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## Improving care for red blood cell alloimmunized pregnant women

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# Chapter 4

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## **Facilitators and barriers for RhD-immunized women to become and remain anti-D donors**

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## Abstract

**Background:** The successful introduction of prophylaxis with anti-RhD Ig has resulted in a significant decline of pregnancy-related RhD immunizations, but also in decreasing availability of naturally immunized women as (new) anti-D donors. An influx of new donors is necessary to maintain a sufficient pool of anti-D donors. We investigated motivators, barriers and predictors for anti-D donorship in RhD-immunized women.

**Study design and methods:** A mixed-methods design was applied, including focus group discussions and questionnaires. The focus groups (two, including 11 women) served as input for the questionnaire.

**Results:** 47.6% out of 750 anti-D donors and potential donors completed the questionnaire (50.4% donors; 38% non-donors; 11.6% ex-donors). Almost 70% of the non-donors would have become a donor if they had known about the possibility. (Travel) time investment was reported as disadvantage; half of the donors mentioned no disadvantages. Motivators for anti-D donorship were 'doing something in return' (31.2%) and 'preventing others having a sick child or losing a child' (33.9%). In multivariable analysis, living single (OR 5.8;p=0.02) and living partnered without resident children (OR 7.9;p=0.03), compared with living partnered with children, were predictors for anti-D donorship. Not being registered as organ donor (OR 0.25;p<0.001) predicted not being an anti-D donor.

**Conclusion:** The main barrier for anti-D donorship was a lack of knowledge. Positive predictors of anti-D donorship were living without resident children, altruism and being registered as an organ donor. A blood bank should develop targeted recruitment strategies with the focus on spreading knowledge about anti-D donorship among RhD-immunized women.

**Key Words:** donors, intravenous immunoglobulin, HDN

## Introduction

Before the introduction of anti-D immunoprophylaxis, RhD immunization was a major cause of perinatal death.(1, 7, 20) Since the 1960s, RhD-negative pregnant women in developed countries have received anti-D immunoglobulin (anti-D) within 48 hours after delivery or in situations during pregnancy creating a risk of fetomaternal hemorrhage (FMH).(77) In the Netherlands, postnatal anti-D prophylaxis was introduced in 1969.(45) Routine antenatal anti-D prophylaxis in the 30<sup>th</sup> week was introduced in 1998. From 2011 onwards, fetal RhD genotyping in maternal plasma has been performed first, restricting prophylaxis to women pregnant with an RhD-positive foetus.(24, 44) These preventive measures have together substantially reduced the risk of RhD alloimmunization and subsequent hemolytic disease of the foetus and newborn (HDFN). HDFN is known as Rhesus disease in the Netherlands. Nowadays, in the Netherlands, the number of newly immunized women is estimated to be about 50 per year (data from registration of alloimmunized pregnancies at Sanquin Diagnostic Services, national reference center).

To safeguard the anti-D prophylaxis program in the Netherlands, anti-D immunoglobulins are partly obtained from the plasma of RhD-immunized donors and partly imported from abroad.(57) In the Netherlands, most anti-D donors are RhD-negative women between 45 and 70 years old, who are immunized naturally after pregnancy and delivery of an RhD-positive child.(116) Some – both male and female – donors are intentionally immunized by administering a small amount of RhD-positive erythrocytes. To meet the national demand for anti-D prophylaxis, approximately 32,000 vials are needed, corresponding to 3200 donations per year – one donation being sufficient for ten products.(117) Assuming an average of five donations per donor per year, 640 donors would be required to reach self-sufficiency in the Netherlands.(116, 118) However, the group of active anti-D donors has decreased over the last years from 501 in December 2010 to 406 in December 2015 because dropout of donors exceeds influx of new donors, the negative result of a successful prophylaxis program. An important dropout reason concerns anti-D donors who were immunized by a pregnancy and delivery before introduction of anti-D prophylaxis in 1969 and reached the maximum age for donation of 70 years. The proportion of old-age stoppers reached its peak in 2014 and is now stabilized at 2–7% yearly.(116) As fewer women are newly immunized by pregnancy and delivery it becomes more important to recruit a higher proportion of newly or already immunized women to become anti-D donors in order to increase and stabilize the donor population.

