Transfusion Testing During Routine Pregnancies: Consensus Recommendations from a Modified Delphi Process

Heather VanderMeulen, MD, MSc;[1] Mira Shuman, MD, CFFP, MScCh;[2] Poh Nyuk Fam, MD, RM, RN;[3] Robyn Berman, RM, MBA;[4] Jeannie Callum, BA, MD;[2,5] Gwen Clarke, MD;[6,7] Lani Lieberman, MD;[8,9] Catharine Walsh, MD, MEd, PhD;[10,11] Julie Thorne, MD, MPH;[12,13,*] Matthew T.S. Yan, MD[14,15,*]

[1]Department of Medicine, University of Toronto, Toronto, ON

[2]Sunnybrook Health Sciences Centre, Toronto, ON

[3]Clinical Science Division, Northern Ontario School of Medicine University, Thunder Bay, ON

[4]The Ottawa Birth and Wellness Centre, Ottawa, ON

[5]Department of Pathology and Molecular Medicine, Kingston Health Sciences Centre and Queen's University, Kingston, ON

[6]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB

[7]Island Health, Victoria, BC

[8]Department of Clinical Pathology, University Health Network, Toronto, ON

[9]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON

[10]Division of Gastroenterology, Hepatology and Nutrition and the Research and Learning Institutes, The Hospital for Sick Children, Toronto, ON

[11]Department of Paediatrics, The Wilson Centre, and Temerty Faculty of Medicine, University of Toronto, Toronto, ON

[12]Women's College Hospital and Mount Sinai Hospital, Toronto, ON

[13]Department of Obstetrics and Gynaecology, University of Toronto, Toronto, ON

[14]Canadian Blood Services, Canada

[15]Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC

ABSTRACT

Objectives: To standardize perinatal transfusion testing and Rh immunoglobulin (RhIG) administration in low-risk pregnancies through the creation of expert consensus statements.

Methods: A modified Delphi consensus process involving iterative rounds of voting on statements by a national expert panel. After each round, responses were analyzed and resent to the panel for further ratings until consensus was achieved, defined as Cronbach's alpha >0.95 or a maximum of 3 voting rounds. Once consensus was achieved, statements with a median score ≥ 4 out of 5 were included.

Results: Forty-six expert panellists participated, with representation across Canadian provinces and care providers including maternal–fetal medicine, obstetrics, family practice, transfusion medicine, neonatology, midwifery, nursing, and a patient representative. Twenty-one statements related to perinatal transfusion testing and RhIG administration met criteria for inclusion in the final set of statements. The 2 statements with the lowest proportion of "strongly agree" votes pertained to eliminating the 28-week group and screen in those with negative first-trimester screens and eliminating the need for RhIG before 12^0 weeks in threatened, spontaneous, or therapeutic abortions.

Conclusions: These 21 expert consensus statements aim to harmonize perinatal practice across Canada, addressing conflicting guidelines and resource limitations, especially in rural settings. This is the first set of expert consensus statements that captures the Canadian context, with coverage from the first trimester to the birth of the neonate. These statements follow Choosing Wisely principles. Some are practice-changing and will require efforts to ensure implementation into practice.

Keywords: pregnancy; transfusion medicine; perinatology; Delphi technique

Corresponding author: Matthew T.S. Yan, Matthew.yan@blood.ca

*Julie Thorne and Matthew Yan are co-senior authors.

Disclosures: Heather VanderMeulen has consulted for CSL Vifor and Canada's Drug Agency. Gwen Clarke is on the medical advisory board for Janssen Pharmaceuticals. Jeannie Callum has received research support from Canadian Blood Services and Octapharma. This work was supported by the Ontario Regional Blood Coordinating Network, the Ontario Ministry of Health and Long-Term Care, and Canadian Blood Services.

Each author has indicated they meet the journal's requirements for authorship.

Received on February 13, 2025

Accepted on March 3, 2025

Available online July 10, 2025

RÉSUMÉ

Objectif : Normaliser les épreuves de transfusion périnatale et l'administration d'immunoglobulines anti-D (Ig anti-D) en cas de grossesse à faible risque par la création de déclarations de consensus d'experts.

Méthodes : Processus de consensus Delphi modifié impliquant des tours itératifs de vote sur les déclarations par un panel d'experts nationaux. Après chaque tour, les réponses ont été analysées et renvoyées au panel pour une nouvelle évaluation jusqu'à ce qu'un consensus soit atteint, défini par un score alpha de Cronbach supérieur à 0,95 ou un maximum de 3 tours de vote. Une fois le consensus atteint, les déclarations ayant un score médian de 4 ou plus sur 5 ont été incluses.

Résultats : En tout, 46 experts ont participé au panel, représentant toutes les provinces canadiennes et les différentes sphères de la prestation de soins, dont la médecine fœto-maternelle, l'obstétrique, la médecine familiale, la médecine transfusionnelle, la néonatologie, la pratique sage-femme, les soins infirmiers ainsi qu'un représentant des patientes. Au total, 21 déclarations relatives aux épreuves de transfusion périnatale et à l'administration d'Ig anti-D répondaient aux critères d'inclusion dans la série finale de déclarations. Les deux déclarations ayant obtenu la plus faible proportion de votes « tout à fait d'accord » concernaient l'élimination du groupage et phénotypage à 28 semaines d'aménorrhée en cas de dépistage négatif des anticorps au premier trimestre ainsi que l'élimination de la nécessité d'administrer des Ig anti-D avant 12 semaines d'aménorrhée en cas de menace d'avortement, d'avortement spontané ou d'interruption médicale de grossesse.

