Blood utilization in sub-Saharan Africa: a systematic review of current data

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Abstract

Background: Data on the use of blood products in sub-Saharan Africa (SSA) are scarce. A systematic review of published data on blood utilization according to diagnosis in SSA was performed.

Study design and methods: Studies published from January 2000 to June 2018 were searched in PubMed, Embase and African Index Medicus. Data were extracted and synthesized. The proportion of blood products used for different diagnostic categories is presented.

Results: 37 studies representing 159,746 transfusions to 96,690 patients from 14 countries in SSA were included. Data from six of 37 studies were pooled to determine blood product use according to diagnosis. The primary diagnostic categories were pediatric malaria (20%), sickle cell anemia [SCA] (18%), obstetric hemorrhage (16%), and other causes of bleeding (16%). About 8%, 6% and 2% of products were used for other infections, cancer treatment, and surgery respectively. Overall, 58.5% of the products transfused were red blood cells, 31.7 % whole blood, 7.2% fresh frozen plasma, and 2.6% as platelets. Estimated blood product use per population in SSA was 5.3 transfusions per 1000 people, compared with 52 and 34 per thousand for Australia and United States respectively.

Conclusion: This study provides a systematic attempt to quantify blood utilization for SSA. Blood products in SSA are used primarily for pediatric malaria, SCA, obstetric hemorrhage and other causes of bleeding. Studies such as this represent an important early step towards improving hemovigilance in SSA.

Key words: blood products, utilization, transfusion, sub-Saharan Africa

Introduction

Blood and blood products are used in clinical care to treat disease conditions that cannot be effectively managed by other means, thus averting their morbidity and mortality risk potential.[1] In most low and middle income countries, blood products are in short supply, presenting enormous challenges related to their effective utilization. National blood transfusion services (NBTS) were established in most African nations in the early part of this century in line with the World Health Assembly resolution WHA28.72 on utilization and supply of human blood and blood products. While these services have improved the situation, shortages remain. Documenting blood utilization in sub-Saharan Africa (SSA) is an important step in understanding the current level of population-based utilization and to forecast future demand for blood.[2] Both of these factors are fundamental to hemovigilance and to improvement of transfusion practice and healthcare systems in SSA.

In SSA, published data on the clinical use of blood and blood products are limited, although estimates for the common indications for transfusion have been made. It has been estimated that about 80% of all blood transfusions in SSA are given to three disease conditions, namely; malaria, obstetric hemorrhage, and trauma.[3] However, some reports have highlighted the possibility that recent improvements in the prevention of malaria and the promising progress towards its elimination in some parts of the region may have had an impact on blood utilization.[4-6] Moreover a few recent studies have suggested that in some settings blood utilization has shifted to the support of patients suffering from cancer and other non-communicable diseases.[7,8] More comprehensive evidence is therefore needed.

Materials and methods

Where applicable, the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines[9] were followed in designing and reporting this review. We reviewed the published literature on the use of blood and blood products for transfusion in SSA (which includes 49 countries). An experienced medical Librarian (RS) searched PubMed, Embase (through Ovid) and African Index Medicus for articles from January 1, 2000 up to 18 June 2018. The search terms used were "Transfusion", "Blood Transfusion", "Blood Component Transfusion", "Exchange Transfusion, Whole Blood", and "Plasma Exchange". Our search included studies published in English or French. We restricted the date of publication to after January 1, 2000, because most African nations established national blood transfusion services (NBTS) around the year 2000.[10]

The search strategies are reported in Appendix 1. These searches were loaded into EndNote software version X7 (Clarivate Analytics, Philadelphia, PA, USA) and duplicates for overlapping references were removed. In addition, systematic snow balling was used to search other resources by looking at the reference lists of included articles using 'Scopus citation database'.

Selection of studies: We included cross-sectional studies reporting the use of blood products in SSA. Studies reporting on transfusion with any one or more of the following products were selected: red blood cells (RBCs), whole blood (WB), platelets (PLTs), and plasma or fresh frozen plasma (FFP). Case reports and case series were excluded. Studies were selected using a pre-determined eligibility criteria stipulated in the protocol in Appendix 2. One review author (AD) screened all titles and abstracts of articles identified. Only clearly ineligible studies were excluded at this stage. Subsequently, full texts of all the remaining 110 studies (3 in French and 107 in English) were retrieved and read for detailed evaluation.

