Stakeholder Perspectives on Maternal Alloimmunization and Resultant Hemolytic Disease of the Fetus and Newborn (HDFN)

Allo Hope Foundation

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Contact:
Molly Sherwood
Director of Research
Allo Hope Foundation
molly@allohopefoundation.org

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Project Background

Maternal red cell alloimmunization is a rare pregnancy condition in which a person develops antibodies to a blood type unlike their own. This typically occurs during fetal and maternal blood mixing during a previous pregnancy, or during exposure to foreign blood through a blood transfusion. Once a person of childbearing potential becomes alloimmunized, they carry these antibodies for the rest of their life. If the alloimmunized person becomes pregnant and the fetus has a blood type which corresponds with the mother's antibodies, the mother's antibodies can cross the placenta and destroy fetal red blood cells, causing fetal and neonatal anemia. This condition in the baby is called hemolytic disease of the fetus and newborn (HDFN). If untreated or not treated promptly, HDFN can cause fetal ascites, hydrops, heart failure, kernicterus and death.

Currently, the only available treatment in utero for babies with HDFN is an intrauterine transfusion (IUT), a highly specialized fetal procedure where a maternal fetal medicine clinician inserts a needle through the mother's abdomen and into the fetus' umbilical vein to transfuse blood. Though not all alloimmunized pregnancies result in IUT, those that do often require multiple IUTs and assume the risks of complications such as fetal death, maternal hemorrhage, emergency c-section and others.

Close monitoring and access to skilled maternal fetal medicine specialists who routinely conduct IUTs is critical to ensure fetal survival. Considering the disease's rarity (about 0.7-1.7% of pregnancies in the U.S. are alloimmunized [1-3]), clinicians do not often have the opportunity to develop expertise or comfort in disease management. Research in this population is lacking not only due to the disease's rarity but because of the challenges in studying vulnerable populations including infants and pregnant women. As a result, patients often bear the burden of advocating for proper care and risk preventable fetal and neonatal morbidity and mortality. The impact on maternal mental health is significant. Mothers develop anxiety over their sense of responsibility to manage their own nuanced condition as well as managing oversight of many practitioners including obstetricians, maternal fetal medicine specialists, neonatologists, pediatricians, and hematologists. Further, these health specialists often practice in silos, so many mothers are responsible for coordination of care across all of these specialties and ensuring critical information is seamlessly transferred from one provider to the next. This is further compounded by feelings of isolation as most alloimmunized women do not personally know another woman with this condition, and feelings of guilt in knowing that her own body is attacking her baby's blood. Inequities in management of this disease are exaggerated by its complex nature and limited publicly available resources, making advocacy difficult for patients with low health literacy.

There is a desperate need to identify research and advocacy needs for the alloimmunized patient population and their families affected by HDFN. The Allo Hope Foundation (AHF) serves patients, families and providers navigating alloimmunization and HDFN through research, advocacy, and education. AHF manages an extensive website with online resources and clinical decision support tools, offers a podcast series, speaks at international conferences, and provides daily patient counsel through its closed online patient support group of over 1,500 alloimmunized patients. Through this work a continued unmet need for patient-centered research and advocacy initiatives presented itself.

The Allo Hope Foundation developed a stakeholder engagement strategy that is organized into three phases to address the needs of the maternal alloimmunization/HDFN community. Phase one involves a series of virtual listening sessions and surveys with patients, clinicians, industry leaders and researchers to discuss needs of the disease community, proposed research concepts and barriers and facilitators to participating in future research initiatives. Special emphasis was placed on the maternal mental health impact of alloimmunization and methods to address this challenge. Phase two is a roundtable discussion with a smaller group of patients, researchers, and clinicians to collaborate and develop an actionable short- and long-term research plan for AHF based on the learnings from the virtual listening sessions. The third and final phase of the capacity building engagement effort by AHF includes development and dissemination of this whitepaper, an engagement guide for patient advocacy groups, and an actionable short- and long-term research plan for AHF to the broader community with great emphasis on the stakeholder community. AHF anticipates dissemination platforms will include updates on the AHF website, AHF newsletter, and PCORI website.

This initiative was launched as a component of a contract funded by the Patient Centered Outcomes Research Institute (PCORI) Eugene Washington Engagement Awards program. Emphasis herein is focused on methods and key findings from the virtual listening sessions and associated surveys in phase one of the stakeholder engagement strategy.

Protection of Human Subjects

This initiative is not human subjects research. Research is defined as “a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge” [45 CFR 46.102(I)]. A research *plan* will be generated in phase two of this stakeholder engagement strategy, however, this initiative does not include research. Stakeholders may feel compelled to share their personal experience, however, this was not a requirement. This initiative included pre- and post-listening session participation surveys. E-mail addresses tied to these surveys were removed and responses analyzed in aggregate. These surveys were limited to stakeholder feedback about the engagement experience and quality of PCOR/CER education they received. No identifying information or protected health information will be elicited in this survey.

While we do not anticipate that there is any risk to stakeholder participants who engaged in this project, we acknowledge a risk of recall stress which may be brought on when patients recall the events during their alloimmunized pregnancies. For this reason, we always provide resources for mental and health and grief support in our public interactions and on our website. These resources were also made readily available during each listening session and also provided again in the post-listening session participation survey.

Listening Session Methodology

Listening Session Structure

There were a total of four virtual multistakeholder listening sessions that each lasted approximately two hours. Stakeholders were invited to attend one listening session only. In an attempt to accommodate the diverse schedules of the stakeholder groups, two listening sessions were offered in the evenings (after 6 pm ET) and two were offered during the day (between 9 am and 5 pm ET) over the span of a 4-week time period.

Stakeholders registered for the listening session via a virtual form sent to their email address. This virtual form also included pre-participation questions that stakeholders were required to complete prior to attending the listening session. Once the registration form/pre-participation questions were submitted, AHF staff contacted the participant within the next two business days via an email with the selected listening session meeting invitation.

Registered participants were sent an email reminder of the upcoming event prior to each listening session. This email also included a Pre-Listening Session Educational Handout which included information on Maternal Alloimmunization/HDFN, Patient Centered Outcomes Research, and planned discussion topics (see **Appendix A**). Participants were asked to review this document prior to the scheduled listening session to establish common baseline knowledge and shared language for the group discussion. It was also recommended to have this document accessible to reference during the session.

The virtual platform used for the listening sessions was Zoom and the presentation content was the same for each listening session. AHF staff shared presentation slides throughout the session to provide educational content integrated with group discussion questions on identified topics to facilitate dialogue with stakeholders. Stakeholders were able to provide verbal feedback and written feedback via the chat box feature at any time. The chat box feature gave participants the option to share public messages visible to all participants or private messages visible to the AHF hosts only. Additionally, structured questions were presented via MentiMeter tools so participants could provide anonymous, live, written feedback. Offering a variety of participation options for stakeholder response during the listening sessions was intended to allow for easy participation in a method that feels comfortable for each stakeholder. At the close of the listening session, information on project phases two and three was provided (roundtable discussion and development/dissemination of deliverables, respectively). Importantly, it was explained that the learnings from the listening sessions and associated surveys would be summarized in the whitepaper and shared with the stakeholder community after completion. The project team recognizes transparency, communication, and dissemination of findings fosters trust between AHF and the stakeholder community, which in turn builds sustained engagement and collaboration on future efforts.

Post-participation survey questions were intentionally developed after completion of all four listening sessions to incorporate questions based on the collective learnings from the listening sessions. Therefore, participants were emailed a virtual form with the post-participation questions on the same date no matter their date of participation. At the close of the survey, participants were provided with access to patient-centered outcomes research training tools and resources for support. Additionally, participants were given AHF contact information, resources around how to continue to engage with AHF in future efforts, and invited to share via an email to AHF any feedback or thoughts that they did not have the opportunity to share during the live session.

Participant Outreach

The AHF team used strategic outreach efforts to engage a representative variety of stakeholder groups for listening session participation. The targeted stakeholder groups included patients (who also serve as caregivers to their children who develop HDFN), researchers, industry, and clinicians. Outreach efforts began two months prior to the first listening session and were predominantly through direct invitation from AHF staff. There were a limited number of slots allotted for each stakeholder group at each listening session to create an intimate environment for meaningful group discussion. Slots were available for registration on a first-come basis. The strategic outreach for each stakeholder group is detailed below and briefly summarized in **Table 1**.

AHF staff communicate regularly with a large network of patients with red cell alloimmunization. Contact with patients is predominantly through the AHF Facebook support group, a private social media group facilitated by AHF and only open to individuals with alloimmunization. This support group offers resources, peer-to-peer support, and access to one-on-one counsel with AHF staff. Patients who have previously participated in one-on-one counsel with AHF staff were directly invited to participate in the listening sessions. Additionally, listening session information was posted on the AHF Facebook support group and on its general social media channels two months prior to the scheduled listening sessions and interested members were encouraged to contact the AHF team to participate.

Further, AHF staff maintains strong relationships with relevant industry and research organizations who have a shared interest in research and improvement of disease management and outcomes for alloimmunization/HDFN. Individuals from these stakeholder groups who have relationships with AHF staff were personally invited to participate in the listening sessions. Additionally, the invited research stakeholder representatives were asked to refer other individuals within their field for participation.

AHF's Medical Advisory Board consists of specialized healthcare providers who are active in the treatment and research of maternal alloimmunization/HDFN and are consistently endorsed by patients in the alloimmunized community. The Medical Advisory Board members were invited to participate in the listening sessions as representatives of the clinician stakeholder group. Additionally, the board members and patients were asked to identify other interested clinical stakeholders for listening session participation. Importantly, AHF was deliberate in also inviting clinicians with interest in the subject matter but who do not necessarily possess specific expertise in the treatment of this disease. These stakeholders were largely selected based on patient recommendation. This allowed for a more diverse perspective during listening sessions and hopefully also resulted in clinical education as a byproduct.

Though the majority of the outreach efforts were through direct invitation from AHF staff and referrals, the listening session information was also shared in the AHF newsletter two months prior to the scheduled listening sessions. The AHF newsletter is available to any individual who signs up to receive it via the AHF website and is approximately half clinicians. Outreach for participation via the newsletter enabled the broader community to participate in the listening sessions if interested.

Table 1. Stakeholder Participant Outreach Methods

Stakeholder group	Method of outreach facilitated by AHF for listening session participation
Patients	One-on-one outreach, AHF newsletter, support group invitations
Researchers	One-on-one-outreach, AHF newsletter, referral from other researchers
Industry	One-on-one outreach, AHF newsletter
Clinicians	One-on-one outreach, AHF newsletter, referral from Medical Advisory Board members and patients

Pre- and Post-Participation Surveys

Listening session participants completed a total of two surveys each - one pre-participation survey prior to attending a listening session and one post-participation survey after attending a listening session. In each survey, participants were asked to self-select which stakeholder group(s) they identify with so the specific perspectives, needs, and barriers for each group could be analyzed. The multiple selection feature for this question was enabled so participants could select as many stakeholder groups they identify with since individuals may be representative of more than one group. For example, some individuals with alloimmunization may also be clinicians, some clinicians may also be researchers, and so on.

The pre-participation survey included 12 questions (in addition to the registration and contact information questions). The question formats included multiple selection checkboxes, rating scales, and free text responses. Generally, this pre-participation survey gathered information pertaining to alloimmunization/HDFN research needs and participant interest in research involvement, current management of alloimmunized pregnancies from stakeholders' perspectives, perceived mental health of alloimmunized patients, and PCOR/CER baseline knowledge. The survey responses were reviewed in aggregate by AHF prior to the listening sessions. The general findings were integrated into the listening session presentation slides to share the results with stakeholders and also to serve as talking points for group discussion. The complete pre-participation survey can be reviewed in **Appendix B**.

The post-participation survey included 11 questions (in addition to the contact information question). Importantly, the post-participation survey was developed after completion of all four listening sessions to incorporate questions based on the collective learnings from the listening sessions, especially regarding identified research gaps and proposed solutions. The question formats included multiple selection checkboxes, rating scales, and free text responses. Generally, this post-participation survey gathered information pertaining to feedback on the listening session content, stakeholder prioritization of research/advocacy initiatives proposed during the listening sessions, and repeat questions from the pre-participation survey to assess potential changes in perspectives about PCOR/CER and research needs. The survey responses were reviewed in aggregate by AHF after completion of the listening sessions. The findings are incorporated into this whitepaper and will also be used to develop the objectives for phase 2 of this project (roundtable discussion to develop a research plan). The complete post-participation survey can be reviewed in **Appendix C**.

Incentives and brief synopsis of the timeline

Phase one of the stakeholder engagement project included stakeholder outreach, four virtual listening sessions, and associated pre-/post-participation surveys. The overall timeline from the initial outreach efforts to completion of the post-participation survey spanned about five months (**Table 2**).