Conclusion : Ces 21 déclarations de consensus d'experts visent à harmoniser la pratique périnatale au Canada en rectifiant les directives contradictoires et en tenant compte des ressources limitées, surtout en régions rurales. Il s'agit de la première série de déclarations de consensus d'experts qui reflète le contexte canadien et couvre la période allant du premier trimestre à la naissance. Ces déclarations sont conformes aux principes de la campagne Choisir avec soin. Certaines d'entre elles modifient la pratique et nécessiteront des efforts pour assurer leur mise en application.

© 2025 The Author. Published by ELSEVIER INC. on behalf of The Society of Obstetricians and Gynaecologists of Canada/La Société des obstétriciens et gynécologues du Canada. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

J Obstet Gynaecol Can 2025;47(9):103034

https://doi.org/10.1016/j.jogc.2025.103034

INTRODUCTION

Hemolytic disease of the fetus and/or newborn (HDFN) occurs when clinically significant red blood cell (RBC) alloantibodies cross the placenta and bind to antigen-positive fetal RBCs. Outcomes range in severity from asymptomatic to fetal anemia and hydrops. With advances in Rh immunoglobulin (RhIG) prophylaxis, RhD alloimmunization can be substantially mitigated in RhD-negative people. Although RhIG has reduced the risk of anti-D formation to less than 1%, anti-D remains the most common cause of severe HDFN in Canada, suggesting there is room for improvement and standardization.[1]

Timely access to routine perinatal testing and care can be challenging in Canada, as many Canadians lack a primary care provider and experience delays in accessing testing, especially in rural locations.[2] This is further complicated by multiple guidelines with differing recommendations on transfusion testing and RhIG administration.[3] As a result, practices are highly variable among clinicians, with recent surveys identifying inconsistencies in fetomaternal hemorrhage (FMH) testing and RhIG dosing.[4]

To address the challenges in providing standardized perinatal care, a modified Delphi process was used to generate consensus statements from a multidisciplinary panel representing a broad range of Canadian health care professionals, inclusive of rural practice, a patient representative, and representation from national societies that publish guidelines. This is the first set of expert statements that details HDFN risk mitigation and diagnosis from conception to the birth of the neonate. Presented within this publication are consensus statements that cover low-risk pregnancies, specifically for people who are not known to be alloimmunized at the first prenatal visit.

METHODS

Design

A modified Delphi panel consensus process, which involved iterative rounds of voting on statements by a national expert panel, was used to develop consensus on statements related to perinatal transfusion.[5]

Participants

Panellists were selected from across Canada and included obstetricians, abortion providers, maternal–fetal medicine specialists, transfusion medicine specialists, pediatricians, family physicians (inclusive of rural practice), midwives, nurses, medical laboratory technologists, and a patient representative. Panel participation was voluntary and non-remunerated. Attendance at the in-person consensus conference and participation in each round of voting were mandatory.

Statement Generation

A steering committee (LL, GC, JC, NS) selected panellists, and the committee chairs (LL, GC) drafted 46 preliminary

statements based on available evidence, international guidelines, Canadian practice, and expert opinion when evidence was lacking. Twenty-one statements addressed low-risk perinatal testing and RhIG administration. To standardize panellists' knowledge prior to the Delphi voting process, a 2-day consensus conference was held in Toronto, Ontario, to review the evidence and discuss each proposed statement.

Delphi Process: Consensus

Iterative rounds of electronic Delphi surveys were then used to achieve consensus. During the first round, panellists were asked to vote anonymously on their level of agreement with each statement on a 1 ("strongly disagree") to 5 ("strongly agree") Likert scale. Panellists were also given the opportunity to comment on the wording of each statement and could abstain from voting if they lacked sufficient expertise. In subsequent voting rounds, panellists re-rated the remaining statements using the same 5-point Likert scale and provided comments. Additionally, they were provided with the mean, median score, and range for each statement from the previous round.

After each survey round, panellists' anonymized responses were analyzed, and the Delphi process continued until consensus was achieved, defined as a Cronbach alpha >0.95 or a maximum of 3 voting rounds. Once consensus was achieved, based on pre-defined criteria, statements with a median rating ≥ 4 were included, while those with <4 were excluded. Statements where panellists had proposed significant content changes were reviewed in a follow-up online meeting. The meeting was recorded, and statement wording was adjusted if full agreement was reached. The revised statements were then re-rated in an abbreviated voting round, and the final list of statements was circulated to the Delphi panel for review and comment.

Data Collection and Analysis

The online surveys were distributed using Research Electronic Data Capture (REDCap), an electronic data capture tool. Descriptive statistics were calculated after each round using Excel (Microsoft 365 Apps for enterprise). Ethical approval was not required for this study.

RESULTS

Forty-six panellists participated in the modified Delphi consensus process (Table 1). Three rounds of voting resulted in 21 low-risk statements divided under 3 topic areas: antenatal testing, RhIG administration, and FMH testing (Figure 1, Table 2[6-24]). The vote distribution for each statement, including the number of abstaining panellists, is presented in Figure 2.