Data extraction: Two review authors (AD and EKB) independently extracted data for each study using a piloted data extraction form. We extracted data on the general aspects about the study such as the first author, country, study setting, and study duration, as well as the outcome variable – the use of blood products. Blood product use was defined as an individual transfusion episode for each blood product. The primary outcome was the proportion of blood products used for different diagnostic categories, and was calculated as; the number of transfusions for a given diagnostic category divided by the total number of blood products transfused. Where the data were not clear in an individual study, attempts were made to clarify via email to the respective authors. Health facilities were grouped by level, based on a three-tier healthcare delivery system. We defined tertiary health facility level as: national referral, regional referral or provincial, and university teaching and specialist hospitals; while secondary included district level or general hospitals and state hospitals, and primary as health centers and health posts. Transfusion index was computed as: number of blood products transfused divided by the total number of patients transfused.

Statistical analysis: The abstracted data were entered into an Excel spreadsheet (Excel 2010, Microsoft Corp., Redmond, WA), and exported into SPSS Statistics 23.0 (IBM Corp., Armonk, NY) for analysis. The primary outcome graph was made using Prism 7 software (GraphPad, La Jolla, CA). Continuous data were summarized with medians and interquartile ranges (IQR), while categorical data were summarized with frequencies and percentages. Sub-group analysis was done for different patient populations, as per the included studies.

Results

We screened 2143 abstracts, and reviewed 110 full-text articles, from which only 37 studies were included. The other 74 studies were excluded for reasons as outlined in Fig. 1.

The 37 studies included were conducted in 14 of the 49 countries across the SSA region, representing 159,746 blood products transfused to 96,690 patients (Appendix 3.1).

10 of these studies reported data on general patient populations, while the rest were among specific patients groups. By geographical location, these were fairly well distributed, although the size of the studies included varied widely, as shown in Fig. 2.

Quantitative analysis

Approximately 75% of the included studies came from tertiary level healthcare facilities in urban settings. More than half were retrospective, with a median (IQR) sample size of 144 (100 – 670) patients. Median study duration (IQR) was 12 (5 – 34) months, and the median number of transfusions was 238 (141 – 887) (Table 1).

Primary outcome measure

Data from ten studies that reported on general patient populations[7, 8, 11- 18] were considered for analysis of the primary outcome, but only six studies[7,13-16, 18] could be used for this analysis because two did not report specific diagnostic categories[12,17] and the other two did so using ICD-10 disease categories[8, 11] (Appendix 3.2). We found that among the general patient population, the majority of blood products were used for the following diagnostic categories: pediatric malaria (20%), sickle cell anemia (18%), obstetric hemorrhage (16%), and other causes of bleeding (16%), as shown in Fig. 3 and Appendix 3.2. The six studies[7,13-16, 18] used to determine the primary outcome were conducted in only five of the 49 countries across SSA, in which 37,195 products were transfused to 33,229 patients (Appendices 3.1 and 3.2). Seven

of the 10 general studies[7,12-16, 18] also reported on blood utilization by the different wards, including pediatrics which used the majority (47%) of blood products (Table 2).

Sub-groups analysis

Blood utilization among the other patient populations of pediatrics, obstetrics and gynecology, Cesarean section births, and newborns are shown in Appendices 3.3 – 3.7. The studies among pediatric patients[23-31] showed that 64% (2810/4387) of blood products were transfused for malaria. Post-partum hemorrage (PPH) at 24% (524/2228) and cesarean sections at 22% (485/2228) were the most transfused diagnostic categories among the obstetrics and gynecology patients,[32-36] with abortions and cancer accounting for only 10% and 8% of transfusions respectively. Within the cesarean section only studies,[37-39] placenta previa at 27% (47/431) and obstructed labor at 25% (44/431) were the leading indications for transfusion. Among newborn babies, whole blood and packed RBCs products were used in relatively equal measure, and neonatal jaundice and bleeding together accounted for 66% (218/477) of the products transfused overall.[40-42]

Blood products

Among the 10 studies on general patient populations,[7, 8, 11- 18] transfusions of whole blood (WB), red blood cells (RBCs), fresh frozen plasma (FFP), and platelets (PLTs) were 31.7 % (46,653/147,310), 58.5% (86,236/147,310), 7.2% (10,662/147,310) and 2.6% (3,759/147,310), respectively (Table 3).

