

Targeted Literature Review to Explore the Patient Experience of Hemolytic Disease of the Fetus and Newborn (HDFN)

AUTHORS: Jennifer Norma Barthelmes,^{1*} Katie Mellor,² Andras Borsi,³ Chris Marshall,²

AFFILIATIONS: ¹Janssen Cilag GmbH, Germany; ²Clinical Outcomes Assessment, Clarivate, UK; ³Janssen Cilag, UK

Background

- Hemolytic Disease of the Fetus and Newborn (HDFN), is a red blood cell disorder in which maternal alloantibodies attack the red blood cells of fetuses and newborn babies¹
- HDFN can have critical outcomes for infants such as anemia, organ damage or death
- Although HDFN is asymptomatic for mothers, it may negatively impact maternal emotional wellbeing and psychosocial functioning^{1,2}
 - Positive antibody screening results are associated with perinatal anxiety in women as they undergo further monitoring to assess HDFN risk²
- Patient-reported outcome (PRO) measures assess patients' perceptions of how they feel and function, for example evaluating mental well-being and ability to perform daily tasks
- Regulatory and best practice guidance outlines the need to ensure that PRO measures used in clinical trials are fit-for-purpose in the context of use and population of interest³⁻⁵
- Currently, no fit-for-purpose PRO measures exist to assess HDFN-related emotional/psychological burden to mothers
- The first step in providing evidence that a PRO measure is appropriate for the population of interest is to obtain an understanding of the patient experience of HDFN

Objectives

- A targeted literature review was conducted to identify qualitative patient experience data and determine outcomes of importance to characterize the maternal experience of HDFN

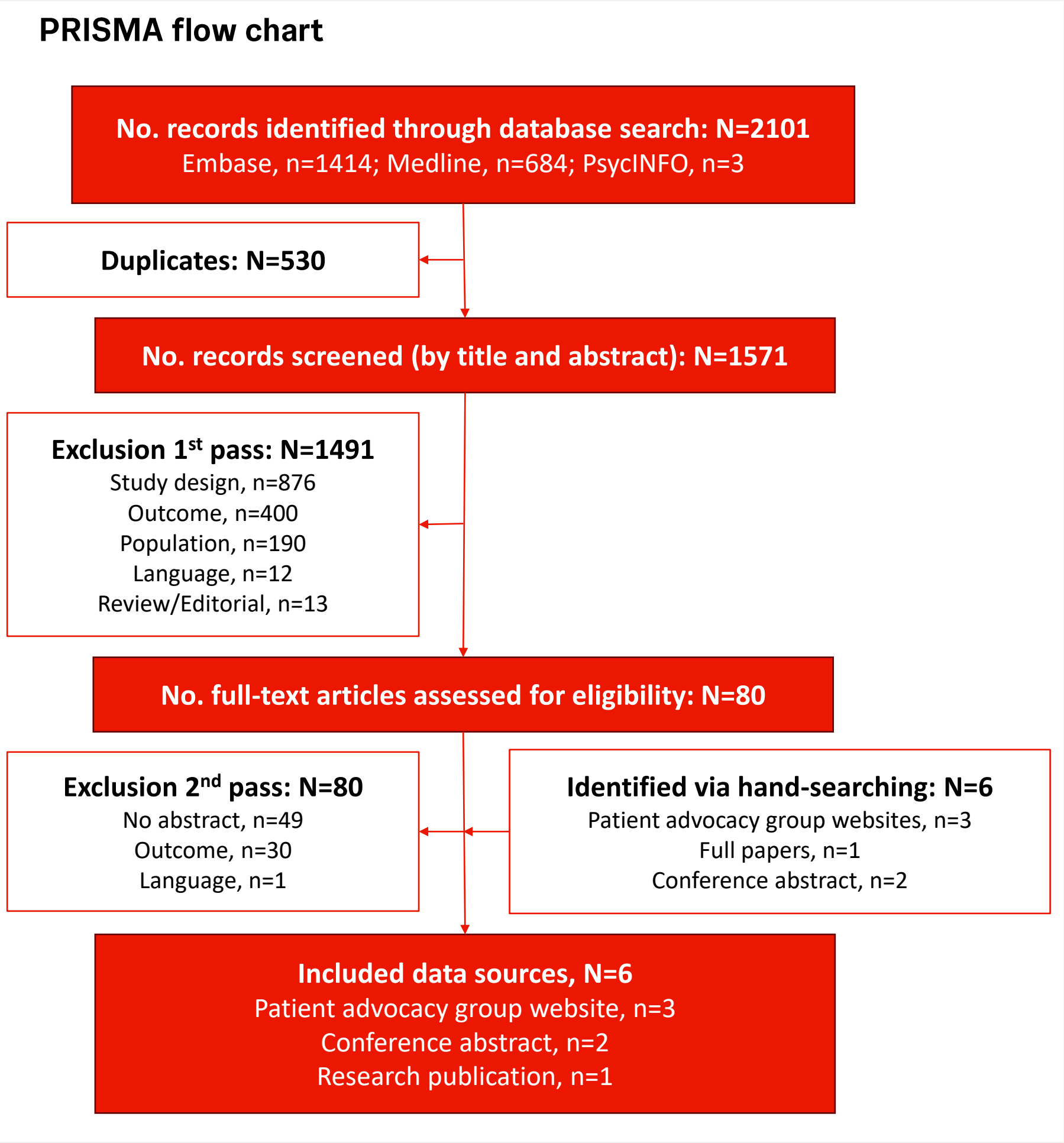
Methods

- Data sources searched through Ovid (in February 2024) included:
 - Embase, Medline and PsycINFO
 - Hand-searching of: FDA & EMA Websites for relevant meetings, workshops or forums; reference lists of included studies; patient advocacy group websites or online forums
- Eligible sources described the maternal experience of HDFN, including descriptions of symptoms, side effects, and health-related quality of life
 - Publications were not restricted by date