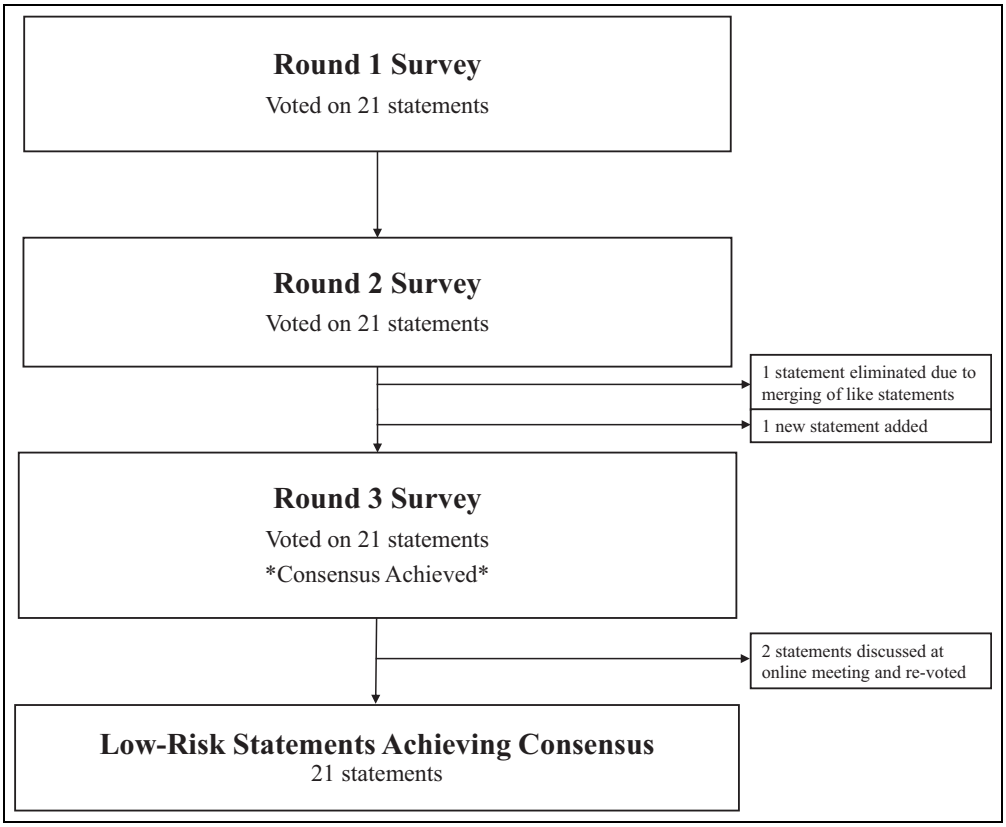
Table 1. Demographics of expert panellists participating in the modified Delphi consensus process

Expert panellists (n = 46)	n (%)
Professional designation	
Physician[a]	36 (78.3)
Transfusion medicine specialist	16 (44.4)
High-risk obstetrician/ gynaecologist	10 (27.8)
Pediatric hematologist	5 (13.9)
Family Physician	4 (11.1)
Pediatrician with neonatology responsibilities	3 (8.3)
Neonatologist	3 (8.3)
Low-risk obstetrician/ gynaecologist	3 (8.3)
Hematopathologist	1 (2.8)
Medical Laboratory Technologist	4 (8.7)
Nurse	3 (6.5)
Midwife	2 (4.3)
Patient Representative	1 (2.2)
Region	
Central Canada	35 (76.1)
Atlantic region	5 (10.9)
Prairie Provinces	3 (6.5)
West Coast	2 (4.3)
North	0 (0)
International	1 (2.2)
Years of expertise	
0–4.9	4 (8.7)
5–9.9	4 (8.7)
10–14.9	8 (17.4)
15–20	7 (15.2)
More than 20	23 (50.0)
Type of centre	
Academic centre	33 (71.7)
Community hospital	6 (13.0)
Other[b]	5 (10.9)
Community office	2 (4.3)
Region	
Central Canada	35 (76.1)
Atlantic region	5 (10.9)
Prairie Provinces	3 (6.5)
West Coast	2 (4.3)
North	0 (0)
International	1 (2.2)

[a]Respondents could select more than one subspecialty type.

[b]Other responses include: birthing centre; blood supplier (specialized testing); community and academic centre and international work; provincial nursing consultation.

Figure 1. Flow of the low-risk statement throughout the modified Delphi process.



Two statements were significantly revised based on panellist feedback and required an additional round of voting. The wording of statement L2, which addresses the routine practice of a 28-week group and screen, was softened from "not suggested" to "may not be necessary". Statement L7, regarding the timing of RhIG administration for abortions, was revised from 8^0 weeks to 12^0 weeks following new evidence from Horvath et al.[12] and guideline updates from several societies.[6,14,15] Both statements were approved in their updated form following a Supplemental Vote.

Aside from statement L21 on fetal maternal hemorrhage testing by flow cytometry, at least 80% of panellists submitted votes for each of the statements (Figure 2). Statement L8 had the highest proportion of "strongly agree" votes at 89%, followed by statements L6 and L13, both at 70%. Conversely, statements L7 and L2 had the smallest proportion of "strongly agree" votes at 33% and 35%, respectively, and the largest proportion of votes between "uncertain" to "strongly disagree" at 26% and 13%. Only 2 statements, L1 and L7, received any "strongly disagree" votes.

DISCUSSION

The perinatal consensus statements generated by the expert panel represent a comprehensive set of Canadian guidance for transfusion testing and RhIG administration in low-risk pregnancies, from conception to the postpartum period (Figure 3). In accordance with Choosing Wisely principles, these statements are patient-focused, evidence-based, and multiprofessional. The panellists represented diverse perspectives, including a patient and rural care providers. Although all statements are based on available evidence and guidelines, considerations for access and logistics were also considered. As a result, the 21 consensus statements presented here have similarities with guideline recommendations but also differ, given the nature of the modified Delphi approach compared to guideline development methodology.