Recruiting naturally immunized women has some advantages compared with intentionally immunized males. Firstly, recruiting naturally immunized women prevents future problems in intentionally immunized donors, when they need a transfusion themselves. The presence of RhD antibodies can delay the process of

preparing suitable donor blood, especially when people are travelling to Asia, where there are fewer RhD-negative people than in Western countries.(119) Secondly, voluntary unpaid blood donation is recommended by all international authorities (WHO/ Council of Europe/ ISBT/ EBA) because they are the best way to strive for self-sufficiency in blood products of all kinds, while maintaining an optimal level of quality and safety for recipients as well as for donors.(120-122)

Although much is known about the behavior and motivations of whole blood donors,(123) less research has been focused on the motivational and psychological factors associated with plasma donor behavior.(124) In the specific group of anti-D plasma donors, to the best of our knowledge, no research has been performed. Factors playing a role in the intention to donate whole blood are educational level, age, gender and marital status.(125) Several studies pinpointed motivators positively associated with becoming and remaining a donor. These factors include a positive attitude towards donating blood, social pressure to donate, perceived behavioral control or self-efficacy, the importance of being a blood donor, altruism and feeling an obligation.(123) In addition, donor career influences return behavior: the longer donors actively remain donating, the more likely they become committed donors. (126) Between whole blood donors and plasma donors few recognizable differences exist. Plasma donors have a higher donation intention, self-efficacy, attitude and conscientiousness, and a lower anxiety than whole blood donors.(124) It is not unlikely that anti-D donors may also differ in some ways from whole blood and nonspecific plasma donors. They emerge from a special group of women which has potentially experienced severe disease of their unborn or newborn child, or maybe even loss of a child through HDFN. These confrontational memories might influence their intention to donate both positively and negatively.

Based on knowledge about RhD-immunized women and their considerations to donate anti-D, targeted recruitment strategies and retention interventions could be developed to guarantee a continuous supply of anti-D plasma from voluntary, immunized, unpaid donors in the Netherlands. To this end, we investigated motivators, barriers and predictors, and appreciated recruitment strategies for anti-D donorship in RhD-immunized women, who are potentially eligible to become an anti-D donor.

## **Materials and Methods**

### **Design**

We applied a mixed-methods study design, combining qualitative and quantitative approaches. Qualitative data were collected by means of focus groups, quantitative data by a questionnaire. The main objective of the qualitative approach was to

identify key themes central to motivations and barriers of (potential) anti-D donors, serving as input for the development of a quantitative questionnaire. We chose to use focus group discussions so that the effect of mutual interaction on the motivation for anti-D donorship and the relation with experiences and preferences could be more easily identified. This study was part of a larger project to gain more insight into the willingness of obstetric care providers to play a role in the recruitment of new anti-D donors. The opinion of obstetric care providers will be elaborated in another paper. The Medical Advisory Council of the Leiden University Medical Center (LUMC) approved the study.

## Participants

Participants were anti-D donors and potential new anti-D donors, i.e. naturally RhD-immunized women between 43 and 65 years of age. Age limits were defined based on the ability to be hyperimmunized (after 45 years of age) and the age limit for donating (70 years of age). Participants were selected from the database of anti-D donors at the Sanquin Department of Donor Relations and from the database of the LUMC, the reference center for the management and treatment of pregnancies with severe RhD immunizations in the Netherlands.

For the focus group discussions, 100 RhD-immunized women were selected from the LUMC database. These were the patients seen most recently at the LUMC mixed with some older women from their neighborhood. They received an invitational letter and informed consent form from the obstetric care providers of the LUMC. Consenting women were contacted to make an appointment for the focus group discussion by the first author. The focus groups were put together using purposive sampling. In each focus group, active and potential anti-D donors were included, and variation in age and severity of offspring HDFN was pursued. The groups consisted of four to seven women and were organized (if possible) in the neighborhood of the participants. Focus groups were organized until data saturation was achieved.

For the questionnaire, RhD-immunized women from the LUMC database received a letter on behalf of their obstetric care provider with a link to the online questionnaire. Current anti-D donors were approached via the Sanquin Department of Donor Relations by email.

