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## **Improving care for red blood cell alloimmunized pregnant women**

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# Chapter 7

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**Knowledge, attitude and practices of obstetric careproviders towards maternal red-blood-cell immunization during pregnancy**

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## Abstract

**Background and objectives:** A successful routine RBC alloantibody screening programme should not lead to unnecessary emotional burden during pregnancy due to inadequate counselling on the risk of severe Haemolytic Disease of the Foetus and the Newborn (HDFN). Rareness of this disease may result in insufficient knowledge and subsequent inadequate information transfer to women, diagnosed with RBC antibodies. We investigated the current knowledge, views and experiences of Dutch obstetric care providers regarding RBC alloimmunisation during pregnancy.

**Materials and methods:** We performed a quantitative cross-sectional study, using a structured digital questionnaire to measure knowledge, attitude and practices (KAP) regarding maternal RBC alloimmunisation among Dutch obstetric care providers in 2016.

**Results:** About 10% of obstetric care providers completed the questionnaire. A sufficient level of knowledge was found in 7% of all participants (N=329). Knowledge about RhD immunisation and prophylaxis was sufficient in 60% of the responders. Knowledge gaps were found concerning the relevance of non-RhD RBC antibodies, the indications for giving extra RhD-prophylaxis and the interpretation of laboratory test results. Health care providers estimated their own level of knowledge “sufficient” (primary/secondary care) to “good” (tertiary care) and all participants considered their professional role important within the screening programme.

**Conclusion:** Dutch obstetric care providers showed a lack of knowledge regarding maternal RBC immunisation. Awareness of the lack of knowledge is necessary to help obstetric care providers to be careful in giving information and even to decide to contact the expert centre before counselling the patient.

## Introduction

Haemolytic disease of the foetus and new-born (HDFN) is still a known cause of pregnancy complications. HDFN is caused by red blood cell (RBC) antibodies developed by the mother and transferred to the foetus. (7, 10, 25) Untreated HDFN may result in progressive foetal anaemia, hydrops, neonatal icterus and even death. (8, 9) Antibodies causing severe HDFN are mostly of the anti-Rh(D) type, and less frequent of the anti-Kell (anti-K1) or anti-Rh(c) type. Severe HDFN is rarely caused by other Rh-antibodies, and only very rarely by non-Rh antibodies (Duffy, Kidd, or S). (4, 10)

Preventive measures such as prenatal and postnatal RhD-immunoglobulin prophylaxis, matched blood transfusions for Rh- and K antigens to women of fertile age (<45 years) and routine prenatal screening for RBC antibodies, together with improvements in monitoring and therapeutic possibilities, have substantially reduced the risk on maternal alloimmunisation and improved outcome of HDFN over the past decades. (10, 32, 44, 91, 163).

Obstetric care providers nowadays only see a few immunised pregnant women during their career, due to the success of the maternal red blood cell alloimmunisation prevention programme. This might result in insufficient knowledge, inadequate information transfer and substandard care to women who are diagnosed with RBC antibodies. In the Netherlands, approximately 180,000 pregnant women are year are entering the screening program. Thanks to a well-organized obstetrical network with multiple safety nets during the process, the coverage of the national prevention programme is almost 100% (57). The reference laboratories (Sanquin Diagnostics and BIBO Groningen) and the national expert centre for the management of alloimmunisation in pregnancy (Leiden University Medical Center, LUMC) are at any time available for advising and consultation on the rare occasion of RBC alloimmunisation.

Pregnancies complicated by the presence of maternal RBC antibodies are monitored by laboratory measurements, consisting of maternal serum testing for antibody levels (quantification of titre) and, in the Netherlands, the antibody dependent cell-mediated cytotoxicity (ADCC) test. (19, 160) If laboratory findings indicate that a pregnancy is at risk for development of HDFN, frequent monitoring is started with ultrasound and Doppler middle cerebral artery (MCA) peak systolic velocity (PSV) measurements, to reliably predict foetal anaemia. (18, 29) If severe foetal anaemia develops, treatment with intrauterine transfusions (IUT) is started and/or preterm delivery is induced, usually followed by neonatal phototherapy and/or (exchange) transfusions. (28, 30)

A Dutch questionnaire survey in 2004, including 233 pregnant women with and without RBC alloimmunisation, showed that women were moderately satisfied with the quantity and comprehensibility of information provided by their obstetric care provider.<sup>(63)</sup> Fifty to 70% of the women, particularly those with RBC antibodies, indicated that they needed more information, preferable orally, about the consequences of the RBC alloantibodies for their child. Supportive written information (e.g., folders / hand-outs) was lacking, both prenatally and postnatally.