These statements are the first in Canada to capture group and screen testing through all phases of pregnancy. Not surprisingly, statement L2 regarding the elimination of the 28-week group and screen for both RhD-positive and

Table 2. Low-risk statements achieving consensus, including rationale

#	Statement	Rationale
	Statements Related to Antenatal Testing	
L1	For routine care, prenatal testing for ABO, RhD, and antibody screen is recommended after 8^0 weeks' gestation, preferably between 11 and 14 weeks.	Testing for ABO, RhD and RBC antibodies in the first trimester is an established practice to identify RhD negative pregnancies requiring RhIG prophylaxis, and pregnancies with clinically significant alloantibodies requiring additional monitoring. The screen for RBC antibodies should be performed after 8^0 weeks, ideally between 11-14 weeks, when enough fetal RBC antigens are expressed to stimulate RBC alloantibodies (e.g., K is expressed on fetal RBC at 10 weeks).[6] However, some evanescent antibodies may not be detectable until an inciting event like a small FMH or transfusion prompts a secondary antibody response, justifying the need for repeat testing after a sensitizing event.[7]
L2	A routine ABO, RhD and antibody screen may not be necessary at 28 weeks' gestation for either RhD positive or RhD negative pregnancies.	
L3	Antibody screening is suggested for all pregnancies (RhD-negative and RhD-positive) following a sensitizing event or after maternal RBC transfusion.	In routine non-alloimmunized pregnancies, the practice of repeating a 28-week group and screen is of very low value, as only 0.01-0.43% of pregnancies with a negative first-trimester antibody screen develop a new alloantibody later in the pregnancy.[7] In those with late alloimmunization, severe HDFN is exceptionally rare.[7,8]
L4	Maternal ABO, RhD, and antibody screen at the time of delivery is only recommended when: a. There is no prior test during the current pregnancy; and/or b. There is a clinically significant antibody, and/or c. The risk of maternal transfusion is increased, and/ or d. The risk of neonatal transfusion is increased.	Repeat group and screen testing prior to delivery is not supported by evidence in low-risk pregnancies where the rate of transfusion is less than 1% for vaginal and C-section deliveries.[7,9] In the rare circumstance that transfusion is required, emergency-issued uncrossmatched O negative, RhD negative, and K negative RBC units can always be provided with minimal risk, particularly in the context of a negative first-trimester antibody screen.[10]
L5	RHD genotyping is recommended in any pregnant person with weak or variably reactive RhD typing.	In up to 1% of the population, RhD serologic typing may be weak, indeterminate, or discrepant with historical results.[11] This may represent a variant RHD allele, which may or may not have the potential for anti-D formation. RHD genotyping is used in these cases to determine RhIG eligibility. Weak D types 1, 2, and 3 will not form anti-D, do not require RhIG, and can be managed as RhD positive.[11] All other RhD variants should be managed as RhD negative and thus RhIG candidates. While genotype results are pending, people should be considered RhD negative.
L6	It is recommended that pregnancies with weak or indeterminate RhD and without available RHD genotype results be considered RhD negative until genotyping results are available.	
L7	For any pregnancy less than 12^0 weeks' gestational age experiencing an abortion (threatened, spontaneous or therapeutic), an ABO, RhD, and antibody screen are not recommended and RhIG is not required.	FMH testing by flow cytometry suggests that the amount of FMH associated with induced abortions prior to 12^0 weeks' gestational age is insufficient to cause RhD alloimmunzation.[12] Additional studies demonstrate that anti-D alloimmunization prior to 12^0 weeks is rare and that RhD alloimmunization rates are no different in the Netherlands compared to Canada, despite the former restricting RhIG to spontaneous abortions 10^0 weeks onwards and therapeutic abortions 7^0 weeks onwards, and Canada's historic practice of administering RhIG to all gestational ages.[13] Several updated societal guidelines allow for the exclusion of RhIG prior to 12^0 weeks' gestation, highlighting factors such as access to care, reduced emergency department visits for RhIG, reduced cost of testing, and variable access to RhIG.[14-17] To omit RhIG prior to 12^0 weeks' gestation, dating of the pregnancy must be certain. If dating is uncertain, RhIG should be administered.
	Statements Related to RhIG Administration	
L8	Informed consent (verbal or written) must be obtained and documented prior to the administration of RhIG.	RhIG is a fractionated product derived from human blood. The 1997 Krever Commission set out standards in practice to assure patient safety in the administration of blood and blood products.[18] Informed consent should be obtained and documented in accordance with current practice standards and according to organization policy.[18,19]
L9	For RhD-negative pregnancies, determination of fetal RhD status by non-invasive prenatal testing (cffDNA testing of maternal plasma) is suggested to avoid unnecessary RhIG administration.	The need for RhIG prophylaxis is eliminated if a fetus is confirmed RhD-negative. Other countries offer non-invasive prenatal testing for RhD-negative pregnancies to determine fetal RhD typing and thus RhIG eligibility.[20] At the time of publication, this test is not yet universally available in Canada.
L10	Routine antenatal RhIG at a dose of 300 μg (1500 IU) is recommended for all RhD-negative pregnant people at approximately 28 weeks' gestation.	All RhD-negative people should receive antepartum RhIG prophylaxis if the fetus is RhD positive, indeterminate, or unknown. Although the biggest risk of sensitization is at delivery, the provision of an antepartum dose of RhIG further reduces this risk from 1% to 0.2%. Most studies evaluated a 28-week dose since transplacental hemorrhages in the third trimester were thought to be most likely to cause sensitization.[21]

(continued)