## Data collection procedure

### Focus groups

We conducted two focus group discussions. A skilled moderator guided the participants through an open discussion, stimulating and influencing their thinking to finally generate a maximum number of different ideas and opinions. The discussion was structured around a set of carefully predetermined open questions (Appendix 1) based on evidence about donor motivation and fueled by the researchers' expertise on the topics of blood donor behavior, RhD immunization and the problems of HDFN. The moderator ended the discussion when new ideas and opinions were no longer put forward. The discussion was video-recorded and notes were taken. Each focus group session was transcribed verbatim, also including relevant non-verbal cues. After the first focus group the verbatim protocol was analyzed to identify central topics to be discussed in the following sessions. Participants in the focus groups were offered travel expense refunds and a small gift.

### Questionnaire

Based on the core themes identified in the focus groups (including also the motivators and barriers mentioned), the questionnaire was developed. Specific questions on motivation and donation barriers for (potential) anti-D donors were also included.

The dependent variable was anti-D donor status, asked as: '*Are you currently an anti-D-donor?*' (yes/no/past-donor).

### Independent variables:

*Obstetric medical history:* pregnancies (yes/no, number, year of last pregnancy), spontaneous/induced abortions (<16 weeks, number), severity of HDFN per pregnancy (yes/no perinatal death due to HDFN, prenatal and/or postnatal transfusion, exchange transfusion, phototherapy). The severity of HDFN was classified into four categories, based on the most severe HDFN the women experienced during one or more pregnancies: 1 fetal demise, 2 prenatal fetal transfusion, 3 postnatal neonatal (exchange) transfusion and 4 neonatal phototherapy.

*Knowledge about/attitudes towards anti-D donorship:* '*Do you know what an anti-D injection is and what it is for?*', '*Have you ever heard about anti-D donorship?*' (yes/no, string value for explanation in own words) and for donors: '*How did you come up with the idea to become anti-D donor?*' Motivators: '*I want to do something in return*',



*'It does not cost me much trouble and it delivers much', 'I want to prevent others having a sick child or losing a child', 'Anti-D donors are needed', 'other' (yes/no/string value for explanation in own words) and 'the most important value to become an anti-D donor' (above-mentioned categories, single answer). Negative factors: 'Time', 'Travel time', 'Travel cost', 'Health', 'Confrontations with memories of HDFN', 'Negative experience of blood donation', 'Fear of needles', 'No negative factors', 'Other' (yes/no/string value for explanation in own words). Recruitment: 'mode of recruitment' (social media, magazines, newspapers, door to door flyers, via obstetric care provider/other health care provider, via obstetric care provider at LUMC, via other blood donors) and timing of contact (during pregnancy, short time after delivery, 6 weeks after delivery, 6 months after delivery, a few years after delivery, approximately ... years).*

*Demographics:* we included a set of standardized measures from the Donor InSight Study (DIS).(117) The questions concerned age (years), postal code (to check for double responses), ethnicity, religion, level of education, working status, family income and family situation (marital status, family composition). Answering categories and descriptive statistics are presented in Table 3.

*Pro-social values and behavior:* we included questions concerning being a registered organ donor (yes/no/choice to relatives) and volunteer work (yes/no). We measured pro-social value orientation differentiated by three scales (answer categories on a five-point Likert scale, 'totally agree' to 'totally disagree'); sum scores were calculated. The first scale, 'trust', comprised two items referring to generalized social trust (maximal total score 10) included in the statements developed by Rosenberg. (127) The second scale, 'altruism', comprised five items (maximal total score 25) referring to altruism, constructed by Gordon and translated into Dutch by Drenth and Kranendonk.(128, 129) The third scale, 'empathic concern', comprised four items (maximal total score 20) referring to empathy, developed by Davis and modified by Bekkers.(130, 131)

## Analysis

Qualitative data were analyzed using thematic content analysis.(132) Coding schemes identifying key categories in facilitators and barriers were revised and expanded, resulting in core themes.

We described the attitude towards anti-D donorship in terms of motivators and negative factors of anti-D donorship. Motivators were mentioned by anti-D donors as well as non-donors who indicated the intention to become a donor. Negative factors were mentioned by anti-D donors and non-donors who were unwilling to become a donor.

For analysis of the quantitative data, we compared motivators and barriers and potential predictors for anti-D donorship between current donors and non-donors, disregarding women who were currently not anti-D donors but had been in the past.