A more recent survey from the UK, performed in the London area, including 270 RhD-negative women, showed that their knowledge about the consequences of screening for RhD-antibodies was limited; 30% of respondents needed more information, via folders or diagrams and through midwives.<sup>(23)</sup> The authors concluded that midwives needed training on this topic. Wee et al. performed a study on knowledge and practices of RhD-prophylaxis among gynaecologists, residents and obstetric care workers in Singapore. Only 49% appeared to have an adequate level of knowledge on this topic.<sup>(164)</sup>

In the Netherlands, after adapting the national screening programme in 2011, training and e-learning were developed and offered. However, it is yet unclear what these refresher courses have brought. More insight in the current knowledge of Dutch obstetric care providers on this topic is needed, to identify gaps in knowledge, and to develop strategies to meet these gaps.

The aim of this research was to investigate the current knowledge, views and experiences of Dutch obstetric care providers regarding RBC alloimmunisation during pregnancy.

## Methods

### Aim/objectives

The aim of the present study was to measure knowledge, attitude and practices (KAP) regarding maternal RBC alloimmunisation among Dutch obstetric care providers. More specifically, the objectives of this KAP study were:

- 1) to investigate the knowledge of Dutch obstetric care providers about the prevention (strategies) and detection of RBC alloantibodies and identification and treatment of HDFN.
- 2) to explore the attitude of Dutch obstetric care providers towards the maternal RBC alloimmunisation prevention programme.
- 3) to examine the practices of Dutch obstetric care providers in participating in the care for pregnant women with RBC alloimmunisation and (risk for) HDFN.

### Design

We designed a quantitative cross-sectional study design, using a structured digital questionnaire. The questionnaire was conducted in 2016.

### Research population

Participants were midwives, obstetricians and general practitioners specialised in obstetrics. In the Netherlands, obstetric care providers are working in three echelons. The first echelon, primary care, is provided by midwives and general practitioners, working independently in home practices. The second echelon, secondary care, is the regional hospital and the third echelon, tertiary care, is the university hospital (with neonatal intensive care unit availability); in these latter two echelons the obstetric care is provided by midwives and gynaecologists. Participants were invited through a personal mail or mass mail.

### Questionnaire

The questionnaire was developed by a medical student (CW), being supervised by a PhD student/midwife (YS) and a PhD/midwife (JK). To reduce the influence of the knowledge questions on the attitude and practice questions, we first posed

the attitude and practical questions. No validated questionnaire was available. We were advised by an expert on questionnaires of the department of Medical Decision Making of the LUMC and by an expert of the education and training Directorate of the LUMC. Additionally, we compared questionnaires with (165-167) Knowledge of the care providers was examined using vignettes, whereby the respondents had to apply their available knowledge. (168) An expert panel (including obstetricians specialized in foetal therapy, midwives and a laboratory specialist) reviewed the items on content and face validity. Finally, we used a checklist designed by the Dutch Interfaculty Center for Teacher Training, Educational Development and Training (ICLON) (Leiden University).

## Measurements

**Professional background.** Questions about professional background, such as: “In which echelon are you working (primary, secondary, tertiary care)?”, year of graduation, work experience (years), prior experienced a pregnancy complicated with maternal RBC alloimmunisation (yes/no), prior experienced a foetus or newborn with haemolytic disease (yes/no), number of deliveries of practice/hospital, latest e-learning (2011, provided by the Dutch National Institute for Public Health and the Environment) done (yes/no), latest training on this topic (year). The variable “year of graduation” was categorised as:  $\leq 1998$ , 1999-2011 and  $>2011$ . These time sets were based on the introduction the routine first trimester screening in 1998, the introduction of the foetal RhD-typing and third trimester screening of Rhc-negative pregnant women in 2011.

**Knowledge.** To test the knowledge about maternal RBC alloimmunisation we used vignettes, case descriptions with questions like “What information do you give your patient?” “What is the right policy in this case?” etc. There were 7 vignettes, the domains were: Screening and prevention of RhD-immunisation (2 questions), Rhc-immunisation (2 questions), K-immunisation (2 questions), risk factors for RhD-immunisation and indications for extra RhD-immunoglobulin prophylaxis (4 questions primary caregivers, 5 questions secondary and tertiary caregivers), laboratory testing for monitoring alloimmunised pregnant women (4 questions), monitoring and treatment of pregnancy with an increased risk of HDFN (only secondary and tertiary care, 2 questions), follow-up of neonate with or without increased risk for hyperbilirubinaemia (2 questions). In total, there were 16 questions to be answered by the primary caregivers and 19 questions for the secondary and tertiary caregivers.

