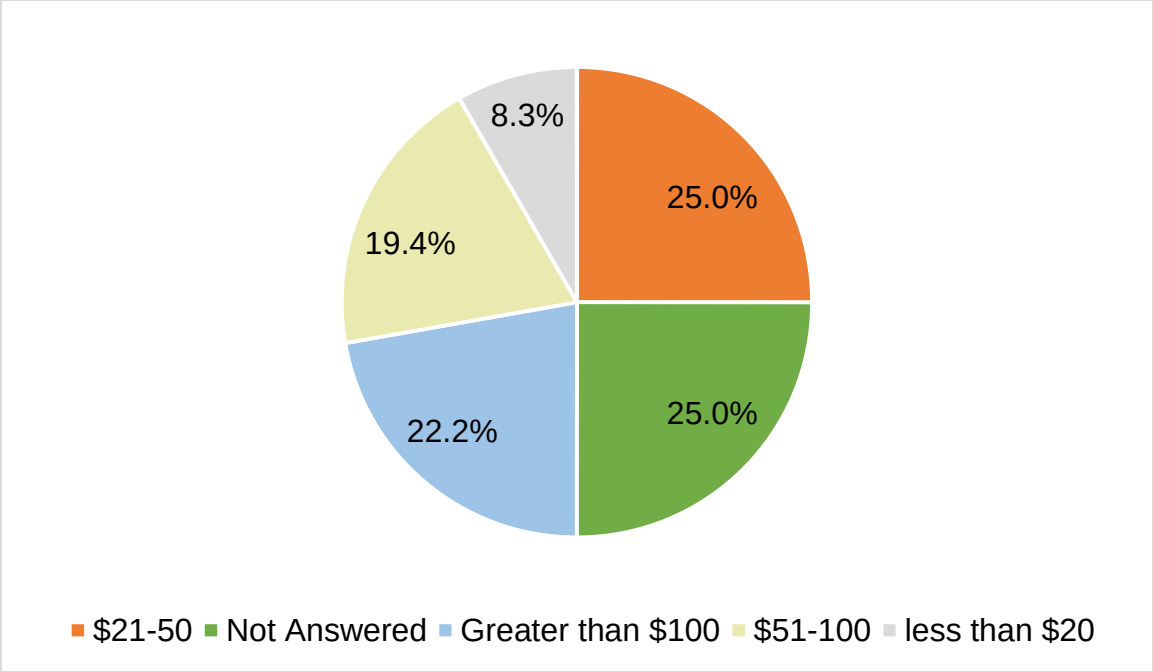

Figure 4.Distribution of co-pay at each visit among the 36 participants who had co-pay requirement

Motivators to Continue Participation in the HBRN Cohort Study

Retention strategies employed at University of Michigan were categorized into 1) incentives, 2) convenience of the visits, 3) overall experience of the visits, 4)patient contact, and 5) communications. Participants were asked if they agreed that the strategies we employ at our site were motivators for their continued participation in the HBRN cohort study. Convenience, overall experience, frequent contacts, and communications with the study team were rated to be more important than incentives for continued participation in HBRN cohort study. For those who agreed financial incentives were important motivators, waiving co-pay (38.4%) was more important than financial compensation (subject fee; 18.6%) at each visit (as noted in Table 5). When asked, which is the most important motivator for continued participation in the HBRN cohort study, 41.9% indicated overall experience of participating in the study, and 37.2% indicated gaining knowledge about their disease, and 10.5% indicated ease of communications with the study team(as shown in Figure 5).

Table 5

Response of participants to questions on Motivators to continue participation in the HBRN Cohort study

	Agree	Neutral	Disagree	Not Answered
Incentive				
Compensation (money paid) at each visit	18.6%	33.7%	44.2%	3.5%
No copay to see the specialist	38.4%	27.9%	30.2%	3.5%
Convenience of the visits				
It is easy to schedule and to reschedule my appointments, and they work with my calendar and are flexible	65.1%	19.8%	11.6%	3.5%
Overall experience for a visit				
Doctors spend more time with me in research visit than they would in clinic	52.3%	32.6%	11.6%	3.5%
I feel research environment is more relaxed compared to visits in regular clinic	64.0%	24.4%	8.1%	3.5%
I feel that I am better cared for in research	62.8%	24.4%	9.3%	3.5%
The research team are experts in my disease	84.9%	9.3%	2.3%	3.5%
Visits are more efficient, with minimal wait times, and blood draw is in the same place	76.7%	16.3%	3.5%	3.5%
Patient contact				
Study staff knows the best way to reach me and respects my preferences on how to be contacted	80.2%	14.0%	2.3%	3.5%
The appointment reminder letters help me keep or reschedule my appointment	75.6%	16.3%	4.7%	3.5%
Communication				
I am learning more about the disease since my participation in the study	77.9%	11.6%	7.0%	3.5%
The staff is easy to reach and answers my questions promptly	82.6%	11.6%	2.3%	3.5%