Dichotomous outcomes were described as number and percentage, normally distributed continuous variables as mean and standard deviation, and non-normally distributed continuous variables as median and P25–P75. Differences between non-donors and current donors were tested univariably by means of Pearson's chi-square test (dichotomous variables), and Student's *t*-test (normally distributed continuous variables) or the Mann–Whitney U-test (not normally distributed continuous variables). All variables with a *p*-value of <0.20 were included in a multivariable logistic regression analysis, to estimate the association between potential predictors and anti-D donorship. The strengths of the associations were expressed as odds ratios (OR) and their corresponding 95% confidence intervals (95% CI). Age (continuous) was included in the model as a potential confounder. Variables with a significant (*p*<0.05) association in the regression analysis were included in a prediction model, predicting anti-D donorship. Data were analyzed using SPSS Statistics version 23.

## Results

### Results from the qualitative focus group interviews

From the 100 RhD-immunized women invited for the focus group discussions, about one in five was an anti-D donor. Twenty-four women gave consent to participate in a focus group. After two focus groups, including a total of 11 women, data saturation was achieved. The remaining 13 women who gave consent were invited for the questionnaire. Eight themes were identified: 'Knowledge of possible anti-D donorship', 'Experiences with Rhesus disease', 'Reasons to become a blood donor', 'Organ donorship', 'Knowledge of Rhesus disease', 'Experiences with blood donation', 'Boosting', 'Ways to recruit anti-D donors' and 'Practical considerations'. These topics were all covered in the questionnaire.

### Quantitative results – responses

We invited all anti-D donors in the Sanquin donor database meeting the inclusion criteria (340/501) reachable by email and all 410 reachable RhD-immunized women between 43 and 65 years of age from the LUMC database to fill in the questionnaire. The overall response rate – excluding ex-donors – was 41.6% (312/750); 32.7% (134/410) in non-donors and 52.4% (178/340) in donors. In the group of responders

57% were anti-D-donors, 43% non-donors. The number of ex-donors not included in the analysis was 41 (10% of total response).