**The attitude part** consisted of 13 items. *The attitude towards professional role* consisted 4 items: the participants indicated the importance of their own role in the whole process of screening, diagnosis and treatment of maternal alloimmunisation



and HDFN. They indicated if they have enough time per patient to well-inform them, if they find it their job to well-inform them and if they feel that this improves the level of care. *The attitude towards competences* consisted 5 items: participants rated their competences in providing information on the several fragments of this topic and their competences to accompany pregnant women with RBC antibodies and/risk of HDFN. *The attitude towards self-assessment of level of knowledge* consisted 4 items: The participants assessed their own level of knowledge and their satisfaction with it. All items were measured at a five-point Likert Scale (1-5, Completely agree-strongly disagree).

**The practices part** contained 5 items in which the participants valued the necessity, importance and intention to improve their knowledge and to attend a training. Furthermore, the participants were asked to indicate how often they provide information about the purpose and possible outcomes of the screening program, just before the blood test was taken. All items were measured at a five-point Likert Scale (1-5, good-poor or completely agree-strongly disagree or always-never).

## Data collection

The questionnaire was made with NetQ version 2014.Q3. The questionnaire was spread in July 2016 and after two reminders, closed for analysis. Data-analysis was done in SPSS version 23 (SPSS, Inc.).

## Data-analysis

On the knowledge questions, the maximum score for primary care was 16 points and for the secondary and tertiary care 19 points. Following the study of Wee et al. and after discussion with the expert panel, it was decided that a score of 80% is a sufficient level of knowledge.

Dichotomous outcomes were described as numbers and percentages, normally distributed continuous variables were described as means and standard deviations, and non-normally distributed continuous variables as median and range. Differences between primary, secondary and tertiary care were tested univariably. All variables with a p value less than 0.20 were included in a multivariable logistic regression analysis to assess the association between those variables and the level of knowledge. We intended to add variables with a significant ( $p < 0.05$ ) association in a regression analysis in a prediction model that predicted level of knowledge of alloimmunisation.

## Ethical considerations

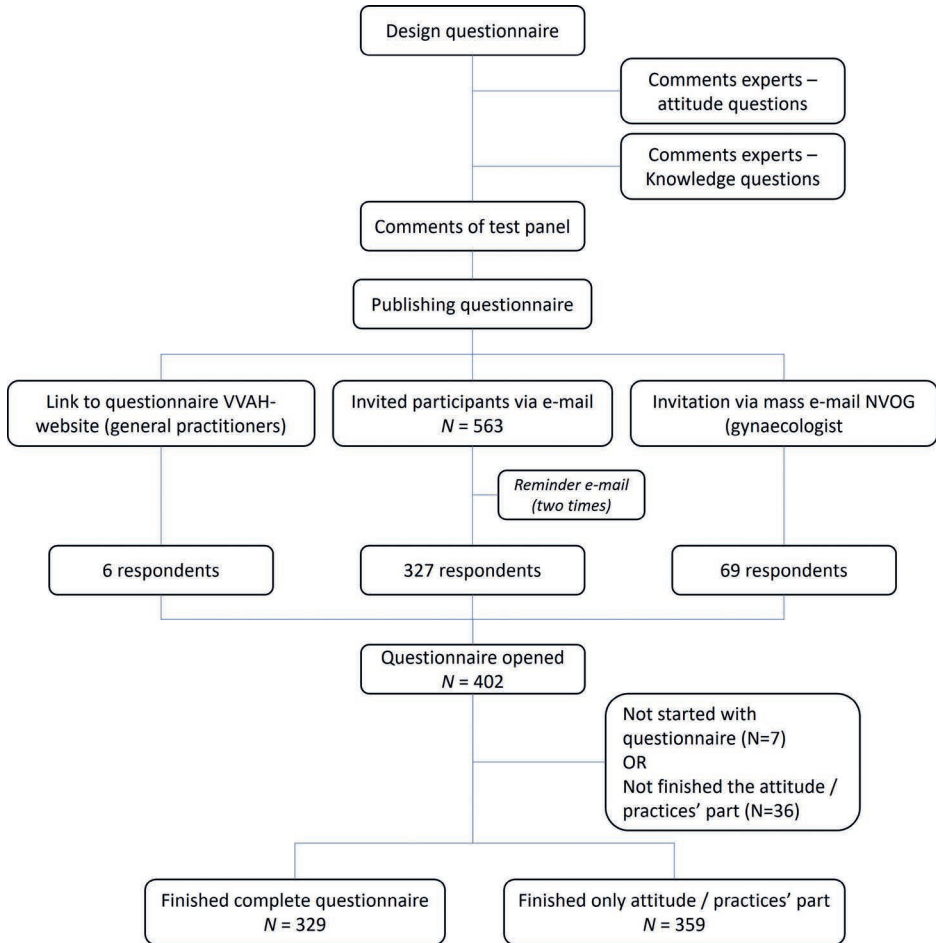
Approval of the Medical Advisory Council of the LUMC was not necessary according to the rules published by the Central Committee on Research involving Human Subjects (<http://www.ccmo.nl/nl/niet-wmo-onderzoek>). The study was approved by the Science Commission of the Department of Obstetrics.

