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# Mapping anticipated advantages and disadvantages of implementation of extensive donor genotyping: A focus group approach

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## Abstract

**Background and objectives:** Current genotyping techniques allow typing of all relevant red cell, human leukocyte and platelet antigens in a single analysis. Even genetic markers related to donor health can be added. Implementation of this technology will affect various stakeholders within the transfusion chain. This study aims to systematically map the anticipated advantages and disadvantages of a national rollout of blood group genotyping of donors, which will affect the availability of rare donors and the implementation of an extensively typed blood transfusion policy.

**Materials and methods:** Two focus-group sessions were held with a wide representation of stakeholders, including representatives of donor and patient organisations. A dedicated software tool was used to collect the reflections of participants on genotyping for blood group antigens and extensive matching. Additionally, stakeholders and experts discussed various prepared propositions. All information collected was categorised.

**Results:** From 162 statements collected, 59 statements (36%) were labelled as 'hopes' and 77 (48%) as 'fears'. Twenty-six (16%) statements remained unlabelled. The statements were divided in 18 categories under seven main themes: patient health, genotyping, privacy issues and ethical aspects, donor management, inventory management and logistics, hospital and transfusion laboratory and general aspects. The discussion on the propositions was analysed and summarised.

**Conclusion:** Stakeholders believe that a genotyped donor pool can result in a reduction of alloimmunization and higher availability of typed blood products. There are concerns regarding logistics, costs, consent for extended typing, data sharing, privacy issues and donor management. These concerns need to be carefully addressed before further implementation.

## 1 | INTRODUCTION

Matching blood group antigens of donors and patients is essential to prevent adverse immune reactions and development of red blood cell



(RBC) antibodies by patients. RBC antibodies can lead to haemolytic transfusion reactions with symptoms ranging from mild fever to death. Therefore, in many countries extensively matched donor blood is selected for transfusion dependent patients or patients with a higher risk to develop alloantibodies.<sup>1–6</sup> During pregnancy RBC antibodies may be transferred from the pregnant women to the foetus and lead to haemolysis. Therefore, prevention of RBC alloimmunization is important for patients with subsequent transfusions as well as for females in reproductive ages.

In the Netherlands, approximately 400 000 RBC units and 54 000 platelet products are issued each year by Sanquin, the national blood supply organisation.<sup>7</sup> All donors are typed serologically for ABO, Rh phenotype and K antigens and a large proportion is typed for other antigens.<sup>8,9</sup> Blood with rare blood types is stored frozen. Blood typing of patients and selection of donor blood is the responsibility of approximately 75 hospital transfusion laboratories and is performed in accordance with the recommendations of the Dutch transfusion guideline.<sup>1</sup> The Dutch population of 17.5 million inhabitants is mainly of Caucasian origin, with a small population of inhabitants with African and Asian genetic roots. There is a thalassemia population of about 300 and a sickle cell disease population of about 2000 patients; the latter group is particularly at risk for alloimmunization and adverse transfusion reactions.<sup>10</sup>

The current Dutch transfusion guideline is designed such that RBC alloantibody formation is prevented by extensive matching in female transfusion recipients under 45 (matching for Rhc, RhE and K), patients with RBC alloantibodies, myelodysplastic syndrome, thalassemia or autoimmune haemolytic anaemia (Rh phenotype and K) and sickle cell patients (Rh phenotype, K, Fy<sup>a</sup>, Jk<sup>a</sup>, Jk<sup>b</sup>, S and if possible s).<sup>1</sup> Between 2007 and 2016, a total of 80 164 new clinically relevant antibodies were added to the national registry system and 712 new antibody formations were registered by the national bureau of hemovigilance in 2019.<sup>11,12</sup> In daily practice, provision of hospitals with sufficient extensively typed units for patients with RBC alloantibodies, or for patients that require extensive matching, remains challenging. Furthermore, it remains difficult to have sufficient products for patients with antibodies against high frequency antigens, or to find units with a specific combination of blood types; for example if these need to be Do<sup>a</sup> or Do<sup>b</sup> negative.

