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ORIGINAL RESEARCH

TRANSFUSION

# Receipt of RhD-positive whole blood for life-threatening bleeding in female children: A survey in alloimmunized mothers regarding minimum acceptable survival benefit relative to risk of maternal alloimmunization to anti-D

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## Abstract

**Background:** Low-titer group O whole blood (LTOWB) for treatment of hemorrhagic shock sometimes necessitates transfusion of RhD-positive units due to short supply of RhD-negative LTOWB. Practitioners must choose between using RhD-positive LTOWB when RhD-negative is unavailable against the risk to a female of childbearing potential of becoming RhD-alloimmunized, risking hemolytic disease of the fetus and newborn (HDFN) in future children, or using component therapy with RhD-negative red cells. This survey asked females with a history of red blood cell (RBC) alloimmunization about their risk tolerance of RhD alloimmunization compared to the potential for improved survival following transfusion of RhD-positive blood for an injured RhD negative female child.

**Study Design and Methods:** A survey was administered to RBC alloimmunized mothers. Respondents were eligible if they were living in the United States with at least one red cell antibody known to cause HDFN and if they had at least one RBC alloimmunized pregnancy.

**Results:** Responses from 107 RBC alloimmmunized females were analyzed. There were 32/107 (30%) with a history of severe HDFN; 12/107 (11%) had a history of fetal or neonatal loss due to HDFN. The median (interquartile range) absolute improvement in survival at which the respondents would accept RhD-positive transfusions for a female child was 4% (1%–14%). This was not

**Abbreviations:** CT, component therapy; HDFN, hemolytic disease of the fetus and newborn; IQR, interquartile range; IRB, institutional review board; IUT, intrauterine transfusion; LTOWB, low-titer group O whole blood; RBC, red blood cell; US, United States.

  

different between females with and without a history of severe or fatal HDFN ($p = .08$ and 0.38, respectively).

**Conclusion:** Alloimmunized mothers would accept the risk of D-alloimmunization in a RhD-negative female child for improved survival in cases of life-threatening bleeding.

**KEYWORDS**

alloimmunization, anti-D, HDFN, hemolytic disease of the fetus and newborn, hemorrhage, low titer group O whole blood, LTOWB, Rh disease, Rh-positive blood, transfusion, whole blood

## 1 | INTRODUCTION

Improving outcomes in children with life-threatening bleeding is critical as mortality rates are higher than in adults. Mortality rates in children with severe bleeding from trauma or medical etiologies range between 36% and 60%,[1] whereas in adults with trauma it ranges between 20% and 24%.[2] Death from traumatic hemorrhage is the most common preventable cause of death after injury due to inadequate or delayed care.[3–6]

Hemostatic resuscitation is a blood-based approach to the treatment of hemorrhagic shock where blood product administration is prioritized over crystalloid and colloid fluids. In the United States, these blood products are administered in either a balanced ratio of blood components or with low titer group O whole blood (LTOWB).[7–10] Based on emerging evidence that demonstrates potential efficacy and safety, LTOWB is now utilized in over 300 US trauma centers in both adults and children with hemorrhagic shock.[5,6,11] Studies in adults and children indicate an independent association with improved 24-hour or 28-day survival.[12–16]

A primary concern related to transfusion of LTOWB is the lack of RhD-negative LTOWB units for use in females of childbearing potential, which also includes children, due to the scarcity of this product. As a consequence, it is sometimes necessary to use RhD-positive LTOWB in instances where recipient's RhD type is unknown, as their blood type often cannot be ascertained within the time necessary to initiate type-specific lifesaving transfusion. An alternative would be to not use LTOWB and use component therapy that includes Rh-negative RBCs, but for the 300 plus trauma centers in the US that have decided to use LTOWB for its potential survival benefit the choice is between a possible acute benefit versus a possible long-term risk. Transfusion of RhD-positive blood products in RhD-negative recipients can potentially result in D-alloimmunization at reported rates of approximately 8%–35% during trauma resuscitation.[17–19] In cases where a fetus in a subsequent alloimmunized pregnancy inherits an incompatible paternal red cell antigen, the maternal RBC antibodies can cross the placenta and attach to the fetal red cells resulting in fetal anemia and even fetal death. This entity is known as hemolytic disease of the fetus and newborn (HDFN). Pregnancy management for a fetus at risk for HDFN includes monitoring through middle cerebral artery Doppler ultrasound and, if required, intervention for fetal anemia through serial intrauterine transfusion (IUT). After birth, neonates with HDFN may require phototherapy, simple or exchange transfusion until maternal antibodies are cleared from neonatal circulation. A recent predictive model calculated the risk of perinatal death from HDFN to be 0.04% in females who are transfused with RhD-positive blood products during their trauma[20]; other models have found future pregnancy risks from HDFN to occur between 0.3% to approximately 6% depending on the inclusion of mild or moderate cases of HDFN, among other parameters.[20–23]

