Transfusion and Apheresis Science ■■ (2015) ■■–■■

Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Review

# Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis

Alain M. Ngoma [a,*], Paulin B. Mutombo [b], Kazuhiko Ikeda [c,d], Kenneth E. Nollet [c,e], Bernard Natukunda [f], Hitoshi Ohto [c]

[a] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada
[b] School of Public Health, University of Kinshasa, Kinshasa, Democratic Republic of the Congo
[c] Department of Blood Transfusion and Transplantation Immunology, Fukushima Medical University, Fukushima, Japan
[d] Department of Cardiology and Hematology, Fukushima Medical University, Fukushima, Japan
[e] Radiation Medical Science Center, Fukushima Medical University, Fukushima, Japan
[f] Department of Hematology and Transfusion Medicine, Faculty of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda

ARTICLE INFO

*Keywords:*
RBC alloantibodies
Haemolytic transfusion reactions
Blood transfusion
Sub-Saharan Africa

ABSTRACT

Background and objectives: Previous studies of Sub-Saharan Africans show significant alloimmunization to red blood cell (RBC) antigens, but country-specific data are limited. Thus, the aim of this study was to estimate, by meta-analysis, the overall proportion of red blood cell alloantibodies among transfused patients.
Methods: We systematically searched Medline, Embase, and the Africa-Wide Information database to identify relevant studies in any language. Case reports, comments, letters, conference abstracts, editorials, and review articles were excluded. Of the 269 potentially relevant articles, 11 studies fulfilled our selection criteria.
Results: Overall proportions of alloimmunization were 6.7 (95% CI: 5.7, 7.8) per 100 transfused patients. With regard to antibody specificity, among clinically significant antibodies, anti-E ranked as the most common, followed by anti-K, anti-C and anti-D.
Conclusion: Meta-analysis of available literature quantifies and qualifies the clinical challenge of RBC alloimmunization among transfused patients in Sub-Saharan Africa. These results should drive policy decisions in favour of routine testing of RBC antigens and irregular antibodies for transfused patients as a standard of care throughout Sub-Saharan Africa.


**Contents**



* Corresponding author. Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Purvis Hall 1020 Pine Avenue West, Montreal, Quebec, Canada H3A 1A2. Tel.: +1 514 398 6258; fax: +1 514 398 4503.
*E-mail address:* alain.ngoma@mail.mcgill.ca (A.M. Ngoma).

http://dx.doi.org/10.1016/j.transci.2015.10.017
1473-0502/

## 1. Background

Red blood cell (RBC) alloantibodies in transfused patients can result in significant morbidity and mortality [1], especially where healthcare resources are limited. Alloimmunization to clinically significant RBC antigens such as those in the Rh, Kell, Kidd and Duffy blood group systems can create formidable challenges in multiply transfused patients by making it difficult or impossible to find compatible units and, thus, jeopardize patient safety [1–3]. Alloantibodies can cause a number of serious transfusion reactions including acute intravascular haemolysis, delayed haemolytic transfusion reactions (DHTRs), and haemolytic disease of foetus and newborn (HDFN) [4]. For instance, in the United States of America (USA), 15% of transfusion-related fatalities are caused by non-ABO HTR [5]. Moreover, it has been reported that single-antibody haemolytic transfusion reactions are among the leading causes of transfusion-related mortality in the USA [5]. Thus, routine RBC antibody screening should be a public health imperative integrated into any system of blood banking and transfusion medicine.