The use of FFP and PLTs was less frequent across the other sub-group studies. Similarly, some products were notably reported by very few studies. For example, cryoprecipitate use was reported in only one study.[11] The two studies that exclusively evaluated the use of autologous whole blood and another two on PLTs are summarized in Appendix 3.8. The transfusion index, defined as the number of products per transfused-patient, computed using all 37 studies was 1.65 (159,746 products per 96,690 transfused-patients).

Estimating the number of transfusions per population

The number of transfusions per population may represent a novel measure of the utilization of blood products suitable for comparison across different healthcare regions. We attempted to estimated this for SSA using Tanzania, for which *Drammeh et al* has documented the national annual blood use.[12] An estimate of 244,535 red cell units were issued in 2013 in Tanzania for an estimated Tanzania national population of 46,142,004 million people in 2013, based on the 2012 population and housing census.[19] We can estimate the number of transfusions in 2013 in Tanzania as; 244,535/46,142,004 = 5.3 transfusions per 1000 people. By comparison in the same year, Australia issued 1,185,732 blood products with a population of 22,730,000 people, giving an estimate of 52.1 transfusions per 1000 people;[20] and the United States (AABB member facilities) transfused a total of 10,962,000 products (RBCs, WB, PLT, FFP and Cryoprecipitates) with a population of 319,330,000, representing 34.3 transfusions per 1000 people.[21, 22]

Qualitative synthesis

All the 37 eligible studies reported utilization of blood and blood products, but with slight variations in the scope and quality. Regarding the scope, eight studies reported use of blood products among hospitalized general patient populations,[7, 11,13-18] while two studies used national blood transfusion databases.[8,12] These 10 studies were used for the primary outcome calculation. The rest of the studies evaluated blood utilizations among specific patient groups: nine studies among pediatric patients only;[23-31] five on obstetrics and gynecology patients;[32-36] three among cesarean section deliveries;[37-39] three among newborn babies;[40-42] two among elective surgical operations;[43,44] two exclusively on the use of platelets;[45,46] two on the use of autologous blood;[47,48] and one among hepato-gastroenterology patients.[49] Most studies made a

clear distinction between the number of patients transfused and the number of blood products used for transfusion. The majority reported both, while eight studies reported on one of the two. We contacted the eight authors in order to get clarification, but received no response from them. We therefore assumed the number of patients transfused and that of products transfused to be equal. Similarly, studies did not specify the number of platelet units used in standard platelet transfusions. Thus, in the case of platelets, the number of blood products is more likely to represent the number of transfusion episodes.

Studies varied considerably in the way they reported the disease conditions for which transfusions were given. The majority reported discrete diagnostic categories; however, two studies[8,11] used the International Classification of Diseases (ICD-10) diagnostic categories, with many patients grouped into "Other ICD-10 diseases" and "Diseases of blood and blood forming organs". We performed a sensitivity analysis with the assumption that the category "Other ICD-10 diseases" falls into our category "Other non-communicable diseases and organ disorders", while "Diseases of blood and blood forming organs" falls into "Other medical conditions such as chronic or unknown anemia". The results showed remarkable differences in the outcome measure, especially given the large numbers of blood units in the two ICD-10 categories from the study performed by *Pitman et al*.[8] We therefore decided not to include these two studies in the primary outcome analysis, since it would be misleading to combine data with heterogeneous diagnostic categories.

Regarding quality of the studies, one concern was the inconsistency by some studies in reporting values, particularly varying denominators in different results tables as well as mixing up the indications for transfusion.[32-34] In such cases, we resorted to reporting broad diagnostic categories or re-calculated the proportions for the blood products, using the rates of

transfusion for the individual study. In two instances where the totals from the manuscript tables could not be reconciled with those in the text,[11,13] the totals from the tables were used.