Table 2. Timeline Overview

Month	Activity
1	Stakeholder outreach efforts began
2	Stakeholder outreach efforts continued, registration form (including the pre-participation survey) sent to interested individuals
3	Two virtual listening sessions hosted
4	Two virtual listening sessions hosted
5	Post-participation survey sent to all listening session participants; monetary incentives dispersed to eligible participants

Full participant engagement in phase one of this project included 1) completion of the pre-participation survey, 2) participation in one two-hour virtual listening session, and 3) completion of the post-participation survey. A monetary incentive was offered to participants upon completion of all three engagement requirements.

The beginning of the listening session registration form detailed the engagement expectations and the requirements to receive the monetary incentive. This was done to ensure participants could review the expectations prior to committing to attending a listening session. Additionally, the pre-participation survey questions were included as a component of the listening session registration form to ensure participant completion of the survey questions. Full completion of this registration form was required in order to receive an invitation to participation in a listening session.

Listening session attendance was monitored via the virtual platform and reviewed by AHF administration in real time to account for any potential errors. After completion of all four listening sessions, the post-participation survey was emailed to participants who attended a listening session. Upon completion of all three engagement requirements (pre-participation survey completion, participation in one listening session, and post-participation survey completion), AHF staff contacted participants via email to facilitate mailing the monetary incentive.

Listening session content

The four virtual listening sessions presented the same content and followed the same discussion outline (**Table 3**).

Table 3. Listening session content and discussion outline

Section	**Content**
Welcome	Introductions Purpose Outline of session
Language review	Review of common alloimmunization/HDFN terminology to establish shared language before discussion
PCOR review	Traditional Research vs Patient-Centered Research Research concepts (CER/PCOR) PCOR role in improving outcomes in alloimmunization/HDFN community
Group discussion of needs, gaps, & barriers	Diagnosis and monitoring ● Summary of standard practice ● Related quotes from patients reported in a previously conducted IRB-approved anonymous patient questionnaire study ● Discussion question prompts
	Interventions in utero ● Summary of standard practice ● Related quotes from patients reported in a previously conducted IRB-approved anonymous patient questionnaire study ● Discussion question prompts
	Post-birth care ● Summary of standard practice ● Related quotes from patients reported in a previously conducted IRB-approved anonymous patient questionnaire study ● Discussion question prompts

	Continuity of care - Summary of standard practice - Related findings from patients reported in a previously conducted IRB-approved anonymous patient questionnaire study - Discussion question prompts
	Maternal mental health - Related results from pre-participation survey - Related findings from patients reported in a previously conducted IRB-approved anonymous patient questionnaire study - Discussion question prompts
Summary of key needs	Group review/discussion of identified key needs and ideas of how these needs can be addressed through research
Next steps & close	Summary of next steps for after listening session AHF contact information

Though AHF staff guided the discussions, the purpose of the listening sessions was to listen to the feedback and concerns of the stakeholders regarding alloimmunization/HDFN care and outcomes. Considering each listening session included a dynamic group of stakeholders, none of the listening sessions were identical but all were equally informative.

Collection and analysis of stakeholder feedback

Stakeholder feedback was collected prior to the listening sessions, during the listening sessions, and after completion of the listening sessions. All collection and analysis was completed by AHF staff, and all feedback was reviewed in aggregate. A summary of the methods for collecting and analyzing stakeholder feedback is provided in **Table 4**.

Table 4. **Summary of methods for collecting and analyzing stakeholder feedback**

Feedback collection	Feedback analysis
Prior to listening sessions	
Pre-participation survey*	Survey results exported Cross tabulation of data by stakeholder group Thematic assessment of free text responses
During listening sessions	
Verbal discussions**	Verbal discussions transcribed Thematic assessment of transcribed content

Written feedback (chat)	Downloaded written messages from chat feature Thematic assessment of chat content
MentiMeter tool***	MentiMeter results exported Cross tabulation of data by stakeholder group Thematic assessment of free text responses
After listening sessions	
Post-participation survey*	Survey results exported Cross tabulation of data by stakeholder group Thematic assessment of free text responses Comparison of repeat pre-/post-survey questions

**Responses were reviewed in aggregate and e-mail addresses were delinked.*

***Participants were notified that listening sessions were being recorded; participants could voluntarily leave the listening session at any time.*

****MentiMeter tools collect anonymous responses.*

Stakeholder Profile

The AHF team used strategic outreach efforts to engage a representative variety of stakeholder groups for listening session participation. The targeted stakeholder groups included patients (who also serve as caregivers to their children who develop HDFN), researchers, industry, and clinicians. These four groups were identified as key stakeholders because of their unique perspectives and anticipated contribution to future efforts to improve outcomes in the alloimmunization/HDFN community (**Table 5**). Across all four listening sessions, there were a total of 51 stakeholders who identified as patients (N=27), researchers (N=7), industry (N=5), clinicians (N=14), and three individuals who identified as other stakeholders (numbers do not sum to 51 because participants could select more than one stakeholder category). A total of 60 participants completed the pre-participation survey though some were ultimately unable to join the listening sessions. A total of 50 participants who participated in the listening sessions completed the post-participation survey (98% completion rate).

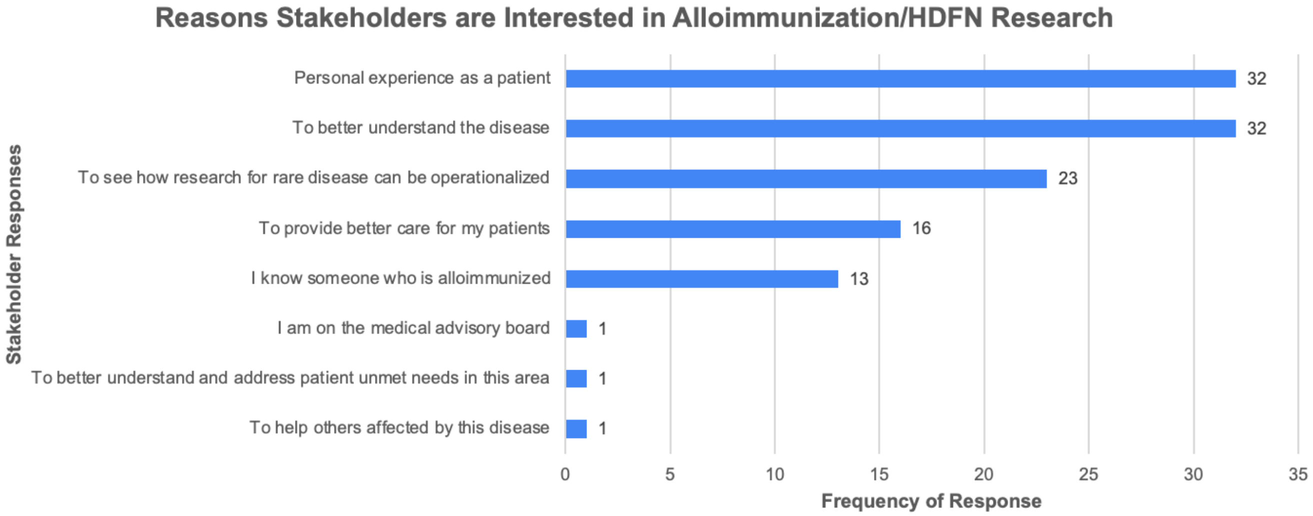
Table 5. Key stakeholder perspectives and anticipated contributions to future efforts

Stakeholder group	Stakeholder perspectives and anticipated contributions
Patients	Provide lived experience as an alloimmunized mother and caregiver to fetus/newborn affected by HDFN; Provide input on barriers to access and participation in research; Provide insight on engagement methods for future research efforts; Educate other stakeholder groups on reality of patient experience
Researchers	Share input on motivations to collaborate in research for this disease; Provide insight on feasibility of research efforts; Provide guidance on funding and partnership opportunities; Amplify AHF's voice on social media and in professional networks
Industry	Share input on motivations to collaborate in research for this disease; Provide insight on feasibility of research efforts; Provide guidance on funding and partnership opportunities; Amplify AHF's voice on social media and in professional networks
Clinicians	Share input on barriers to providing quality care to alloimmunized mothers/infants with HDFN; Share motivations to partner for research efforts; Offer potential mechanisms to reach other clinicians and research hospitals; Facilitate clinical research partnerships

Every listening session brought together a dynamic group of stakeholders. They came to the discussions with diverse lived experiences, varying degrees of exposure to research, and differing levels of knowledge of alloimmunization/HDFN. AHF acknowledged that perceived and real power dynamics among stakeholders could impact some individual's comfort level and willingness to participate in group discussions. Therefore, AHF launched each listening session by establishing an environment of even footing across all stakeholders. It was emphasized that each stakeholder's participation was valued independent of their personal experience or education about the topics at hand. It was also reiterated that by choosing to participate, all stakeholders demonstrated their genuine interest in better understanding the needs of this disease population. Offering a mixed media of participation options (as previously discussed) promoted engagement and responsiveness as well. Individuals were able to share their perspectives in ways that most align with their comfort, thus allowing more voices to be heard. Additionally, the pre- and post-participation surveys gave participants opportunities to provide anonymous feedback outside of the listening sessions.

As a part of the pre-participation survey, the stakeholders were asked to share why they were interested in alloimmunization/HDFN research. This question allowed multi-selection of responses as well as a free text option. Many participants selected more than one reason. The majority responded that they were interested because of personal experience as a patient and to better understand the disease. The other reasons for stakeholder interest are detailed below in **Figure 1**.

Figure 1. Stakeholder reasons for interest in Alloimmunization/HDFN research (N=60)



*N=61; some participants who completed the pre-participation survey were not able to attend the listening session and therefore were not included in the post-participation survey group.

Learnings: Core Challenges Across the Disease Course

The discussion prompts for these listening sessions were separated into the following categories: diagnosis and monitoring, treatments in pregnancy, treatments after birth, continuity of care, and maternal mental health. Stakeholders were invited to share their perspectives on areas requiring attention and improvement within each of these subcategories.

Diagnosis and Monitoring

> *"I've been working in this field for 20 years and* ***I think every single alloimmunized patient that I have seen has had to advocate for themselves*** *to get to see me through a sea of primary care providers who don't understand the disease and really the only patients I've seen where their disease prevention treatment course has gone really smoothly are return patients."* - Clinician

Screening for red cell alloimmunization is part of the standard first trimester bloodwork in the United States. If an antibody screen returns positive, the patient requires referral to a high-risk specialist in maternal fetal medicine (MFM), and, depending on fetal antigen status, continued monitoring will be required. Timely monitoring is a critical component of disease management as the maternal antibodies can cross the placenta and destroy fetal red blood cells, resulting in rapidly developing anemia which can progress to ascites and hydrops without close monitoring and treatment. Overall, stakeholders voiced concerns around the following topics.

Obstetrician understanding of necessary testing. Once a mother's antibody screen is positive, the next step is to determine whether the fetus carries the antigen which the mother's antibody attacks. This is a nuanced process which sometimes requires specialized laboratory tests. Stakeholders expressed concerns over improperly ordered tests or lack of follow up care resulting in preventable morbidity and mortality.

> *"It's never smooth. It's never the timely, proper referral. It's amazing to me how poorly understood this is, even in the MFM [maternal fetal medicine] community to some degree, but certainly in the OB [obstetrician], midwifery, family practice community. I get emails every week from providers about type and screen results and countless sad stories.* ***I feel like patients have to do lots of advocating for themselves to get to the right person and to get to specialists and often by that point, things are too late.*** *This is exactly what my experience has been, hearing my patients."* - Clinician

Referral protocols. Maternal fetal medicine specialists in attendance expressed concern that patients were not being referred to them by the obstetrician, midwife, or family practice clinician in time for the right treatment for their babies. Some patients in attendance shared experiences of not being referred to specialists at all and losing children due to absence of care.

> *"My impression from everything that I've heard today is that our largest challenge is up*

> *front in the frontline providers and many of these frontline providers are not necessarily MFMs, they're nurse practitioners, certified nurse midwives, family medicine physicians and OBGYNs. So it seems to me that we probably have to tackle that group and probably their organizations [...]. We probably have to collaborate with these other specialties to help disseminate this information because, I think somebody mentioned earlier,* ***by the time somebody reaches us it's kind of late in the process****."* - *Clinician*

Inconsistent frequency of monitoring. The frequency at which patients should be monitored by specialized ultrasounds called MCA Dopplers is inconsistent in the currently available literature. Clinicians voiced that there is not enough research detailing the impact of conducting MCA Doppler ultrasounds weekly or every two weeks. Some patients expressed that because their babies became severely anemic rapidly and require urgent intrauterine transfusion (IUT) for survival, MCA Dopplers every two weeks would have resulted in increased morbidity and mortality. Nonetheless, current guidelines are unclear about the ideal frequency.

HDFN Treatments in Pregnancy

The only currently available treatment for a fetus with HDFN is an IUT. These are highly-specialized procedures which must be conducted by a skilled MFM with the right supportive staff, access to blood products, and with the ability to conduct prompt intervention. There are additional non-invasive treatments including intravenous immune globulin (IVIG) and plasmapheresis which are sometimes utilized in severely affected pregnancies to delay the onset of fetal anemia. Literature on the use of IVIG and plasmapheresis is scarce and largely limited to pregnancies with a history of previous fetal loss or previous need for extremely early IUTs (prior to 24 weeks gestation). Overall, stakeholders voiced concerns around the following topics.