## Results

### Response

A total of 402 obstetric healthcare providers opened the link to the questionnaire, 359 of which filled in the attitude/practices part completely and 329 completed the questionnaire (Figure 1).

On January 1<sup>st</sup>, 2016, approximately 3,321 midwives were active, of them 8.2% (272/3321) filled in at least the attitude/practices part of the questionnaire. Of 66 registered general practitioners specialized in obstetrics, 12.1% filled in at least the attitude/practices part of the questionnaire (ref registration CHBB). In 2009, 842 actively practicing gynaecologists were registered, more recent data are not available, of whom 8.2% filled in the questionnaire at least partly (<https://nvl004.nivel.nl/nivel-2015/sites/default/files/bestanden/Rapport-de-arbeidsmarkt-voor-gynaecologen-in-Nederland.pdf>).



**Figure 1:** Flowcharts of study design, distribution of the questionnaire and overview of the responders.

*Background variables*

Table 1 shows the background variables of the obstetric healthcare providers who filled in the questionnaire completely (n=329). From all participants, 54% graduated between 1999 to 2011. Most had less than 20 years of work experience. The average number of births supervised annually per clinic/practice was between 250 and 500 in the home practices (primary care), in secondary care, 54% of obstetric care providers attended 1000-2000 births annually and 35% more than 2000 births/year. In tertiary care 59% of the care providers had supervised between 1000 and 2000 births/year. The chance of experiencing a case of maternal alloimmunisation or of HDFN increased from primary to secondary care. Forty-two percent of participants followed a training in RBC alloimmunisation and prevention less than five years ago, 25% between 5-10 years ago or longer than 10 years ago. One fifth of obstetric healthcare providers did not know if or when the last training on this topic was attended. The 2011 e-learning was completed by 32% of all participants.

**Table 1:** Background variables of participants divided into three echelons: primary, secondary and tertiary care.

		Primary care n=252	Secondary care n=60	Tertiary care n=17
		n (%)	n (%)	n (%)
Profession	Midwife	246 (98)	7 (12)	1 (6)
	General practitioner	6 (2)	0	0
	Gynaecologist	0	53 (88)	16 (94)
Graduation year	Until 1998	66 (26)	12 (20.0)	2 (12)
	1999 – 2011	144 (57)	27 (45)	8 (47)
	>2011	42 (17)	21 (35)	7 (41)
Work experience	0-10 year(s)	116 (46)	22 (37)	2 (12)
	11 - 20 years	89 (35)	23 (38)	11 (65)
	21 – 30 years	33 (13)	15 (25)	3 (18)
	31 - 50 years	14 (6)	0	1 (6)
Average number of births attended	<250	130 (52)	0	0
	251 – 500	105 (42)	0	0
	501 – 750	13 (5)	1 (2)	0
	751 – 1000	2 (1)	2 (3)	0
	1001 – 1500	2 (1)	3 (5)	10 (59)
	1501 – 2000	0	20 (33)	3 (18)
	>2000	0	13 (22)	4 (24)

**Table 1:** Background variables of participants divided into three echelons: primary, secondary and tertiary care. (continued)

		Primary care n=252	Secondary care n=60	Tertiary care n=17
Experienced a foetus or new-born with haemolytic disease?	yes	53 (21)	21 (35)	15 (88)
Experienced a pregnancy complicated with RBC antibodies?	yes	171 (68)	44 (73)	17 (100)
Last training about alloimmunised pregnant women	< 5 years ago	102 (41)	56 (93)	12 (71)
	5-10 years ago	45 (18)	24 (40)	2 (12)
	>10 years ago	18 (7)	12 (20)	2 (12)
	Unknown	87 (35)	3 (5)	1 (6)
Latest (2011) followed e-learning provided by the RIVM*?	yes	92 (37)	21 (35)	5 (29)
	No	113 (45)	10 (17)	11 (65)
	Unknown	47 (19)	34 (57)	1 (6)