Because the majority (20/37) of included studies were retrospective chart reviews of paper-based records, the risk concern for information bias resulting from missing data from the archives cannot be overlooked. Few studies made a mention of missing records, and only one,[8] explained in detail how this matter was handled. We regarded the risk of information bias as high for one study in the pediatric population that excluded transfusions done at the emergency ward.[31] Because of the same challenge of missing data, two large studies that used NBTS database,[8,12] used the assumption that all blood products distributed by NBTS were transfused to the same patients, as requested. In this case, we considered the actual number of blood products issued, rather than those requested. In addition, because the proportions of products used for the different indications were not reported, we assumed that the proportions of requested and issued products would remain the same.

Discussion

This review analyzes 37 studies that reported on the use of blood products in SSA, from which six studies, reporting on a general hospitalized patient population, [7, 13-16, 18] were used to estimate current blood utilization in the region. The results suggest that pediatric malaria, sickle cell anemia (SCA), obstetric hemorrhage, and other causes of bleeding are the most common indications for which blood is transfused in SSA. We found parallel patterns both for the individual hospital wards, with most products being given to the pediatric ward, as well as for sub-group patient populations. In the pooled analysis of the nine studies that included only children[23-31] it was found that 64% of blood products were used for children with severe malaria. Similarly, from the five pooled studies in obstetrics and gynecology[32-36] over half (54%) of blood products were used for obstetric hemorrhage (represented here by the diagnostic categories of post-partum hemorrhage [PPH], antepartum hemorrhage [APH], and cesarean deliveries). The current review has shown that 'other cause of bleeding' is the fourth leading transfusion indication, using up to 16% of blood products. This category constituted non-traumatic bleedings, with the largest single diagnosis being gastrointestinal bleeding.

Our review confirms evidence from earlier reports that have shown pediatric malaria, obstetric hemorrhage, and SCA to be the leading disease conditions for blood transfusion in SSA.[3,50,51] Although our review includes publications as early as the year 2000, the burden of each of these diseases still remains high in SSA. Globally malarial anemia is the third most common cause of anemia,[52] while the prevalence of the sickle cell gene in some parts of SSA ranges between 10% and 18%,[53,54] with up to 3% of hospitalized children suffering from SCA.[55] Similarly, the prevalence of PPH (the most common type of obstetric hemorrhage) in SSA ranges between 10% and 23% of deliveries.[56]

Two recent reports (*Butler et al* and *Pitman et al*) have indicated that changes are taking place in the use of blood in some SSA settings, with blood being used more for cancer and non-communicable diseases.[7,8] Nevertheless, our review has found that pediatric malaria, SCA and obstetric hemorrhage still remain the top indications for blood utilization, similar to earlier reports. The differences in findings between the present systematic review and the two recent studies could relate to the broader assessment of this systematic review and to specific aspects of the patient populations included in the two studies. For example, the study by *Butler et al* was conducted at a national referral health facility that handles mainly specialized patient care, including cancer care.[7] The findings from *Pitman et al* may be confounded by possible mis-categorization of malaria transfusions, a study limitation the authors acknowledge in their paper.[8]

Whereas blood utilization in most developed countries have been documented to be generally decreasing,[57] the picture in SSA still remains uncertain due to limited data. Some reports have suggested that the decrease in blood transfusions in some settings follows a decline in the malaria edemicity.[4-6] These observations still need to be confirmed by larger prospective studies. Blood utilization tends to vary considerably by health care specialty and by level of health facility.[58] The current review was unable to study these possible trends, because there were too few studies to compare urban versus rural setting, tertiary versus secondary level health facilities, or studies conducted in early 2000 versus recent years.

We estimated a transfusion index, defined as number of products per transfused patient, and found a much lower transfusion index for SSA compared with the United States (1.65 and 2.72 respectively).[21] Similarly, the use of the different blood products varied between SSA and high income countries such as the United States with 58.5%, 31.7%, 7.2% and 2.6%,

versus 66%, 0.1%, 19% and 14% for RBCs, WB, FFP and PLTs, respectively.[21] Possible explanations for these findings, especially the high percentage of WB use in SSA, could be factors associated with limited clinical awareness, the high cost of component separation, as well as the local blood demand for WB. Whereas the latter aligns with the WHO recommendation for blood products use,[1] in general policies and practices related to component use in SSA remain unclear. [59] However, lower FFP and PLT use in SSA may be related to the high cost investment required to prepare and store these components.