Recent developments in genotyping provide potential benefits in three different areas: (1) increasing availability of extensively typed blood units; (2) revealing the presence of rare high frequency antigen negative donors; and (3) preventing alloimmunization by increasing the level of blood matching between donor and recipient. From previous studies on the immunogenicity of red blood cell antigens it was concluded that preventive matching for C, c, E, K and Jk<sup>a</sup> will be most effective in reducing alloimmunization, while other immunogenic antigens seem to be less important for matching because antibodies are less clinically important (i.e. Lu<sup>a</sup>, Le<sup>a</sup>) or have a low frequency in the population (i.e. Cw).<sup>13,14</sup> Pre-emptive matching for a larger set of most clinically relevant RBC antigens (Rh phenotype, K, Fy<sup>a</sup>, Fy<sup>b</sup>, Jk<sup>a</sup>, Jk<sup>b</sup>, S and s) could prevent 94% of transfusion-related alloimmunization.<sup>15</sup> The development of a donor genotyping platform<sup>16–22</sup> makes

simultaneously typing of the most-clinically relevant RBC, human platelet (HPA), and human leukocyte (HLA) antigens possible. A genotyped donor pool will also increase the availability of matched platelet products for patients to prevent HLA alloimmunization or to match if a patient is refractory for platelet transfusions. Finally, it may be used to increase the availability of typed stem cell donors.

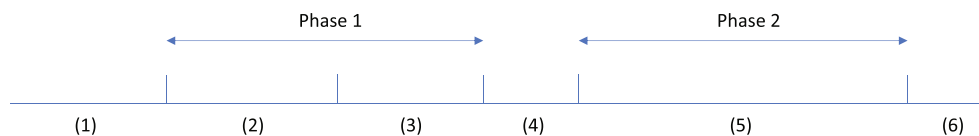
Seizing the promises of extended blood group genotyping of blood donors in a practical strategy will require many changes throughout the blood transfusion chain. With the implementation of genotyping and an extended matched transfusion strategy, there will be consequences for the registration of extended (e.g. more than currently routinely available ABO, Rh phenotype, K, Fy, Jk and MNSs typing) donor blood profiles, for extended routine patient typing (e.g. beyond ABO, D and for all blood recipients) and pretransfusion compatibility testing and it will change RBC logistics and stock management.<sup>21</sup> Databases with patient and donor data and a system to allocate units to patients with a linkage of blood bank and hospital inventories will be required.<sup>21</sup> Some red blood cell phenotypes are associated with clinically relevant morbidity<sup>23</sup> or carry a higher risk on foetal alloantibody-mediated disease (e.g. negativity for Human Platelet Antigen type 1a<sup>24</sup>) or are associated with certain diseases (e.g. HLA types). For example, in the Netherlands, currently, only male donors are typed for HPA-1a and only a subset of donors is typed for HLA antigens; it may have impact on donor counselling if donors will be typed for a large set of red blood cell, platelet and HLA antigens. To enable the foreseen change in daily transfusion practice with extensively genotyping of the donor cohort, it is paramount to know the views and concerns of all stakeholders involved in the affected areas. Involving stakeholders and being able to assess and tackle foreseen challenges based on their practical experience will be valuable to develop a strong implementation plan. In this study, we therefore aimed to systematically map the anticipated advantages and disadvantages of the implementation of blood group genotyping of donors and an extensively typed blood transfusion policy. Insights were obtained from different experts in the transfusion chain, including donor and patient representatives, utilising focus group sessions. This paper provides a description of these focus group sessions, a summary of our findings and recommendations derived.

## 2 | METHODS

### 2.1 | Focus group sessions

To collect perceptions of stakeholders on the implications of the implementation of genotyping and extensive matching, two focus group sessions were organised. It was strived to recruit a wide representation of relevant expertise and domains of stakeholders (all referred to as 'experts' in this paper).

The focus group sessions were held online and a dedicated software tool (Xleap, MeetingSphere GmbH) was used to collect information during the meetings, while Microsoft Teams was used for communication. The session started with a short introduction of the



**FIGURE 1** Timetable for the focus group sessions.

(1) Introduction of experts and informative presentation by Sanquin	(20 minutes)
(2) Experts enter statements and define these as hope, fear or undefined	(20 minutes)
(3) Experts assign statements to a part of the bloodtransfusion process	(15 minutes)
(4) Break	(10 minutes)
(5) Experts discuss several propositions	(45 minutes)
(6) Plenary summary and conclusion of the focus group	(10 minutes)

Area of expertise	Focus group 1	Focus group 2	Total
Blood bank			
Donor management	1	1	2
Donor screening laboratory	1	1	2
Clinical consultant transfusion medicine	0	3	3
Operations (logistics, ICT, finance)	3	2	5
Hospital			
Treating physician	2	3	5
Laboratory pathologist/clinical chemist	2	1	3
Research			
Researchers (donor management, immunohematology)	3	1	4
Experience experts			
Donor representatives	1	1	2
Patient representatives	1	1	2
Total	14	14	28

**TABLE 1** Participants of the two focus groups per area of expertise.

Notes: All participants were categorised based on their main area of expertise. However, treating physicians also have experience as clinical consultants in transfusion medicine. In addition, some clinical consultants have experience as laboratory pathologists. In addition, one combined donor management with clinical consultancy.

experts and an informative presentation from the researchers. Next, the participating experts were able to provide input anonymously and independently. The outline of the focus group sessions is shown in Figure 1.