Africa is the second-largest and second most populous continent on the planet. Based on forecast, by 2050, Africa will record the world's largest population growth and Sub-Saharan Africa will account for the majority of the increase [6]. This population growth will impact health care delivery, which has already been facing enormous difficulties, including the provision of adequate and safe blood. In 2010, the prevalence of anaemia in Sub-Saharan Africa has been estimated to be 60%, much of this due to malaria and malnutrition. Perinatal haemorrhage persists as a cause of death and is a leading indication for RBC transfusion [7]. Accessing safe blood products represents one of the biggest challenges in Sub-Saharan Africa. Over the past decades, much effort has been dedicated to preventing transfusion-transmitted infections (TTIs) and many African blood services routinely screen blood components to mitigate the risk of TTIs [8,9]. However, RBC alloantibodies outside the ABO blood group system are not routinely screened in most healthcare institutions, thus increasing the risk of immune haemolysis and its significant morbidity and mortality [10–12]. Furthermore, management of patients with alloantibodies and the associated complications, such as DHTRs and HDFN, imposes enormous medical and economic challenges. Studies reporting the prevalence of RBC alloantibodies in Sub-Saharan Africa are scanty and a previous narrative review that included three studies conducted in two countries revealed that 1–6% of transfused patients displayed clinically relevant RBC antibodies [12]. In this context, it is critical to integrate previous estimates and ascertain the actual burden of RBC alloantibodies in patients in Sub-Saharan Africa. We believe that this is the first comprehensive meta-analysis on RBC alloimmunization in Sub-Saharan Africa and we hope it will drive changes in pre-transfusion immunohaematologic testing that will advance patient safety.

## 2. Methods

### 2.1. Search strategy and study selection

This review was prepared and conducted in accordance with PRISMA guidelines [13]. Medline, Embase, and the Africa-Wide Information databases were searched for studies in any language published up to July 1st, 2015. Key search themes were "blood transfusion", "isoimmunisation", and "Africa" and were described by medical subject heading terms and keywords. The search strategy is shown in Table 1. Duplicates were removed using Endnote X7 software and two authors (A.M.N. and P.B.M.) carefully examined all articles independently. Studies were included if they report on the frequency of red cell alloantibodies in transfused patients in sub-Saharan Africa. Complete articles that met inclusion criteria were downloaded. The bibliographies of selected articles were examined to identify additional relevant literature that had not been identified during the screening of databases. These two authors then read the full-text articles and screened them according to pre-defined inclusion and exclusion criteria. We also included one grey literature source, a master's thesis. Case reports, comments, letters, conference abstracts, editorials, or narrative review articles were excluded.

### 2.2. Data extraction

Data extraction was conducted independently by two investigators (A.M.N. and P.B.M.) and disagreements were resolved by consensus. Extracted data included study design, population under study, study size, number of alloimmunized patients, and types of alloantibodies detected.

### 2.3. Statistical analysis

Data were analysed using the statistical software package R version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria) with the command "Metaprop" (R package: meta; Schwarzer 2014) [14]. Proportions were logit transformed and pooled within the DerSimonian and Laird

**Table 1**
Systematic review search strategy.

| | |
|---|---|
| 1. | exp Isoantibodies/ |
| 2. | (alloantibodies or irregular antibodies or red cell antibodies or rbc antibodies or irregular erythrocyte antibodies or allo immunization or alloimmunization or alloimmunisation).tw. |
| 3. | exp africa/ |
| 4. | exp blood transfusion/ |
| 5. | blood transfusion*.tw. |
| 6. | 1 or 2 |
| 7. | 4 or 5 |
| 8. | 3 and 6 and 7 |

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017

random effect model to account for possible heterogeneity between studies [15,16]. The logit-transformed proportions were back-transformed and results were presented as percentages. The logit transformation was used to avoid studies with few events from being weighted too heavily in the random-effects model [17,18]. Heterogeneity in results across the studies was assessed using the I-squared ($I^2$) statistic. $I^2$ value represents the proportion of total variation in the study estimates that are due to variation between studies rather than to chance, and according to Higgins and colleagues, $I^2$ values of 25%, 50%, and 75% are considered as low, moderate and high heterogeneity [19]. Funnel plots were used to visually check for the possible existence of publication bias (small study effects). When appropriate, the Egger's regression asymmetry and the Begg's rank method were conducted to test the significance of funnel plot's asymmetries [20,21].