Results expressed as percent of participants

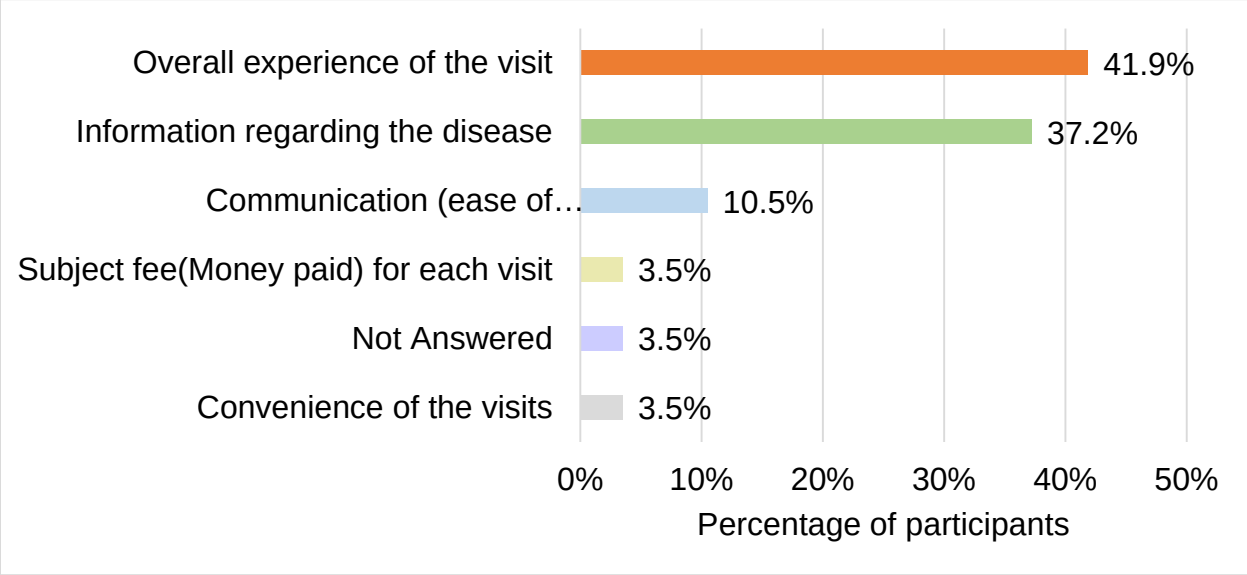

Figure 5.Main motivator to continue participation in the study

Demotivators to Continue Participation in the HBRN Study

When participants were asked whether certain aspects of the study such as need for fasting, amount of blood drawn, amount of questionnaire to be completed, and not receiving treatment bothered them, majority (around 65%) disagreed (Table 6).

Table 6

Responses of participants to questions on demotivators to continue participation in the HBRN Cohort study

	Agree	Neutral	Disagree	Not swered
8 hours of fasting at annual visits bothers me	10.5%	20.9%	67.4%	1.2%
The amount of blood drawn at each visit for research purposes bothers me	9.3%	23.3%	66.3%	1.2%
The amount of questionnaires to be completed for research at each visit bothers me	10.5%	24.4%	64.0%	1.2%
The concept of just being observed and not getting any treatment bothers me	10.5%	23.3%	65.1%	1.2%

Likelihood of Staying in the HBRN Cohort Study

The vast majority (88.4%) of participants responded they are likely to stay in the study that is currently projected to end in late 2019, 7% were neutral, and only 2.3% said no (Figure 6).