## Knowledge

Table 2 shows the number of correct answers per question of primary, secondary and tertiary caregivers. The questions on the indications for RhD prophylaxis administered in pregnancy were correctly answered by 95% of primary care participants, compared with 15% and 6% respectively of the secondary and tertiary care participants. The question about the indication and quantity of RhD prophylaxis after caesarean section was significantly better answered by secondary and tertiary caregivers. The knowledge about indication for RhD-prophylaxis in case of a spontaneous abortion (72%) as well the indication of RhD-prophylaxis in case of an abortion with curettage was less frequently correctly answered by participants in primary care (43%). The indication for RhD prophylaxis in case of fetal demise was poorly answered; this question was only submitted to secondary and tertiary caregivers. The knowledge score of screening of RhD and Rhc-negative women was over 80%, hence sufficient, in all echelons, but the purpose of the third trimester screening of Rhc-negatives appeared to be often unclear. Less than 20% of all participants gave the correct answers to the question about purpose and policy in case of K-immunisation. In general, questions about laboratory monitoring were moderately to poorly answered. The score for questions about detection of HDFN prenatally or postnatally was in general sufficient. Only tertiary care participants had some difficulties with correctly answering a question about unexpected hyperbilirubinemia.

**Table 2:** Correctly answered questions by participants of primary, secondary or tertiary care.

Question	Primary care	Secondary care	Tertiary care	p-value*
	n=252	n=60	n=17	
Correct	n (%)	n (%)	n (%)	
1a Screening policy RhD-negatives	244 (97)	60 (100)	17 (100)	0.286
1b Antenatal RhD-prophylaxis	231 (96)	9 (15)	1 (6)	<0.001
1c RhD-prophylaxis policy caesarean	16 (6)	35 (58)	11 (65)	<0.001
1d RhD-prophylaxis policy abortion (9 weeks)	229 (91)	53 (88)	14 (82)	0.473
1e RhD-prophylaxis policy abortion (12 weeks)	181 (72)	57 (95)	15 (88)	<0.001
1f RhD-prophylaxis policy abortion + curettage (12 weeks)	109 (43)	56 (93)	16 (94)	<0.001
2a Screening policy Rhc-negatives	252 (100)	60 (100)	17 (100)	-
2b Purpose third trimester screening Rhc-negatives	52 (21)	18 (30)	4 (24)	0.294
3a Screening policy K-immunisation	48 (19)	6 (10)	3 (18)	0.250
3b Follow-up K-immunisation	22 (9)	11 (18)	3 (18)	0.067
4a RhD-prophylaxis policy foetal demise	-	34 (57)	8 (47)	0.483
5a Risk HDFN ADCC-test 10%/ titre 1:8	74 (29)	27 (45)	8 (47)	0.031
5b Policy ADCC-test 10%/ titre 1:8	106 (42)	8 (13)	2 (12)	<0.001
5c Risk HDFN ADCC-test 35%/ titre 1:16	78 (31)	23 (38)	12 (71)	0.003
5d Policy ADCC-test 35%/ titre 1:16	168 (67)	34 (57)	14 (83)	0.113
5e Doppler monitoring to detect foetal anaemia	-	57 (95)	16 (94)	<0.001

**Table 2:** Correctly answered questions by participants of primary, secondary or tertiary care. (continued)

Question	Primary care	Secondary care	Tertiary care	p-value*
5f Frequency of doppler monitoring	-	48 (80)	15 (88)	<0.001
6a follow-up neonate with negative RBC screening	239 (95)	53 (88)	16 (94)	0.179
7a Cause hyperbilirubinaemia neonate and negative third trimester screening	198 (79)	42 (70)	9 (53)	0.031

\*comparing primary, secondary and tertiary care (or secondary and tertiary care when restricted question); Pearson's chi-square test, Fisher's Exact with expected value < 5 in 1 or more cells.

### Level of total knowledge of participants

Table 3 shows how many participants from primary, secondary and tertiary care achieved a sufficient score on the test (defined as: 13, respectively 15 correctly answered questions in primary and secondary/tertiary care). Only 7% of all participants achieved a sufficient score. No significant differences between the echelons were measured. None of the background variables showed an association with the total test-result with a p-value < 0.20. When the cut-off was lowered from 80% to 60% or 70%, 35%, respectively 21% of all participants had a sufficient score.