## 3. Results

### 3.1. Search results

We identified a total of 269 citations in the initial electronic search and an additional 13 citations were identified through hand searching (Fig. 1). After duplicates were removed, 231 citations were screened by title and 122 were excluded because titles were unrelated to our focus. The remaining 109 citations were assessed by abstract, including predefined eligibility criteria, and 88 were excluded (41 not in Sub-Saharan Africa, 18 irrelevant, 12 case reports, 10 reviews, 5 conference abstracts, and 2 letters). A total of 21 articles were assessed in the full-text review and 10 were excluded because transfused patients were not the main focus of their studies. In the end, only 11 relevant studies meeting all the inclusion criteria were selected for data

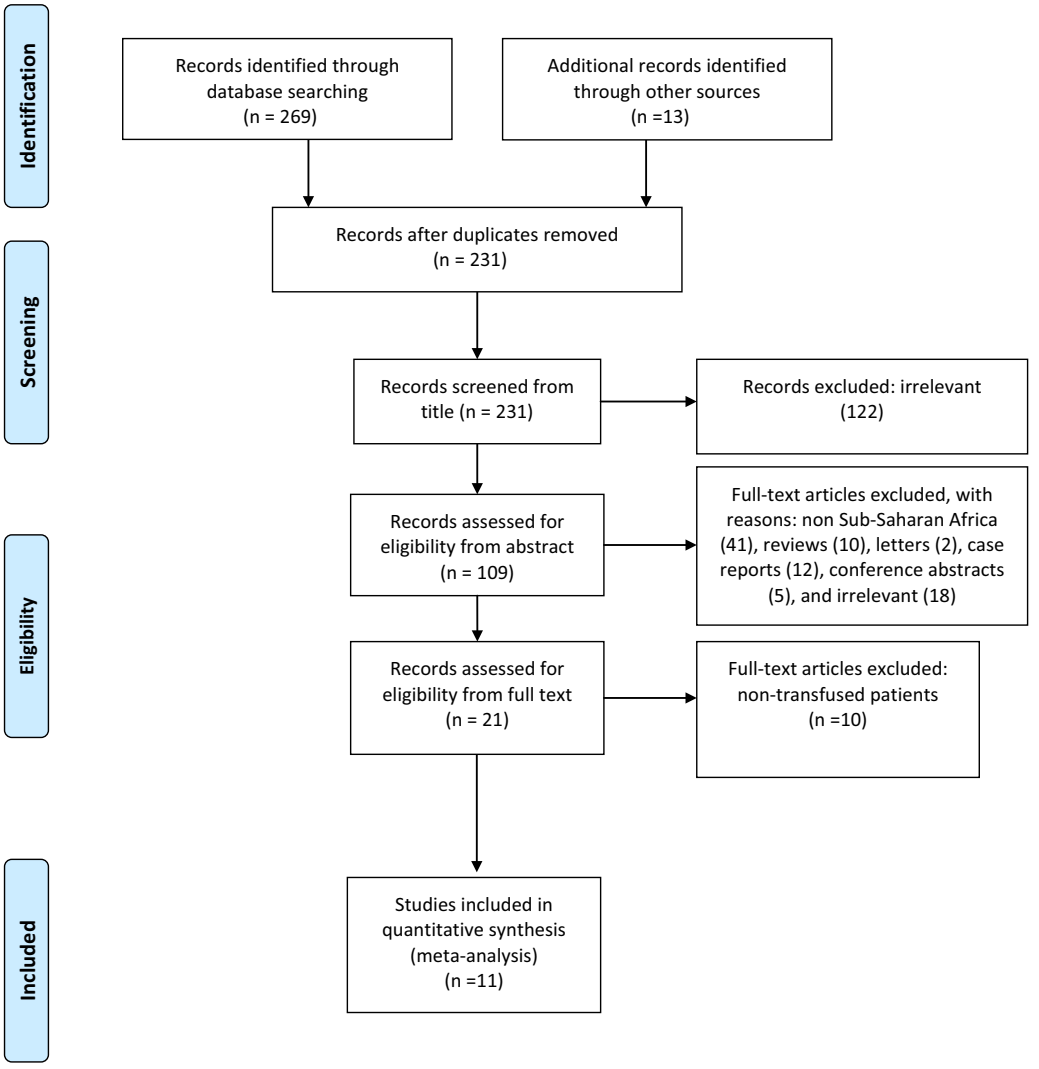


**Fig. 1.** Summary of data extraction history.

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017

**Table 2**
General characteristics of eligible studies.

| Author (year) | Country | Design | Sample size | Alloimmunized patients | Proportion (%) | Screening method[a] |
|---|---|---|---|---|---|---|
| Abbas et al. (2013) | Sudan | Cross-sectional | 100 | 4 | 4.0 | Tube technique |
| Aguiah Vianou (2006) | Benin | Cross-sectional | 210 | 16 | 7.6 | Tube technique |
| Baby et al. (2008) | Mali | Prospective | 78 | 8 | 10.3 | Column agglutination |
| Batina Agasa et al. (2010) | Congo | Retrospective | 127 | 13 | 10.2 | Column agglutination |
| Diarra et al. (2013) | Mali | Prospective | 90 | 4 | 4.4 | Column agglutination |
| Meda et al. (2014) | Tanzania | Cross-sectional | 365 | 15 | 4.1 | Tube technique |
| Mwambungu and Nathan (2014) | Zambia | Cross-sectional | 1000 | 70 | 7.0 | Tube technique |
| Natukunda et al. (2010) | Uganda | Cross-sectional | 214 | 13 | 6.1 | Column agglutination |
| Natukunda et al. (2010) | Uganda | Cross-sectional | 428 | 26 | 6.1 | Column agglutination |
| Ndahimana et al. (2013) | Rwanda | Cross-sectional | 187 | 12 | 6.4 | Tube technique |
| Ugwu et al. (2015) | Nigeria | Cross-sectional | 86 | 8 | 9.3 | Tube technique |