Table 2. *(Continued)*

#	Statement	Rationale
L11	For sensitizing events in RhD-negative pregnancies, RhIG dosing varies depending on the gestational age of the pregnancy: a. Less than 8^0 weeks: no RhIG required b. 8^0 to 11^6: 120 μg (600 IU) for ectopic or molar pregnancies, trauma or invasive prenatal testing (see statement L7: RhIG not required for abortion) c. 12^0 to 19^6 weeks: 300 μg (1500 IU) for all sensitizing events d. $\geq 20^0$ weeks: 300 μg (1500 IU) for all sensitizing events with FMH quantification to determine need for additional doses	Sensitizing events refer to any opportunity for fetal blood to enter the maternal circulation and thus trigger alloimmunization. Except for first-trimester abortion (therapeutic, spontaneous or threatened), RhIG should be administered for sensitizing events to RhD-negative pregnant people if the fetus is RhD positive, indeterminate or unknown. The actual risk of alloimmunization from percutaneous fetal procedures (e.g., selective fetal termination, relief of lower urinary tract obstruction) and ectopic or molar pregnancies is unclear.[21] If the dating of the pregnancy is unclear, RhIG should be administered. Refer to statement L7 for abortion prior to 12^0 weeks, and to statement L17 for FMH testing guidance. The current evidence for RhIG omission between 8 and 12 weeks' GA focused on early abortions. The panellists did not feel comfortable extrapolating this to the care of ectopic or molar pregnancies.
L12	If an immune anti-D is detected, RhIG is not recommended	There is no benefit in administering RhIG to people with an immune anti-D (i.e., those who are already sensitized to RhD). If there is uncertainty about whether an anti-D antibody is passive from recent RhIG vs. immune, the pregnant people should be managed as RhIG eligible. There is no reliable test to differentiate passive and immune anti-D.
L13	RhIG is recommended for routine prophylaxis and for sensitizing events in RhD-negative pregnancies when antibodies other than anti-D are present	Besides RhD, alloimmunization can occur to other blood group antigens. In this situation, RhD-negative people remain RhIG eligible so long as immune anti-D is absent.[22]
L14	In the setting of ongoing or recurrent antepartum bleeding starting at 20^0 weeks' gestation in an RhD-negative pregnancy, both RhIG and FMH testing are recommended	In pregnancies affected with recurrent or continuous uterine bleeding after 20^0 weeks' gestation, RhIG should be administered and FMH testing performed at 3-to 6-week intervals. If there is an increase in the severity of bleeding, the frequency of FMH testing should be increased to every 2 weeks.[22] If FMH testing detects fetal cells, additional RhIG should be administered in accordance with a validated dose calculator (see statement L19).
L15	Following delivery of an RhD-positive neonate in an RhD-negative pregnancy, RhIG is required within 72 hours of delivery	Delivery represents one of the largest risks for RhD alloimmunization in an RhD-negative person. If an RhD-negative person delivers an RhD-positive infant, RhIG administration should occur as soon as possible within 72 hours postpartum.[21] If RhIG is not administered in this time frame, the protective benefits of RhIG may extend up to 28 days from delivery.[6]
L16	Postnatal RhIG dosing (300 μg (1500 IU) or 120 μg (600 IU)) may vary depending on access to FMH test results	Postnatal RhIG protects an RhD-negative people against alloimmunization by RhD-positive fetal RBCs at the time of delivery. FMH testing at delivery identifies people requiring additional RhIG beyond the standard dose given. A 120 μg (600 IU) dose of RhIG is sufficient for FMH bleeds up to 12 mL of fetal blood (6 mL of fetal RBCs), and a 300 μg (1500 IU) dose for FMH bleeds up to 30 mL of fetal blood (15 mL of fetal RBCs).[6] Rapid identification of the minority of people with more than 12 mL of FMH (6 mL of fetal RBCs) enables the provision of additional RhIG still within the 72-hour window. In these cases, a 120 μg (600 IU) standard dose may be considered. Where ready access to flow cytometry for FMH quantification is not available, the 300 μg (1500 IU) dose should be used, which will be sufficient prophylaxis for more than 99% of deliveries.[21]
Statements Related to Maternal–Fetal Hemorrhage Testing		
L17	Quantitative FMH testing prior to 20 weeks' gestation is not routinely recommended for RhIG dose guidance	The role of quantitative FMH testing is to determine if the volume of FMH exceeds that covered by standard doses of RhIG. Prior to 20^0 weeks' gestation, a standard dose of RhIG covers the entire fetal-placental blood volume of a singleton pregnancy.[23] The increased fetoplacental blood volume in multiple gestation pregnancies must be considered, and expert opinion should be sought to guide RhIG dosing prior to 20^0 weeks in these pregnancies.
L18	Quantitative FMH testing is required starting at 20^0 weeks' gestation for pregnancies with a sensitizing event that may lead to FMH	Starting at 20^0 weeks' gestation, RhIG candidates should receive 300 μg (1500 IU) RhIG following a sensitizing event, which covers up to 30 mL of fetal whole blood (15 mL of fetal RBCs).[6] Quantitative FMH testing is required to determine the need for additional doses using a validated calculator.[6,23] Note that current FMH tests are not sensitive enough to justify withholding a standard dose of RhIG based on a negative test. FMH testing is not required if the person is not eligible for RhIG (e.g., presence of immune anti-D, cffDNA predicts fetus to be RhD negative).
L19	For sensitizing events starting at 20^0 weeks, RhIG dosing should be based on quantitative FMH assessment with use of a validated calculator	

(continued)