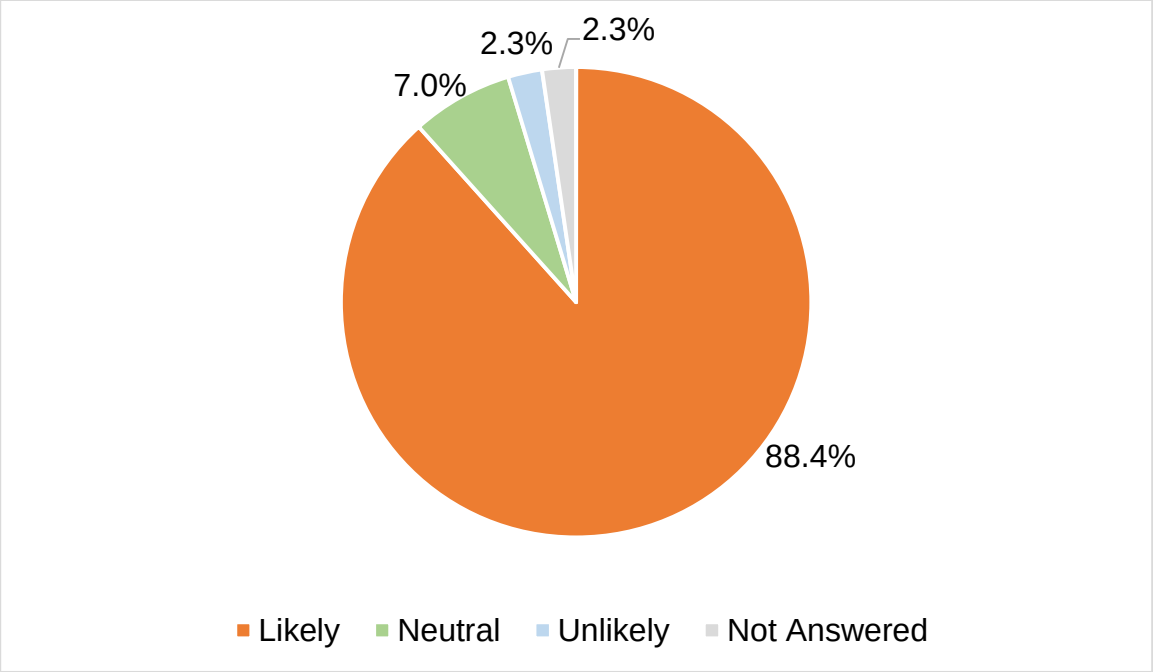

Figure 6. Distribution or participants' response regarding likelihood of staying in the HBRN Cohort Study

Main Reasons for Discontinuation in HBRN Cohort Study:

When participants were asked what would be their main reason to discontinue participating in HBRN cohort study, the most common reason (59.3%) was if they were to move away from the study site followed by loss of insurance or high co-pay (17.5%) as shown in Figure 7.

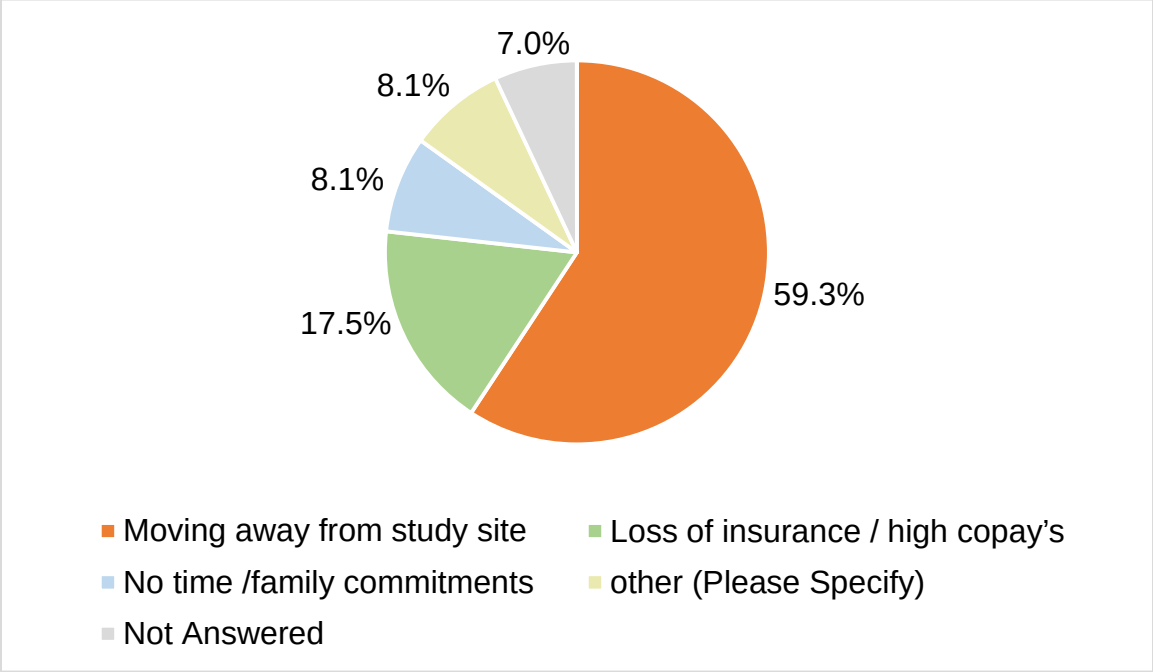

Figure 7.Possible reasons that may lead to withdrawal from the HBRN Cohort study

Comments from Participants. When participants were asked to provide suggestions for additional strategies that would help them stay in the study, only 33 (38.37%) responded, 15 of whom indicated no changes needed, 10 would like to have financial assistance, and 4 would like to be seen in satellite research clinics closer to their homes (as noted in Table 7). Participants were asked to provide additional written comments towards the end of the survey. Twenty-two (25.58%) did so, of these 9 participants expressed their gratitude towards the study team and/or for the opportunity to participate, 5 expressed appreciations for the study team and 4 had other suggestions for us (as noted in Table 8).