[a] Principle of the procedure involves testing unknown serum/plasma against a set of a standard group O reagent red cells.

extraction and quantitative analysis. Table 2 summarizes the general characteristics of studies included in the analysis. Two were conducted in Uganda [22,23], two in Mali [24,25], and the six others in Sudan [26], Tanzania [27], Benin [28], Rwanda [29], Zambia [30], the Democratic Republic of Congo [31], and Nigeria [32]. These studies were conducted between 2006 and 2015. The 11 studies reported results for transfused 2885 transfused patients.

### 3.2. Proportion of RBC alloantibodies

The pooled analysis of the proportion of RBC alloimmunization led to a cumulative sample size of 2885 transfused patients. Pooling of the 11 studies yielded overall proportions of 6.7 (95% CI: 5.7, 7.8) per 100 transfused individuals, with low heterogeneity ($I^2$ = 13.1%, Fig. 2).

### 3.3. RBC alloantibody specificities

With regard to blood group systems, the majority of alloantibodies belonged to the Rhesus, Kell, and Lewis blood group systems. Among clinically significant antibodies, anti-E ranked as the most common, followed by anti-K, anti-C and anti-D (Table 3).

### 3.4. Publication bias and heterogeneity

In order to ascertain whether publication bias might be affecting the estimated pooled proportions, funnel plots were constructed, as illustrated in Fig. 3. As the figure shows, the funnel plot is relatively symmetric. Moreover, the probability values calculated by Egger and Begg's tests were greater than 0.05 (0.78 and 0.94, respectively), indicating that publication bias was unlikely. With respect to heterogeneity, the relatively low heterogeneity results suggest that between-study variability was reasonable.

## 4. Discussion

Results from this comprehensive meta-analysis indicate that 6.7 (95% CI: 5.7, 7.8) per 100 transfused individuals in Sub-Saharan Africa have clinically significant RBC alloantibodies. This study also found that anti-E, anti-K, anti-C, and anti-D were the most prevalent clinically significant