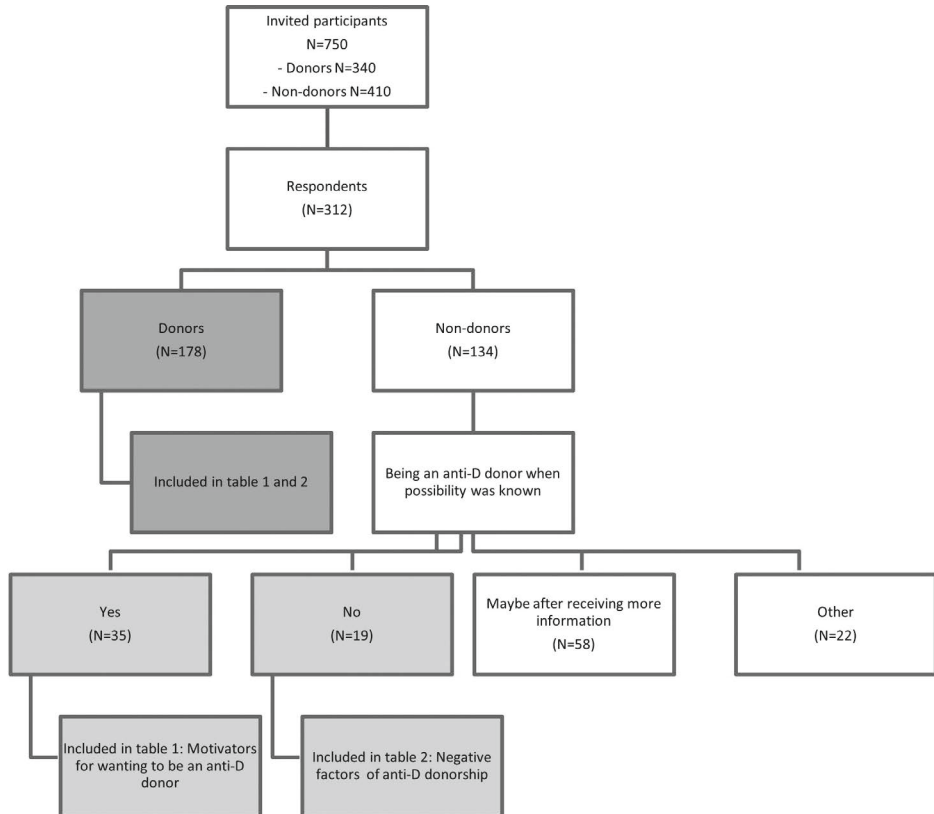


Figure 1. Flowchart of included participants table 1 and 2

## Attitudes towards anti-D donorship

Almost all responders had ever heard about anti-D injections (98.3%, 347/353) and 94% (332/353) could explain more or less the purpose of anti-D injections. The majority of the 134 non-donors indicated that they would have become a donor if they had known about the possibility (69.4%, 93/134) (Figure 1). Of them, 43.3% pointed out that they wanted to receive more information first. To the question 'in the future I will certainly sign up as anti-D donor', asked to non-donors only, 47% (63/133) gave a neutral response and 35% (47/133) agreed or totally agreed. Table 1 shows the results on motivators for being or becoming an anti-D donor of donors and non-donors with the intention to become a donor (n=35). Anti-D donors gave the reason 'anti-D donors are needed' twice as often as non-donors ( $p < 0.001$ ). Non-

donors responded slightly more often 'they want to do something in return' ( $p=0.09$ ) or 'want to prevent others having a sick child or losing a child' ( $p=0.14$ ). Those two reasons (31.2% and 33.9% respectively) were also the most important values for non-donors with the intention to become a donor.

Frequently mentioned negative factors of anti-D donorship by anti-D donors were time investment (63/174) and travel time investment (37/174) (Table 2). Half of them could not think of any negative factors. Respondents who certainly did not want to become an anti-D donor ( $n=19$ ) named as their reason 'time investment' (42%) and 'negative experiences with blood drawing in the past' (31%). 'Being confronted with memories referring to HDFN' was not mentioned as a major negative factor in either group (anti-D donors 6% and 16% non-donors).

**Table 1.** Motivators for being or becoming an anti-D donor

| Motivator  | Anti-D donor<br>(N = 178)<br>N (%) | Non-donor*<br>(N = 35)<br>N (%) |
|--|------------------------------------|---------------------------------|
| 'I want to do something in return'                               | 84 (47.8)                          | 22 (62.9)                       |
| 'It does not cost me much trouble and it delivers much'          | 108 (60.6)                         | 21 (60.0)                       |
| 'I want to prevent others having a sick child or losing a child' | 82 (45.6)                          | 21 (60.0)                       |
| 'Anti-D donors are needed'                                       | 150 (83.9)                         | 16 (45.7)                       |

\*Non-donors with the intention to become a donor.

Multiple answers were possible.

**Table 2.** Negative factors of anti-D donorship

| Negative factor                       | Anti-D donors<br>(N = 174)<br>N (%) | Non-donors*<br>(N = 19)<br>N (%) |
|---------------------------------------|-------------------------------------|----------------------------------|
| Time                                  | 63 (36)                             | 8 (42)                           |
| Travel time                           | 37 (21)                             | 4 (21)                           |
| Travel cost                           | 7 (4)                               | 4 (21)                           |
| Health                                | 6 (3)                               | 2 (13)                           |
| Confrontations with memories of HDFN  | 10 (6)                              | 3 (16)                           |
| Negative experience of blood donation | 7 (4)                               | 6 (32)                           |
| Fear of needles                       | 0 (0)                               | 4 (21)                           |
| Negative factor                       | 87 (50)                             | 0 (0)                            |
| Other                                 | 16 (9)                              | 3 (2)                            |

**Table 2.** Negative factors of anti-D donorship (continued)

| Negative factor             | Anti-D donors<br>(N = 174)<br>N (%) | Non-donors*<br>(N = 19)<br>N (%) |
|-----------------------------|-------------------------------------|----------------------------------|
| Purpose of immunization     | 2 (1)                               | 0 (0)                            |
| No fee                      | 0 (0)                               | 1 (6)                            |
| Problems with blood drawing | 10 (6)                              | 2 (13)                           |
| Opening hours               | 4 (2)                               | 0 (0)                            |

\*Non-donors unwilling to become a donor.

Multiple answers were possible.