Table 7

Comments from participants on what more can be provided to help them stay in the study

Comments from the patients	**Count (n=33)**
No changes Desired	
Nothing	9
Continue as is	4
Study team is doing its best	2
Total	15
Financial Assistance	
Cover Co-pays	6
More Compensation	1
Food Vouchers	1
Treatment if needed	1
Low priced Drug	1
Total	10
Satellite research clinics	4
Total	4
Other	
Provide Study results	1
No wait time	1
Transparency on which physician is seeing me	1
Provide efficient Phlebotomists	1
Total	4

Table 8

Other comments from the study Participants

Other Comments From Participants	Count 22)
Gratitude	
Appreciate being part of the study	2
Thank you for caring/Receiving Proper Care	3
Thank you for studying a disease that has been somewhat forgotten	1
Happy to help	3
Total	9
Appreciation For The Study Team	5
Other	
Provide More information regarding disease	1
Invent Cure	1
Provide study results on Regular basis	1
Research coordinator discusses results	1
Total	4

A major goal for this survey study is to identify strategies to improve retention in the HBRN cohort study and to share best practice with other sites. Although most (88.4%) of our participants responded that they are likely to complete the study that is projected to end in late 2019, 10 participants (11.6%) have either not responded to the question, said that they are neutral or they are unlikely to complete the study. Characteristics of these 10 participants are similar to those who indicated they are likely to stay in the study (Table 9). A higher percent of participants who had been in the HBRN study for longer than 2 years indicated they are likely to stay in the study than those who joined the study more recently.

Table 9

Characteristics of participants who are likely vs. those who are unlikely to stay in the study

	Likely		Neutral, Not Answered, Unlikely	
Characteristic	*Number*	*Percent*	*Number*	*Percent*
Gender				
Female	36	47.37%	4	40.00%
Male	38	50.00%	6	60.00%
Not Answered	2	2.63%		
Age groups				
20-40 yrs	23	30.26%	3	30.00%
40-60 yrs	38	50.00%	5	50.00%
60-80 yrs	15	19.74%	2	20.00%
Ethnicity				
Hispanic or Latino	2	2.63%	1	10.00%
Not Hispanic or Latino	69	90.79%	9	90.00%
Not Answered	5	6.58%		
Race				
Asian, Chinese	36	47.37%	2	20.00%
Asian, non-Chinese	15	19.74%	2	20.00%
Black or African American	4	5.26%	1	10.00%
Other	3	3.95%	1	10.00%
White	18	23.68%	4	40.00%
Highest level of school you attended				
High school graduate or less	8	10.53%	1	10.00%
Some college & College graduate	28	36.84%	2	20.00%
Some graduate school & Graduate / professional Degree	40	52.63%	7	70.00%
Total household income ($) per year				
Less than $50,000	15	19.74%	1	10.00%
$50,001- $100,000	20	26.32%	3	30.00%
Greater than $100,000	35	46.05%	4	40.00%
Not Answered/ Unknown	6	7.89%	2	20.00%
Health insurance status				
Government medical insurance	10	13.16%	1	10.00%
Private medical insurance	66	86.84%	9	90.00%

Table 9 (continued)

Number of years in the study				
< 2 years	14	18.42%	5	50.00%
>=2 years	60	78.94%	4	40.00%
Not answered	2	2.63%	1	10.00%

To understand which participants are more likely to have missed study visits, characteristics of the participants who reported having missed at least one visit in the HBRN cohort study were compared to those who reported they had never missed a visit. (Table 10, Figure 8). Younger age was the most important factor associated with having missed a visit.

Table 10

Comparison of participants with vs. without missed visits in the HBRN

	No		Yes	
Characteristic	*Number*	*Percent*	*Number*	*Percent*
Gender				
Female	29	43.3%	11	57.9%
Male	38	56.7%	6	31.6%
Not Answered			2	10.5%
Age groups				
20-40 years	18	26.9%	8	42.1%
40-60 years	33	49.3%	10	52.6%
60-80 years	16	23.9%	1	5.3%
Ethnicity				
Hispanic or Latino	2	3.0%	1	5.3%
Not Hispanic or Latino	63	94.0%	15	79.0%
Not Answered	2	3.0%	3	15.8%
Race				
Asian, Chinese	31	46.3%	7	36.8%
Asian, non-Chinese	13	19.4%	4	21.1%
Black or African American	2	3.0%	3	15.8%
Other	3	4.5%	1	5.3%
White	18	26.9%	4	21.1%
Highest level of school you attended				
High school graduate or less	8	11.9%	1	5.3%
Some college & College graduate	24	35.8%	6	31.6%
Some graduate school & Graduate / Professional degree	35	52.2%	12	63.2%
Total household income ($) per year				
Less than $50,000	13	19.4%	3	15.8%
$50,001- $100,000	19	28.4%	4	21.1%
Greater than $100,000	29	43.3%	10	52.6%
Not Answered/ Unknown	6	9.0%	2	10.5%
Health insurance status				
Government medical insurance	10	14.9%	1	5.3%
Private medical insurance	57	85.1%	18	94.7%

Discussion

The goals of this survey study are to determine HBRN Cohort Study participants' evaluation of the University of Michigan retention strategies, to identify other strategies that will improve retention rate among HBRN Cohort Study participants at University of Michigan and to develop best practices for retention in the HBRN Cohort Study that can be shared with other sites.