Provider uncertainty regarding the use of IVIG and plasmapheresis. Clinicians consistently noted a lack of research on the utilization of IVIG and plasmapheresis for pregnancies complicated by red cell alloimmunization, leading to inconsistent use and clinician concern around attempting IVIG and/or plasmapheresis.

Lack of insurance coverage for IVIG and plasmapheresis. Depending on their region in the U.S., patients and providers expressed difficulty obtaining insurance coverage for the use of IVIG and plasmapheresis in alloimmunized pregnancies, especially in pregnancies where the mother had not previously lost a child. Some clinicians expressed that they have developed packets including letters and literature to submit to insurance companies for approval, however, they noted that the approval was more likely to be granted in a peer-to-peer environment led by the clinician rather than by the patient themselves.

Lack of provider expertise in conducting IUTs. Because alloimmunization is a rare condition, many MFMs do not have the opportunity to develop expertise in conducting IUTs. Stakeholders discussed that in small European countries, IUT outcomes may be better because they have centralized referral centers. The concept of establishing a centralized referral network was discussed often.

HDFN Management in the Newborn

> *"I have a question, this might be really naïve… but why can't every HDFN child who is over a certain threshold immediately be sent to hematology until 3-4 months… again, sorry if this belies a great level of naivety here, but why can't every HDFN baby be followed?"* - Patient
> *"They should be. But there's a lack of knowledge."* - Clinician

After a baby with HDFN is delivered, their care is transferred to new providers, sometimes outside the hospital and sometimes in the neonatal intensive care unit (NICU). HDFN babies sometimes require interventions up to 3-4 months after birth. Babies after birth often display high bilirubin levels (hyperbilirubinemia) as their body attempts to metabolize broken down red blood cells that the maternal antibodies have destroyed. Treatment for hyperbilirubinemia is aggressive phototherapy and sometimes exchange transfusion, an invasive procedure with a risk of infection. In addition to high bilirubin, the second primary concern is delayed onset anemia, which is continued anemia resulting from maternal antibodies remaining in the neonatal circulation. This is treated as well with top up or exchange transfusion. Overall, stakeholders voiced concerns around the following topics.

Lack of consistency in medical record transfer. Because many HDFN babies have received treatments in utero, they are born with a pre-existing fetal "medical history". This history oftentimes is not relayed to the post-birth care team and is not reflected in the infant's medical record.

Lack of knowledge amongst neonatologists, hematologists and pediatricians. Stakeholders universally reported a lack of knowledge around the treatment of HDFN in infants. One clinician, when discussing how he explained this problem to a colleague in a European country with excellent post-birth protocols, stated,

> *"When I told him that I send patients to pediatric hematologists and even have them meet prenatally with patients he was aghast, he was like why can't the general pediatrician follow the baby's hematocrit and know when to transfuse them? And I said* ***there's no prayer that's gonna happen in the United States****."* - Clinician

Lack of neonatal protocols for HDFN management. Several patients shared stories of being sent home from the hospital with no follow-up care, later ending up in the emergency room with a lethargic infant with near-fatal anemia. All stakeholders agreed on a need for standardized best practices for neonatal management of HDFN.

Continuity of Care

> *"We've become very siloed and very specialized and very shift-driven and I don't know how to fix that."* - Clinician

Alloimmunization and HDFN is a nuanced condition because it involves a pregnancy diagnosis of alloimmunization for the mother, and a diagnosis of HDFN for the fetus and neonate. The care team involved in an alloimmunized pregnancy may include an obstetrician or midwife, an MFM, an oncologist/hematologist, a neonatologist, a pediatrician, and a pediatric hematologist. Ensuring continuity of care across specialties in a rare disease presents many challenges. Stakeholders voiced an overarching concern for **lack of continuity of care across providers.** Transfer of medical records was often discussed. One NICU nurse expressed, "I don't even know if I have taken care of a baby who I knew had an IUT already… I don't even know where I would find that information." An MFM echoed this sentiment, sharing, "that pediatrician never sees that baby in the hospital, the neonatologist is hospital-based, and again, the baton gets passed over and the records may or may not get there."

Many clinicians who attended the listening sessions have a special interest in the management of alloimmunization and HDFN, employing uncommon but exemplary comprehensive care. One clinician reflected on who should bear the burden of managing the continuity of care as he spoke to the patients in the listening session.

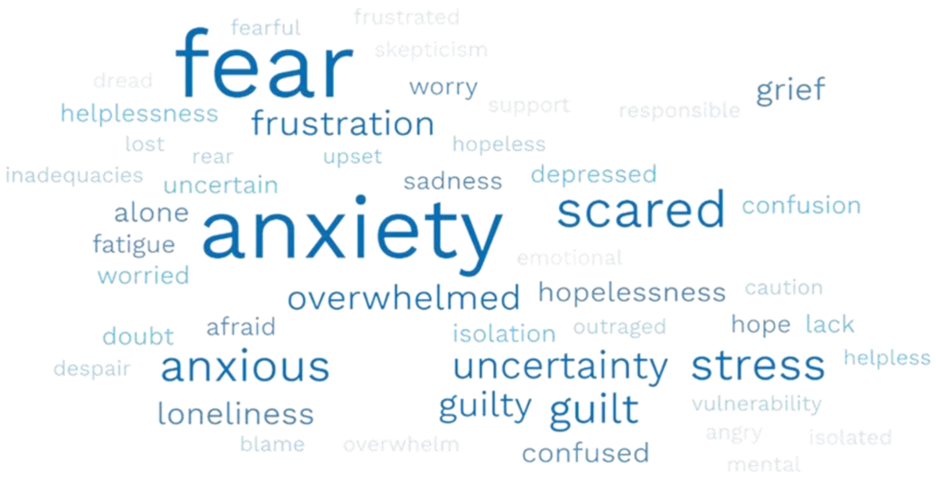
> *"I think it is my responsibility to pass that baton to the right person as a provider because the race isn't over when the baby's out. The APGAR score is the beginning. And I hold the MFMs responsible for going to the delivery room door and saying "I'm done." I really do. If they understand this disease, they know half the race has been won. And they want the best baby for you, that's why they work so hard during the pregnancy. But the general way we teach MFMs is once the baby's done, neonatology and other people do that, we don't do that. We have more knowledge than they do about these diseases and I think we cannot let the MFMs off the hook, who is interested in this disease, to not educate pediatric specialists about what this means or we have not done our job.* ***Mom should be plan B. She's stressed enough. We've heard that over and over again.*** *She's got postpartum blues, she's not sleeping at night, there's lots of things going on, and y'all should be plan B, you should be the backup. I agree that you all should be knowledgeable and you need to do this, but* ***I think the medical profession needs to wake up a bit and realize we are responsible for passing that baton, not you****. And I feel bad that MFMs don't do that, I think they should." - Clinician*

Maternal Mental Health

> *"I don't think that the mother's job of advocating for care is going to go away." - Patient*
>
> *"The reality is if you're an HDFN patient,* ***it affects you as a human and a mother as much as your child is ill****." - Industry researcher*

Allo Hope Foundation staff has had the fortune of supporting alloimmunized mothers in individualized counsel for more than ten years. The impact of alloimmunization on maternal mental health is monumental. AHF has conducted research on the psychosocial impact of alloimmunization and HDFN which will become available in Spring 2024. Independent of this aforementioned research effort, AHF asked all stakeholders in the pre-participation survey to list the top three emotions that they believe alloimmunized women experience during their pregnancies. The responses were overwhelmingly similar, as detailed below in **Figure 2.**

Figure 2. Stakeholder-reported most common feelings experienced by alloimmunized mothers during their pregnancies.



The burden on mothers experiencing this disease, whether or not their pregnancy resulted in the loss of their child, is not adequately addressed in the U.S. healthcare system. Clinicians expressed concern that while more mental health screening tools are becoming available, the infrastructure is not in place to follow up with women experiencing negative mental health effects and provide them with adequate resources and care. Patients in attendance expressed compelling experiences which speak volumes to the extent of this challenge.

> *"It's a heavy burden on mothers once you're sort of freed from the care of your MFM who you've come to know and trust and all of a sudden you're in the wild west of having an HDFN baby in the NICU and you're hormonal and you're exhausted and* ***every time you open your mouth you burst into tears*** *and it's difficult to know how to be prudent but also to know how to advocate for your child."* - Patient

> *"****Having to teach someone first about your disease before receiving empathy from them is really difficult and that's when the isolation comes in.*** *When people ask how they can help with this disease or support the foundation and I'm not talking monetarily, they can learn about it, they can tell someone about it, they can make it feel less rare, so that the community around us, something rings a bell when someone says I have this condition."* - Patient

> *"I think most moms I've talked to agree that after you have your baby it's supposed to be the best time in your life, you're supposed to be super happy, things are supposed to be great.* ***It's really hard to admit that you don't feel happy when you have a living baby in your arms****."* - Patient

There was consistent mention of a **lack of support from care teams and community**. Feelings of guilt sometimes kept mothers from being honest about their levels of anxiety, depression and stress. Many patients expressed that the mental health burden felt exaggerated in cases where they did not receive high quality care or strong continuity of care, as the patient undertook the additional burden of advocating for their child and fearing preventable trauma and loss.

Maternal Health of Underrepresented Populations

Alloimmunization/HDFN advocacy is challenging given it is a rare disease with limited publicly available resources and limited access to clinical interventions. These challenges are further complicated for underrepresented populations due to systemic inequities in quality of care.

> *"As far as barriers I also want to call attention to the one that we hear about sometimes which is the barrier of women of color not being able to receive quality maternal health care. I found that to be true; we're already just by the nature of what we're dealing with just in a small population and then couple that with the fact that as a woman of color, my voice is not heard, I'm often not taken seriously, I actually had to have my midwife navigate or advocate for me. [...] I just think in general that is something to consider when you're looking at these cases as well as underrepresented populations and those that already have so many barriers with access to even get to this point to get healthcare. What about if you only have Medicare? Or Medicaid? There's so many things that can be a factor to even just to get [...] diagnosed and then to get the follow up care that you need." -Patient*
>
> *"Access to treatment is unfairly based on location, money, ability to take time off work and travel, or other factors people cannot control." -Patient*

These systemic challenges in access to support for underserved populations are further exaggerated by the nuanced and complex nature of alloimmunization and HDFN, making self-education and advocacy challenging for those with limited health literacy. In an attempt to offset this, AHF has recently relaunched its website with more inclusive language and has made a concerted effort (through search engine optimization and search ads) to reach audiences more broadly who may be seeking information about antibodies in pregnancy. During the listening sessions, increasing access to resources to patients who do not otherwise know to look for it was a common topic, and some solutions were posed to address this challenge, detailed below.

Learnings: Proposed Solutions

As the discussions around challenges specific to alloimmunization closed, the meeting facilitator guided participants back to the most commonly cited challenges. The groups returned to these needs and offered suggestions for research initiatives and supplemental resources that could best address these gaps.

Research Initiatives

Meeting facilitators took notes throughout the listening sessions as stakeholders proposed solutions through research or other efforts to commonly stated challenges. These were revisited as the session shifted towards a discussion of PCOR-related solutions. **Table 6** below reviews the core challenges, proposed research initiative, and its intended impact (total N respondents = 50). In the post-participation survey, all stakeholders were presented with each of the below research proposals. They were asked to select up to 5 that they believed to be the most important, and up to 5 that they believed to be the most feasible. Note that not all of these initiatives fall in the category of patient-centered outcomes research but are nonetheless significant contributions to the improvement of care practices and outcomes related to alloimmunization/HDFN.

Table 6. Core challenges, research concepts and intended impacts proposed by stakeholders to improve outcomes related to alloimmunization and HDFN.