In phase one, the experts were asked to express their perceptions related to genotyping and extensive matching and entered them as statements into the system. They were then asked to label these as either 'hopes' or 'fears', and to assign the entered items to various parts of the blood transfusion process (Supporting information 1).

In phase two, experts were evenly divided (based on their expertise) into two groups and discussed a number of pre-determined propositions related to three themes (Supporting information 2). The participants first entered their opinions in Xleap, after which these were discussed with two of the researchers (SR, JL, MJ or MdH) and one of the process facilitators (ER or MvdW). After the first focus

group session propositions that were deemed adequately discussed (no new input was given or required within the discussion time in session one), were replaced with new propositions. Subjects that were deemed valuable to explore further (discussion needed more time than available or new questions were brought up), were adjusted and re-implemented for the second focus group session.

## 2.2 | Participants

The main areas of expertise of the experts are shown in Table 1. Experts may have experience in multiple areas. Both professionals with a strategic, administrative role in the blood bank and professionals with a more operational role were invited. Donor representatives came from the donor association and donor advisory board, and



Themes	Categories per theme	Description of categories	Hope (n=59) (100%)	Fear (n=77) (100%)	Undefined (n=26) (100%)	Total (n=162) (100%)
<b>Patient health</b>			21 (36%)	0 (0%)	0 (0%)	21 (13%)
	<i>Patient health outcomes</i>	Patient outcomes achieved by a process utilizing genotyping				
	<i>Special patient groups</i>	Patient outcomes in special or non-standard cases				
<b>Genotyping</b>			4 (7%)	5 (6%)	6 (23%)	15 (9%)
	<i>Genotyping of donors</i>	The approach and method of genotyping donors				
	<i>Typing of patients</i>	The approach and method of genotyping and phenotyping of patients				
<b>Privacy issues and ethical aspects</b>			3 (5%)	12 (16%)	3 (12%)	18 (11%)
	<i>Donor privacy</i>	Handling data of donors that is processed due to genotyping				
	<i>Patient privacy</i>	Handling data of patients that is processed due to genotyping				
<b>Donor management</b>			11 (19%)	22 (29%)	5 (19%)	38 (23%)
	<i>Diversity of blood types in the donor pool</i>	Implications of genotyping on the composition of the donor base				
	<i>Donor management</i>	Implications of genotyping on the ability to maintain sufficient (active) donors				
	<i>Attitude of donors</i>	Donor attitudes and behavior towards genotyping				
<b>Inventory management and logistics</b>			4 (7%)	18 (23%)	4 (15%)	26 (16%)
	<i>Logistics</i>	Implications of genotyping on business operations in (between) parts of the blood transfusion process				
	<i>Demand forecasting</i>	Being able to order blood products in time to meet the needs of the patient population				
	<i>Outdating of blood products</i>	Using blood products before the specified expiration date				
	<i>Emergency situations</i>	The working method in situations with urgent need for transfusion				
<b>Hospital and transfusion laboratory</b>			2 (3%)	10 (13%)	1 (4%)	13 (8%)
	<i>Pre-transfusion compatibility testing</i>	The working method at the hospital transfusion laboratory, including pre-transfusion diagnostics				
	<i>Organization in hospitals</i>	Implications of genotyping on hospital operations				
<b>General aspects</b>			14 (24%)	10 (13%)	7 (27%)	31 (19%)
	<i>Costs</i>	Implications of genotyping on the total costs of the blood transfusion process				
	<i>Implementation remarks</i>	Decision-making concerning when to apply genotyping and extensive matching and when to opt for other methods				
	<i>General remarks</i>	General remarks or implications for the whole process (not assignable to a single step)				

**FIGURE 2** Distribution of statements of hope and fear as provided by the experts during phase one of the focus group sessions. For the 18 categories, the distribution of statements labelled as hope or fear and the statements that remained undefined is shown. This distribution is visualised in pie charts, scaled to size according to the total amount of statements per category. Additionally, a description is provided of the content within each category, as well as the themes the categories belong to.

patient representatives from patient organisations for sickle cell disease and thalassemia and for rare haematological diseases. Twenty-eight experts participated in the study and were divided into two groups with similar background and expertise.