Compared with high income countries, the blood product use per population in SSA is very low. We have estimated the annual transfusions per population (using Tanzanian data) to be 5.3 transfusions per 1000 people, compared to 52.1 and 34.3 per 1000 people for Australia and United States respectively. These figures parallel the WHO estimates of 32.0 red cell units (range of 7-49) per 1000 population and 3.41 red cell units (range of 0.32-10) per 1000 population in high-income and low-income countries respectively. [60] The low transfusion rates in low-income nations are linked to lower donation rates, which in turn are to a great extent a result of inadequate funding. WHO data estimate donation rates of only 4.6 donations per 1000 population per year for low-income countries.[61] However, to align with the World Health Assembly resolution WHA63.12 on availability, safety and quality of blood products, SSA nations need to improve blood availability to meet the increasing demand for transfusion.[62]

Limitations: Interpretations of the findings of this current review may be subject to a few uncertainties. First, most studies included were retrospective chart reviews conducted with non-representative sample of patients and associated with missing data. This increases the risk of bias in the individual studies. Moreover, data have not been published for all nations of

SSA: only six studies from 10% (five out of 49) of SSA countries could be pooled for the primary outcome analysis - in which 37,195 products were transfused to 33,229 patients. Secondly, there was heterogeneity across the individual studies in reporting the diagnostic categories. As such, during our quantitative synthesis we tried to re-categorize some similar or over-lapping categories, although we could not do so in the case of two studies that used ICD-10 disease categories. This may have risked introducing bias associated with this process of re-categorizing. These limitations could be largely removed by a more comprehensive hemovigilance program for SSA.

In summary, our study has merit because, it systematically attempts to estimate blood utilization in SSA. Blood products in SSA are used primarily for pediatric malaria, SCA, obstetric hemorrhage, and other causes of bleeding. Compared with high income countries, the transfusion index, transfusions per population and component transfusions for FFP and PLTs still remain low, while the use of WB is relatively high.

Recommendations: Understanding blood utilization in SSA would be improved by standardized documentation of the diseases and diagnostic categories for which transfusion are given. Developing and implementing a standardized quality clinical transfusion use and management reporting system under a multi-nation bio-vigilance program could generate annual trends useful for documenting blood needs. In addition, improvement in diagnostic precision during routine clinical care would minimize the large numbers of 'unknown anemias' that were reported among many retrospective studies. Furthermore, comprehensive and larger prospective studies among a wide range of healthcare settings and levels would provide useful evidence on the possible trends of blood utilization in the region.

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Table 1. Characteristics of studies on blood utilization in sub-Saharan Africa (n = 37)	
Variable	Descriptive statistics
Year of study (starting), Median (IQR*)	2009 (2005 – 2013)
Study duration (in months), Median (IQR)	12 (5.0 – 33.5)
Study design, N (%)	
Retrospective	20 (52.6)
Prospective	16 (42.1)
Mixed	1 (2.6)
Study setting, N (%)	
Urban	27 (71.1)
Rural	6 (15.8)
Mixed	3 (7.9)
Unknown	1 (2.6)
Level of health facility, N (%)	
Tertiary	28 (73.7)
Secondary	5 (13.2)
Mixed	4 (10.5)
Blood products reported on, median (IQR)	2 (1-3)
Number of patients transfused, median (IQR)	144 (100 – 670)
Number of transfusions, median (IQR)	238 (141 – 887)

*IQR = interquartile range

Table 2. Blood utilization by the different wards in sub-Saharan Africa

Author	Number of blood products used by each ward				
	Pediatrics	Medical	Surgical	Accident & Emergency	Obstetrics & Gynecology
Arewa et al (2009) [13]	228	192	150	-	112
Bugge et al (2013) [14]	66	30	-	-	-
Butler et al (2015) [7]	700	1,349	901	517	1,404
Drammeh et al (2017) [12]	4,968	5,320	1,589	-	4,651
Mbanya et al (2001) [15]	17,128	4,999	-	-	4,855
Natukunda et al (2010) [16]	724	453	21	158	318
Traore et al (2011) [18]	-	-	-	-	168
Totals	23,814 (47%)	12,343 (24%)	2,661 (5%)	675 (1%)	11,508 (23%)