Results

Identified records

- A total of 1571 unique data sources were identified through the database searches; none were eligible in the initial database search
- Six records were identified through unautomated hand-searching
- No qualitative research publications in an exclusively HDFN population were identified
- Findings are primarily based on data obtained from blogs or stories written by patients and published on publicly available patient group websites, and findings of relevant qualitative research studies published in conference posters



Summary of included data sources		
	N	Description
Patient advocacy group website patient written blogs or stories	3	Three patient advocacy group websites: Alloimmunization ⁶ , Fetal Health foundation ⁷ and Allo Hope Foundation ⁸
Conference abstract	2	Two conference abstracts presented at ISPOR 2024 ^{9,10} describing the findings of qualitative research to explore patient experience of HDFN in a US patient sample
Research publication	1	A controlled longitudinal survey describing attitudes towards prenatal screening ²

Key findings

- Impacts were identified across five domains: Emotional functioning, Physical functioning, Social, Family planning and Work
- Anxiety[†] was identified across all six records as a key concept to the maternal experience of HDFN; primarily related to the current pregnancy, but also regarding future pregnancies and family planning

Domain	Concepts	Illustrative quotes (all patient reported)
Emotional functioning	<ul style="list-style-type: none">AngerAnxiety and worry[†]ConfusionDepressionDisconnection from babyExtreme distressFearGuiltHelplessnessSadnessShockUncertainty	<ul style="list-style-type: none"><i>“I felt anxious and afraid of what was happening. I didn’t have experience in advocating for medical care”</i>⁶<i>“This diagnosis crushed us. My husband and I wanted a lot of children, and now we were left wondering whether we could even have a second.”</i>⁶<i>“I already felt extremely guilty and worried about things like, ‘did I miss a knock to my bump?’”</i>⁸<i>“I had an anxiety attack post procedure while I was still being monitored—scary!”</i>⁸
Physical functioning	<ul style="list-style-type: none">Bodily pain and/or discomfortDifficulty with normal exercise and activitiesFatigue, tiredness, and reduced energy levelsMobilitySelf-care	<ul style="list-style-type: none"><i>“You know, um, the days that I got the IVlg, I would just come home and try to wr- wrap up my work day and rest, and then those days were usually the worst days just in terms of just physically and mentally just feeling so tired, um, so tired from it.”</i>¹⁰
Social	<ul style="list-style-type: none">Impact (positive and negative) on relationships (with partner, other children, family, friends)Support networks	<ul style="list-style-type: none"><i>“Having a support network is a must! [...] I was so upset after reading Dr Google and not knowing what to expect. My mum found the Facebook page and the information there cleared up so much stuff.”</i>⁸
Family planning	<ul style="list-style-type: none">Advice from medical professionals (both positive and negative)Decisions about future pregnancies (both positive and negative)	<ul style="list-style-type: none"><i>“We have decided not to have any more children based on the anti-K antibodies.”</i>⁸<i>“[M]y maternal fetal specialist had pretty much told me it probably wasn’t a good idea [to have another baby]. So I don’t think I ever really seriously thought about it.”</i>⁹
Work	<ul style="list-style-type: none">AbsencePerformance declineSupport needs	<ul style="list-style-type: none"><i>“For my ultrasounds, I thankfully didn’t need to take off an entire day, but I was gone for at least 2 hours of my workday. Um, obviously nobody does ultrasounds after business hours, so (laughs)... Um, for my procedures, they were a full-day thing. And so I had to take an intermittent leave...”</i>¹⁰

References:

1. Delaney M, et al. *Hematology Am Soc Hematol Educ Program*. 2015;(1):146-151. 2. Koelewijn JM, et al. *BMC Pregnancy Childbirth*. 2008;8:49. 3. Food and Drug Administration (FDA). Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. 2009. 4. Patrick DL, et al. *Value in Health*. 2011;14(8):967-77. 5. Patrick DL, et al. *Value in Health*. 2011;14(8):978-88. 6. <https://www.alloimmunization.org/> 7. <https://www.fetalhealthfoundation.org/> 8. <https://allohopefoundation.org/> 9. Pease S, et al. *ISPOR 2024. Value in Health*. 2024;27(6):S1 10. Scippa K, et al. *ISPOR 2024. Value in Health*. 2024;27(6):S1

Presented at: International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe Annual Meeting; Nov 17-20, 2024; Barcelona, Spain

Key takeaway



Limited qualitative data exist to describe the patient experience of HDFN and inform the development or validation of PRO measures

Conclusions



A diagnosis of HDFN is known to cause increased levels of maternal anxiety



It is challenging to discern the additive impact of HDFN-induced anxiety from any existing pregnancy-associated anxiety



The true extent of HDFN-related maternal impacts is unknown due to limited published qualitative data, possibly due to the summative challenges of conducting research during pregnancy and in a rare condition



Qualitative research has been initiated to provide insight into the patient experience of HDFN and identify relevant outcomes for future patient-centered research^{9,10}, however future qualitative research, in a global sample, is recommended

Acknowledgments

This study was sponsored by Janssen Global Services, LLC. Review of the poster abstract was provided by Lori Alquier, Marie Fitzgibbon, May Lee Tjoa, Sheryl Pease and Jannine Williams, all employees of Janssen Global Services.

Disclosures

JNB and AB are employees of Janssen Global Services, KM and CM are employees of Clarivate, which received funding from Janssen for this analysis.

Hemolytic Disease of the Fetus and Newborn (HDFN)