The Allo Hope Foundation is a patient advocacy organization for families affected by red cell alloimmunization and their clinicians. The Foundation educates alloimmunized females about their condition and how to find the best care to treat HDFN and reduce the risk of preventable perinatal neonatal morbidity and mortality. Individuals connected with this organization have a unique understanding of RBC alloimmunization and might also have firsthand experience with its impact on their lives and pregnancies. Their opinion provides valuable insight into the risks that patients will assume in accepting RhD-positive LTOWB during their resuscitation from massive bleeding. The objective of this study was to survey females associated with the Allo Hope Foundation who had at least one RBC alloimmunized pregnancy at risk for HDFN on their willingness to accept RhD-positive LTOWB if RhD-negative LTOWB is not available relative to the risk of future HDFN complications for a female child experiencing life-threatening hemorrhage.

## 2 | STUDY DESIGN AND METHODS

This survey study was approved and classified as minimal risk by the IRB at the University of Pittsburgh (Study 21120095). Recruitment took place in June and July 2023. The Allo Hope Foundation maintains a database of females who have previously opted in to be contacted for participation in research studies; these females were sent an email that introduced the survey and provided a weblink to access the survey. Survey invitations were also made available in the Allo Hope Foundation's online patient support group. Unique responses were identified by email addresses. Respondents were eligible to participate if they were adults living in the United States with at least one red cell antibody known to cause HDFN and if they had at least one completed alloimmunized pregnancy that ended in live birth or fetal death. Participation was voluntary with informed consent. Participants who completed the survey were compensated with a $50 gift card. Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at the University of Pittsburgh. REDCap is a secure, web-based software platform designed to support data capture for research studies.[24,25]

This survey was modeled utilizing the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) to reduce risk of bias.[26] The survey was piloted for clarity and content in three alloimmunized patients. Survey questions included demographic questions and pregnancy history. Participants were asked what HDFN treatments they or their children have received, if they had lost children to HDFN, whether they had female children, and the RhD-type of their children, if known. Alloimmunization history including the specificity(ies) of red cell antibody(ies), treatment history, and fetal and neonatal outcomes were also queried. Severe HDFN was defined as a history of fetal or neonatal death due to HDFN or HDFN treatment complications (i.e., complications from IUT), fetal or neonatal hydrops, or receipt of an IUT.

Participants were presented with a scenario where an RhD-negative female child could be offered RhD-positive LTOWB during a massive hemorrhage if RhD-negative product was unavailable. A baseline mortality rate of 24% was used based on the available literature[2] and respondents were asked to shift a slider icon to the percent mortality risk that they would accept if RhD-positive blood was given to their RhD-negative female child, given their understanding of the implications of potential RhD-alloimmunization (Appendix). Only complete questionnaires were analyzed. Survey respondents who completed the survey within 1 min or less were contacted by email to confirm their legitimacy. Those who did not confirm legitimacy were excluded from analysis. Respondents with at least one completed alloimmunized pregnancy were included in the analysis.

Due to feedback from several participants and a wide range of responses that may have been due to a lack of comprehension of the question being posed or the response method, investigators sent two clarification emails to all survey participants. The purpose of these emails was to rephrase the mortality reduction to that of improvement in a survival benefit. Investigators asked respondents to either verify that their initial response remained the same or change their response given the additional clarity provided on the intent of the question.

Descriptive analysis was conducted in Microsoft Excel (Irvine, CA). Parametric data are described as mean (standard deviation). Nonparametric data are described as median (interquartile range, IQR). SAS (Cary, USA) 9.4 was used for risk reduction assessment within demographic or pregnancy history groups. Wald Chi-squared tests compared the risk reduction scores that were fewer than or equal to the median (0%–4%) or above the median (≥5%), while Wilcoxon tests assessed median survival benefit scores continuously. Responses were grouped when necessary to avoid identifiability.