## Recruitment of anti-D donors

Among the current anti-D donors 44% became a donor on their own initiative, and 51% via a blood bank flyer or a recruitment campaign. A small group (14%) was made aware of the possibility to donate by a health care provider. Frequently mentioned preferred recruitment strategies were 'personally by the obstetric care provider' (69%), 'personally by the LUMC, the reference center for Rhesus disease' (67%) and 'through social media' (49%). The right timing frequently mentioned was 6 weeks (31%) or 6 months after delivery (33%); 80% of the responders mentioned that they would like to have received a personal letter from the LUMC to make them aware of the possibility of anti-D donorship.

## Univariable regression analysis

The general demographics, pro-social values and obstetric medical history, and their contributions in the univariable analysis are described in Table 3. There were no significant differences between anti-D donors and non-donors in religion, educational level and employment. Anti-D donors were slightly older than non-donors (not statistically significant). Overall, non-donors had experienced more severe HDFN in their obstetric history ( $p < 0.001$ ). Anti-D donors were more often a registered organ donor and participated more frequently in volunteer work.

To assess the reliability of the altruism and empathy scales used Cronbach's alpha was determined ( $\alpha = 0.73$  and  $\alpha = 0.65$  respectively). Only the altruism scale showed good reliability and was significantly different between anti-D donors and non-donors. The trust scale consisted of only two items; Cronbach's alpha was therefore not determined.

**Table 3.** Demographics, pro-social values and severity of HDFN and their univariable contributions in predicting anti-D donorship

| Variable                                  | Anti-D donors<br>N = 178<br>(57%) | Non-donors<br>N = 134<br>(43%) | P-value§ |
|---|-----------------------------------|--------------------------------|----------|
| Age mean (SD)                             | 51.7 (± 9.6)                      | 50.4 (± 4.5)                   | 0.16     |
| <b>Family composition</b> n (%)           |                                   |                                | 0.001    |
| Husband/wife and children                 | 122 (68.5)                        | 106 (79.1)                     |          |
| Husband/wife                              | 31 (17.4)                         | 7 (5.2)                        |          |
| Alone                                     | 14 (7.9)                          | 4 (3.0)                        |          |
| Single parent with children               | 11 (6.2)                          | 17 (12.7)                      |          |
| <b>Religion</b> n (%)                     |                                   |                                | 0.48     |
| Roman Catholic                            | 43 (24.2)                         | 35 (26.1)                      |          |
| Protestant                                | 47 (26.4)                         | 35 (26.1)                      |          |
| Muslim                                    | 0 (0)                             | 2 (1.5)                        |          |
| None                                      | 81 (45.5)                         | 55 (41.0)                      |          |
| Christian other                           | 7 (3.9)                           | 6 (4.5)                        |          |
| <b>Education</b> n (%)                    |                                   |                                | 0.65     |
| None/lower education                      | 27 (15.1)                         | 15 (11.1)                      |          |
| Secondary education                       | 64 (35.9)                         | 59 (44.0)                      |          |
| Higher education                          | 72 (40.4)                         | 50 (37.3)                      |          |
| University                                | 14 (7.9)                          | 9 (6.8)                        |          |
| <b>Employed</b> n (%)                     | 136 (76.4)                        | 105 (78.4)                     | 0.66     |
| <b>Registered organ donor</b> n (%)       | 122 (68.5)                        | 50 (37.3)                      | < 0.001  |
| <b>Volunteer work</b> n (%)               | 88 (49.4)                         | 51 (38.0)                      | 0.05     |
| <b>Pro-social values</b> median (P25–P75) |                                   |                                |          |
| Trust scale*                              | 7 (6–8)                           | 7 (6–8)                        | 0.84     |
| Empathy scale†                            | 16 (14–16)                        | 16 (14–17)                     | 0.18     |
| Altruism scale‡                           | 19 (17–20)                        | 20 (18–21)                     | 0.05     |

**Table 3.** Demographics, pro-social values and severity of HDFN and their univariable contributions in predicting anti-D donorship (continued)

| Variable  | Anti-D donors<br>N = 178<br>(57%) | Non-donors<br>N = 134<br>(43%) | P-value§ |
|---|-----------------------------------|--------------------------------|----------|
| <b>Severity hemolytic disease of foetus and newborn<br/>n (%)</b> |                                   |                                | < 0.001  |
| No disease  | 53 (29.8)                         | 10 (7.5)                       |          |
| Fetal demise  | 14 (7.9)                          | 24 (17.9)                      |          |
| Prenatal transfusion  | 27 (15.2)                         | 56 (41.8)                      |          |
| Postnatal transfusion   | 64 (36)                           | 27 (20.1)                      |          |
| Phototherapy only   | 20 (11.2)                         | 17 (12.7)                      |          |

Dependent variable is anti-D-donors and independent variable is non-donors. \*Cronbach's  $\alpha = 0.49$ ; †Cronbach's  $\alpha = 0.65$ ; ‡ Cronbach's  $\alpha=0.73$ .§ Pearson's chi-square test, Student's t-test or Mann-Whitney U-test.