## 2.3 | Data analysis

The statements provided by the experts in phase one of the focus group sessions were analysed for similarities and differences. Two researchers (JL and SR) independently categorised and assigned all statements to self-determined categories and themes. These results were compared, after which consensus was reached on a definitive set of categories, themes and assignments of stakeholder statements.

## 3 | RESULTS

### 3.1 | Expressed hopes and fears

During phase one of the focus group sessions 172 statements were obtained. Ten statements were excluded from further analysis, either because these were part of the instruction by the focus group facilitators, did not apply to the transfusion process, or were uninterpretable. Of the 162 remaining statements 59 (36%) were categorised by the experts as hopes, 77 (48%) as fears and 26 (16%) statements remained unlabelled. Two statements labelled as both hope and fear were counted as 0.5 in each group. The 162 statements were divided in 18 categories under seven themes. These themes are described in Figure 2 and under 'Summary per theme'. The hopes and fears obtained from the two focus group sessions were regarded as not significantly different between both focus group sessions (Supporting information 3).

### 3.2 | Summary per theme

#### 3.2.1 | Patient health

In the category *patient health outcomes* the experts foresaw a reduction of alloimmunization in (poly)transfused patients. Additionally, the experts expected faster availability of better-matched blood and safer blood transfusions for patients. One participant described hope that donors and patients could be matched at other (biochemical) characteristics than RBC antigens.

The experts foresaw advantages for some *special patient groups* in particular. First of all, the possibility of better matching for complex patients (e.g. patients with rare RBC antibodies, rare Rh phenotypes, post-transfusion AIHA or red cell aplasia), because rare RBC blood types will become easier available. Secondly, lower alloimmunization risk could increase treatment options, for example, improved chronic transfusion schemes or apheresis therapy for patients with sickle cell disease.

#### 3.2.2 | Genotyping

Three experts expressed fear that large scale genotyping of donors is not yet possible. However, others described that genotyping of donors can be well organised. It was mentioned that phenotyping is faster and effective when searching for a specific genotype. Additionally, it was suggested that genotyping of the whole population early in life is likely to become routine practice.

Concerning the extended RBC antigen typing of patients, it was questioned where the responsibility and costs for the typing of patients should lie, and whether this should be organised centralised or decentralised. Furthermore, practical questions were raised on topics such as the quantity and type of samples needed for genotyping. Three experts feared that the turn-around time of typing would be unsatisfactory for patients with an acute transfusion indication.

#### 3.2.3 | Privacy issues and ethical aspects

Focus group participants feared the violation of donor privacy due to recognizability of specific donors through their genetic profile. There was fear that the use of DNA could lead to the misuse of private data that people do not want shared. It was believed that donors could feel uncomfortable by the use of their DNA and might worry about the privacy of the data obtained. It was proposed that donors should explicitly be asked for consent for determining a donor profile by genotyping. Experts mentioned that informing donors could involve the number of typed RBC, platelet and other antigen systems, and the related clinical implications related to the obtained data. The possibility of a national registry for blood types obtained by genotyping was mentioned. An appropriate method of labelling donors in the blood bank information system needs to be determined.

Concerning patient privacy, the vulnerability of storing and sharing patient data was feared. Several questions were related to managing a centralised storage of patient data. It was noted that hospitals and Sanquin Blood Bank currently do not share data on antigen types required and availability of typed RBCs. Data sharing could become necessary and this might raise ethical and privacy issues. Patients may not want this data to be shared. Another question concerned obtaining consent to type specific patients, for example, children.

Genotyping offers opportunities to obtain additional data on other health topics that are not purely intended to be used in facilitating blood transfusions (e.g. genetic indicators for iron metabolism or disease associations). The experts considered acquiring this information as undesirable, because it may provide information that a person does not want to know. This could result in ethical problems and would not be in line with the general accepted rules concerning the screening for diseases, such as assessing treatability.

#### 3.2.4 | Donor management

Experts expect an improvement in diversity of blood types in the donor pool that is, better availability of typed products and more



typing information from donors from non-Caucasian origin. Expressed fears concerned a shortage of donors most in demand. This demand could be increased by introducing an extended matching strategy as more patients with uncommon antigen profiles need to be matched.

Having sufficient donors was stated as a challenge in donor management. There were fears about a possible increased donation frequency of certain donors, new donor acceptance criteria and differing donation frequencies between donors with different profiles. It was stated that donors with rare blood types should be protected against excessive donation.