## 3 | RESULTS

Email invitations with the survey link were sent to 126 Allo Hope Foundation members and 78/126 (62%) members of the email group responded. The additional respondents were alloimmunized females who saw the survey advertisement on the Allo Hope Foundation online patient support group, which requires verification of alloimmunization prior to joining. Fifty-seven responses were determined to be invalid (three duplicate email addresses, 54 with a survey completion time of 1 min or less). A total of 117 validated users initiated the survey and a total of 110 participants completed the survey. Three respondents were currently pregnant with their first alloimmunized pregnancy (i.e., the pregnancy was not complete) and were excluded from analysis for a total of 107 responses. The average (±standard deviation) age at time of survey completion was 34 (±4) years and 82/107 (77%) had at least one female child. Additional demographics are listed in Table 1.

The various antibodies that complicated the respondents' pregnancies are reported in Table 2. Multiple antibodies were present in 52/107 (47%) of the respondents. The most commonly reported red cell antibody was anti-D (47/107, 44%). Perinatal and neonatal treatment history for HDFN is reported in Table 3. A history of severe disease was reported in 32/107 (30%) of responses and 12/107 (11%) had a history of fetal/neonatal loss.

**TABLE 1** Participant demographics and pregnancy history.

| | Participants ($N = 107$) | |
|---|---|---|
| | ***N*** | **%** |
| Race | | |
| White | 101 | 94% |
| Non-White | 6 | 6% |
| Education | | |
| Some high school or high school graduate | 25 | 23% |
| Associate or Bachelor's degree | 50 | 47% |
| Master's degree | 24 | 22% |
| Doctorate or other professional degree | 8 | 7% |
| Annual household income | | |
| $0–60,000 | 21 | 20% |
| $60,001–90,000 | 25 | 23% |
| $90,001–120,000 | 20 | 19% |
| >$120,000 | 41 | 38% |
| Number of completed alloimmunized pregnancies[a] | | |
| 1 | 51 | 46% |
| 2 | 37 | 37% |
| 3+ | 19 | 18% |
| History of child with severe HDFN | | |
| Yes | 32 | 30% |
| No | 75 | 70% |
| History of fetal or neonatal death from HDFN | | |
| Yes | 12 | 11% |
| No | 95 | 89% |
| Number of female children[b] | | |
| 0 | 25 | 25% |
| 1 | 34 | 31% |
| 2 | 28 | 25% |
| 3+ | 20 | 19% |

[a]Participants were asked, "How many completed alloimmunized pregnancies have you had that progressed beyond 12 weeks (meaning pregnancies that are now over)? This includes pregnancies monitored for hemolytic disease of the fetus and newborn (HDFN), even if the baby was later determined to be antigen negative."
[b]Includes female children in both alloimmunized and non-alloimmunized pregnancies.

**TABLE 2** Red cell antibody prevalence among survey participants.

| | Participants ($N = 107$) | |
|---|---|---|
| | ***N*** | **%** |
| Antibody prevalence | | |
| Multiple antibodies | 52 | 47% |
| One antibody | 55 | 53% |
| Specific antibody[a] | | |
| Anti-D | 47 | 44% |
| Anti-E | 41 | 38% |
| Anti-C | 22 | 21% |
| Anti-c | 22 | 21% |
| Anti-K | 17 | 16% |
| Anti-Fya | 9 | 8% |
| Anti-Jka | 7 | 7% |
| Anti-G | 4 | 4% |
| Anti-S | 3 | 3% |
| Anti-k | 2 | 2% |
| Other | 7 | 7% |

[a]Values do not sum to 100% because some participants had more than one red cell antibody.

**TABLE 3** Perinatal and neonatal hemolytic disease of the fetus and newborn (HDFN) treatment histories among survey participants.

| | Participants ($N = 107$) | |
|---|---|---|
| | ***N*** | **%** |
| Perinatal treatments | | |
| Intrauterine blood transfusion | 26 | 24% |
| Intravenous immune globulin | 14 | 13% |
| Phenobarbital | 7 | 7% |
| Plasmapheresis | 5 | 5% |
| Neonatal HDFN treatments | | |
| Phototherapy | 67 | 63% |
| Intravenous immune globulin | 32 | 30% |
| Top-up transfusion | 33 | 31% |
| Exchange transfusion | 10 | 9% |

The median improvement in survival that would justify receipt of RhD-positive LTOWB transfusion in an Rh-negative female child was 4%; that is, from 76% to 80% (range 0%–24%; IQR 1%–14%); this was not changed after the question was clarified via email. There were 70/107 (65%) respondents who replied to the clarification emails and either verified their response or changed their response. Of these 70, 28/70 (40%) respondents changed their initial answer, while 42/70 (60%) verified their initial response. The final response distributions are demonstrated in Figure 1 for the total cohort and those with a history of severe and fatal HDFN.