Table 2. *(Continued)*

#	Statement	Rationale
L20	FMH testing is required postpartum for RhD-negative pregnancies with an RhD-positive neonate	If a neonate is RhD positive or the neonate's RhD status is unknown, postpartum RhIG and FMH testing (drawn before RhIG administration) are required for RhIG eligible postpartum people.[8] By consensus, the panel agrees with test kit recommendations that maternal samples are collected between 30 minutes to 2 hours from delivery.[23] In theory, this minimizes the risk of under detection of FMH by: (a) providing adequate time for fetal cells to mix with maternal circulation; and (b) testing before fetal cells are rapidly cleared from maternal circulation (e.g., due to maternal–fetal ABO incompatibility). If the neonate is RhD negative (including weak D testing), FMH testing is not required.
L21	Flow cytometry is recommended for confirmation of diagnosis and quantitation of FMH, where feasible.	Assessing for FMH usually begins with a screening test (e.g., Rosette or Betke-Kleihauer test). Positive tests should then be confirmed and quantified using a flow cytometry method. FMH testing by flow cytometry is usually not used as a frontline quantitative test due to both costs and unavailability of the test outside working hours. In certain pregnant populations, such as people with elevated hemoglobin F (commonly seen in those with beta thalassemia, sickle cell disease or hereditary persistence of fetal hemoglobin), consider bypassing the Betke-Kleihauer test and progressing directly to flow cytometry.[23] Flow cytometry is the most precise and accurate method for the detection of FMH.[24] Commonly used methods involve monoclonal anti-D and/or anti-hemoglobin F antibodies (targeting the RhD antigen on fetal RBCs and fetal hemoglobin, respectively).[24]

cffDNA: cell-free fetal DNA; FMH: fetal maternal hemorrhage; HDFN: hemolytic disease of the fetus and/or newborn; RBC: red blood cell; RhIG: Rh immunoglobulin.

RhD-negative pregnancies were controversial despite a strong evidence base supporting the change. This likely reflected some panellists' very low tolerance of any perceived risk for missing late red cell alloimmunization. Although most guidelines recommend performing the 28-week group and screen for all people to assess for new alloimmunization,[7] statement L2 offers a more personalized approach recognizing that people with a negative first trimester screen have an exceedingly low rate of developing a new alloantibody (referred to as late alloimmunization), ranging from 0.01%–0.43%.[7] In those with late alloimmunization, the risk of developing HDFN is 0.05%, where the risk of severe HDFN, defined as requiring intrauterine transfusion, is even lower at <0.01%.[7] The rare risk of HDFN also holds true for anti-c, where a prospective study by Slootweg et al.[8] calculated an HDFN rate of <0.01% for late alloimmunization events related to anti-c. The disconnect between late

Figure 2. Distribution of panellist voting for each statement in the final voting round.

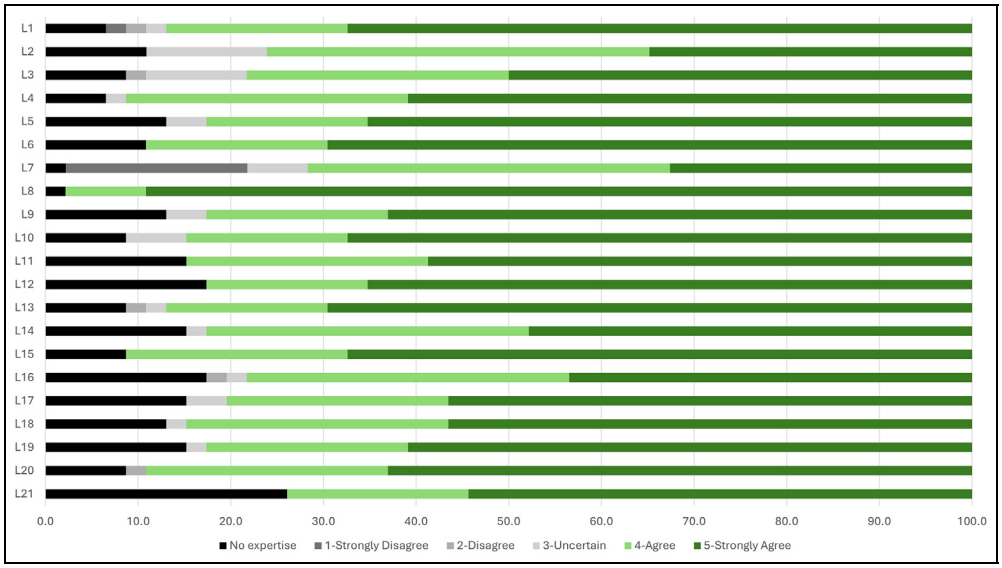
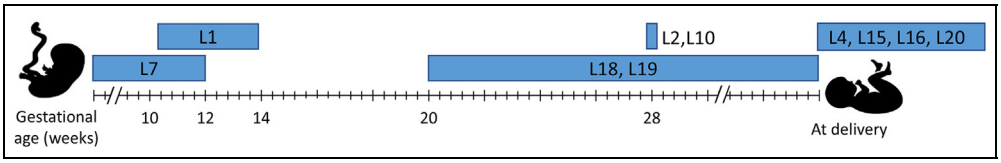


Figure 3. Gestational timeline of low-risk consensus statements (L#).



alloimmunization and HDFN is likely because most primary alloimmunization events initially present with immunoglobulin M (IgM) antibodies, which cannot cross the placenta and thus do not affect the current pregnancy.[25] More studies are needed.

Likewise, statement L4 acknowledges that a blood group and antibody screen is not routinely required at the time of delivery, given the exceptionally unlikely event of both (a) maternal or neonatal red cell transfusion and (b) late alloimmunization in pregnancy.

It is important to note that statements L2 and L4 are contingent on a negative antibody screen using a high-sensitivity assay performed after 8 weeks' gestation, the absence of any subsequent sensitizing events (e.g., fetomaternal hemorrhage, red cell transfusion, intravenous drug use), and no evidence of fetal anemia. An antibody screen performed before 8^0 weeks' gestation may yield a falsely reassuring result, as fetal expression of RBC antigens, which is required for antibody stimulation, may be limited until at least 8^0 weeks' gestation. High-sensitivity antibody screening assays are universally employed in most high-development index countries. Underlying statement L2 is also recognition that a repeat blood group and antibody screen is not required before RhIG administration.