Additionally, the attitude of donors towards donating could be negatively influenced by their individual opinions on genetic testing or the use of a DNA database. The experts noted that communication with donors about genotyping is important to prevent donor reluctance. In addition, individuals of African genetic origin should be given extra information about their importance as donors for patients with sickle cell disease or thalassemia.

The possibility of improving donor diversity by conducting campaigns to recruit more donors of non-Caucasian origin was an expressed hope. Notably, more attention for specific minorities can be both desirable and undesirable. In the case of partial application of genotyping it was questioned which donors would be selected for extensive genotyping and if selection on ancestry would be possible.

### 3.2.5 | Inventory management and logistics

Nine experts mentioned challenges in logistics that would arise if the blood transfusion chain would include extensive blood group genotyping and extended matching. Advanced matching of blood products from donor to patient was feared to lead to rigid allocation of products and inflexibility of inventory management and logistics. Additionally, experts regarded the time between patient demand and donor blood delivery determinative for the achievable level of blood matching. Stated hopes were inventories better attuned to the demands and that manual typing of donors would no longer be necessary before matching a blood product to a patient.

Fears in the demand-forecasting category concerned the ability of hospitals to timely provide information on which patients need which blood products at what time. Additionally, the demand for certain profiles could increase. Furthermore, the predictability of profiles with the largest demand was questioned.

Three experts feared increased outdating of blood products if more antigens are considered for matching, as it will become more difficult to adhere to administering the oldest products first.

Seven experts expressed fear that, in emergency situations, impossibility to match could delay transfusions, either due to missing antigen profiles of patients or unavailability of matching units. Adhering to the matching strategy could delay transfusions in these situations.

### 3.2.6 | Hospital and transfusion laboratory

Different opinions existed on the necessity of pre-transfusion compatibility testing in case of matching for the most important RBC

antigens. This makes detecting antibodies against the matched antigens unnecessary. However, without pre-transfusion antibody screening, autoantibodies or rare antibodies against high-frequent antigens would be missed. Experts fear that serological antigen typing would have to continue alongside genotyping for patients in urgent need for transfusion, thereby increasing costs.

Extensive matching will result in different consequences for the organisation in hospitals. Fear was expressed for diminishing knowledge about blood types and RBC serology, whilst still needed. Additionally, there was fear about linking new and current IT systems, and the support of IT systems to designate matching products to patients. Education on matching and associated inventory management would be mandatory. It was questioned how to deal with ordered blood that remained unused. Furthermore, it was feared that hospital costs would increase.

### 3.2.7 | General aspects

Five experts expressed concern about the costs and cost-effectiveness of an extensively matched transfusion strategy. In addition, there was concern about a shift of costs in the transfusion chain to other stakeholders. Meanwhile, hope was expressed that extensive typing of donors would reduce costs, due to fewer transportations and improved inventory management.

There were remarks on the implementation of genotyping and extensive matching. It was argued that matching for all RBC antigens is not required, as only clinically relevant antibodies need to be prevented. In addition, it was stated that for many patients extensive matching is not necessary, and an optimum must be found between the number of antigens typed and the level of antibody formation prevented. It was questioned whether enough knowledge exists to allocate products, given that in practice there will always be mismatches on some antigens for some patients.

There were several general remarks about extensive matching. Expressed hope concerned the prospects of being able to work with improved techniques. Additionally, it was hoped that collecting data for other research, including determining how much clinically relevant alloimmunization occurs after elective transfusions, would become possible. The experts mentioned that the advantages of genotyping have to be made very explicit before it will become accepted by hospitals.

## 3.3 | Discussed propositions

### 3.3.1 | Dealing with data obtained from the typing of donors and patients

The experts argued that genetic information from donors and patients related to blood group profiles and HLA typing may be stored with the aim of reducing antibody formation and side effects of transfusions, if performed in accordance to European privacy laws (GDPR).<sup>25</sup>

Properly informing donors and patients, obtaining consent, storing and granting access to data, are important. Additionally, it was discussed that data should be stored centrally, with genotyping being required once per individual. However, obtaining health-related information of donors or patients was regarded legally and ethically complex, for example in case of disease-related risk factors (certain HLA types) or blood types more prone to foetal-maternal incompatibility. Between groups there were different views on the preferred course of action. One group mentioned that reporting on health risks is not within the goal of the blood bank, which is to provide a safe transfusion for recipients. Additionally, 'the right to not know' was mentioned as an important point. Contrarily, another group discussed that obtaining health data can be valuable for donors, and should be possible with consent of well-informed donors. It was concluded that guidelines are needed on the provision of health-related data.