Our response rate of 94.7% was much higher than most survey studies likely related to our long relationship with the participants and multiple modalities of completing the survey (hard copy in person at study visit, by return mail, or electronic link via email).

Our study population differs from the general population in the U.S. in having a high proportion of Asians, with high education level, and high income, and 100% having some form of health insurance. In the United States, the prevalence of chronic hepatitis B is low in the general population but 10-fold higher among Asians thus explaining the high proportion of Asians in this survey study (Roberts et al., 2016). The high education level and high income level among our participants might be related to the location of our study site in a college town. Because the HBRN cohort study is an observational study with standard of care testing billed to participant insurance, it is not surprising that 100% of our participants have some form of health insurance.

Although the HBRN Cohort Study is an observational study we conducted study visits at our clinical research unit instead of the regular clinic. The clinical research unit differs from the regular clinic in that the unit is equipped with a lab, and staffed by specially trained nurses and medical assistants in addition to the HBRN research team. This set-up allows efficient evaluation of participants, and blood draw and sample processing at the same location. The spacious facility also provides a more relaxed environment for participants and ample private space for completion of questionnaire.

Our unique set-up may explain why the retention rate at our site is substantially higher than the overall retention rate of HBRN Cohort Study. In addition to the resources available through the clinical research unit, we also adopted several strategies from inception of the study, including emphasizing on investigator meeting the participants at each visit and having the same study coordinator in charge of the study. This allows us to build a strong relationship with the participants. We also adopt many strategies to optimize communications and to facilitate scheduling and rescheduling of study visits including flexibility in scheduling appointments, sending reminder letters, planning future visits in advance, responding to participants' questions and concerns promptly, and checking for changes in participants' contact information at each visit. Finally, the principal investigator who is a world renowned expert in hepatitis B and a native Chinese who can speak Chinese is on hand to evaluate the participants at more than 50% of the study visits and provides updates on hepatitis B and the study to the participants. Indeed, the overall experience of study visits was the most important reason why participants remain in the study whereas financial incentive was a minor factor. However, co-pays remained a hurdle for some participants. Although we do not charge (neither insurance carrier nor participant) for the office visits, blood tests are performed at each visit for all participants and ultrasounds for a subgroup of participants. Almost half of our participants reported they had co-pays for these tests that can exceed $100 per visit though similar copays would be required if the participants were monitored in clinical practice. We have tried to mitigate this by covering tests for participants who have temporary lapse in their insurance or when participants have unusually high co-pays. In addition, we refer participants to social services to help their financial situation when appropriate. For participants whose insurance changed during the study and their new insurance makes us out of network, we work with participants' primary care physician to order the labs and get them

drawn locally. Elimination of co-pays was more important for our participants than the $25 subject fee which we offer after completing each visit; whether responses would be different if a higher amount of subject fee is provided is unclear. Overall experience of the study visits and provision of information regarding the disease were the two most important motivating factors for continued participation in the HBRN cohort study. Compared to clinical trials, observational studies do not offer free medications or testing instead observational studies involve lengthy office visits, multiple questionnaires to be answered, and blood draws for research with no direct benefit to the participants. Nevertheless, only 10% of our participants were bothered by these study procedures. Clearly explaining the purpose of the study, visits and procedures required, and risks and benefits upfront minimize participant resent or regret after consenting. Half of our participants responded that they signed up for the study to help future patients with the same disease and not for their own personal gain.

Although only 11% of our participants may not stay until the end of the study, understanding participants' concerns and removing those barriers are important to maximize retention.

Strategies that can be implemented to maintain and to improve retention rate at our site. Overall experience at the study visit is the most important motivator our participants stay in the study, and we will strive to maintain the quality of this experience. In addition, based on the survey results we will implement several new strategies to enhance that experience. These include the following:

1) Provide flow sheet with serial test results and study newsletter to participants when they check-in.This strategy will encourage participants to review their past results

and to read the newsletter and stimulate them to ask more questions and have a better understanding of their disease and the study.

2) Continue to mail reminder appointment letters to all participants 2 weeks before appointment and to add phone or email reminder to participants 1–2 days before the scheduled visit date.
3) Review patient care study budget and determine whether it is possible to cover or waive co-pays for participants with high co-pays or financial hardship.