The absolute improvement in survival at which alloimmunized mothers would accept Group O

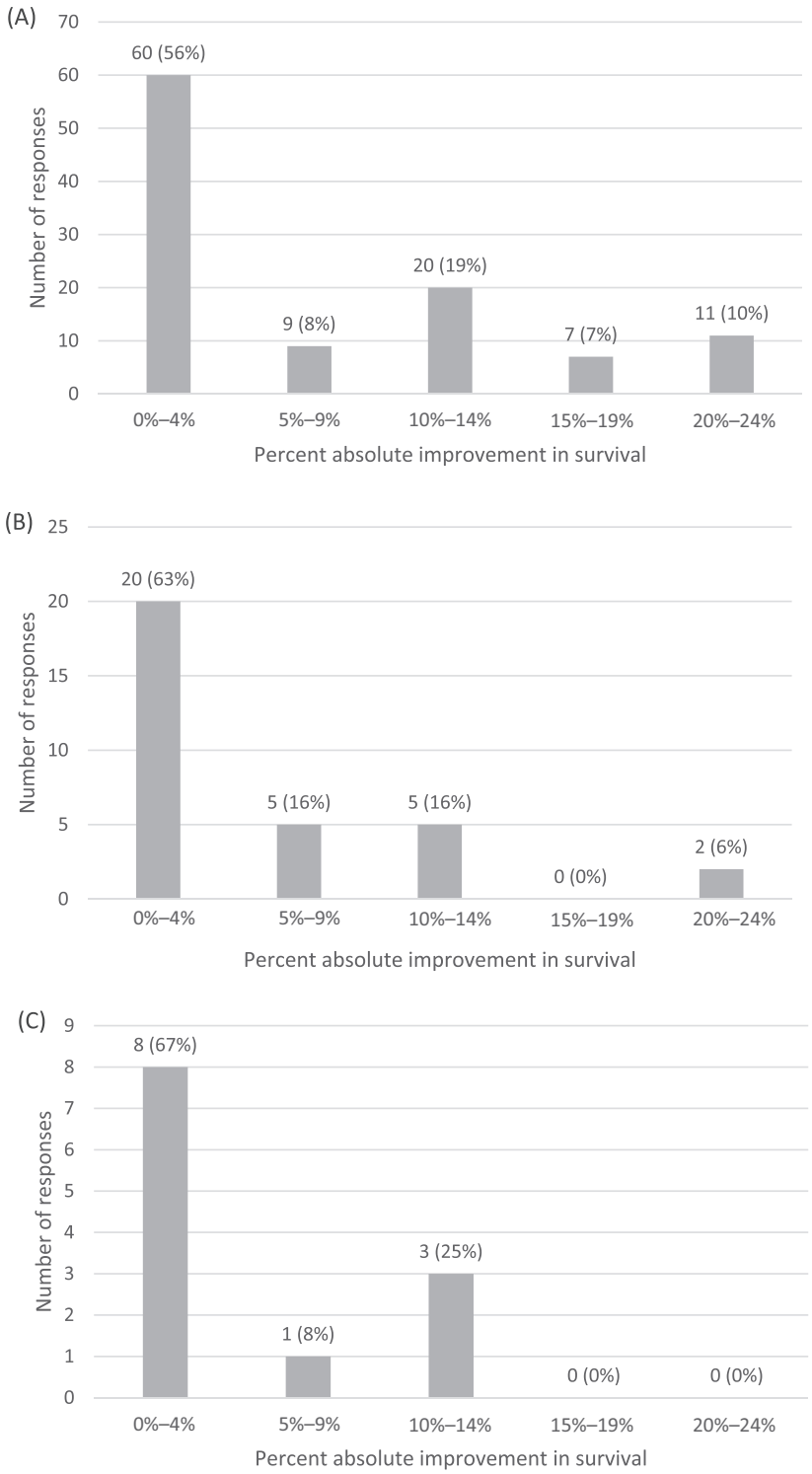


**FIGURE 1** Percent absolute improvement in survival required by red blood cell alloimmunized respondents to accept Rh-positive whole blood for a Rh-negative female child in (A) total survey cohort ($N = 107$); (B) subgroup analysis of respondents with a history of severe hemolytic disease of the fetus and newborn (HDFN) ($N = 32$); (C) subgroup analysis of respondents with history of fetal/neonatal loss to HDFN ($N = 12$).