### 3.3.2 | Testing prior to a blood transfusion and the selection of blood products

There were contrasting expectations about the effect of genotyping on pre-blood transfusion testing. The experts expected that the number of tests prior to transfusion will decrease. Patients saw advantages in reducing immune responses and fewer required blood tests prior to transfusion. However, although it can become easier to select blood for a transfusion, it could also become more difficult when searching for the optimal match. It will occasionally not be possible to select a fully matched blood product, which has to be dealt with. It was concluded that it should be clear what is considered an acceptable match.

### 3.3.3 | Consequences for logistics

It was discussed that combining transports to several hospitals in standard deliveries can keep transportation costs low. The experts stated that the target numbers of specific products per individual hospital when administering blood for transport are a currently existing challenge. However, it was said that a form of competition between hospitals would be created regarding the availability of widely applicable ('easy to match') or of rare blood, as these are finite. Furthermore, it was argued that, as tailor-made delivery is a current challenge, changing to a demand-driven system will be considerably challenging. Thus, automation will be important in facilitating this change. In addition, unnecessary typing should be minimal to keep the adapted system sustainable: 'we should not start overtyping'. A solution that the experts mentioned was to implement genotyped based matching step-by-step (per antigen).

## 4 | DISCUSSION

This study resulted in an overview of anticipated advantages and disadvantages of a national rollout of blood group genotyping of donors

and an extensively typed blood transfusion policy, categorised in a set of comprehensive themes. Genotyping with chip array technology is now within reach and makes large-scale genotyping of donors possible for many blood group systems as well as other transfusion-related genetic characteristics.<sup>16</sup> To provide guidance for a successful implementation of genotyping it is paramount to know the views and concerns of all stakeholders involved. Moreover, all experts have been asked to remain involved in any further discussions for practical implementation.

The participating experts saw important advantages for patients. They expected a reduction in alloimmunization in transfused patients, and positive effects for patients with, for example, sickle cell anaemia and AIHA. In addition, blood provision for patients with rare antibodies against high frequency antigens would greatly improve. In general, increased availability of typed units for patients that are already provided with extensively typed units generated enthusiasm. Experts did not spontaneously propose that all patients could receive units matched for Rh, K and additional blood group antigens, but agreed that it would be beneficial for all transfusion recipients to receive more matched units.

In the focus groups a matched transfusion strategy with a genotyped donor pool for all patients was proposed. However, in practice only about 10% of repeatedly transfused patients will become alloimmunized,<sup>13</sup> and until now it is impossible to distinguish these patients. The difference in clinical relevance of antibodies and immunogenicity between antigens makes that the importance of matching varies per antigen.<sup>13,14,26</sup> Because many patients will never make antibodies or will not require a follow-up transfusion, the efficiency and feasibility of a fully matched transfusion strategy is questionable.<sup>27-29</sup> Currently a substantial part of donors are typed serologically for Rh, K, Fy, Jk and Ss antigens<sup>8,9</sup> and genotyping is used on indication; for example when serological typing is not possible (i.e. Dombrock antigens and rare blood types). Preventive matching is implemented for many risk groups,<sup>1</sup> but large scale donor genotyping offers possibilities to protect much larger groups with an increased alloimmunization-risk, because of repeated blood transfusion; as for example patients suffering from inflammatory bowel disease.<sup>30</sup> Further evaluation is needed of better-matched transfusion strategies for broader groups of patients.

Many experts in this study warned for acquiring genetic health information that is not directly related to the typing of blood group antigens and regarded this as undesirable. Certain health data can be informative for the donor or blood bank (i.e. to determine donation frequency), but the right to not know was emphasised. Contrarily, other experts were less opposed to gaining disease-related information related to blood group polymorphisms, given donors are well informed. Donor representatives emphasised the importance of information provision regarding genotyping, and donor physicians pointed out that this would require considerable time and attention. An ethics review could gain more insight into these comments and could be incorporated as part of the implementation plan.

The experts noticed disadvantages when discussing new transfusion strategies. Important are logistical challenges and costs of a new



transfusion strategy using comprehensive blood group typing of donors and patients. A health economics analysis is required to evaluate these logistical implications and costs and could be part of the implementation plan.