Best practices for retention in the HBRN cohort study. Though having a dedicated research clinic may not be feasible for every site involved in the study, several of the strategies that work well for our site can be easily implemented at other sites where participants are seen in clinics by multiple providers who may not be part of the research team:

1) Informing participants who they will be seeing at the next visit and having the same study coordinator seeing participants at each visit will help develop strong relationship with patients.
2) If participants raise concerns about high co-pays, evaluating if some tests can be deferred to the next visit or done locally.
3) When ordering labs, reviewing the labs ordered with participants to reassure them the tests are required labs for monitoring their health and not just for research.
4) If participants relocate, transfer cares to another HBRN site if possible, if not, encourage the participants to participate remotely. Even though the participant can't be physically seen and the study would be missing physical exam information and research bloods, it is still possible to capture useful data such as labs, progression of liver disease, and initiation or discontinuation of treatment for hepatitis B.

5) Review study visit window and compare to scheduled clinic follow-up appointment and work with the clinical team to minimize missed visits.
6) Remind patients of their upcoming follow-up clinic visits and remind them they will also be seen for the study.
7) Provide study coordinators phone number for easy access, facilitate communications with clinical team, and respond to questions related to the research study promptly.

Chapter 5: Conclusion

Providing a pleasant experience to the participants at each visit, engaging in good communication with participants, establishing a strong trusting patient-doctor relationship, minimizing turnover of staff, using specialized phlebotomists for blood draw, decreasing wait time at the visits, and providing information about their health and progress of the study are motivating factors important to our participants. Though incentives (monetary and non-monetary) are not important to most participants, a substantial proportion would like to see decrease or waiving of co-pays but implementation will be difficult due to budget constraints. Having a physician that is expert in their disease and a familiar study team is a very good motivating factor for participants to come back. Study teams should also identify participants that frequently miss their visits and put special efforts in retaining these participants. These study results will be shared with the entire network with the goal of improving retention at all sites.

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Appendix A: University Of Michigan IRBMED (Institutional Review Board) Notice of Exemption

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Road, Building 520, Suite 3214, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Anna Lok

From:

Michael Geisser
Alan Sugar

Cc:

Sravanthi Kaza
Anna Lok

Subject: Notice of Exemption for [HUM00116670]

SUBMISSION INFORMATION:
Title: Survey of HBRN Cohort patients
Full Study Title (if applicable): What motivates patients to remain in longitudinal observational studies?
Study eResearch ID: HUM00116670
Date of this Notification from IRB: 6/13/2016
Date of IRB Exempt Determination: 6/13/2016
UM Federalwide Assurance: FWA00004969 (For the current FWA expiration date, please visit the UM HRPP Webpage)

IRB EXEMPTION STATUS:
The IRBMED has reviewed the study referenced above and determined that, as currently described, it is exempt from ongoing IRB review, per the following federal exemption category:

EXEMPTION #2 of the 45 CFR 46.101.(b):
Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a

manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Note that the study is considered exempt as long as any changes to the use of human subjects (including their data) remain within the scope of the exemption category above. Any proposed changes that may exceed the scope of this category, or the approval conditions of any other non-IRB reviewing committees, must be submitted as an amendment through eResearch.

Although an exemption determination eliminates the need for ongoing IRB review and approval, you still have an obligation to understand and abide by generally accepted principles of responsible and ethical conduct of research. Examples of these principles can be found in the Belmont Report as well as in guidance from professional societies and scientific organizations.

SUBMITTING AMENDMENTS VIA eRESEARCH:
You can access the online forms for amendments in the eResearch workspace for this exempt study, referenced above.

ACCESSING EXEMPT STUDIES IN eRESEARCH:
Click the "Exempt and Not Regulated" tab in your eResearch home workspace to access this exempt study.

Michael Geisser
Co-chair, IRBMED

Alan Sugar
Co-chair, IRBMED

Appendix B: University Human Subjects Review Committee (UHSRC) Notice of Exemption

RESEARCH @ EMU

UHSRC Determination: **EXEMPT**

DATE: **June 22, 2016**

TO: **Sravanthi Kaza**
Department of Health Sciences
Eastern Michigan University

Re: **UHSRC: # 920504-1**
Category: Exempt category 2
Approval Date: June 22, 2016

Title: **What motivates patients to remain in longitudinal observational studies?**

Your research project, entitled **What motivates patients to remain in longitudinal observational studies?,** has been determined **Exempt** in accordance with federal regulation 45 CFR 46.102. UHSRC policy states that you, as the Principal Investigator, are responsible for protecting the rights and welfare of your research subjects and conducting your research as described in your protocol.

Renewals: Exempt protocols do not need to be renewed. When the project is completed, please submit the **Human Subjects Study Completion Form** (access through IRBNet on the UHSRC website).

Modifications: You may make minor changes (e.g., study staff changes, sample size changes, contact information changes, etc.) without submitting for review. However, if you plan to make changes that alter study design or any study instruments, you must submit a **Human Subjects Approval Request Form** and obtain approval prior to implementation. The form is available through IRBNet on the UHSRC website.