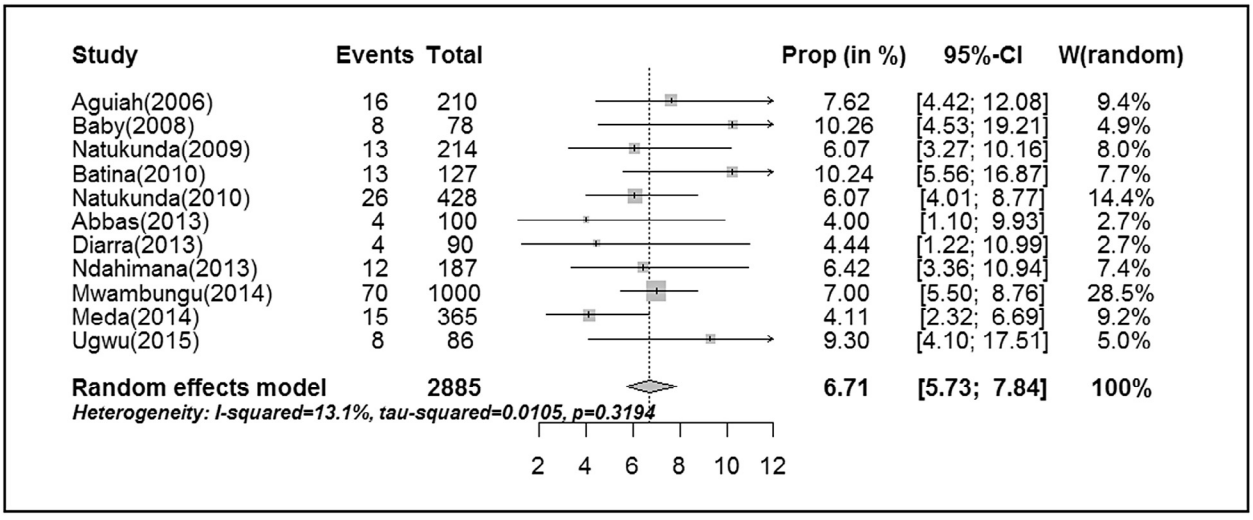


**Fig. 2.** Forest plot of proportion estimates of RBC alloantibodies in transfused patients.

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017

**Table 3**
Red blood cell alloantibody specificities in transfused patients and antigen frequency in black population.

| Blood group system | RBC alloantibodies | Number of antibodies | Antigen frequency (%)* |
|---|---|---|---|
| RH | D | 17 | 92 |
| | C | 19 | 27 |
| | c | 4 | 96 |
| | E | 57 | 22 |
| | e | 3 | 98 |
| | $C^w$ | 5 | 0.01 |
| | **Sub-total** | **105** | |
| MNS | M | 10 | 74 |
| | N | 1 | 75 |
| | S | 11 | 31 |
| | s | 2 | 94 |
| | **Subtotal** | **24** | |
| Kidd | $JK^a$ | 5 | 92 |
| | $JK^b$ | 5 | 49 |
| | **Sub-total** | **10** | |
| Kell | K | 36 | 2 |
| | k | 0 | 99.9 |
| | $Kp^a$ | 4 | <1 |
| | $Kp^b$ | 1 | >99 |
| | $JS^a$ | 0 | 20 |
| | $JS^b$ | 1 | 99 |
| | **Sub-total** | **42** | |
| Duffy | $Fy^a$ | 2 | 10 |
| | $Fy^b$ | 4 | 23 |
| | **Sub-total** | **6** | |
| Lewis | $Le^a$ | 23 | 23 |
| | $Le^b$ | 6 | 55 |
| | **Sub-total** | **29** | |
| Lutheran | $Lu^a$ | 3 | 5 |
| | $Lu^b$ | 1 | >99 |
| | **Sub-total** | **4** | |
| | **Total** | **220** | |

* Source: Adapted from Reid ME, Lomas-Francis C, Olsson ML. *The Blood Group Antigen FactsBook*. Third Edition, 2012, Academic Press.

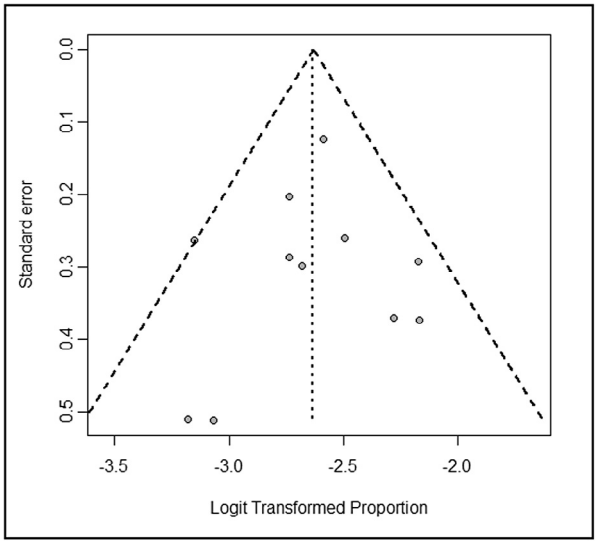


**Fig. 3.** Funnel plot of logit event estimate in transfused patients.

antibodies. To our knowledge, this is the first study that uses meta-analysis of the available evidence to quantify and qualify RBC alloimmunization in transfused patients. One major advantage of this approach over narrative reviews is that it provides a more objective summary to guide policy-making.