**Table 3:** Total test-result of participants shown as sufficient with cut-off at 80% correctly answered questions.

	Sufficient	
	N	%
Primary care	19	7.5%
Secondary care	3	5.0%
Tertiary care	1	5.9%
p-value *	0.843	

\* Comparing primary, secondary and tertiary care; Pearson's chi-square test, Fisher's Exact with expected value < 5 in 1 of more cells.

## Attitude and practices

Table 4 shows the median scores on self-assessed attitude and practices per question per echelon (N=359). For several domains a Cronbach's alpha was calculated, showing that only the domain "Attitude to competences" turned out to be 0.84, while the other domains were between 0.24 and 0.49 (respectively "practices" and "knowledge").

The tertiary health care providers estimated their own level of knowledge significantly higher (median score "good") than primary care and secondary care (median score "sufficient"). The tertiary care participants were more satisfied with their own level of knowledge and found it less necessary to participate in trainings than participants of primary and secondary care. The tertiary care participants considered their role within the screening programme and treatment of RBC immunisation and HDFN less important. The primary care participants considered themselves less capable in the care of pregnant women with RBC alloimmunisation without signs of foetal anaemia. All participants considered it their task to well inform pregnant women about the prevention programme. The opinion about time available to well inform pregnant women about the prevention programme was significant different between echelons, varying from surely enough time (tertiary care) to neutral (secondary care).

Primary care providers felt themselves significantly less competent (median score "partly agree" vs "completely agree") in providing information about the development of RBC antibodies during pregnancy and in explaining the blood test results to women with newly identified RBC antibodies, as well as on possible risk of HDFN. The secondary care providers explained significantly less frequent to the patient (median score "often" vs "always") that the routine first trimester screening includes the ABO blood group, Rhesus-D antigen typing and presence of RBC antibodies.



**Table 4:** Overview of median scores on the attitude and practices questions divided in primary, secondary and tertiary care.

	Primary care (n=270)	Secondary care (n=70)	Tertiary care (n=19)	P-value**
	Median (P25-P75)	Median (P25-P75)	Median (P25-P75)	
<b>Attitude towards professional role</b>				
I'm important within the trajectory of detection and treatment of RBC alloimmunisation and HDFN	1 (1-2)	2 (1-2)	2 (1-2)	<0.001
It is my job to well inform the pregnant women about the goal of the RBC screening	1 (1-1)	1 (1-1)	1 (1-1.75)	0.322
Providing information about the prevention programme alloimmunisation improves the level of care	1 (1-2)	1 (1-2)	1 (1-2)	0.694
The time per pregnant women is sufficient to well inform the pregnant women about the goal of the RBC screening programme	2 (1-4)	3 (2-4)	1.5 (1-3.75)	0.011
<b>Attitude towards competences</b>				
I am competent in explaining the meaning of the titre and ADCC result to pregnant women with RBC antibodies	2 (2-3)	1 (1-2)	1 (1-1.75)	<0.001
I am competent to accompany a pregnant woman with RBC antibodies without any signs of haemolytic disease of the foetus	2 (1-3)	1 (1-1)	1 (1-1)	<0.001
I am competent to provide information about alloimmunisation during pregnancy	2 (1-2)	1 (1-2)	1 (1-1.75)	0.003
I am competent in explaining the blood test result to pregnant women for whom RBC antibodies have been found	2 (1-2)	1 (1-1.5)	1 (1-1)	<0.001
I feel competent to provide information about the possible risk of haemolytic disease due to RBC antibodies during pregnancy	2 (1-2)	1 (1-2)	1 (1-1.75)	<0.001

**Table 4:** Overview of median scores on the attitude and practices questions divided in primary, secondary and tertiary care. (continued)