RhD-positive LTOWB for an RhD-negative female child (%) stratified by selected participant characteristics is described in Table 4. Analyses were conducted for responses at or below the median response (0%–4%) versus above the median response (≥5%) and for the median absolute survival benefit as a continuous variable. Participants with a history of severe HDFN reported a median (IQR) response of 1% (1%–9%); those with a history of fetal death due to HDFN reported a median (IQR) response of 2% (1%–10%). There was no significant difference based on number of alloimmunized pregnancies, presence of female children, anti-D alloimmunization compared to other RBC antibodies, history of severe HDFN, or history of loss due to HDFN.

**TABLE 4** Absolute improvement in survival at which alloimmunized mothers would accept Group O RhD-positive low-titer group O whole blood for an Rh-D negative female child (%) stratified by selected participant characteristics.

| Absolute improvement in survival needed | 0%–4% | | ≥5% | | | Median (IQR) percent absolute improvement in survival | |
|---|---|---|---|---|---|---|---|
| | *N* | % | *N* | % | *p*-Value | | *p*-Value |
| Number of completed alloimmunized pregnancies | | | | | | | |
| 1 | 28 | 47% | 23 | 49% | 0.79 | 4% (1%–14%) | .54 |
| 2 | 20 | 33% | 17 | 36% | | 4% (1%–14%) | |
| ≥3 | 12 | 20% | 7 | 15% | | 4% (1%–9%) | |
| Number of female children | | | | | | | |
| 0 | 16 | 27% | 9 | 19% | 0.36 | 4% (1%–12%) | .99 |
| ≥1 | 44 | 73% | 38 | 81% | | 4% (1%–14%) | |
| Alloimmunized with Anti-D | | | | | | | |
| Yes | 23 | 38% | 23 | 49% | 0.27 | 5% (1%–14%) | .13 |
| No | 37 | 62% | 24 | 51% | | 4% (1%–12%) | |
| History of severe HDFN | | | | | | | |
| Yes | 20 | 33% | 12 | 26% | 0.38 | 1% (1%–9%) | .08 |
| No | 40 | 67% | 35 | 74% | | 4% (1%–14%) | |
| History of loss due to HDFN | | | | | | | |
| Yes | 8 | 13% | 4 | 9% | 0.43 | 2% (1%–10%) | .38 |
| No | 52 | 87% | 43 | 91% | | 4% (1%–14%) | |

Abbreviations: HDFN, hemolytic disease of the fetus and newborn; IQR, interquartile range.

## 4 | DISCUSSION

The transfusion of LTOWB continues to be adopted at trauma centers and in the prehospital setting while access to RhD-negative product remains limited. The question remains as to whether the survival benefits of offering RhD-positive LTOWB to a female of current or future childbearing potential outweigh the risk of her becoming D-alloimmunized and subsequently having a pregnancy affected by HDFN.

Red cell alloimmunization is a rare complication of pregnancy with only 0.6%–1.2% of pregnant patients having a red cell antibody associated with HDFN found at the time of their first prenatal visit.[27,28] Thus the average parent when confronted with a decision as to whether to accept RhD incompatible blood in cases of hemorrhagic shock in their female child will have little knowledge of the consequences of HDFN.

The findings of this survey provide valuable insight by offering the perspective of patients with real-life experience and understanding of the implications of RBC alloimmunization and HDFN. Overall, although responses varied, most of the alloimmunized females in this survey would accept RhD-positive LTOWB for an RhD-negative female child if it resulted in an improved survival of 4%. These results are consistent with several other surveys of non-alloimmunized respondents who generally favored receiving a transfusion of RhD-positive whole blood in order to improve their chances of survival in trauma, even knowing that there is a risk of HDFN complicating a future pregnancy.[29–32]