Problems: All major deviations from the reviewed protocol, unanticipated problems, adverse events, subject complaints, or other problems that may increase the risk to human subjects **or** change the category of review must be reported to the UHSRC via an **Event Report** form, available through IRBNet on the UHSRC website

Follow-up: If your Exempt project is not completed and closed after **three years**, the UHSRC office will contact you regarding the status of the project.

Please use the UHSRC number listed above on any forms submitted that relate to this project, or on any correspondence with the UHSRC office.

Good luck in your research. If we can be of further assistance, please contact us at 734-487-3090 or via e-mail at human.subjects@emich.edu. Thank you for your cooperation.

Sincerely,

Sonia Chawla, PhD
Research Compliance Officer

Appendix C: Introduction to Survey through Qualtrics

UNIVERSITY OF MICHIGAN

PATIENT SURVEY

Study Team: Anna Lok, MD

University of Michigan, Internal Medicine-Gastroenterology

Sravanthi Kaza, B.Pharm,CCRP

University of Michigan, Internal Medicine-Gastroenterology

Thank you for taking the time to respond to our survey! The survey should take about **15 minutes** of your time and no identifiable information will be collected.

You are being invited to participate in this study as you're currently enrolled in **HBRN (Hepatitis B Network) observation study.** The purpose of this study is to get a direct input from you on the strategies that are employed by University of Michigan for subject Retention and to identify strategies we can implement to improve patient retention rate.

Participating in this study is completely voluntary. You can decide not to participate. Even if you decide to participate now, you may change your mind and stop at any time. You may choose not to answer any of the survey questions for any reason.

In the questions that follow, there is no right answer. We are interested in YOUR opinion. The information you provide on this form will be kept confidential and your responses are strictly anonymous.

If you have any questions about this research study, you can contact the study coordinator, Sravanthi Kaza at sravanth@med.umich.edu, (734) 615-3853.

By completing and submitting this survey, you are indicating your consent to participate in the study. Your participation is appreciated.

Appendix D: Introduction to Survey: In Person

UNIVERSITY OF MICHIGAN

PATIENT SURVEY

Study Team: Anna Lok, MD

University of Michigan, Internal Medicine-Gastroenterology

Sravanthi Kaza, B.Pharm,CCRP

University of Michigan, Internal Medicine-Gastroenterology

Thank you for taking the time to respond to our survey! The survey should take about **15 minutes** of your time and no identifiable information will be collected.

You are being invited to participate in this study as you're currently enrolled in **HBRN (Hepatitis B Network) observation study.** The purpose of this study is to get a direct input from you on the strategies that are employed by University of Michigan for subject Retention and to identify strategies we can implement to improve patient retention rate.

Participating in this study is completely voluntary. You can decide not to participate. Even if you decide to participate now, you may change your mind and stop at any time. You may choose not to answer any of the survey questions for any reason.

In the questions that follow, there is no right answer. We are interested in YOUR opinion. The information you provide on this form will be kept confidential and your responses are strictly anonymous.

If you have any questions about this research study, you can contact the study coordinator, Sravanthi Kaza at sravanth@med.umich.edu, (734) 615-3853.

By completing and submitting this survey, you are indicating your consent to participate in the study. Your participation is appreciated.

PLEASE RETURN THE SURVEY TO THE RESEARCH STAFF.

Appendix E: Introduction to Survey: By Mail

UNIVERSITY OF MICHIGAN

PATIENT SURVEY

Study Team: Anna Lok, MD

University of Michigan, Internal Medicine-Gastroenterology

Sravanthi Kaza, B.Pharm,CCRP

University of Michigan, Internal Medicine-Gastroenterology

Thank you for taking the time to respond to our survey! The survey should take about **15 minutes** of your time and no identifiable information will be collected.

You are being invited to participate in this study as you're currently enrolled in **HBRN (Hepatitis B Network) observation study.** The purpose of this study is to get a direct input from you on the strategies that are employed by University of Michigan for subject Retention and to identify strategies we can implement to improve patient retention rate.

Participating in this study is completely voluntary. You can decide not to participate. Even if you decide to participate now, you may change your mind and stop at any time. You may choose not to answer any of the survey questions for any reason.

In the questions that follow, there is no right answer. We are interested in YOUR opinion. The information you provide on this form will be kept confidential and your responses are strictly anonymous.

If you have any questions about this research study, you can contact the study coordinator, Sravanthi Kaza at sravanth@med.umich.edu, (734) 615-3853.

By completing and submitting this survey, you are indicating your consent to participate in the study. Your participation is appreciated.

PLEASE USE THE RETURN ENVELOPE TO RETURN THE SURVEY TO THE RESEARCH STAFF.

Appendix F: Survey questions

Questionnaire:

Demographics:

What is you Gender? ___Male ___Female

How old are you? ____

Which best describes your race?

___ White

___ Black or African American

___ Asian, Chinese

___ Asian, non-Chinese

___ American Indian or Alaska Native

___ Native Hawaiian or Other Pacific Islander

___ Other

Which best describes your ethnicity?