Importance (N votes)	Feasibility (N votes)	Research concept	Rationale
33	14	Develop, publish and disseminate consensus guidelines for the management of alloimmunization/HDFN during pregnancy and after birth with expert voting committee, systematic literature review and Delphi analysis methods	While a brief guideline is available from the American College of Obstetricians and Gynecologists (ACOG), this is only intended for obstetricians and does not include management information for the MFM in enough detail to properly plan for and accommodate patients with severe disease. There are no known management guidelines for the neonatal management period of HDFN.
25	29	Develop, distribute, analyze and publish a knowledge survey amongst obstetricians regarding their understanding of alloimmunization/HDFN	One previous study has been conducted on provider knowledge of alloimmunization/HDFN in the Netherlands (4), the country with the most prolific publication and strongest

			management protocols for this disease in the world. This study found that only 7% of obstetricians had adequate understanding of alloimmunization/HDFN. A similar finding and call to action amongst US practitioners may assist in improving awareness and shifting clinician attention to improving care practices.
23	5	Develop and launch a virtual nurse navigator/patient advocate program to assign an advocate to enrolled alloimmunized patients in order to facilitate quality, streamlined care; evaluate neonatal morbidity/mortality outcomes and maternal mental health outcomes	A consistent challenge for the alloimmunized patient population is the burden of advocacy and managing their own treatment. This contributes to significant anxiety and other adverse mental health impacts on the patient and increases the risk of preventable fetal morbidity and mortality. Due to the rarity of this disease, isolating patient advocates to specific hospital systems may not be reasonable. Facilitating a virtual program allows for a more sustainable and inclusive program.
22	25	Offer virtual support groups to alloimmunized mothers hosted by patients and mental health professionals based on patient history (e.g., history of loss) or pregnancy phase (e.g., matched by trimester); evaluate neonatal morbidity/mortality outcomes and maternal mental health outcomes	The burden of alloimmunization/HDFN on maternal mental health is overwhelming in this patient population. In light of national mental health provider shortages, a virtual mental health program may provide critical patient support in a sustainable model. Both maternal mental health as well as direct neonatal morbidity/mortality should be measured as stakeholders hypothesize that mothers participating in these groups may feel more empowered in managing their healthcare which may directly impact health outcomes beyond maternal mental health.
21	19	Grassroots outreach to obstetrician offices by patients to share information about alloimmunization/HDFN with	The in-person “lunch-n-learn” model has long been accepted in the private practice and hospital setting. In order to reach obstetrician offices across the

		virtual lecture by AHF Medical Advisory Board member; evaluate provider feedback	nation, trained alloimmunized patients can facilitate outreach directly and offer a virtual lecture by a member of AHF's Medical Advisory Board complemented with the traditional lunch-n-learn model.
21	5	Clinical evaluation and publication of predictors of severe disease such that providers can better manage alloimmunized pregnancies and patients can determine what technical expertise may be required to manage their pregnancy	Currently, the best available indicator of disease severity is the maternal antibody titer. However, this has been demonstrated to fluctuate for unknown reasons, and, conversely, some fetuses born to mothers with extremely high titers are not as severely affected by HDFN as mothers with lower titers. Understanding predictors of severe disease allows the patient the opportunity to coordinate highly specialized care for severe cases.
20	10	Development of a centers for excellence program based on aforementioned best practice guidelines; evaluate outcomes in patients managed at these centers against those who do not	There was significant discussion in the listening sessions around the technical skill required to conduct intrauterine transfusions (IUTs). These specialized fetal procedures were compared to other fetal interventions such as laser surgery for twin-to-twin transfusion. Such interventions are managed at only a handful of fetal centers with high volume. This model has not been implemented in the U.S. for alloimmunization/HDFN but could contribute to improved outcomes in pregnancies requiring IUTs.
15	10	Facilitate a publicly available disease registry with clinician-reported treatment outcomes to aid in patient selection of appropriate clinicians (potentially a reporting requirement among centers for excellence)	Some medical specialties report on procedure-related outcomes and adverse events in a standardized format (5). This model could be implemented for management of alloimmunization/HDFN to allow patients to make informed decisions about the best provider for their condition, and to bolster clinician understanding of predictors of

			preventable morbidity and mortality.
14	18	Launch a national Rh immune globulin education initiative to improve national disease awareness and patient empowerment	Rh immune globulin (often known by the trade name RhoGAM) is the only available preventative treatment to avoid development of Anti-D antibodies, the most commonly developed red cell antibody. It is administered in developed countries to pregnant women with negative blood types. Stakeholders that many women do not realize why they have received this injection which perpetuates a lack of awareness of alloimmunization/HDFN.
13	10	Interview alloimmunization/HDFN pregnancy management experts regarding their IUT techniques and assess findings using the Delphi analysis method; publish results to improve technical understanding of proper conduct of IUTs	Stakeholders agreed that clinicians have little opportunity to develop skill in conducting IUTs. This often leads to preventable fetal morbidity and mortality if an IUT is conducted by an inexperienced clinician. Publishing on the technical aspects of a successful IUT may help improve outcomes or allow clinicians to self-select for their appropriateness to conduct such procedures.
13	21	Facilitate maternal mental health screening through AHF using existing mobile apps and initiate referral to support group or local mental health professional; evaluate impact on maternal mental health outcomes	Stakeholders discussed a lack of access to mental health support and a reluctance to directly disclose feelings of anxiety, shame and depression to their providers. A mental health screening tool offered through AHF could help to flag patients in need of further support.
9	18	Publish case reports/series detailing cases of severe alloimmunization/HDFN	Patients expressed concern that severe and unique cases of alloimmunization/HDFN can result in fetal/neonatal morbidity and mortality that could be prevented with timely monitoring and treatment beyond that which is currently recommended. Shedding light on severe cases and their

			optimal management through publication can provide clinician education and promote awareness of this disease on a broader scale.
9	15	Offer a travel assistance program to alloimmunized mothers with demonstrated need who must travel to receive necessary care; evaluate burden of disease, fetal and neonatal outcomes and maternal mental health	Some stakeholders expressed concern that a byproduct of promoting a centers for excellence model for management of alloimmunization may be inaccessibility to the proper care by patients who are unable to afford childcare and travel. To remedy this, AHF could launch a fundraising campaign to support mothers who require assistance in order to travel to receive appropriate care.
6	9	Morbidity/mortality reviews at specific centers facilitated by AHF and led by the Medical Advisory Board	Some patients, particularly patients who experienced fetal loss, expressed that their clinician or hospital system remain unaware of the way their pregnancy could have been managed differently to prevent fetal death. AHF historically has conducted virtual morbidity/mortality reviews in third world hospital systems as an educational opportunity and a point of closure for the grieving family. Some stakeholders expressed interest in this being offered by AHF upon request and agreement with the local institution.
244	**208**		

As outlined above in the methodology of this report, the proposed initiatives discussed in these listening sessions will be reviewed in a virtual roundtable session with a small group of patients, researchers and providers to isolate short and long-term research goals and map out a funding and execution trajectory.

Other Supportive Efforts

In addition to specific initiatives as described above, stakeholders, largely patients, often requested specific resources be developed and offered to patients and providers.

> *"I do feel like at least for me personally, feeling armed with the right information throughout the care for before delivery and during and after, I feel like some of these feelings of anxiety of guilt they would be off set at least a bit if you could have access to the right information and the proper care." - patient*

The Allo Hope Foundation currently offers the following resources. All resources are developed by AHF staff and reviewed and approved by the Medical Advisory board or Patient Advisory Board as appropriate:

- Provider Primer reviewing disease management in detail
- Clinical decision tree reviewing disease management
- Excellent Care Practices checklist
- Letter to Providers for patients to bring to appointments
- Comprehensive Prenatal Booklet and Newborn Booklet reviewing prenatal and neonatal disease information, management suggestions and interactive spaces for patients to log their records, available by mail for free on request
- Extensive in-depth learning modules on the Allo Hope Foundation website

In addition to the currently available resources which AHF provides, the following supportive content was suggested during the listening sessions. In the post-participation survey, these resource ideas were presented to stakeholders. Some of the resources proposed below were in response to a concern that underserved patients may not seek AHF's resources. A solution to this limitation was to focus on a top-down approach to inform clinicians about disease management and to distribute resources to clinicians to pass along to their alloimmunized patients.

Stakeholders were asked to rate the need for each resource from 1 being the least needed to 5 being the most needed (total N respondents = 50). While most resources were found to be near equally beneficial, the results are displayed below in **Table 7** sorted from highest rated to lowest rated in necessity.

Table 7. Most needed resources to further support patient and provider education surrounding alloimmunization/HDFN management

Resource	Necessity (1 being lowest, 5 being highest)
Accredited continuing education (CE) online course for maternal fetal medicine (MFM) specialists	4.46
Accredited continuing education (CE) online course for obstetricians	4.40
Clinical decision tree for neonatal period	4.40
Accredited continuing education (CE) online course for neonatologists	4.28

Fetal Health Record document where family can complete fetal treatment history to hand off to neonatal/pediatrics team with management recommendations	4.26
Resource document for hematologists/pediatricians regarding the effects of IUTs of newborns with HDFN	4.20
Distilled resource page for HDFN neonatal management	4.12
Insurance "packet" with standard letter and supportive literature to aid with insurance approvals for necessary treatments	4.06
Accredited continuing education (CE) online course for neonatologists	4.04
Mail patient-facing materials to obstetricians such that they can give newly diagnosed patients a resource	4.02
Resource page for blood bankers to improve flagging and recommendations on positive antibody screens	3.82

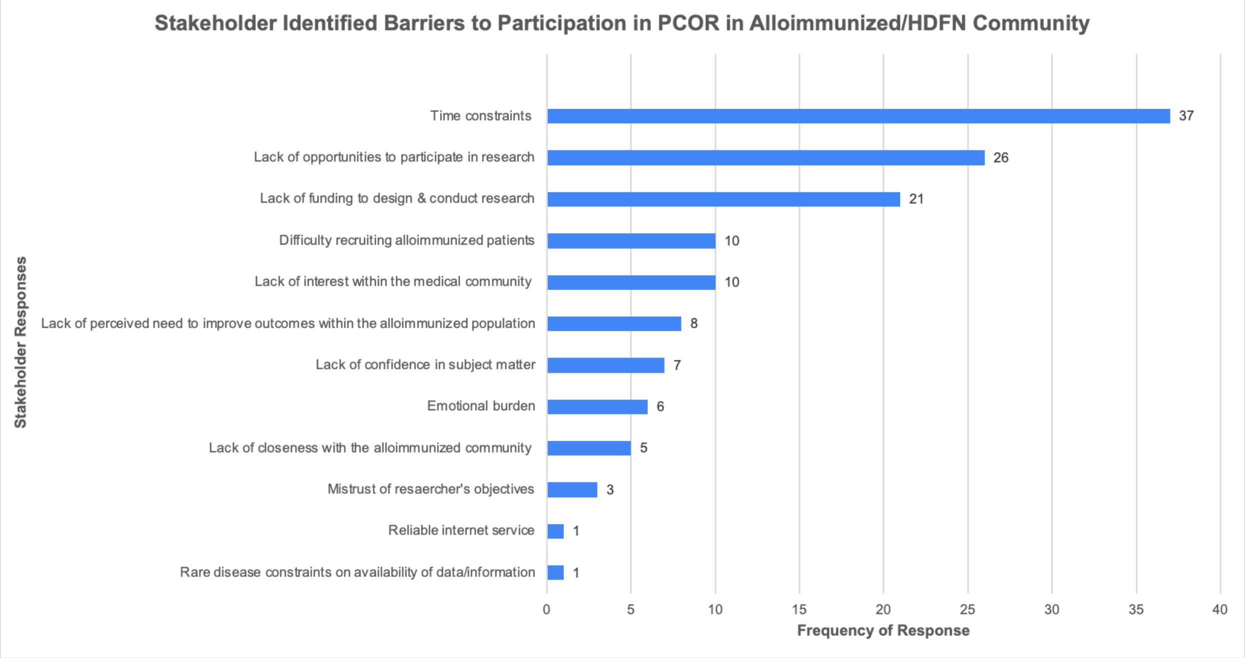
The AHF team will utilize this feedback to generate a selection of new resources in the coming year. AHF has previously engaged potential partners to facilitate the development of accredited CE programs and will discuss the feasibility of these initiatives during the roundtable session slated for phase two of this effort.

Learnings: Barriers to Participating in PCOR

AHF recognizes stakeholder involvement in every aspect of research is necessary to make meaningful and sustainable changes to improve quality of care and outcomes for the alloimmunized/HDFN population. For this reason, stakeholders were asked to share their perceived barriers to participation in PCOR.

As a part of the pre-participation survey, the stakeholders were asked to respond to the following question: *From your perspective and experience, what barriers prevent you from participating in research efforts to improve care in this community? (Answers may differ between patients, clinicians, researchers, industry and others.).* This question allowed multi-selection of responses as well as a free text option. Many participants selected more than one reason. The top three stakeholder identified barriers to participation in research were 1) time constraints, 2) lack of opportunities to participate in research, and 3) lack of funding to design & conduct research. The other barriers to participation in PCOR from the stakeholders' perspectives are detailed below in **Figure 3**.

Figure 3. Stakeholder identified barriers to participation in Alloimmunization/HDFN research (N=60).



The pre-participation survey responses were also shared and discussed with participants during the virtual listening sessions. During these dialogues, stakeholders echoed the same common barriers as depicted in the graph above. Additionally, stakeholders expressed other barriers to participation in research during the listening sessions that were not captured in the pre-participation survey responses.

During a listening session discussion about research ideas to address maternal mental health needs, a clinician expressed the need to get IRB consent for research in some situations which can be challenging to do proactively.

> *"One of the problems with that [...] is that [...] if we're going to publish it which we hope to do, you have to get an IRB consent because it involves mental health and some identifying characteristics. It's hard to get patients to do that ahead of time, but we have come up with a way to do online consenting." -Clinician*

During another listening session, stakeholders were discussing challenges with obtaining insurance approval for certain treatments because of the lack of research publications on those specific treatments. They shared that enrolling the appropriate numbers of study participants is challenging in the rare disease community, which presents a barrier for conducting, and consequently participating in, certain types of research.

> *"[...] the proper type of trial that would be accepted by insurance companies would be a randomized controlled double-blinded trial that no ones ever going to do unfortunately because it's [alloimmunization diagnosis] so rare and you'd need a lot of patients." - Clinician*

Additionally, stakeholders discussed the need for adequate funding to implement research initiatives to improve outcomes in the alloimmunization/HDFN population. The magnitude of this identified barrier to research participation may vary across geographical locations.

> *"[...] we have an organized state collaborative that's funded partly by the [...] state legislature, so we have a budget from the [...] state legislature of about a million dollars a year just to improve maternal-child health outcomes in the state, so if you live in a state that doesn't have something like that, if you're a provider you should try to form something like that, there's about half the states in the country that have some type of state-funded perinatal initiative quality initiative and that's been super helpful." - Clinician*

Identifying and quantifying these barriers serves a critical role in facilitating meaningful and sustainable POCR in the future. The findings enable research teams to proactively address and mitigate these barriers when planning and implementing research initiatives. Nonetheless, despite the numerous barriers stakeholders identified, they in many ways were offset by stakeholders' passion for improving outcomes in the alloimmunized/HDFN community as evidenced from feedback shared below.

Learnings: Facilitators to Participating in PCOR

The stakeholders' willingness to participate in future efforts to improve outcomes in the alloimmunized/HDFN population was evident based on their strong engagement throughout the virtual listening sessions. Post-participation survey responses and listening session discussion transcripts were analyzed to identify common themes of facilitators to PCOR participation. Facilitators were categorized as follows: perceived benefit to self and others in the alloimmunized/HDFN community, ease of access to research opportunities, availability of less expensive research options, trust in the patient-provider relationship, consistent and clear communication, and access to evidence transferable to the alloimmunized/HDFN population. Impactful quotes from stakeholders relevant to each facilitator category are shared below.

Additionally, there was a common sentiment among participants that the research process needs to be flexible and adaptable to accommodate alloimmunized individuals. Many are balancing personal health needs, medical appointments, other family commitments, and work obligations while also managing the emotional and financial stressors of this rare disease. Each facilitator category below should be considered within the context of this sentiment.

Perceived benefit to self and others in the alloimmunized/HDFN community:

> *"Thank you for letting me be a part of this. I feel it is truly important and would love to keep helping in any way!" -Anonymous Post-Participation Survey Response*
>
> *"Thank you for the time and effort that you have all put into advancing care for alloimmunized patients and their families. I am grateful for the work you are doing and look forward to assisting in future research initiatives." -Anonymous Post-Participation Survey Response*
>
> *"This is an amazing working group. I would be pleased to continue collaborating with it and assisting in whatever way would be most helpful." -Anonymous Post-Participation Survey Response*
>
> *"I love being part of this research and discussions! I am excited to work further and hopefully make a difference in this confusing/rare disease. Thank you so much for including me." -Anonymous Post-Participation Survey Response*
>
> *"I would be so willing to find the 10 closest OB offices and [...] I could go and present a pamphlet and present 'I know it's rare, but if you could just keep this in a file for the one day that you see the patient, it would mean a lot to me personally because I have real-life experience.' And if we had a conglomerate of mothers who were willing to do that, I don't know if it would be enough to make a massive difference, but I think [it's] that kind of in-person 'we're coming to you mentality' that this is important. It could make a big difference." -Patient*

Ease of access to research opportunities:

> *"[...] Patients don't always mind traveling if they can get some help getting to a center of excellence, so that should be part of that discussion as you create those [...] how do we get them there because they're going to come more than once."* - Clinician

Availability of less expensive research options:

> *"[...] A lot of what I've heard today kind of jived with my own experience is that there's a lot of low hanging fruit that would be inexpensive research to do to just improve like warning systems, dissemination of guidelines, kinds of studies where you do something like try to implement an automatic warning system for any positive antibody screen on a pregnant person or something like that. [...] there's some low hanging fruit that would probably be almost more impactful because we could have the best therapy in the world and patients still come too late."* -Clinician

Trust in the patient-provider relationship:

> *"I also had a really good team for my IUTs and I think that helped reduce a lot of the trauma for me, knowing that I was in good hands for that treatment part."* -Patient
>
> *"We found that ours [doctor] was very very knowledgeable and very open to the Allo Hope Foundation and she wanted to know more about it and that made me feel like I could trust her a little better."* -Patient
>
> *"Then we made the hard decision in the end to be delivered in [removed] as well, not by my OB who had delivered my two other babies and she just said "I'm sorry. I can't consciously do this, your baby wouldn't even be cared for the way they need to in this NICU." [...] It was a hard thing for her to say to me, she didn't say "I can't treat you, I won't treat you" but she said "I don't know what to do, you need to take this step." So for those doctors to have an understanding and be gracious enough to say that but also bold enough to say that to a patient."* -Patient
>
> *"It's hard to also be an extremely strong advocate in the face of people who are intimidating."* -Patient

Consistent and clear communication:

> *"[...] it was a research hospital and it helped that my MFM was at the same hospital where the NICU was but I think this is a good example of where it can actually work smoothly if all parties involved communicate with each other and share the records and relevant information."* -Patient

Access to evidence transferable to the alloimmunized/HDFN population:

> *"That has been possible with other multidisciplinary conditions. Take for example, traumatic brain injury. [...] Of course, it takes funding to do so, but the brain injury guidelines are a great example to follow to be able to accomplish this [...]."* -Clinician
>
> *"Most physicians are always worried about starting something new that they haven't done before because they're worried about and adverse effects from the therapy, more than they're worried about not adequately treating the disease [...] so what they need is*

some high-quality level of evidence to start to initiate a new therapy that they haven’t started before.” -Clinician

“[...] if we can somehow work together to develop the evidence, not just on new treatments, but on what are your experiences what are the gaps that you can bring very strongly to all kinds of places to convince people and it helps all these efforts[...]” - Patient

Session Effectiveness

The post-participation survey incorporated questions to evaluate the listening session effectiveness. Additionally, further evaluation of session effectiveness will be ongoing throughout the entirety of this capacity building engagement effort (phases one through three). The overall findings will be used to develop an engagement guide for patient advocacy groups with special emphasis on considerations of psychosocial impact of disease management on patients. The engagement guide is intended for alloimmunization/HDFN-specific audiences within stakeholder groups such as patients/caregivers, clinicians, researchers, nonprofit programs, and funding organizations. Dissemination of the engagement guide will be in phase three of this project. This section herein will discuss the post-participation findings used to evaluate the listening session effectiveness in phase one of this project.

Stakeholders were asked to rate their satisfaction with the meeting content in the post-participation survey. The overwhelming majority of respondents "strongly agreed" topics of importance to them were expressed and respected (**Figure 4**), the session enhanced their awareness of the needs of the alloimmunized community (**Figure 5**), and the session met their expectations for content and quality (**Figure 6**).

Figure 4. Participant satisfaction rating of meeting content: Question 1 (N=50)

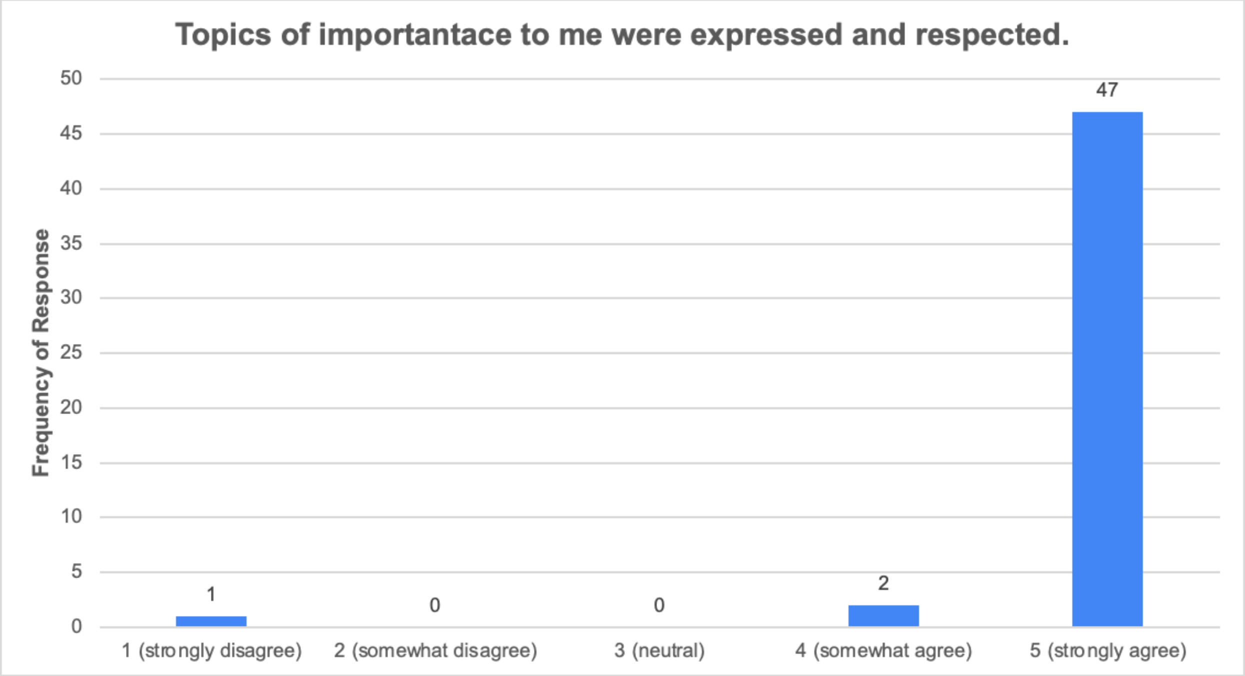


Figure 5. Participant satisfaction rating of meeting content (N=50)

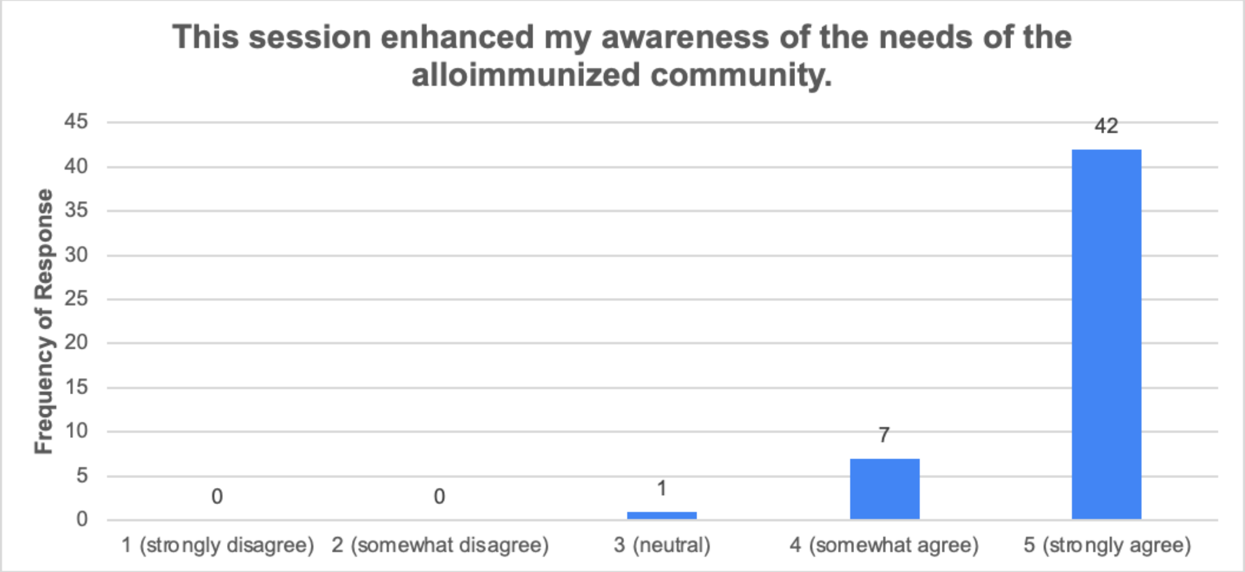
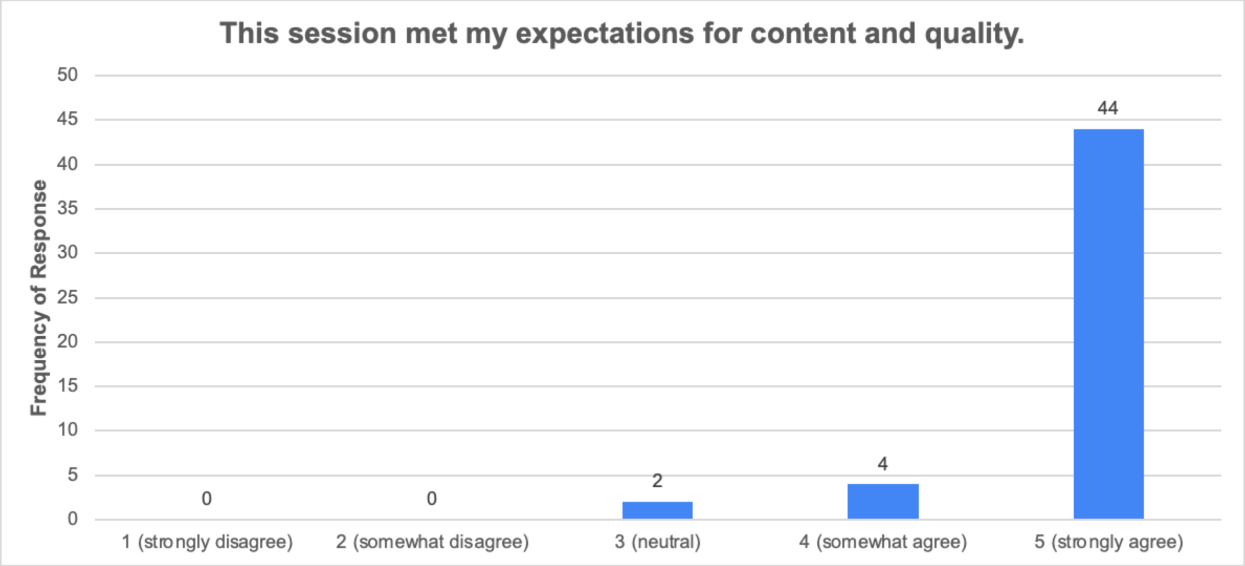


Figure 6. Participant satisfaction rating of meeting content (N=50)



Participants were also asked in the post-participation survey to share one specific thing discussed during the session (by another participant or by AHF) that broadened their perspective on alloimmunization/HDFN. Common themes included learning about both the patient and physician experience, the need for more clinician education, barriers to care, and the mental health impact of the disease among others. Some anonymous participant responses to the survey question are shared below.

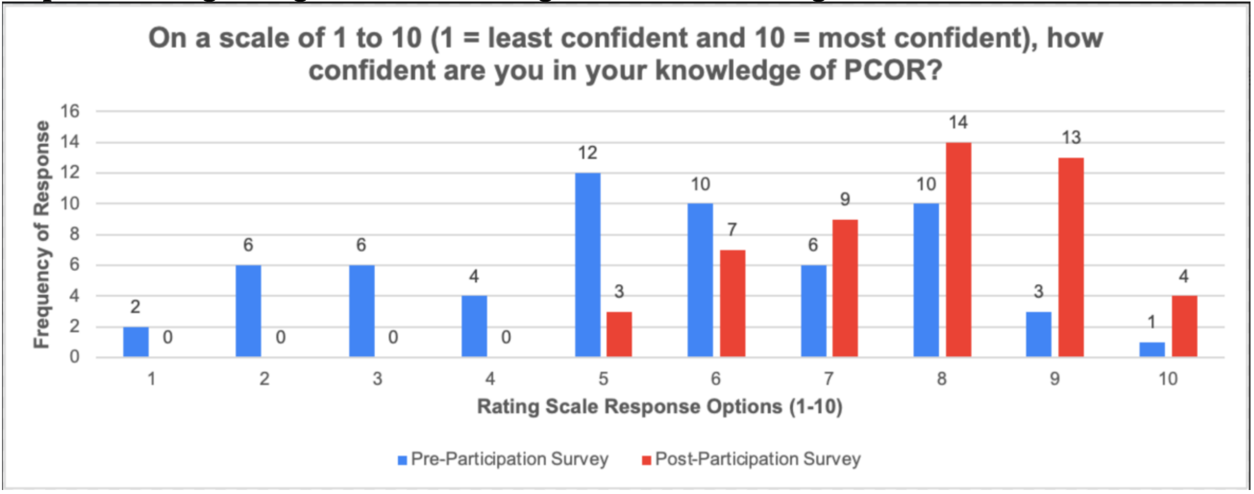
> *"It was interesting to learn more about the patient experience, and how much physician and provider education is still needed in the general obstetrical and MFM community."*

> *"The ongoing need for disease education/awareness for providers."*
>
> *"Social/emotional implications for the whole family."*
>
> *"I hadn't even thought about access to mental health assistance for parents specifically dealing with alloimmunization."*
>
> *"I was shocked to learn that it is not incredibly uncommon for Allomoms to NOT receive mental health assessments during their pregnancies. I completed several assessments at my MFMs office and then post-delivery. This an alarming disservice to any expecting mother, and especially to those having a high-risk pregnancy that can be so unpredictable, volatile and traumatic (physically and mentally). An absence of maternal health assessment (and care) during and after an allo-pregancy is completely unacceptable."*

Additionally, participants were asked in the post-participation survey to share one specific thing that could be improved in future meetings of this nature. The most common responses were related to discussion time management and time constraints on discussions. Some responses suggested longer sessions for more discussion time, others preferred shorter sessions overall, some recommended splitting each session into two sessions to allow for more discussion time, and others proposed incorporating breakout rooms for smaller discussions. The majority of time management recommendations offered ideas to allow more time for meaningful conversations together. Overall, this spectrum of responses emphasizes the need to have more stakeholder discussions in the future, though it will be important to incorporate a variety of discussion formats to meet stakeholder preferences.

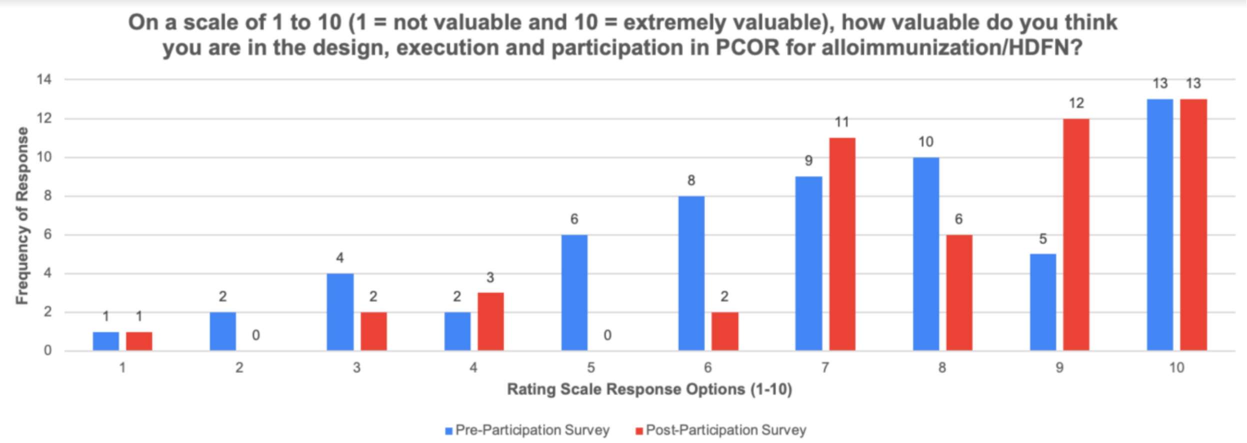
There were three questions in the post-participation survey that were repeated from the pre-participation survey to observe any changes after the sessions. Repeat question one responses (**Figure 7)** demonstrate participants were more confident in their knowledge of PCOR after the listening sessions. Repeat question two responses (**Figure 8**) demonstrate participants' perceived self-value of their involvement in the design, execution, and participation in PCOR for alloimmunization/HDFN increased after the listening sessions. In both the pre- and post-participation surveys, this question was accompanied by the following phrases to reiterate AHF values each stakeholder participating in the listening sessions: *If you are invited to participate in this session, you are valuable. This question is about your perceived value given what you know about PCOR research.*

Figure 7. Pre-participation survey responses* compared to post-participation survey responses regarding confidence rating of PCOR knowledge**



**Total N responses = 60*
***Total N responses = 50*

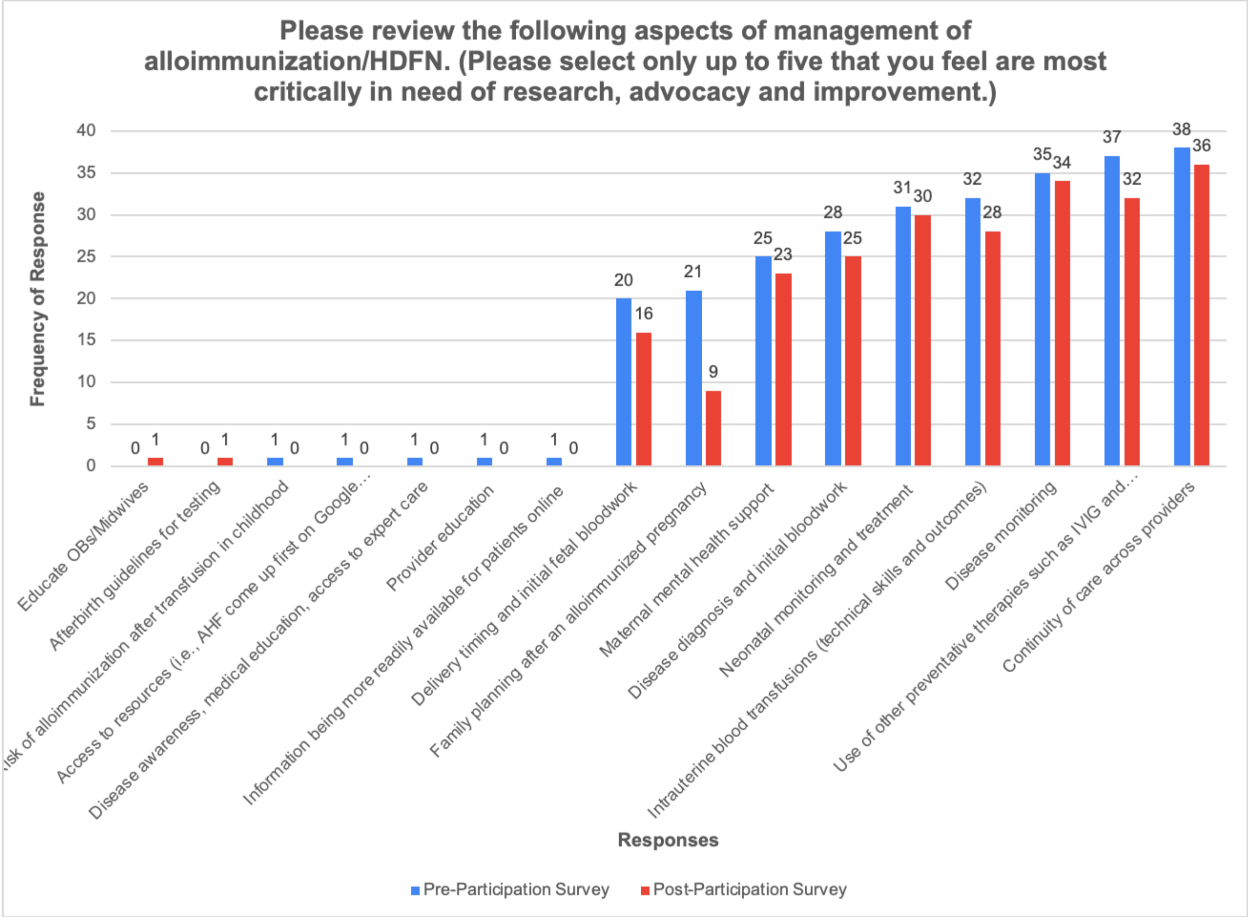
Figure 8. Pre-participation survey responses* compared to post-participation survey responses perceived self-value in PCOR**



**Total N responses = 60*
***Total N responses = 50*

Repeat question 3 asked stakeholders to select up to five alloimmunization/HDFN management aspects most in need of research, advocacy, and improvement in the pre-participation survey. This question allowed multi-selection of responses as well as a free text option, and many participants selected more than one aspect. **Figure 9** demonstrates that stakeholders' responses were similar in the pre-and post-participation survey. Specifically, the top five identified aspects remained the same despite slight variation in the order of importance.

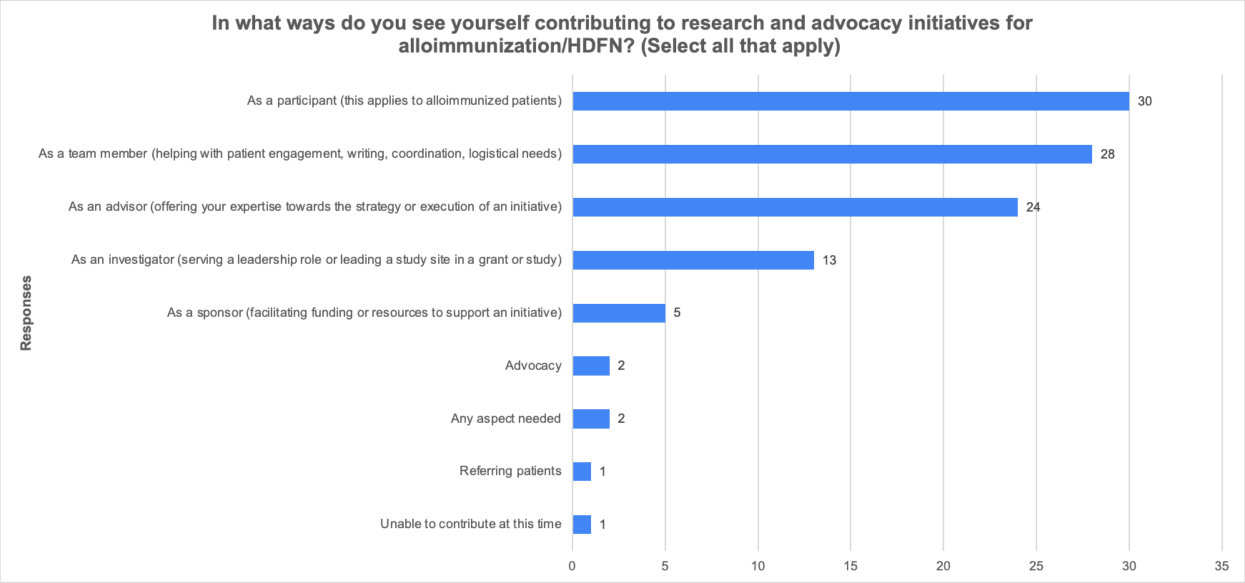
Figure 9. Pre-participation survey responses* compared to post-participation survey responses regarding alloimmunization/HDFN management aspects most in need of research, advocacy, and improvement**



**Total N respondents = 60*
***Total N respondents = 50*

Participants were also asked in what ways they saw themselves contributing to research and advocacy initiatives for alloimmunization/HDFN. It was specified that their responses did not obligate them to contribute to further initiatives, but instead they may be contacted in the future to gauge their interest based on their responses. This question allowed multi-selection of responses as well as a free text option, and participants were instructed to select all that apply. The responses indicate stakeholders are committed to engaging in future research efforts to improve outcomes in the alloimmunization/HDFN community (**Figure 10**).

Figure 10. Post-participation survey responses regarding stakeholder involvement in future research and advocacy initiatives for alloimmunization/HDFN (N=50)



At the close of the post-participation survey, stakeholders were asked if there was anything else they wanted to share. Free text responses were enabled. Stakeholders provided overwhelmingly positive feedback regarding their experiences with the listening sessions. A few anonymous participant responses to the survey question are shared below.

> *"I'm honored to be a part of this."*
>
> *"This was one of the better discussions I have had the opportunity to be involved with. Very good!"*
>
> *"Frequent sessions are necessary and valuable."*
>
> *"Excellent session and discussion!"*
>
> *"Thank you so much for including me. I was so scared during my last pregnancy, and being apart of this gave me the confidence I need to advocate for myself and have future babies. I want women with this condition to feel empowered to advocate for themselves and their babies. Bug me anytime!!"*

Collectively, the post-participation survey responses indicate the listening sessions were impactful to the stakeholders. Further, stakeholders actively shared their perspectives and ideas for the future throughout the entirety of phase one of this project. Their willingness to contribute to the conversation, the thoroughness of their survey responses, and their interest to be involved with future initiatives are testaments to the stakeholders' commitment to improve outcomes in the alloimmunized/HDFN community. It was also evident that the listening sessions created a space for stakeholders to have conversations that really resonated with them. They were empowered to voice their experiences and concerns in a supportive space. As one patient shared during a listening session conversation, *"I apologize that I keep talking, but my heart is racing because this is really specific to my experience."*

Summary

The learnings from the four listening sessions in the first phase of this engagement project provided a multitude of actionable research opportunities. The opportunities determined by stakeholders to be most critical will be reviewed during the next phase of this project, where a virtual roundtable discussion will review the proposed initiatives for alignment with AHF's mission and for feasibility. Funding sources, potential partner sites and collaborators, brief study outlines and timelines will be developed based on this session. Upon completion of the research plan, AHF will shift its attention towards the dissemination of findings and the development of an engagement guide for advocacy groups with special accommodation for navigating disease topics which impose a high degree of mental health burden.

The degree of engagement and enthusiasm from stakeholder participants in this series was robust and productive. AHF attributes this success not only to the strong engagement methodology and experience and passion of the staff, but to the collective commitment from stakeholders in the alloimmunization community who are called to contribute to change. There was consistent, repeated willingness from nearly all stakeholders to offer more time, energy and insight into further research and engagement initiatives to improve quality of care and support to patients navigating alloimmunization and HDFN.

Appendix A

Appendix A includes both the pre-listening session email reminder with instructions to review the educational handout as well as the educational handout.

Pre-listening session email reminder sent to registered participants two days prior to each scheduled listening session:

Hello,

Please find attached the *Pre-Listening Session Educational Handout*. This document includes information on Maternal Alloimmunization/HDFN, Patient Centered Outcomes Research, and planned discussion topics.

Please review this document prior to the scheduled listening session. We also recommend having this document accessible to reference during the session.

Your listening session is [removed date]. *If at all possible, please join the Zoom from a computer rather than a phone.*

Topic: PCORI Listening Session #[removed number]
Time: [removed time]

Join Zoom Meeting: [removed link]

Meeting ID: [removed number]
Passcode: [removed number]

We are looking forward to connecting with you soon!
AHF team

Pre-Listening Session Educational Handout:

Stakeholder Engagement in PCOR/CER Planning in Support of Maternal Alloimmunization/HDFN

Pre-Listening Session Educational Handout

Thank you for your upcoming participation in the upcoming listening session hosted by the Allo Hope Foundation! This document includes information about **1) Maternal Alloimmunization/HDFN**, **2) Patient Centered Outcomes Research,** and **3) Planned discussion topics for the listening session** for review prior to the listening session. You are welcome to bring this document to the listening session to reference as needed.

Purpose of this document: Our goal is to maximize discussion time during the scheduled listening session to learn from each of you. We recognize some people may be quite familiar with maternal alloimmunization/HDFN and patient centered outcomes research language, while it may be completely new to others. Please use this document to familiarize yourself with the content. Doing so will help us create shared language so we can be ready for meaningful discussion. We appreciate the perspectives each of you will bring to the table.

Maternal Alloimmunization/HDFN

Acronyms and frequently used terms specific to alloimmunization/HDFN	
Ascites	Fluid build up in the abdomen as a result of anemia from HDFN.
CBC	Complete blood count: This is a blood draw run on cord blood when baby is born, and includes hemoglobin and hematocrit to check for anemia in babies with suspected HDFN.
cffDNA	Cell free fetal DNA: a blood draw on the mom where fetal DNA circulating in the mother’s bloodsteam is found and tested for certain genetic diseases or, in the case of alloimmunization, tested for a certain antigen. cffDNA is currently offered to check fetal antigen status for the D, C, c, E, K, and Fya antigens.
DAT	Direct agglutination test (also called Direct Coombs test or just Coombs test): A blood test on baby done at birth to see if antibodies are attaching to their red blood cells. A positive Direct Coombs test indicates HDFN.
Erythropoietin	An injection given to some HDFN babies after birth to help stimulate production of new red blood cells.
HDFN	Hemolytic Disease of the Fetus and Newborn (the disease caused by maternal alloimmunization)
Hydrops	Fluid buildup and swelling in multiple locations as a result of advanced HDFN. Hydrops can be prevented with proper treatment (prompt IUTs).
IUT	Intrauterine Blood Transfusion (the only way to provide blood to an anemic fetus in utero)
IVIG	Intravenous Immunoglobulin (a treatment both for the mother and for the baby after birth)
Kernicterus	Permanent brain damage resulting from extremely high bilirubin levels. Kernicterus is preventable with aggressive phototherapy and transfusion.

MCA	Middle Cerebral Artery (a MCA Doppler ultrasound screens for fetal anemia in utero)
MoM	Multiples of the Median (an MoM of 1.5 or higher in an MCA Doppler ultrasound indicates likely fetal anemia and a need to an IUT)
Plasmapheresis	A treatment sometimes used prenatally in conjunction with IVIG in cases of severe alloimmunization whereby plasma (where maternal antibodies are contained) is removed from the mother's bloodstream
Transfusion (top-up)	A procedure where new, antigen negative blood is given to the fetus/newborn
Transfusion (exchange)	More invasive than a top-up transfusion, an exchange transfusion involves removing all of the baby's blood and replacing it with antigen negative donor blood

Key Alloimmunization/HDFN Concepts

Alloimmunization vs. HDFN, which is which?

- Mom's condition: *red cell alloimmunization*
    - Mother has antibodies which may cross the placenta and attach to their baby's blood cells, destroying them
- Baby's condition: *hemolytic disease of the fetus and newborn (HDFN)*
    - The disease that results when mom's antibodies attack baby's red blood cells
    - Hemolytic anemia and hyperbilirubinemia are two major consequences

What can happen to babies with HDFN?

- Most common consequences of HDFN
    - Anemia (measured by hemoglobin/hematocrit)
    - Hyperbilirubinemia (measured by bilirubin)
- Anemia and hyperbilirubinemia can cause…
    - Ascites (fluid buildup in the abdomen)
    - Hydrops (fluid buildup and swelling in multiple locations including organs and abdomen)
    - Kernicterus (brain damage from extremely high bilirubin)
    - Organ failure and death

****With proper, timely treatment, these poor outcomes are avoidable****

How are mom and baby with Alloimmunization/HDFN monitored?

- Monitoring

    - Titers: used to see if antibody level is rising. Considered “critical” if 16 or greater for all antibodies EXCEPT Kell. Kell is considered “critical” if any antibodies are present at all. Once a titer indicates “critical”....
        - MCA Doppler scans: special ultrasounds to look for fetal anemia
        - Results from MCA Doppler scans are measured in Multiples of the Median (MoM). An MoM of 1.5 or higher indicates the baby requires a transfusion for anemia.

What are the treatment options for Alloimmunization/HDFN?

- Treatment in-utero
    - Plasmapheresis and/or intravenous immunoglobulin (IVIG) for very high titers or for history of severe disease beginning in first trimester
    - Intrauterine blood transfusions (IUTs) as soon as 15 weeks in experienced centers
    - Phenobarbital given to mom before delivery to help develop baby’s liver
    - Potential future treatment: nipocalimab (once weekly infusion for mom; currently in development)
- Treatment after Birth
    - Phototherapy to break down bilirubin
    - Top-up transfusion or exchange transfusion for hyperbilirubinemia and/or anemia
    - Intravenous immunoglobulin (IVIG) to help baby process antibodies and bilirubin
    - Erythropoietin to stimulate production of new red blood cells
    - Bloodwork sometimes required for up to 12-15 weeks after birth

Patient Centered Outcomes Research (PCOR)

Term/Acronym	Definition*
Comparative Effectiveness Research (CER)	Studies that compare two or more treatments to find out which is more effective for which people.
Patient-Centered Outcomes Research (PCOR)	A special kind of CER that focuses on answering questions that matter most to patients, caregivers, clinicians, or other healthcare stakeholders. In other words, like CER, PCOR compares two or more treatments to find out which is more effective for which people but it always investigates questions that patients care about.

Stakeholder	Patients, family, caregivers, clinicians, payers, researchers, and anyone else who is invested in health outcomes.

*Reference: https://www.pcori.org/sites/default/files/PCORI-Research-Fundamentals-Approach-PCOR.pdf

For more information on PCOR and the role of stakeholders, review the following:
The PCORI Approach to Patient-Centered Outcomes Research
(https://www.pcori.org/sites/default/files/PCORI-Research-Fundamentals-Approach-PCOR.pdf).

Overview of the Research Process:

1. Developing research questions
2. Designing the research study
3. Planning patient-centered consent and study protocols
4. Sampling, recruiting, and retaining study participants
5. Understanding and sharing research findings

Planned Discussion Topics

We will review, discuss and vote on the aspects of alloimmunization/HDFN monitoring and treatment which require the most improvement. Stakeholders who are not patients or clinicians should offer questions or feedback on any of these items, even if they are new to them. A casual and dynamic discussion is welcomed. These issue areas will fall into the following categories:

1. Diagnosis, initial bloodwork and monitoring
2. Pregnancy interventions for HDFN
3. After birth management for HDFN
4. Continuity of care
5. Hard conversations between providers and patients
6. Maternal mental health during an alloimmunized pregnancy

We will be summarizing the major challenges in alloimmunization/HDFN treatment and monitoring and determining the best way to address these challenges through future research.

Appendix B

Appendix B includes the complete wording of the listening session registration and pre-participation survey questions. These items were both included in one virtual form to be completed online. In this appendix, the survey questions and response options are presented in a table format. All names and personal email contacts for AHF staff have been removed for privacy.

Alloimmunization/HDFN Listening Session Registration
This is an invite-only form for participation in Allo Hope Foundation's PCORI-funded engagement award. The Allo Hope Foundation is conducting a series of listening sessions to discuss the needs of the alloimmunized patient population, barriers to providing and accessing care, and research needs of this population. We welcome patients, clinicians, researchers, industry, and other nonprofit representatives to participate.

This engagement includes completion of:
1) The brief survey below
2) Participation in one two-hour listening session, and
3) One brief 15-minute survey following your listening session.