Following feedback from the expert panel, statement L2 was softened to "may not be necessary" to allow for individual risk assessment and for practitioners to use discretion based on their local practice. Some panellists felt that despite a high number needed to screen to detect 1 case (1 in 31,000), even a single event should be prevented, whereas others argued that any impacted neonate would still present with jaundice, leading to appropriate management. Panellists encouraged sites to publish their observations (in the presence or absence of a 28-week group and screen) to help inform a more definitive statement in the future.

Statement L7, regarding the restriction of RhIG to abortions at 12^0 weeks' gestation or later, also stirred controversy. This statement is dependent on reliable dating and was initially written with a gestational threshold of 8^0 weeks, which represented a change from usual Canadian practice, where all RhD-negative pregnancies with a sensitizing event received RhIG regardless of gestational age. This change reflected growing evidence that anti-D sensitization does not occur before 8^0 weeks' gestation due to the limited amount of fetal RBCs present in maternal circulation, and was a move towards alignment with international practice, where RhIG is not routinely administered for all early abortions.[13,22,26] Wiebe et al.[13] found no difference in red cell alloimmunization events when comparing population data between Canada, which follows a conservative RhIG administration policy for all potential sensitizing events, and the Netherlands, where RhIG is recommended only for induced abortions beginning at 7^0 weeks, and spontaneous abortions beginning at 10^0 weeks. Benefits of reducing RhIG use in early gestation include more timely access and improved confidentiality in abortion care, fewer emergency department visits for pregnant people, elimination of interference caused by RhIG in transfusion testing, and preservation of the limited RhIG supply for those sensitizing events occurring later in gestation.

Statement L7 was revised to 12^0 weeks during the Delphi process to align with the updated World Health Organization recommendations, and as more international guidelines removed the requirement for RhIG in all early abortions.[14-17,27,28] Some of these changes followed the study published by Horvath et al., which demonstrated that first-trimester induced abortions did not result in enough circulating fetal RBCs to trigger RhD sensitization.[12] Although statement L7 reached consensus, some panellists expressed concerns, as the study did not directly measure RhD alloimmunization as its primary outcome. Additionally, the Society of Obstetrics and Gynecology in Canada guidelines were updated to allow consideration of RhIG between 8–12 weeks in risk-averse people,[6] and the Society for Maternal-Fetal Medicine in the United States continues to recommend RhIG for all abortions if accessible.[29] The panel consensus to omit RhIG administration between 8 and 12 weeks for threatened, spontaneous, and therapeutic abortions takes into consideration existing evidence, along with practical factors that impact equity in access to care, including when and where RhIG can be

accessed (often only through emergency departments), its potential to impede abortion care, and the cost to the health care system in the absence of high-quality evidence demonstrating further reduction in RhD alloimmunization already afforded by routine 28-week and postpartum administration.[30] The panel believed there is insufficient evidence to support RhIG omission for ectopic and molar pregnancies between 8 and 12 weeks' gestation. This area warrants future study.

The remainder of the statements had minimal disagreement among the panellists. Statement L9 was included to advocate for non-invasive prenatal testing (NIPT) in RhD-negative pregnancies, even though the test is not yet performed in Canada at the time of writing. NIPT has become the standard for all RhD-negative pregnancies in many countries to determine RhIG prophylaxis eligibility.[20] Testing of cell-free fetal DNA can eliminate the need for RhIG if the fetus is predicted to be RhD-negative, which accounts for approximately 40% of RhD-negative pregnancies. NIPT is extremely accurate, with a false negative rate of less than 1%, especially if performed at 11 weeks' gestation or later. The benefits of NIPT have been well documented, including the ethical approach of RhIG avoidance in those with no risk, resource savings, and the adoption of personalized care.[20]

Limitations

Although the expert panellists were selected to represent a broad range of national practitioners, there is an overrepresentation of Central Canada and a lack of territorial and Indigenous representation. To address this, the steering committee ensured the inclusion of panellists from rural areas and those who may provide coverage for people from northern communities. Further, only 1 patient representative was included in the panel. As with any Delphi consensus process, there is always a risk of recruiting panellists with similar opinions, especially when the topic is very specialized. However, based on the range of voting observed, the multitude of disciplines represented, and the comments received throughout each round of voting, balance was likely achieved.

CONCLUSION

These 21 expert consensus statements for testing and RhIG administration in pregnancies represent a concerted Canadian effort to standardize care in an area where guidelines sometimes conflict. Although some statements may represent a change in practice, they aim to provide high-quality, patient-centred care by prioritizing equitable access and reduced interventions over minimal alloimmunization risks. Knowledge translation efforts are underway, especially as newer technologies such as NIPT may soon be available in Canada.

Acknowledgements

The authors would like to acknowledge the following people for their participation in the consensus panel and review of the manuscript: Michael Angers, Susan Ellis, Batya Grundland, Catherine McAuley, Neil Naik, Claire Osepchook, Dorien Rujis, Barb Silveri, and Julia Stewardson. The authors would also like to acknowledge Tracy Cameron for providing administrative support and Elona Turley for her expertise in the area of flow cytometry.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jogc.2025.103034