___ Hispanic or Latino

___ Not Hispanic or Latino

What is the highest level of school you attended?

___ Some high school or less

___ High school graduate

___ Some college

___ College graduate

___ Some graduate school

___ Graduate / Professional Degree

What is your total household income ($) per year?

___ Less than $25,000

___ $25,001-50,000

___ $50,001-75,000

___ $75,001-100,000

___ More than $100,000

___ Unknown

Which of the following best describes your health insurance status? ***(May select more than one)***

___ I have government medical insurance (for example: Medicare, Medicaid)

___ I have private medical insurance (for example: HMO, PPO, Blue Cross)

___ I do not have medical insurance

Affinity to participate in research studies:

Have you participated in any other research studies (Other than the HBRN Cohort study)?

___ Yes ___ No

What is your biggest motivation to participate in the HBRN study (Select One)?

___ I signed up because it is an interesting study

___ I signed up because this study might be able to help future patients in my situation.

___I signed up because I can get better care through this study

___I signed up because my liver doctor asked me to

___I signed up because of the compensation (money) for participation.

___Other reasons: _____

How long have you been participating in the HBRN study? ____ years

Have you missed any visits as part of the HBRN study? ___Yes ____No

If Yes,

How many visits have you missed? ____

What is the main reason for you to miss the visit/s?

___ I forgot the appointment

___ Appointment was not at a convenient time

___ Weather didn't permit

___ Didn't have time/ family commitments

___ Didn't have a ride

___ I was out of town/country at that visit window

___ I was dealing with other major health problem

___Other

If other , please Specify _____

What is the distance from your home to University of Michigan Hospital?

_____(approx. miles) _____(driving time – minutes)

Do you have copays for the tests we order at each HBRN visit for standard of care purposes?

___ Yes ___No

If Yes,

What is the average amount you pay per visit _____ (in USD)?

Are you currently receiving any treatment (Medication) for Hepatitis B? ___ Yes ___No

Motivation to continue Participation

For each statement below related to your ***motivation to continue participation in the HBRN Cohort study***, please indicate how much you agree or disagree. Rate on Scale of 1 (completely Disagree) to 5(Completely Agree).Choose only **One** response for each statement.

	Completely disagree (1)	Somewhat disagree (2)	Neutral (3)	Somewhat agree (4)	Completely agree (5)
Incentive					
Compensation(money paid) at each visit tivates me to come back	1	2	3	4	5
No copay to see the specialist motivates to come back	1	2	3	4	5
Convenience of the visits					
It is easy to schedule and to reschedule appointments, and they work with my ndar and are flexible	1	2	3	4	5
Overall experience for the visit					
Visits are more efficient, with minimal t times, and blood draw is in the same ce	1	2	3	4	5
Doctors spend more time with me in earch visit than they would in clinic	1	2	3	4	5
I feel research environment is more xed compared to visits in Regular clinic	1	2	3	4	5
I feel that I am better cared for in earch	1	2	3	4	5
The research team are experts in my ease	1	2	3	4	5

Patient contact					
The appointment reminder letters help to keep or reschedule my appointment.	1	2	3	4	5
Study staff knows the best way to reach and respects my preferences on how to be tacted	1	2	3	4	5
Communication					
The staff is easy to reach and answers questions promptly	1	2	3	4	5
I am learning more about the disease ce my participation in the study.	1	2	3	4	5

Which factor is most motivating for you to stay in the study? (Select one)

___ Subject fee for each visit

___ Convenience of the visits

___ Overall experience of the visit

___ Communication (ease of communication with study team)

___ Information regarding the disease

Demotivators to continue Participation in observational studies like HBRN Cohort study

For each statement below related to your **de-*motivators to continue participation in the HBRN Cohort study***, please indicate how much you agree or disagree. Rate on Scale of 1 (completely Disagree) to 5(Completely Agree).Choose only **One** response for each statement.

	Completely disagree (1)	Somewhat disagree (2)	Neutral (3)	Somewhat agree (4)	Completely agree (5)
8 hours of fasting at annual visits hers me	1	2	3	4	5
The amount of blood drawn at each visit research purposes bothers me	1	2	3	4	5
The amount of questionnaires to be npleted for research at each visit bothers	1	2	3	4	5
The concept of just being observed and getting any treatment bothers me	1	2	3	4	5

Please answer the question below. Rate on Scale of 1 (Extremely unlikely) to 5 (Extremely likely). Choose only **one** response.

	Extremely likely (1)	Unlikely (2)	Neutral (3)	likely (4)	Extremely likely (5)
How Likely will you stay in the study **till the** currently projected to be late 2019 ?	1	2	3	4	5

If you were to discontinue participation in the study, what would be the main the reason?

__ Moving away from study site

__ Loss of insurance / high copay's

__ No time /family commitments

__ other

If other, Please Specify _____

What else can we do to facilitate your staying in the study?

_____

Other comments: