Patient Preferences and Experiences in the Treatment of Severe Hemolytic Disease of the Fetus and Newborn: A Mixed-Methods Study

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Background

- Hemolytic disease of the fetus and newborn (HDFN) is caused by an incompatibility between maternal and fetal red blood cell (RBC) antigens, leading to the transfer of maternal alloantibodies to the fetus (Badami et al, 2014; Baker et al, 2021).
  - HDFN can result in severe outcomes such as anemia, hydrops fetalis, and fetal demise.
  - The emotional burden of severe HDFN on affected individuals is significant.
- Once diagnosed, treatment options are limited.
  - Intrauterine transfusions (IUTs) are used to improve fetal survival in severe cases (Sutton and Visintini, 2018), but they carry significant risks such as perinatal mortality, bradycardia, bleeding, and fetal loss (Zwiers et al, 2017).
  - There is a need for effective, less invasive treatments than IUT for severe HDFN.
  - Whether individuals with pregnancies at risk of severe HDFN would accept medical treatment during pregnancy to improve their infant's outcomes depends on both treatment and individual factors.
- This study aims to explore the experiences and treatment priorities of individuals with HDFN-affected pregnancies using a mixed-methods approach.

Methods

- This is a non-interventional study done in partnership with a patient advocacy group (PAG – the Allo Hope Foundation) that employed a mixed-methods approach to explore patient preferences and experiences in the treatment of severe HDFN.
- The Allo Hope foundation recruited participants, provided valuable insights into the patient community, and helped to develop study materials.
- The study consisted of three components:

1. Best-Worst Scaling (BWS) Survey:

- **Objective:** Understand treatment priorities for severe HDFN.
- **Attributes:** Delaying IUT, reducing number of IUTs, birth near/full-term, home administration, structured schedule, preventing NICU hospitalization, reducing complications for baby/mother.
- **Format:** Online questionnaire (on invitation only from Allo Hope).

2. Qualitative Interviews:

- **Objective:** Explore participants' experiences and decision-making and refine TT survey design
- **Discussion guide:** developed by the team and reviewed and approved by Allo Hope, the guide covered diagnosis, monitoring, birth, and post-partum experience.
- **Format:** Semi-structured 1:1 telephone interviews post-BWS survey.

3. Threshold Technique (TT) Survey:

- **Objective:** Measure acceptable trade-offs between benefits and risks of HDFN treatments.
- **Attributes:** Risk of serious infections for the baby, length of NICU hospitalization, risk of serious infections for the mother.
- **Format:** Online questionnaire (on invitation only from Allo Hope), Figure 1.

Figure 1. Example of TT choice task

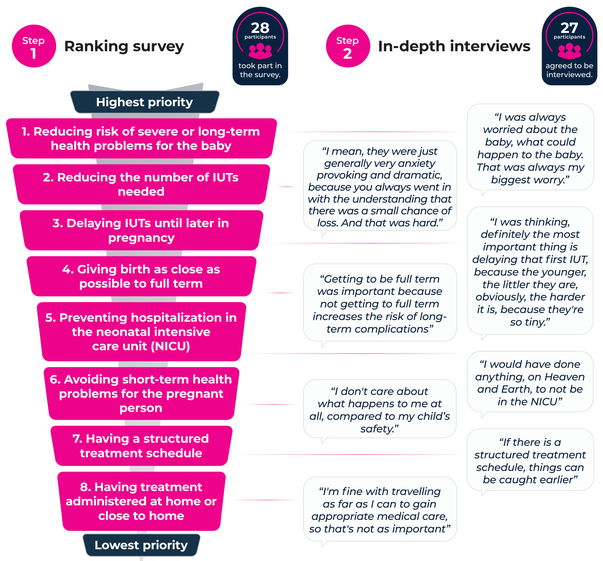
Medicine feature	Medicine A	Medicine B
Number of IUTs needed throughout your pregnancy	4 IUTs	3 IUTs (reduced by 1)
Risk of serious infections for the baby in the first year of life	10% (10 out of 100 babies)	30% (30 out of 100 babies)
Which medicine would you prefer?	○	○