### Predictors associated with anti-D donorship

All variables with a p-value < 0.20 in the univariable regression were included in the multivariable logistic regression (Table 4). Volunteer work and the empathy scale were not significantly associated with anti-D donorship in the multivariable analysis and were subsequently excluded from the final prediction model. The model was adjusted for age.

Family composition affected donorship; in particular, single women and partnered women without resident children were more likely to be an anti-D donor. Not being registered as an organ donor and 'leaving the choice for organ donation to relatives' were also negatively associated with anti-D donorship. Women who had experienced fetal or neonatal disease, especially women who had experienced severe disease such as fetal demise or prenatal transfusion, were less likely to be an anti-D donor. A higher score on the altruism scale was positively associated with anti-D donorship.

**Table 4.** Multivariable logistic regression: predicting the likelihood of anti-D donorship

| Variable  | Crude OR<br>(95% CI) | Adjusted* OR<br>(95% CI) | Multivariate<br>p-value |
|---|----------------------|--------------------------|-------------------------|
| <b>Demographics</b>                                     |                      |                          |                         |
| <b>Family composition:</b>                              |                      |                          |                         |
| Husband/wife and children                               | Ref                  | Ref                      | Ref                     |
| Husband/wife  | 6.28 (2.29–17.17)    | 7.88 (2.68–23.11)        | 0.03                    |
| Alone   | 4.60 (1.09–19.28)    | 5.79 (1.32–25.31)        | 0.02                    |
| Single parent with children                             | 0.83 (0.32–2.12)     | 0.84 (0.32–2.17)         | 0.71                    |
| <b>Pro-social parameters and behavior</b>               |                      |                          |                         |
| Altruism scale  | 1.12 (1.01–1.24)     | 1.12 (1.01–1.23)         | 0.04                    |
| <b>Registered organ donor</b>                           |                      |                          |                         |
| Yes   | Ref                  | Ref                      | Ref                     |
| No  | 0.25 (0.14–0.47)     | 0.25 (0.14–0.46)         | < 0.001                 |
| Choice to relatives                                     | 0.46 (0.21–1.02)     | 0.46 (0.21–1.01)         | 0.05                    |
| I don't know  | 1.13 (0.05–22.21)    | 0.91 (0.05–18.4)         | 0.95                    |
| <b>Severity hemolytic disease of foetus and newborn</b> |                      |                          |                         |
| No disease  | Ref                  | Ref                      | Ref                     |
| Fetal demise  | 0.08 (0.03–0.22)     | 0.08 (0.03–0.27)         | < 0.001                 |
| Prenatal transfusion                                    | 0.09 (0.04–0.22)     | 0.09 (0.04–0.22)         | < 0.001                 |
| Postnatal transfusion                                   | 0.45 (0.18–1.10)     | 0.44 (0.18–1.08)         | 0.07                    |
| Phototherapy only                                       | 0.26 (0.24–0.67)     | 0.23 (0.08–0.64)         | 0.005                   |

CI = confidence interval; OR = odds ratio.

\*Multivariable analysis adjusted for age.

Goodness-of-fit tests showed no evidence of lack of fit (Hosmer and Lemeshow  $p = 0.65$ ); explained variance 24% (Nagelkerke  $R^2$ ).



## Discussion

We tried to gain a better understanding of motivators and barriers of RhD-immunized women to become and remain anti-D donors and to identify the most promising way to approach this specific group of (potential) donors. The results showed that almost 70% of non-donors might have become a donor if they had been informed of the possibility, while almost half of them first wanted to get more information before deciding on becoming an anti-D donor. This finding implies that a lack of knowledge about the possibility of becoming an anti-D donor is a major barrier for becoming one. This was confirmed by the explanation frequently heard in the focus group interviews that the potential donors thought that they could not be a whole blood donor because of the presence of RBC antibodies. Negative factors found were time investment and travel time investment, but half of the donors mentioned no negative factors of being an anti-D donor. 'Being confronted with memories referring to HDFN' was not mentioned as a major disadvantage of anti-D donorship in either focus group. Motivators of non-donors to become an anti-D donor were 'want to do something in return' (31.2%) and 'want to prevent others having a sick child or losing a child' (33.9%).