Alloimmunization and HDFN is a serious and sometimes severe disease, and prevention of maternal alloimmunization to RBCs and subsequent HDFN in the fetus and newborn where possible remains a global necessity.[33] Since the widespread adoption of Rh immune globulin in the 1960s, HDFN has become a rare disease in developed countries. With proper management and timely treatment by skilled maternal fetal medicine specialists and hematologists, HDFN is a treatable condition with little to no long-term consequences in the properly managed child.[34] With prompt intervention by skilled practitioners at large referral centers, fetal survival among the fraction of alloimmunized pregnancies severe enough to require intrauterine transfusion (24% in this sample) is upward of 97%.[35] However, due to the relative rarity of HDFN in any one center, clinician experience in management of HDFN has understandably decreased. It is for this reason that alloimmunized patients report inconsistent care resulting in preventable morbidity and mortality[36] and fetal outcomes are variable across sites,[37] evidenced by 11% of this sample experiencing loss due to HDFN. Alloimmunized patients also frequently report anxiety, isolation, and depression in their pregnancies

independent of the severity and outcomes in their disease, in large part due to the burden of spearheading their own care and feelings of uncertainty about their child's survival.[36,38] Widespread education initiatives for the multidisciplinary group of clinicians who care for these patients will help to alleviate this burden; important topics include the provision of evidence-based, expeditious, skilled treatment; referring sensitized patients to fetal centers with specific experience in alloimmunized pregnancy management and the conduct of intrauterine transfusions; and offering sensitized patients referrals and resources such as those provided by the Allo Hope Foundation that allow them to advocate for quality care and reduce the social and emotional burden that often accompanies an alloimmunized pregnancy.

While randomized controlled trials have not yet been completed, clinicians must make management decisions based on the currently available data, which suggests there may be benefits to the use of LTOWB over CT in children. There is no data that support the use of individual component therapy improves outcomes compared to LTOWB in the literature, and due to the potential benefit of LTOWB some centers have opted to use this alternative product for clinical care as trials are being performed to definitively determine efficacy. Data from the trauma quality improvement project (TQIP) indicates that LTOWB is used in 302 out of 795 (38%) trauma centers in the United States. At least 11 pediatric trauma programs utilize LTOWB.[6] Of these centers six will use RhD+ LTOWB in female children if RhD-LTOWB is not available. Randomized clinical trials examining use of LTOWB in adults are ongoing (NCT05638581) and the Massive Transfusion in Children-2 (MATIC 2) trial (NCT06070350) designed to evaluate mortality in massively bleeding children who receive LTOWB compared to CT has been initiated.

This survey has several limitations. As the study population was US-based, these results may not be applicable to other countries with variable healthcare systems. This survey focused on the specific question of LTOWB use for life-threatening hemorrhage and did not explore patient perspectives on the use of component therapy with Rh-negative RBCs that are also available since this would require explaining the current data and differences in product availability which was beyond the scope of this survey. This survey required convenience sampling from a nonprofit patient support group due to the rarity of the disease population, therefore the generalizability of these findings is not certain. However, it is the first survey of its kind to focus on the opinions of females who have experienced HDFN. Additionally, the participants were likely to be White, having high income, and highly educated. Though this may aid in the respondents' understanding of the primary research question, it may not reflect the population of female trauma patients. Future investigation in a subset of patients who did not seek support through a patient advocacy organization in their pregnancies may provide a more complete perspective. Lastly, the nature of the topic at hand is extremely complex and it might be difficult to properly communicate the intention behind the mortality risk scenario. For this reason, investigators made every effort to ensure participant clarity on the topic, but the potential for lack of participant understanding remains. Future research may include qualitative interviews to better depict the delicate scenario of considering RhD-positive LTOWB. Prospective database studies in female children and adults receiving transfusion to examine true alloimmunization prevalence and downstream impacts on pregnancies would be a challenging but valuable effort.

The findings outlined herein provide a patient-reported perspective on the risk benefit assessment of using an RhD-positive blood product that may improve survival compared to the risk of future HDFN for a female child. Although 11% of participants had previously experienced fetal death due to HDFN and 30% had a history of a child with severe HDFN, the majority of respondents would be willing to risk future HDFN for even a small improvement in trauma survival from receipt of RhD-positive LTOWB. Promoting disease education in practitioners and patients alike, routine screening for alloimmunization after exposure to RhD-positive blood products to an RhD-negative female, and referring alloimmunized patients to centers with specific experience in managing RBC-alloimmunized pregnancies is an appropriate plan to reduce morbidity and mortality due to HDFN.