The design of this study with the use of focus groups has some implications. Firstly, the number of stakeholders of whom views were collected was limited. However, expectably the most important advantages and disadvantages have been collected as no significantly new inputs were retrieved from the second focus group. Another limitation of the study was the anonymity of the inputs by the experts. It is uncertain whether each participant contributed equally. Additionally, the experts were selected by the researchers with the aim to include all stakeholders. However, this might have influenced the discussions. In addition, the focus group sessions started with an informative presentation about genotyping and extended matching. Although information was provided objectively, the framing may have influenced the experts. On the other hand, the experts may already have had a biased view on the topic because of their expertise. The influence of group dynamics on the opinions of participants was limited by the use of two separate groups and a digital platform for data input.

The obtained insights from this study can be valuable for other countries for decision making on genotyping and extended matching. In the Netherlands extensive preventive matching is already implemented for certain groups of transfusion recipients, making the rate of alloimmunization already low. In other settings with less preventive matching, opinions may be different. Additionally, differing social values and opportunities in other countries may lead to a unique set of challenges not identified in this study.

In conclusion, many experts believe that utilising genotyping offers possibilities to improve transfusion practice, with positive effects on patient health. However, there are undisputable fears about the logistical consequences, costs involved, and data generated by genotyping. This study resulted in the derivation of categories and themes that bring structure to potential relevant areas of change as a result of the implementation of genotyping technology. This structure will be helpful when designing an actual plan for implementation. Further discussion on these topics is needed to capitalise on the opportunities of blood group genotyping of donors and to determine the optimal course of action for implementation. It is therefore advised to proceed with the implementation of genotyping technology in manageable steps and in continuous close collaboration with various experts and stakeholders.

## AUTHOR CONTRIBUTIONS

Jessie S. Luken, Sebastien P. Ritsema, Masja de Haas and Mart P. Janssen had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the analysis. Concept and design: All authors. Focus group sessions: Jessie S. Luken, Sebastien P. Ritsema, Mart P. Janssen, Masja de Haas, Merel M. Van der Wal and Etiënne A. J. A. Rouwette. Data analysis: Jessie S. Luken, Sebastien P. Ritsema. Data interpretation and drafting of the manuscript: Jessie S. Luken, Sebastien P. Ritsema, Mart P. Janssen and

Masja de Haas. Critical revision of the manuscript for important intellectual content: All authors.

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## CONFLICT OF INTEREST

The authors have no competing interests.

## DATA AVAILABILITY STATEMENT

Data available upon request.

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## REFERENCES

1. Federatie Medisch Specialisten. Blood transfusion guidelines. 2019. Accessed December 21, 2021. <https://richtlijnendatabase.nl/richtlijn/bloedtransfusiebeleid>
2. Australian & New Zealand Society of Blood Transfus. Guidelines for transfusion and immunohaematology laboratory practice. 2020. Accessed December 21, 2021. [https://anzsbt.org.au/wp-content/uploads/2021/04/Guideline\\_-for\\_Transfusion\\_and\\_Immunohaematology\\_Laboratory\\_Practice\\_FINAL\\_Published\\_20210426.pdf](https://anzsbt.org.au/wp-content/uploads/2021/04/Guideline_-for_Transfusion_and_Immunohaematology_Laboratory_Practice_FINAL_Published_20210426.pdf)
3. British Committee for Standards in Haematology, Milkins C, Berryman J, et al. Guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories. *Transfus Med*. 2013;23(1):3-35.
4. Bundesärztekammer. Querschnitts-Leitlinien zur Therapie mit Blutkomponenten und Plasmaderivaten; Gesamtnovelle. Bundesärztekammer; 2020.
5. HAS Haute Autorité de santé. *Transfusion de globules rouges homologues: produits, indications alternatives. Méthode Recommandations pour la pratique clinique*. HAS Haute Autorité de santé; 2014.
6. Compennolle V, Chou ST, Tanael S, et al. Red blood cell specifications for patients with hemoglobinopathies: a systematic review and guideline. *Transfusion*. 2018;58(6):1555-1566.
7. Sanquin: Jaarverslag (Annual report). 2020. Accessed December 21, 2021. Available from [https://www.sanquin.org/binaries/content/assets/nl/over-sanquin/jaarverslagen/sanquin\\_stichting\\_jaarverslag\\_2020.pdf](https://www.sanquin.org/binaries/content/assets/nl/over-sanquin/jaarverslagen/sanquin_stichting_jaarverslag_2020.pdf)
8. Jongerius JM, Boujnan M, Bos HJ, de Wit HJC. Typeren van donorytrocyten. *Tijdschrift voor Bloedtransfusie*. 2013;6(4):62-64.
9. Vreeswijk N, Jongerius J, van Weert A, Bos H. Vijftien miljoen typeringen van het donorbestand biedt tijdswinst en ondersteunt adequate preventie van immunisatie rondom bloedtransfusies. *Ned Tijdschr Klin Chem Labgeneesk*. 2015;40:64-67.
10. Pirenne F, Yazdanbakhsh K. How I safely transfuse patients with sickle-cell disease and manage delayed hemolytic transfusion reactions. *Blood*. 2018;131(25):2773-2781.