This study shows that (potential) anti-D donors differ from whole blood and plasma donors in gender, almost exclusively women, while in whole blood donors the gender ratio is more balanced and regular plasma donors are predominantly male.(124) Secondly, in this study, demographic variables as educational level, age and marital status were also associated with the intention to donate.(125, 133)

To indicate pro-social behavior, we used 'altruism', 'organ donorship' and 'volunteer work'. Similar to whole blood donors those indicators showed higher odds of being an anti-D donor.(123) Although the confrontation with memories of HDFN was not mentioned as being a negative factor or barrier in focus group discussions, the experience of severe HDFN was associated with higher odds of not being an anti-D donor in the multivariate model. This might be partly explained by an overrepresentation of women with severe HDFN in the non-donor group. A possible further explanation might be that the severity of the disease restrains the obstetric care worker from discussing the possibility of anti-D donorship with the patient.

For this particular group of potential donors, tailored recruitment strategies should be designed. The obstetric care provider can play a major role in creating awareness of anti-D donorship in women with RhD antibodies. Although responders to this

questionnaire mentioned they would like to have been contacted personally by the obstetric care provider 6 weeks to 6 months after giving birth, privacy and ethical considerations might be a barrier for the professional. Further research on this topic, in particular the view of obstetric care workers, will provide more insight. Possibly, a joint protocol might be created between the different parties involved to make it easier for obstetricians to retrieve consent of RhD-immunized women and to enable the blood bank to contact the woman after a certain time to provide her with information about anti-D donorship.

### **Strength and limitations**

To the best of our knowledge, this is the first study on motivators and barriers of women with RhD antibodies to be or to become anti-D donors. The overall response rate of this study was 42%, comparable with other donor studies.(124, 134) In both anti-D donors and non-donors, we achieved a sufficient response; the response in the anti-D donor group was higher. Possibly, selective response exists among non-donors, since women with a positive attitude to anti-D donorship will be more inclined to respond to both the questionnaire and the focus group discussions than non-donors with a more negative attitude. This might have resulted in overestimation of the proportion of women with a willingness to become anti-D donors. However, we think our results provide a good overview of motivators and barriers to becoming an anti-D donor.

A major strength of our study is that we designed our questionnaire based on two focus group discussions in which we identified themes related to anti-D donorship. Moreover, we used validated scales to measure pro-social values and behavior, which were also used in the DIS.(117) In doing so, we believe that our questionnaire covered all themes. A limitation of the questionnaire was that we asked donors and non-donors who would certainly not want to become an anti-D donor (n = 19) only about negative factors of anti-D donorship. Therefore, information about negative factors of non-donors with the intention to be a donor is still lacking. Non-donors from the focus groups, like the anti-D donors, also indicated that too much time and travel investment might be negative factors for becoming an anti-D donor.

Because we identified non-donors via the LUMC, the reference center for the monitoring and treatment of alloimmunized pregnant women, we might have included a group of non-donors who experienced more severe HDFN than RhD-immunized Dutch women who were not referred to the LUMC. This might partly explain the contradiction in our results that the experience of severe HDFN was associated with not being an anti-D donor, while donors as well as non-donors did not consider being confronted with memories of HDFN as a major disadvantage of anti-D donorship.

## Conclusion

The main barrier for women with RhD antibodies to be an anti-D donor is lack of knowledge about anti-D donorship. The profile of (potential) anti-D donors is different from whole blood and plasma donors, mainly because they are women and are eligible to become donors through immunization during pregnancy. Important motivators for being or becoming an anti-D donor mentioned often are 'want to do something in return' and 'want to prevent others having a sick child or losing a child'. Predictive factors positively associated with anti-D donorship are family composition and altruism. Negatively associated predictive factors are 'not being registered as an organ donor' and 'severity of the experienced HDFN'. A blood bank and obstetric care providers should find a way to work together to better inform, recruit and retain women to anti-D donorship.