## CONFLICT OF INTEREST STATEMENT

MRS, SC, and MY have disclosed no conflicts of interest. CML: BARDA funding for a trial comparing whole blood to components in children. KJM: Member, Medical Advisory Board for Allo Hope Foundation. PCS: BARDA funding for a trial comparing whole blood to components in children.

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## APPENDIX: COMPLETE SURVEY ADMINISTERED TO RESPONDENTS

### Screener

1. Do you currently live in the United States? (Yes/no)
2. Are you at least 18 years of age? (Yes/no)
3. Have you been diagnosed with red blood cell antibodies (maternal alloimmunization) known to cause hemolytic disease of the fetus and newborn (HDFN) including at least one of the below:

   K, k (Kell blood group)
   D, E, C, c (Rh blood group) Fya, By3 (Duffy blood group)
   Jka, Jkb, Jk3 (Kidd blood group)
   M,N,S,s,U,Mia(MNSsbloodgroup)Mta,Vw,Mur,Hil,Hut (MSSsbloodgroup)Lua,Lub(Lutheranbloodgroup)
   D1a, Dib (Diego blood group)
   Xg PP (Tja) Yta, Ytb, Lan, Ena, Ge, Jra, Coa, Co1-b-(Public antigens)
   Batty, Becker, Berrens, Biles, Evans, Gonzales, Good, Heibel, Hunt, Jobbins, Radin, Rm, Ven, Wrighta, Wrightb, Zd (Private antigens)

4. Have you had at least one alloimmunized pregnancy that progressed beyond 12 weeks? This includes pregnancies monitored for HDFN even if the baby was later determined to be antigen negative. (Yes/no)

### Demographics

1. What is your age? (integer)
2. What is your race?
   a. Black or African American
   b. White
   c. American Indian or Alaska Native
   d. Asian
   e. Native Hawaiian or Other Pacific Islander
   f. Prefer not to say
   g. Other (free text)
3. What is the highest level of education that you have completed?
   a. Elementary school
   b. Some high school or high school graduate
   c. Associate degree or Bachelor's degree
   d. Master's degree
   e. Doctorate or other professional degree (MD, DDS, JD)

4. What is your annual household income?
   a. <$30,000
   b. $30,001–$60,000
   c. $60,001–$90,000
   d. $90,001–$120,000
   e. >$120,000
5. Are you currently pregnant?
   a. Yes
   b. No
6. How many completed alloimmunized pregnancies have you had that progressed beyond 12 weeks (meaning pregnancies that are now over)? This includes pregnancies monitored for HDFN even if the baby was later determined to be antigen negative. (integer)
7. How many living children do you have? (integer)
8. How many living children do you have from your alloimmunized pregnancy/pregnancies? (integer)
9. How many children have you lost due to HDFN or complications from HDFN? (integer)
10. How many female children do you have? (integer)
11. What is your child's/children's Rh type? Your child's Rh blood type is the symbol portion of their blood type. For instance, if their blood type was A positive (A+), their Rh blood type would be positive (+). If you have multiple children, check all that apply.
    - ☐ Positive (+)
    - ☐ Negative (−)
    - ☐ I'm not sure

**Alloimmunized pregnancy and HDFN experiences**

Please think about your experience with your alloimmunized pregnancy/pregnancies that progressed beyond 12 weeks. This includes pregnancies monitored for HDFN even if the baby was later determined to be unaffected. If you are currently pregnant with your first alloimmunized pregnancy, you may proceed with your current pregnancy in mind.