Results

- The descriptive statistics of the participants are summarized below:

Variable	Output
Age (Mean, SD)	34.8, 4.4
Location (N, %)	
US:	26, 92.9%
Canada:	2, 7.1%
Distance from treatment center (N, %)	
Less than 10 miles away:	4, 14.3%
10–49 miles away:	14, 50.0%
50–99 miles:	3, 10.7%
100–500 miles away:	7, 25.0%
Number of visits to treatment center (N, %)	
1–5:	5, 17.9%
6–10:	1, 3.6%
11–20:	2, 7.4%
21–50:	12, 42.9%
50:	8, 28.6%
Longest distance travelled for treatment (N, %)	
Less than 10 miles away:	1, 3.6%
10–49 miles away:	14, 50.0%
50–99 miles:	5, 17.9%
100–500 miles away:	7, 25.0%
500 miles away:	1, 3.6%
Week during which IUT received for most recent pregnancy (N, %)*	
Earlier than week 25:	11, 42.3%
Week 26 or 27:	7, 26.9%
Week 28 or 29:	2, 7.7%
Week 30 or later:	5, 19.2%
I did not receive an IUT in my most recent HDFN pregnancy:	1, 3.9%
Number of IUTs received (Median, Min, Max)**	4, 1, 11
Level of education (N, %)	
Some college or technical school:	7, 25.0%
College graduate:	9, 32.1%
Advanced or graduate/post-graduate degree:	12, 42.9%

- The mean family size was 4.7 members (including parents), mean number of HDFN-affected pregnancies was 4.1 and the mean number of IUTs received in the worst affected pregnancy was 4.5 (qualitative interviews, N = 22-26).



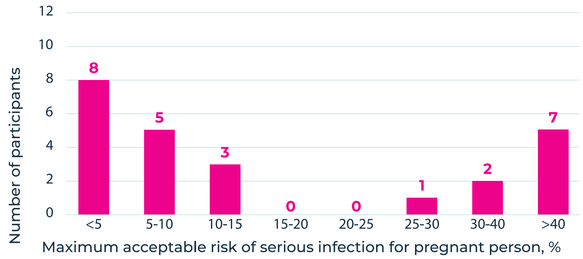
Results (cont'd)

Outcome A: Risk of serious infections for the baby in the first year of life

27 participants took part in the final part of the study.

16 people would be willing to accept up to **15% increased risk** of their child getting a serious infection, relative to the standard of care, to receive 1 fewer IUT.

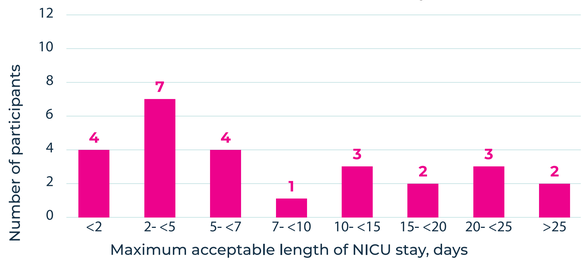
10 people would be willing to accept more than **25% increase in risk** of serious infection for their child, relative to standard of care, to receive 1 fewer IUT.



Outcome B: Length of NICU hospitalization after delivery

The maximum number of days acceptable ranged from under 2 days to more than 25 days.

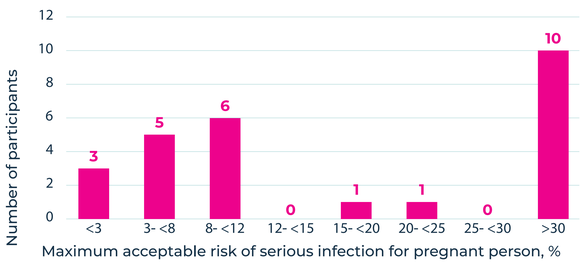
- The most common range was between **2-5 days**, by **7** people.
- **16 out of 25** (almost 2/3) people said they would accept a NICU stay of **up to 10 days** to receive 1 fewer IUT.



Outcome C: Risk of serious infections for the pregnant person that require medical attention

To avoid 1 UT, about half **(13 out of 25)** of the participants would be willing to accept a **0-12% increased risk** of expericing a serious infection.

10 people were willing to accept an **increased risk of more than 30%** relative to the standard of care to avoid 1 IUT.



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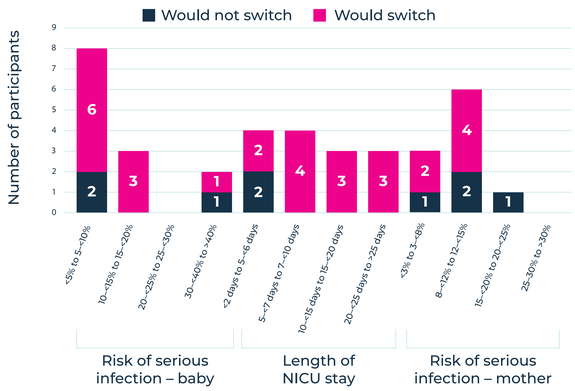

- Among respondents in the TT who picked the lower risk in the last question in each series, more than 75% switched treatment to the higher risk when presented with an increased benefit of a reduction in 2 IUTs rather than 1.

Discussion

- Partnership with the PAG (Allo Hope) was essential to improve and optimize the study protocol, the survey and the recruiting, and to contextualize results.
- **Key Findings based on the integration of the findings from the three methods:**
  - **Neonatal Outcomes:** Preventing severe complications for the baby is paramount; new treatments should prioritize neonatal health.
  - **Support Systems:** Significant emotional and practical burdens highlight the need for comprehensive support, better communication, and reliable information.
  - **Risk Tolerance:** Participants showed higher risk tolerance when benefit increased to a reduction to 2 IUTs rather than 1 (from 4 to 2 rather than 3).
  - **Tailored Plans:** Variability in risk tolerance among participants necessitates personalized treatment plans.

Conclusion

- These insights align with existing literature on the importance of patient-centered care and the need for tailored approaches in managing complex medical conditions.
- By incorporating patient preferences into treatment planning, healthcare providers can improve the overall care experience and outcomes for individuals with HDFN-affected pregnancies.

Disclosure

Marco Boeri, Adele Barlassina, and **Divya Mohan** are employees of OPEN Health. OPEN Health received funding from J&J to conduct the study used to create this abstract. **Ellen Janssen, Alexis Krumme, Laura Bozzi** are employees of Johnson & Johnson, the sponsor of this study, and own company stock/stock options. All authors participated in the design of the study, in the analysis and interpretation of data, and in creating this poster.

References

Badami KG, Parker J, Kenny A, Warrington S. Incidence of maternal sensitisation to rh (d) in christchurch, new zealand and reasons for prophylaxis failures. NZ Med J. 2014;127(1388):40-6.

Baker JM, Campbell DM, Pavenski K, Gnanalingam A, Hollamby K, Jegathesan T, Zipursky A, Bhutani V, Sgro M. Infants affected by rh sensitization: A 2-year canadian national surveillance study. Paediatrics & Child Health. 2021;26(3):159-65.

Sutton D, Visintini S. Off-label use of intravenous immunoglobulin for neurological conditions: A review of clinical effectiveness. Canadian Agency for Drugs and Technologies in Health, Ottawa (ON); 2018.

Zwiers C, van Kamp I, Oepkes D, Lopriore E. Intrauterine transfusion and non-invasive treatment options for hemolytic disease of the fetus and newborn–review on current management and outcome. Expert review of hematology. 2017;10(4):337-44.