Upon completion of these three steps, AHF staff will contact you via e-mail to facilitate payment of $[removed] in a paper check to your mailing address.

Event Timing: You will select only one date and time below.
Event Address: All listening sessions will be via Zoom.
Contact us at [removed]

Your e-mail address will be used to send a meeting invite for the listening session and for gathering your mailing address after session completion to mail your compensation. Your email is used for listening session coordination only and will not be shared for any other purpose.

Responses to this survey are reviewed in aggregate and e-mail addresses will be delinked.

[removed - free text box for participants to enter their preferred email]

[removed - "What day and time will you attend? (Sessions last two hours)" multiple choice question with four session options provided]

	Pre-participation survey question and response options	***Format***
1	Select which stakeholder group(s) you identify with. ● Researcher ● Clinician (physician, nurse, and other health professionals) ● Alloimmunized patient ● Industry	Multiple selection checkboxes

	● Nonprofit leader ● Other (free text fill in)	
2	Why are you interested in alloimmunization/HDFN research? ● Personal experience as patient ● To provide better care for my patients ● I know someone who is alloimmunized ● To better understand the disease ● To see how research for rare disease can be operationalized ● Other (free text fill in)	Multiple selection checkboxes
3	Please review the following aspects of management of alloimmunization/HDFN. Please select only up to five that you feel are most critically in need of research, advocacy and improvement. ● Disease diagnosis and initial bloodwork ● Disease monitoring ● Intrauterine blood transfusions (technical skills and outcomes) ● Use of other preventative therapies such as IVIG and plasmapheresis ● Delivery timing and initial fetal bloodwork ● Neonatal monitoring and treatment ● Continuity of care across providers ● Maternal mental health support ● Family planning after an alloimmunized pregnancy ● Other (free text fill in)	Multiple selection checkboxes (up to five total)
4	Please rate how confident you believe providers feel in managing alloimmunized pregnancies in the U.S. (1=least confident, 10=most confident)	Rating scale
5	Please rate how equipped you believe providers are in managing alloimmunized pregnancies in the U.S. (1=least equipped, 10=most equipped) (*An equipped provider has technical expertise to promptly perform necessary procedures, incorporates counsel from other experts, and has enough support staff to execute necessary care and procedures).*	Rating scale
6	Consider the aspects of an equipped provider mentioned above. When thinking about management of alloimmunized pregnancies, what aspects do you believe require the most improvement (1=needs no improvement, 5=needs the most improvement) ● Technical expertise to perform necessary procedures ● Ability to incorporate counsel from other experts ● Access to necessary support staff to execute necessary care and procedures	Rating scale (rating scale applied to each bullet point)

7	Please list the top three emotions (separated by commas) that you believe alloimmunized mothers feel during their pregnancies.	Free text response
8	Keeping the feelings in mind from the previous question, how do you think this impacts activities of daily living during an alloimmunized pregnancy?	Free text response
9	How do you think these emotions affect activities of daily living after experiencing an alloimmunized pregnancy?	Free text response
10	On a scale of 1 to 10 (1=least confident and 10=most confident), how confident are you in your knowledge of patient-centered outcomes research (PCOR)?	Rating scale
11	On a scale of 1-10 (1=not valuable and 10=extremely valuable), how valuable do you think you are in the design, execution and participation in patient-centered outcomes research (PCOR) for alloimmunization/HDFN? *(If you are invited to participate in this session, you are valuable. This question is about your perceived value given what you know about PCOR research).*	Rating scale
12	From your perspective and experience, what barriers prevent you from participating in research efforts to improve care in this community? *(Answers may differ between patients, clinicians, research, industry and others).* Select all that apply. ● Time constraints ● Emotional burden ● Lack of confidence in subject matter ● Lack of opportunities to participate in research ● Lack of funding to design & conduct research ● Mistrust of researcher's objectives ● Lack of closeness with the alloimmunized community ● Lack of interest within the medical community ● Difficulty recruiting alloimmunized patients ● Lack of perceived need to improve outcomes within the alloimmunized population ● Other (free text fill in)	Multiple selection checkboxes

Thank you.

You will be contacted in the next two business days with your meeting invitation to participate in your selected listening session.

Upon participation in the listening session and a 15-minute follow-up survey, AHF's accounts manager will contact you within two business days via e-mail to issue your $[removed]

participation incentive. If you have any questions or concerns related to this participation incentive, please contact [removed name] at [removed email].

DO NOT FORGET TO PRESS "SUBMIT" BELOW.

Appendix C

Appendix C includes the complete wording of the listening session post-participation survey questions. These items were included in one virtual form to be completed online. In this appendix, the survey questions and response options are presented in a table format. All names and personal email contacts for AHF staff have been removed for privacy.

Alloimmunization/HDFN Listening Session Post-Survey

Thank you for participating in the Allo Hope Foundation's PCORI-funded listening sessions. These sessions allowed key stakeholders (patients, clinicians, researchers, industry, and other nonprofit representatives) to gather and discuss the needs of the alloimmunized patient population, barriers to providing and accessing care, and research needs of this population. We thank you for your contributions to these important conversations.

If you have completed the brief pre-survey and participated in one two-hour listening session, **your last step is to complete the brief 10-minute survey by [removed].**

Upon completion of these three steps, AHF staff will issue $[removed] in a paper check to your mailing address on [removed] (please allow time for shipping). If you have corresponded with [removed] to make different arrangements, please know that these are accounted for.

Contact us at [removed]

[removed - free text box for participants to enter their preferred email]

	Post-participation survey question and response options	***Format***
1	Select which stakeholder group(s) you identify with. ● Researcher ● Clinician (physician, nurse, and other health professionals) ● Alloimmunized patient ● Industry ● Nonprofit leader ● Other (free text fill in)	Multiple selection checkboxes
2	Please rate your satisfaction with the meeting content. (1=strongly disagree, 2=somewhat disagree, 3=neutral, 4=somewhat agree, 5=strongly agree) ● Topics of importance to me were expressed and respected. ● This session enhanced my awareness of the needs of the alloimmunized community. ● This session met my expectations for content and quality.	Rating scale (rating scale applied to each bullet point)

3	What was one specific thing discussed during the session (by another participant or by AHF) that broadened your perspective on alloimmunization/HDFN?	Free text response
4	What is one specific thing that could be improved in future meetings of this nature?	Free text response
5	In what ways do you see yourself contributing to research and advocacy initiatives for alloimmunization/HDFN? (This does not obligate you to contribute to further initiatives - you may be contacted in the future to gauge your interest based on your responses today) (Select all that apply) ● As a participant (this applies to alloimmunized patients) ● As a sponsor (facilitating funding or resources to support an initiative) ● As an investigator (serving a leadership role or leading a study site in a grant or study) ● As an advisor (offering your expertise towards the strategy or execution of an initiative) ● As a team member (helping with patient engagement, writing, coordination, logistical needs) ● Unable to contribute at this time ● Other (free text fill in)	Multiple selection checkboxes
6	Initiatives proposed during the sessions are listed in brief below. Please select which you believe are the highest priority, which you believe are the most feasible, and any which you would be willing to contribute to in some capacity (note that checking this box does not obligate you to participate in the future - we will simply include you on future communications for that initiative should it be pursued). *Note - The initiatives were listed in one column. To the right of the initiatives, there were three columns with the following instructions: Select up to 5 in this column that you think are most important; Select up to 5 in this column that you think are most feasible (i.e., easiest to accomplish); Select all that you may be willing to contribute to in the capacity you provided in the previous question.* ● Develop and maintain a national care coordinator/nurse navigator program ● "Grassroots" education for obstetricians through office lunches and virtual presentations ● Develop and maintain an AHF Centers for Excellence program ● Conduct a detailed analysis of necessary steps for successful IUT and publish results ● Develop a publicly available registry where MFMs report on their IUT outcomes	Multiple selection checkboxes

	● Conduct research across alloimmunized pregnancies to better predict why some cases of HDFN are more severe than others ● Partner with apps/online platforms that offer maternal mental health screening and make these tools available to alloimmunized mothers ● Launch online Zoom support groups for alloimmunized mothers matched to their current pregnancy stage or history, measure impact on mental health ● Bring experts together to publish new consensus guidelines on best practices for management of alloimmunization/HDFN ● Education initiative for RhIG prophylaxis (RhoGAM) and knowing your blood type to places such as WIC, low income family health centers, Medicaid offices ● Mail a survey to OBs to determine their knowledge of alloimmunization/HDFN, identify knowledge gaps, and publish results ● AHF to coordinate morbidity/mortality reviews at centers after a fetal death due to HDFN ● Publish case reports on severe disease to inform clinicians ● Establish a program for donors to contribute flight miles, hotel points and resources to women traveling for care	

7	The following resources were discussed during sessions. Please rate how important you believe these resources are. (Note, AHF currently offers a detailed Provider Primer for OBs/MFMs, a comprehensive printed prenatal and newborn booklet, a pregnancy management flow chart, a two-page Letter to Providers with critical information for pregnancy management, and an Excellent Care Checklist to distinguish what should be offered in a well-managed alloimmunized pregnancy). (Rate each bullet point; 1=less important and 5=most important) ● Flow chart for management from pregnancy through infant period ● Continuing education online course for OBs ● Continuing education online course for MFMs ● Continuing education online course for neonatologists ● Continuing education online course for pediatricians ● Brief resource page for newborn period ● "Fetal Health Record" where family can complete fetal treatment history and hand off to neonatologist/pediatrician with recommended next steps ● Mail patient materials to OBs such that they can give newly diagnosed patients a resource ● Resource document for hematologists/pediatricians about the effects of IUTs on newborn HDFN ● Resource page for blood bankers to improve flagging and recommendations on positive antibody screens ● Insurance "packet" with standard letter and supportive literature to aid with insurance approvals	Rating scale (rating scale applied to each bullet point)
The three questions below are repeated from our pre-survey to observe any changes after the sessions.		
8	On a scale of 1 to 10 (1=least confident and 10=most confident), how confident are you in your knowledge of patient-centered outcomes research (PCOR)?	Rating scale
9	On a scale of 1-10 (1=not valuable and 10=extremely valuable), how valuable do you think you are in the design, execution and participation in patient-centered outcomes research (PCOR) for alloimmunization/HDFN? *(If you are invited to participate in this session, you are valuable. This question is about your perceived value given what you know about PCOR research).*	Rating scale
10	Please review the following aspects of management of alloimmunization/HDFN. Please select only up to five that you feel are most critically in need of research, advocacy and improvement.	Multiple selection checkboxes

	• Disease diagnosis and initial bloodwork • Disease monitoring • Intrauterine blood transfusions (technical skills and outcomes) • Use of other preventative therapies such as IVIG and plasmapheresis • Delivery timing and initial fetal bloodwork • Neonatal monitoring and treatment • Continuity of care across providers • Maternal mental health support • Family planning after an alloimmunized pregnancy • Other (free text fill in)	(up to five total)
11	Anything else you would like to share?	Free text response

You have completed the survey. Please proceed to the thank you page for next steps. (You must continue to the next page in order to click "SUBMIT").

Thank you.

DO NOT FORGET TO PRESS "SUBMIT" BELOW

For those interested in participating in future patient-centered outcomes research, this Research Fundamentals training package offers free, easy to understand content to help understand the language and logic of the research process and PCOR.

We acknowledge the full spectrum of emotions the listening session may have brought up and may continue to bring up; please know the Allo Hope Foundation is available to support you through our website and Facebook Support Group as well as the resources below:

- Postpartum Support International
- International Stillbirth Alliance
- Star Legacy Foundation
- Pregnancy After Loss Support
- National Maternal Health Hotline

References

1. Geifman-Holtzman O, Wojtowycz M, Kosmas E, Artal R. Female alloimmunization with antibodies known to cause hemolytic disease. *Obstet Gynecol*. 1997;89(2):272-275. doi:10.1016/S0029-7844(96)00434-6

2. Moinuddin I, Fletcher C, Millward P. Prevalence and specificity of clinically significant red cell alloantibodies in pregnant women - a study from a tertiary care hospital in Southeast Michigan. *J Blood Med*. 2019;10:283-289. Published 2019 Aug 20. doi:10.2147/JBM.S214118

3. Smith HM, Shirey RS, Thoman SK, Jackson JB. Prevalence of clinically significant red blood cell alloantibodies in pregnant women at a large tertiary-care facility. *Immunohematology*. 2013;29(4):127-130.

4. Slootweg YM, Walg C, Koelewijn JM, Van Kamp IL, De Haas M. Knowledge, attitude and practices of obstetric care providers towards maternal red-blood-cell immunization during pregnancy. *Vox Sang*. 2020;115(3):211-220. doi:10.1111/vox.12883

5. Martin GR, Anderson JB, Vincent RN. IMPACT Registry and National Pediatric Cardiology Quality Improvement Collaborative: Contributions to Quality in Congenital Heart Disease. *World J Pediatr Congenit Heart Surg*. 2019;10(1):72-80. doi:10.1177/2150135118815059