1. What red blood cell antibodies do you have? (Select all that apply)
   - ☐ Anti-D
   - ☐ Anti-E
   - ☐ Anti-C
   - ☐ Anti-c
   - ☐ Anti-K
   - ☐ Anti-k
   - ☐ Anti-Fya (Duffy)
   - ☐ Anti-By3 (Duffy)
   - ☐ Anti-Jka (Kidd)
   - ☐ Anti-Jkb (Kidd)
   - ☐ Anti-Jk3 (Kidd)
   - ☐ Anti-M
   - ☐ Anti-N
   - ☐ Anti-S
   - ☐ Anti-s
   - ☐ Anti-U
   - ☐ Anti-Mia
   - ☐ Other (please type)
2. Please check all of the following that has happened during any of your alloimmunized pregnancies:
   - ☐ IVIG treatment (IV treatments started early in your pregnancy to reduce high antibody levels)
   - ☐ Plasmapheresis treatment (IV treatments started early in your pregnancy to reduce high antibody levels)
   - ☐ Port or permacath placed in you during pregnancy
   - ☐ Phenobarbital given to you before delivery to help baby's liver function (oral medication usually for 3 days)
   - ☐ Steroid shots given to you before delivery to help baby's lungs develop (usually two shots 24 h apart)
   - ☐ Middle cerebral artery (MCA) Doppler ultrasound scans (special ultrasounds to measure for fetal anemia)
   - ☐ Nonstress tests (two monitors strapped to your belly to listen for the baby's heart rate pattern and mother's contractions)
   - ☐ Biophysical profile (BPP) (ultrasounds with or without nonstress tests to check baby's overall activity and well-being)
   - ☐ Cell free fetal DNA (cffDNA) antigen status testing (a blood test on mom to determine baby's antigen status, available for D antigens in the United States; available for E, c, and K by sending blood out of the country for testing)
   - ☐ Chorionic villus sampling/amniocentesis to determine baby's antigen status (a needle inserted into mom's belly to sample amniotic fluid)
   - ☐ Cordocentesis/PUBS (sampling the baby's blood directly from the umbilical cord)
   - ☐ Intrauterine transfusion (IUT) (inserting a needle into mom's baby to give new blood to the baby through their abdomen or umbilical cord)
   - ☐ Complication from IUT
   - ☐ Emergency C-section
   - ☐ None of these
3. Please check all of the following conditions that occurred in your child (or children) affected by HDFN:
   - ☐ Enlarged heart on ultrasound
   - ☐ Ascites on ultrasound
   - ☐ Hydrops on ultrasound
   - ☐ Polyhydramnios on ultrasound
   - ☐ Hyperbilirubinemia after birth (high bilirubin)

- ☐ Anemia at birth
- ☐ Thrombocytopenia (low platelets)
- ☐ Neutropenia (low neutrophils)
- ☐ Hydrops after birth
- ☐ Heart failure
- ☐ Infant death related to HDFN or HDFN treatments
- ☐ Infant death unrelated to HDFN or HDFN treatments
- ☐ None of these
- ☐ Not applicable (my child/children turned out to be unaffected by my antibodies)

4. Please check all of the following treatments that any of your babies from your alloimmunized pregnancies received after birth:
   - ☐ Phototherapy (blue lights, bili blankets)
   - ☐ Intravenous immune globulin (IVIG) treatment for baby
   - ☐ Top-up blood transfusion (baby is given donor blood)
   - ☐ Exchange blood transfusion (baby's blood is removed and replaced with donor blood)
   - ☐ Erythropoietin
   - ☐ Iron supplements
   - ☐ NICU admission
   - ☐ Other
   - ☐ None
   - ☐ Not applicable (I am still pregnant with my first alloimmunized pregnancy)
   - ☐ Not applicable (my child/children turned out to be unaffected by my antibodies)

**Risk assessment**

"Giving an emergent blood transfusion to a child who is bleeding to death from trauma may increase their chance of survival. In many centers, bleeding is treated with multiple component products: red blood cells, plasma and platelets. The most common type of component product given is RhD-negative. Some centers use whole blood, which provides all blood components in one bag. The most common type of whole blood given is RhD-positive, as RhD-negative whole blood is in very short supply, which limits its availability."

"Giving RhD-positive blood to a female child who is RhD-negative has the potential to result in alloimmunization and HDFN in the child's future pregnancy as an adult. Some centers do not transfuse RhD-positive whole blood to any female children to prevent the risk of HDFN. However, recent data indicate that whole blood has the potential to improve survival over giving blood components in an emergency."

"In the situation of severe bleeding from trauma, a child's chance of dying is 24%. If RhD-positive blood is transfused to a child who is RhD-negative, the estimated risk of HDFN in future pregnancies when the child is an adult (mild to severe cases) is 0–6%. The risk of HDFN causing death of the fetus in the child's future pregnancies is estimated to be 0.3%."

"Based on the situation shown above, and with your knowledge and experience of maternal alloimmunization and HDFN, consider a situation where a child is experiencing a massive bleed due to a traumatic event. Would you accept RhD-positive whole blood for an RhD-negative female child if it reduced her chance of dying from 24% to ____%: Slider represents mortality reduction at which you would be willing to accept the RhD-positive blood. For example, by moving your slider to 20, you are suggesting that you would accept O RhD-positive whole blood for your child if it resulted in a mortality reduction from 24% to 20%."