Proportions of patients with alloantibodies reported in this review are higher than what has been reported in the general population [33]. The rate of alloimmunization in transfused patients, mostly sickle cell disease patients, fluctuates considerably depending primarily on the number of RBC transfusions [3]. In addition, other factors including genetic background, the population under study, gender, and racial differences between donors and recipients have been shown to influence RBC alloimmunization and this may explain why our pooled estimate is different from rates reported in studies conducted elsewhere [34]. For instance, comparing SCD patients, only 2.6% of those transfused in Jamaica developed RBC alloantibodies in contrast to those transfused in Manchester, United Kingdom, where 76% displayed antibodies [35]. Furthermore, a study conducted in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukaemia found that alloimmunization occurred in 15% of the patients [36]. Thus, our findings highlight the need to prevent alloimmunization in the first place and implement routine pre-transfusion testing practice including antibody screening and identification in major hospitals in Sub-Saharan African countries as a standard of care, especially for at-risk patients including sickle cell disease and other multi-transfused patients. However, given the austere environment in most of Sub-Saharan African countries, limiting RBC phenotyping to the most immunogenic groups and appropriately matching donors and receivers might be considered interim standards to mitigate alloimmunization. In addition, limiting screening to the most prevalent alloantibodies might be cost-effective in resource-limited circumstances. Altogether, these measures would likely minimize the risk of haemolytic reactions and improve blood safety. Moreover, an economic return-on-investment may accrue by decreasing the subsequent burden of laboratory testing and clinical care needed by alloimmunized patients [37].

With respect to antibody specificity, a lot of variation has been observed among different ethnic groups [37,39]. Despite the current policy of routine D-matched transfusions in Sub-Saharan Africa, this review has revealed significant anti-D alloimmunization among transfusion recipients. As suggested by Natukunda et al., data on blood group heterogeneity are needed, including D variants, in different black subpopulations to better understand alloimmunization and formulate evidence-based recommendations [38].

One of the major strengths of this systematic review was that it included studies from all Sub-Saharan African regions including Eastern Africa (Uganda, Sudan and Tanzania), Western Africa (Benin, Mali, and Nigeria), Southern Africa (Zambia), and Central Africa (Rwanda and Congo DRC). In addition, we used a comprehensive search strategy including multiple sources and a diversity of databases with no language restriction. Two researchers independently screened all articles and extracted data from research studies included in the systematic review. We believe, therefore, that our meta-analysis captured the best available data from Sub-Saharan Africa.

However, some limitations need to be considered. First, the evidence summarized in this review comes largely from

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017

cross-sectional studies, which may underestimate the true frequency of alloantibodies, owing to time needed before antibodies can be detected, and once formed, the chance of titers falling to undetectable levels [40,41]. Second, the majority of included studies employed convenience sampling; therefore, the sampled transfused patients may not have been representative of the broader transfused patients. Third, virtually all of the referenced publications came from various more academic institutions that would disproportionately represent more frequently transfused patients and potentially induce a selection bias. This could inflate the prevalence of these antibodies. Notwithstanding the aforementioned limitations, the results of this study represent the most precise and accurate estimates of RBC alloimmunization among transfused patients living in Sub-Saharan Africa. Our meta-analysis strengthens the case for better and more comprehensive alloantibody prevention strategies throughout Sub-Saharan Africa.

In conclusion, our meta-analysis shows that in comparison with more developed parts of the world where antibody screening is widely implemented, RBC alloimmunization in Sub-Saharan Africa is quantitatively similar, but qualitatively different. This has implications for clinical practice, policy-making, and further research. Continued education of clinicians about the importance of prevention should be a priority. Health care decision-makers should understand the magnitude of this situation and act on the evidence. Additional training in Immunohematology and Blood Transfusion will ensure quality and standardize Transfusion Medicine practitioners in Sub-Saharan Africa. Uniform pre-transfusion testing guidelines should be formulated to inform local transfusion practices. Resource constraints notwithstanding, regional blood group reference laboratories should be established to handle complex serologic problems. Therefore, all stakeholders should place a premium on patient safety by developing the necessary infrastructure and training for routine testing of RBC antigens and irregular antibodies for transfused patients. In such a low resource environment, adding the antibody screen to pre-transfusion testing will be a significant achievement in many of the Sub-Saharan African countries.

## References

[1] Chou ST, Liem RI, Thompson AA. Challenges of alloimmunization in patients with haemoglobinopathies. Br J Haematol 2012;159:394–404.
[2] Moise KJ. Red blood cell alloimmunization in pregnancy. Semin Hematol 2005;42:169–78.
[3] Zalpuri S, Zwaginga JJ, le Cessie S, Elshuis J, Schonewille H, van der Bom JG. Red blood cell alloimmunization and number of red-blood-cell transfusions. Vox Sang 2012;102:144–9.
[4] Lindenburg IT, Smits-Wintjens VE, van Klink JM, Verduin E, van Kamp IL, Walther FJ, et al. Long-term neurodevelopmental outcome after intrauterine transfusion for hemolytic disease of the fetus/newborn: the LOTUS study. Am J Obstet Gynecol 2012;206:141, e1-8.
[5] US Food and Drug Administration, Center for Biologics Evaluation and Research. Fatalities Reported to FDA Following Blood Collection and Transfusion: Annual Summary for Fiscal Year 2012. <http://www.fda.gov/BiologicsBloodVaccines/SafetyAvailability/ReportaProblem/TransfusionDonationFatalities/ucm346639.htm>[accessed 06.14].
[6] Population Reference Bureau (PRB), World Population data sheet 2013. <http://www.prb.org/Publications/Datasheets/2013/2013-world-population-data-sheet/data-sheet.aspx> [accessed 12.14].
[7] Dzik WS, Delaney M. The future of transfusion and Africa. Transfusion 2014;54:2791–4.
[8] Tapko J-BMP, Diarra-Nama AJ. Status of blood safety in the WHO African region: report of the 2006 survey. Brazzaville, Republic of Congo: WHO Regional Office for Africa; 2006 <http://apps.who.int/iris/handle> [accessed 12.14.].
[9] Bloch EM, Vermeulen M, Murphy E. Blood transfusion safety in Africa: a literature review of infectious disease and organizational challenges. Transfus Med Rev 2012;26:164–80.
[10] Lund TC, Hume H, Allain JP, McCullough J, Dzik W. The blood supply in Sub-Saharan Africa: needs, challenges, and solutions. Transfus Apher Sci 2013;49:416–21.
[11] Bugge HF, Karlsen NC, Oydna E, Rake MM, Wexels N, Bendabenda J, et al. A study of blood transfusion services at a district hospital in Malawi. Vox Sang 2013;104:37–45.
[12] Osaro E, Charles AT. The challenges of meeting the blood transfusion requirements in Sub-Saharan Africa: the need for the development of alternatives to allogenic blood. J Blood Med 2011;2:7–21.
[13] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.
[14] Schwarzer G. Package 'meta'. The R Foundation for Statistical Computing 2014. <http://cran.r-project.org/web/packages/meta/meta.pdf> [accessed 12.14].
[15] Fleiss JL. The statistical basis of meta-analysis. Stat Methods Med Res 1993;2:121–45.
[16] Egger M, Smith GD. Meta-analysis. Potentials and promise. BMJ 1997;315:1371–4.
[17] Rucker G, Schwarzer G, Carpenter J, Olkin I. Why add anything to nothing? The arcsine difference as a measure of treatment effect in meta-analysis with zero cells. Stat Med 2009;28:721–38.
[18] Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health 2013;67:974–8.
[19] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
[20] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
[21] Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50:1088–101.
[22] Natukunda BM, Schonewille H, Ndugwa C, Brand A. Red blood cell alloimmunization in sickle cell disease patients in Uganda. Transfusion 2010;50:20–5.
[23] Natukunda B, Schonewille H, van de Watering L, Brand A. Prevalence and specificities of red blood cell alloantibodies in transfused Ugandans with different diseases. Vox Sang 2010;98:167–71.
[24] Diarra AB, Guindo A, Kouriba B, Dorie A, Diabaté DT, Diawara SI, et al. Sickle cell anemia and transfusion safety in Bamako, Mali. Seroprevalence of HIV, HBV and HCV infections and alloimmunization belonged to Rh and Kell systems in sickle cell anemia patients. Transfus Clin Biol 2013;20:476–81.
[25] Baby M, Fongoro S, Cissé M, Gakou Y, Bathily M, Dembélé AK, et al. Frequency of red blood cell alloimmunization in polytransfused patients at the university teaching hospital of Point G, Bamako, Mali. Transfus Clin Biol 2010;17:218–22.
[26] Abbas M, Bolad A, Jiefri N, Mergani A. Red blood cell alloimmunization among Sudanese homozygous sickle cell disease patients. Am J Med Sci 2013;3:61–7.
[27] Meda EMP, Marlow T, Reid C, Roberts DJ, Makani J. Red blood cell alloimmunization in sickle cell disease patients in Tanzania. East Afr J Public Health 2014;11:775–80.
[28] Aguiah Vianou B. Contribution à l'étude de l'Allo immunisation post-transfusionnelle chez les patients transfusés à Cotonou Bénin [Thesis]. Bénin: Université d'Abomey-Calavi. <http://www.memoireonline.com/02/13/6974/> [accessed 12.14].
[29] Ndahimana E, Gothot A, Gérard C, Senyana F, R'zik S, Mukabayire O, et al. Risk of red blood cell alloimmunisation in Rwanda: assessment of pretransfusion crossmatch techniques used in district hospitals. East Afr Med J 2013;90:277–82.
[30] Mwambungu A, Nathan S. Frequency and distribution of RBC alloantibodies among transfused patients at Ndola Central Hospital, Zambia. Int J Sci Res 2014;3:86–9.
[31] Batina Agasa S, Dupont E, Kayembe T, Molima P, Malengela R, Kabemba S, et al. Multiple transfusions for sickle cell disease in the Democratic Republic of Congo: the importance of the hepatitis C virus. Transfus Clin Biol 2010;17:254–9.
[32] Ugwu NI, Awodu OA, Bazuaye GN, Okoye AE. Red cell alloimmunization in multi-transfused patients with sickle cell anemia in Benin City, Nigeria. Niger J Clin Pract 2015;18:522–6.
[33] Issitt PD, Anstee DJ. Applied blood group serology. 4th ed. Durham (NC): Montgomery Scientific; 1998. p. 873–5.