	Primary care (n=270)	Secondary care (n=70)	Tertiary care (n=19)	P-value**
	Median (P25-P75)	Median (P25-P75)	Median (P25-P75)	
<b>Attitude towards self-assessment of level of knowledge</b>				
My knowledge about alloimmunisation is: ~	3 (3-3)	3 (2-3)	2 (1-3)	<0.001
It is necessary to extent my knowledge about alloimmunisation.	2 (2-3)	2 (2-3)	4 (2.25-5)	0.027
My plan is to extent my knowledge about alloimmunisation.	2 (2-3)	2 (2-3)	4 (3-5)	0.126
I'm satisfied with my level of knowledge	3 (2-3)	3 (1-3)	2 (1-2)	0.044
<b>Practices followed courses, actual information provided and intention or need for training</b>				
I would attend a training/ course on providing information	2 (1-2.25)	2 (1-2.5)	2.5 (2-3)	0.007
I find it important to follow a training/ course about RBC alloimmunisation	2 (1-2)	1 (1-3)	2 (1.25-3)	0.363
Attending the e-learning about prevention and detection of RBC alloimmunisation was useful/relevant # (primary care n=149, secondary care n=17, tertiary care n=8)	1 (1-2)	1 (1-2)	1 (1-1)	0.207
Before the first trimester screening, I explain that the blood test contains the ABO and RhD blood group and RBC antibodies*	1 (1-1)	2 (1-3)	1 (1-2)	<0.001
Before the first trimester screening, I explain the possible test results and the risk of RBC antibodies during pregnancy *	3.5 (3-4)	4 (3-4.5)	3 (2-4.75)	0.329

\*\*Differences between primary, secondary and tertiary care were tested using Kruskal-Wallis test.

1=Completely agree, 2=partly agree, 3=neutral, 4= partly disagree, 5=strongly disagree

~1=very good, 2 = good, 3 = sufficient, 4= insufficient, 5 = poor

#respondents who didn't follow the e-learning were excluded

\*1= always, 2= often, 3= sometimes, 4 = rarely, 5 = never

## Discussion

In this nationwide study with 329 participants, only 7% of obstetric care providers appeared to have sufficient knowledge of all aspects of maternal RBC alloimmunisation, needed to provide sufficient support and counselling during pregnancy. The participants of the tertiary care were more satisfied with their own knowledge on the subject than the participants of primary and secondary care and judged it to be less necessary to follow an additional in-service training on management of maternal RBC alloimmunisation. All echelons considered themselves important within the process of detection and treatment of RBC alloimmunisation and HDFN.

### Strength and weaknesses

For each professional group, the response was approximately 10% of the total number of active care providers. The response may have been negatively influenced by the length of the questionnaire and by sending it around in the summer period. In our opinion, this relatively low response is sufficient to at least have an impression of the level of knowledge. However, selective response of care providers who have an affinity with the subject, may have resulted in an overestimation of the level of knowledge and a too optimistic assessment of the attitude.

### Previous findings and interpretation

Our estimation was that at least half of the obstetric care providers should have sufficient knowledge about RBC alloimmunisation, defined as answering 80% of all questions correctly.<sup>(164)</sup> This cut-off value was also used in a study from Singapore, exploring the knowledge about RhD immunisation and prophylaxis. Our study included questions on all aspects of the screening program, whereas the Singapore study focused on prevention of RhD immunisation. Also in our study, 60% of the questions about RhD screening and prophylaxis were correctly answered. The knowledge gaps we found concerned mainly aspects of non-RhD RBC antibodies, the indications for administering extra Rhlg and the interpretation of ADCC and antibody titre results. This probably does not mean that mistakes are made in the care for pregnant women with RBC alloimmunisation.<sup>(10, 28, 44, 76)</sup> A lack of active knowledge may be explained by the fact that, the care provider receives necessary information about the follow-up policy, and if necessary, advice to consult the expert centre at LUMC, via the laboratory report from the reference laboratories. The finding that obstetric care providers are often not aware of their own low level of knowledge is not only remarkable but also worrisome, as self-knowledge and introspection are

essential to warrant an adequate level of care. Presumably, lack of knowledge has consequences for the adequate counselling and understanding of this complex matter by patients. It therefore may explain the moderate satisfaction of pregnant women with the content and comprehensibility of information they receive on this condition, as we previously showed.(63) Poorly provided information after detection of RBC antibodies or during follow up, can influence the emotional pregnancy experience of women. From the evaluation of similar situations, like informing parents about a positive test result for any of the diseases tested during the new-born screening, Moody et al (2017) advised to arrange direct face-to-face contact between the specialist team and the family, continued support and the availability of accessible condition specific information. Various studies about parents' recommendations how to inform them about a positive new-born screening result suggest that it is important to offer realistic reassurance and hope, to address and support parents through the moments of anxiety and to keep the content simple, clear and actionable.(169-172)

In our study the obstetric care providers considered it important to provide information about the national screening programme and found their own professional role important within the process of detection and treatment of RBC alloimmunisation and HDFN. This positive attitude can form the basis to fill the knowledge gaps by a targeted e-learning based training or by up-to-date information on the web. Awareness of giving the patient news that can cause anxiety, already helps to respond more adequately on emotions and socio-psychological aspects of the message, thus diminishing stress and anxiety in the pregnant woman.(173)

## **Conclusion**

Awareness of the lack of knowledge is necessary to help obstetric care providers to be careful in giving information and even to decide to contact the expert centre before counselling the patient.