REFERENCES

1. Baker JM, Campbell DM, Bhutani VK, et al. Rh sensitization in Canada is not obsolete. Paediatr Child Health 2017;22:238–9.
2. Sutherns R, Bourgeault IL. Accessing maternity care in rural Canada: there's more to the story than distance to a doctor. Health Care Women Int 2008;29:863–83.
3. Fyfe TM, Ritchey MJ, Taruc C, et al. Appropriate provision of anti-D prophylaxis to RhD negative pregnant women: a scoping review. BMC Pregnancy Childbirth 2014;14:411.
4. Ramsey G, College of American Pathologists Transfusion Medicine Resource Committee. Inaccurate doses of R immune globulin after rh-incompatible fetomaternal hemorrhage: survey of laboratory practice. Arch Pathol Lab Med 2009;133:465–9.
5. Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: how to decide its appropriateness. World J Methodol 2021;11:116–29.
6. Fung-Kee-Fung K, Wong K, Walsh J, et al. Guideline no. 448: prevention of Rh D alloimmunization. J Obstet Gynaecol Can 2024;46:102449.
7. Tran A, Clarke G, Callum JL, et al. Reconsidering routine repeat group and screens during pregnancy-personalizing pregnancy care. J Obstet Gynaecol Can 2024;46:102351.
8. Slootweg YM, Koelewijn JM, van Kamp IL, et al. Third trimester screening for alloimmunisation in Rhc-negative pregnant women: evaluation of the Dutch national screening programme. BJOG 2016;123:955–63.
9. Stock O, Beckmann M. Why group & save? Blood transfusion at low-risk elective caesarean section. Aust N Z J Obstet Gynaecol 2014;54:279–82.
10. Ringel F, Schoenfeld H, El Bali S, et al. Safety of uncrossmatched ABO-compatible RBCs in alloimmunized patients with bleeding: data from two decades: results of a systematic analysis in 6,109 patients. Transfus Med Hemother 2022;49:234–9.
11. National Advisory Committee on Blood and BLood Products. RHD genotyping in prenatal patients. Ottawa: National Advisory Committee on Blood and Blood Products; 2022. Available at: https://nacblood.ca. Accessed on September 6, 2024.

12. Horvath S, Huang ZY, Koelper NC, et al. Induced abortion and the risk of Rh sensitization. JAMA 2023;330:1167–74.

13. Wiebe ER, Campbell M, Aiken ARA, et al. Can we safely stop testing for Rh status and immunizing Rh-negative women having early abortions? A comparison of Rh alloimmunization in Canada and the Netherlands. Contraception: X 2019;1:100001.

14. World Health Organization. Abortion care guideline. Geneva: World Health Organization; 2022. Available at: https://who.int. Accessed on September 6, 2024.

15. National Abortion Federation. Clinical policy guidelines for abortion care. Annapolis Junction: National Abortion Federation; 2022. Available at: https://prochoice.org. Accessed on September 6, 2024.

16. Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG). Guidelines for the use of Rh(D) immunoglobulin (anti-D) in obstetrics (C-Obs 6). Melbourne: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; 2023. Available at: https://ranzcog.edu.au. Accessed on September 6, 2024.

17. Royal College of Obstetricians & Gynaecologists (RCOG). Best practice in abortion care. London: Royal College of Obstetricians and Gynaecologists; 2022. Available at: https://rcog.org.uk. Accessed on September 6, 2024.

18. Wilson K. The Krever Commission–10 years later. CMAJ 2007;177:1387–9.

19. CSA Group. Blood and blood components: Toronto (ON), 2020, CSA Group, CSA Standard Z902-20. Clause 11.2.1. Available at: https://www.csagroup.org/. Accessed on September 6, 2024.

20. Johnson JA, MacDonald K, Clarke G, et al. No. 343-routine non-invasive prenatal prediction of fetal RHD genotype in Canada: the time is here. J Obstet Gynaecol Can 2017;39:366–73.

21. Hamel C, Esmaeilisaraji L, Thuku M, et al. Antenatal and postpartum prevention of Rh alloimmunization: a systematic review and GRADE analysis. PLoS One 2020;15:e0238844.

22. Qureshi H, Massey E, Kirwan D, et al. BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. Transfus Med 2014;24:8–20.

23. British Committee for Standards in Haematology. Guidelines for the estimation of fetomaternal haemorrhage. London: British Committee for Standards in Haematology; 2009. Available at: https://b-s-h.org.uk. Accessed on September 6, 2024.

24. Kim YA, Makar RS. Detection of fetomaternal hemorrhage. Am J Hematol 2012;87:417–23.

25. Myle AK, Al-Khattabi GH. Hemolytic disease of the newborn: a review of current trends and prospects. Pediatr Health Med Ther 2021;12:491–8.

26. National Institute for Health and Care Excellence (NICE). Abortion care NICE guideline. London: National Institute for Health and Care Excellence; 2019. Available at: https://nice.org.uk/guidance/NG140. Accessed on September 6, 2024.

27. Vigoureux S, Maurice P, Sibiude J, et al. Prévention de l'allo-immunisation anti-RH1 au premier trimestre de la grossesse : recommandations pour la pratique clinique du Collège National des gynécologues-obstétriciens français [Prevention of Rh D alloimmunization in the first trimester of the pregnancy: French College of Obstetricians and Gynecologists guidelines for clinical practice]. Gynecol Obstet Fertil Senol 2024;52:446–53. French.

28. Horvath S, Goyal V, Traxler S, et al. Society of Family Planning committee consensus on Rh testing in early pregnancy. Contraception 2022;114:1–5.

29. Prabhu M, Louis JM, et al., Society for Maternal-Fetal Medicine. Electronic address: pubs@smfm.org. Society for Maternal-Fetal Medicine Statement: RhD immune globulin after spontaneous or induced abortion at less than 12 weeks of gestation. Am J Obstet Gynecol 2024;230:B2–5.

30. Heuser C, Flink-Bochacki R, Sperling J, et al. A tale of two societies: implications of conflicting Rh-immunoglobulin guidelines. AJOG Glob Rep 2024;4:100380.