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017

[34] Garratty G. Severe reactions associated with transfusion of patients with sickle cell disease. Transfusion 1997;37:357–61.
[35] Olujohungbe A, Hambleton I, Stephens L, Serjeant B, Serjeant G. Red cell antibodies in patients with homozygous sickle cell disease: a comparison of patients in Jamaica and the United Kingdom. Br J Haematol 2001;113:661–5.
[36] Sanz C, Nomdedeu M, Belkaid M, Martinez I, Nomdedeu B, Pereira A. Red blood cell alloimmunization in transfused patients with myelodysplastic syndrome or chronic myelomonocytic leukemia. Transfusion 2013;53:710–5.
[37] Adias TC, Erhabor O. Suboptimal testing for alloantibodies in sub Saharan Africa: bane to effective immunohaematological services delivery. Int J Med Sci 2013;1:13–22.
[38] Natukunda B, Brand A, Schonewille H. Red blood cell alloimmunization from an African perspective. Curr Opin Hematol 2010;17:565–70.
[39] Reid ME, Lomas-Francis C, Olsson ML. The Blood Group Antigen FactsBook. Third ed. Academic Press; 2012.
[40] Schonewille H, Haak HL, van Zijl AM. RBC antibody persistence. Transfusion 2000;40:1127–31.
[41] Reverberi R. The persistence of red cell alloantibodies. Blood Transfus 2008;6:225–34.

Please cite this article in press as: Alain M. Ngoma, et al., Red blood cell alloimmunization in transfused patients in sub-Saharan Africa: A systematic review and meta-analysis, Transfusion and Apheresis Science (2015), doi: 10.1016/j.transci.2015.10.017