This will improve adequate counselling with the aim to empower the pregnant woman and her partner to appropriately translate the message of the presence of RBC alloantibodies into risks for their unborn child, to minimise unnecessary anxiety during pregnancy.

**Table S1:** Knowledge scores classified per level of obstetrical care

		Primary care n=252 n (%)	Secondary care n=60 n (%)	Tertiary care n=17 n (%)	p-values*
<hr/>					
Prevention of maternal alloimmunisation in RhD-negative women					
Screening policy RhD-negative women	Correct	225 (80.9)	7 (11.7)	1 (5.9)	<0.0001
Antenatal anti-D administration					
<hr/>					
Prevention of maternal alloimmunisation in Rhc-negative women					
Screening policy Rhc-negative women	Correct	52 (18.1)	18 (30.0)	4 (23.5)	0.3092
Purpose screening at 27 weeks in Rhesus-c-negative women					
<hr/>					
Screening for maternal K-immunisation	Correct	6 (2.4)	0	1 (5.9)	0.282
Follow-up laboratory tests in K-immunised pregnant women					
<hr/>					
Indications Anti-D					
Anti-D policy caesarean section					
Anti-D policy spontaneous abortion (9 weeks)	Correct	85 (34.0)	28 (46.7)	9 (52.9)	0.075
Anti-D policy spontaneous abortion (12 weeks)					
Anti-D policy abortion + curettage (12 weeks)					
<hr/>					
ADCC-test and titre measurements					
Risk of haemolysis and policy if ADCC-test 10%/ titre 1:8					
Risk of haemolysis and policy if ADCC-test 10%/ titre 1:8	Correct	32 (12.8)	3 (5.0)	1 (5.9)	0.175
Risk of haemolysis and policy if ADCC-test 35%/ titer 1:16					
Risk of haemolysis and policy if ADCC-test 35%/ titer 1:16					

**Table S1:** Knowledge scores classified per level of obstetrical care (continued)

		Primary care n=252	Secondary care n=60	Tertiary care n=17	p-values*
		n (%)	n (%)	n (%)	
Follow-up of the neonate					
Follow-up neonate with negative antibody screening	Correct	186 (74.4)	36 (60.0)	9 (52.9)	0.023
Causes of neonatal icterus with a negative antibody screening at 27 weeks.					

\*Differences between primary, secondary and tertiary healthcare providers, Pearson's Chi-square and Fisher's Exact with a minimal expected value of <5 in 1 or more cells.

**Table S2:** Univariate analysis of the association of background variables with the level of knowledge.

	Sufficient n (%)	p-value*
Profession		
Midwife (n= 254)	17 (6.7)	0.783
General practitioner (n= 6)	0	
Gynaecologist (n= 69)	4 (5.8)	
Year of graduation		
<1998 (n=80)	4 (5.0)	0.547
1999-2011 (n=179)	13 (7.3)	
>2011 (n=70)	4 (5.7)	
Years' of obstetrical experience		
0-10 years (n=130)	10 (7.1)	0.684
11 - 20 years (n=116)	7 (5.7)	
21 - 30 years (n=49)	2 (3.9)	
31 - 40 years (n=12)	2 (14.3)	
41 - 50 years (n=1)	0	
Experienced a foetus or new-born with haemolytic disease		
Yes (n=103)	9 (8.0)	0.378
No (n=205)	12 (5.5)	
Experienced a pregnancy complicated with red blood cell immunisation		
Yes (n=227)	17 (7.0)	0.463
No (n= 81)	4 (4.7)	
Average number births attended per year		
< 1000 (n=239)	17 (6.6)	0.484
>1000 (n=69)	4 (5.5)	
Last training about alloimmunised pregnant women		
< 5 years ago (n=130)	8 (5.8)	0.652
> 5 years ago (n=75)	7 (8.5)	
I don't know (n=103)	6 (5.5)	
Latest (2011) followed e-learning provided by the National Institute for Health and environment?		
yes (n=140)	8 (5.4)	0.741
No (n= 94)	8 (7.8)	
unknown (n=58)	4 (6.5)	

\* Pearson's Chi-square and Fisher's Exact with a minimal expected value of <5 in 1 or more cells.