11. van Gammeren AJ, van den Bos AG, Som N, Veldhoven C, Vossen R, Folman CC. A national transfusion register of irregular antibodies and cross (X)-match problems: TRIX, a 10-year analysis. *Transfusion*. 2019; 59(8):2559-2566.
12. TRIP Foundation. TRIP Report Hemovigilance Extended version. 2019. Accessed December 21, 2021. [https://www.tripnet.nl/wp-content/uploads/2021/07/Trip.basis-stramien.HEMO\\_ENGdef-2019-met-links-voor-website-5.pdf](https://www.tripnet.nl/wp-content/uploads/2021/07/Trip.basis-stramien.HEMO_ENGdef-2019-met-links-voor-website-5.pdf)
13. Evers D, Middelburg RA, de Haas M, et al. Red-blood-cell alloimmunisation in relation to antigens' exposure and their immunogenicity: a cohort study. *Lancet Haematol*. 2016;3(6):e284-e292.
14. Tormey CA, Stack G. Immunogenicity of blood group antigens: a mathematical model corrected for antibody evanescence with exclusion of naturally occurring and pregnancy-related antibodies. *Blood*. 2009;114(19):4279-4282.
15. van de Weem RHG, Wemelsfelder ML, Luken JS, et al. Preventing alloimmunization using a new model for matching extensively typed red blood cells. *Vox Sang*. 2021;117:580-586.
16. Gleadall NS, Veldhuisen B, Gollub J, et al. Development and validation of a universal blood donor genotyping platform: a multinational prospective study. *Blood Adv*. 2020;4(15):3495-3506.
17. Portegys J, Rink G, Bloos P, Scharberg EA, Kluter H, Bugert P. Towards a regional registry of extended typed blood donors: molecular typing for blood group, platelet and granulocyte antigens. *Transfus Med Hemother*. 2018;45(5):331-340.
18. Avent ND, Martinez A, Flegel WA, et al. The BloodGen project: toward mass-scale comprehensive genotyping of blood donors in the European Union and beyond. *Transfusion*. 2007;47(1):40S-46S.
19. Hashmi G, Shariff T, Zhang Y, et al. Determination of 24 minor red blood cell antigens for more than 2000 blood donors by high-throughput DNA analysis. *Transfusion*. 2007;47(4):736-747.
20. Wagner FF, Bittner R, Petershofen EK, Doescher A, Muller TH. Cost-efficient sequence-specific priming-polymerase chain reaction screening for blood donors with rare phenotypes. *Transfusion*. 2008;48(6):1169-1173.
21. Flegel WA, Gottschall JL, Denomme GA. Integration of red cell genotyping into the blood supply chain: a population-based study. *Lancet Haematol*. 2015;2(7):e282-e289.
22. Flegel WA, Gottschall JL, Denomme GA. Implementing mass-scale red cell genotyping at a blood center. *Transfusion*. 2015;55(11):2610-2615.
23. Reid ME, Lomas-Francis C, Olsson ML. Ok blood group system. *The Blood Group Antigen Factsbook*. Third. Elsevier Academic Press; 2012.
24. Dreyfus M, Kaplan C, Verdy E, et al. Frequency of immune thrombocytopenia in newborns: a prospective study. *Blood*. 1997;89(12):4402-4406.
25. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), 2016.
26. Higgins JM, Sloan SR. Stochastic modeling of human RBC alloimmunization: evidence for a distinct population of immunologic responders. *Blood*. 2008;112(6):2546-2553.
27. Wagner FF. Will genotyping replace serology in future routine blood grouping?—opinion 1. *Transfus Med Hemother*. 2009;36(3):226-227.
28. Schonitzer D. Will genotyping replace serology in future routine blood grouping?—opinion 3. *Transfus Med Hemother*. 2009;36(3):230-231.
29. Anstee DJ. Red cell genotyping and the future of pretransfusion testing. *Blood*. 2009;114(2):248-256.
30. Papay P, Hackner K, Vogelsang H, et al. High risk of transfusion-induced alloimmunization of patients with inflammatory bowel disease. *Am J Med*. 2012;125(7):717-e1.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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