Table 3. Distribution of blood products use in sub-Saharan Africa

	Type of blood product used				
Author	RBCs	WB	FFP	PLTs	Totals
Arewa et al (2009) [13]	462	39	72	100	673
Bugge et al (2013) [14]	-	104	-	-	104
Butler et al (2015) [7]	1,970	3,879	132	349	6,330
Drammeh et al (2017) [12]	283	13,416	251	234	14,184
Mafirakureva et al (2015) [11]	3,660	20	444	93	4,217
Mbanya et al (2001) [15]	-	26,982	-	-	26,982
Natukunda et al (2010) [16]	1,151	1,621	-	5	2,777
Pitman et al (2015) [8]	78,660	-	9,751	2,978	91,389
Tobi et al (2014) [17]	50	362	12	-	424
Traore et al (2011) [18]	-	230	-	-	230
Totals	86,236	46,653	10,662	3,759	147,310
	(58.5%)	(31.7%)	(7.2%)	(2.6%)	

Appendices

Appendix 1: The search strategy

Embase (through Ovid);

1. blood transfusion/ or blood component therapy/ or exchange blood transfusion/
2. transfusion.ti,ab,kw.
3. exp "Africa south of the Sahara"/ or sub-Sahara.ti,ab. or sahara.ti,ab. or central africa.ti,ab. or Cameroon.ti,ab. or "Central African Republic".ti,ab. or Chad.ti,ab. or Congo.ti,ab. or "Democratic Republic of the Congo".ti,ab. or Equatorial Guinea.ti,ab. or Gabon.ti,ab. or Eastern africa.ti,ab. or Burundi.ti,ab. or Djibouti.ti,ab. or Eritrea.ti,ab. or Ethiopia.ti,ab. or Kenya.ti,ab. or Rwanda.ti,ab. or Somalia.ti,ab. or Sudan.ti,ab. or Tanzania.ti,ab. or Uganda.ti,ab. or Southern africa.ti,ab. or Angola.ti,ab. or Botswana.ti,ab. or Lesotho.ti,ab. or Malawi.ti,ab. or Mozambique.ti,ab. or Namibia.ti,ab. or South Africa.ti,ab. or Swaziland.ti,ab. or Zambia.ti,ab. or Zimbabwe.ti,ab. or Western africa.ti,ab. or Benin.ti,ab. or Burkina Faso.ti,ab. or Cape Verde.ti,ab. or "Cote d'Ivoire".ti,ab. or Gambia.ti,ab. or Ghana.ti,ab. or Guinea.ti,ab. or Guinea-Bissau.ti,ab. or Liberia.ti,ab. or Mali.ti,ab. or Mauritania.ti,ab. or Niger.ti,ab. or Nigeria.ti,ab. or Senegal.ti,ab. or Sierra Leone.ti,ab. or Togo.ti,ab. or Ivory Coast.ti,ab. or central africa.ad. or Cameroon.ad. or Central African Republic.ad. or Chad.ad. or Congo.ad. or Democratic Republic of the Congo.ad. or Equatorial Guinea.ad. or Gabon.ad. or Eastern africa.ad. or Burundi.ad. or Djibouti.ad. or Eritrea.ad. or Ethiopia.ad. or Kenya.ad. or Rwanda.ad. or Somalia.ad. or Sudan.ad. or Tanzania.ad. or Uganda.ad. or

Southern africa.ad. or Angola.ad. or Botswana.ad. or Lesotho.ad. or Malawi.ad. or Mozambique.ad. or Namibia.ad. or South Africa.ad. or Swaziland.ad. or Zambia.ad. or Zimbabwe.ad. or west africa.ad. or Benin.ad. or Burkina Faso.ad. or Cape Verde.ad. or "Cote d'Ivoire".ad. or Gambia.ad. or Ghana.ad. or Guinea.ad. or Guinea-Bissau.ad. or Liberia.ad. or Mali.ad. or Mauritania.ad. or Niger.ad. or Nigeria.ad. or Senegal.ad. or Sierra Leone.ad. or Togo.ad. or Ivory Coast.ad.

4. 1 or 2
5. 3 and 4
6. (elsevier or embase or canadian).cr.
7. 5 and 6
8. limit 7 to (conference abstract or conference paper or "conference review")
9. 7 not 8
10. case report/
11. 9 not 10
12. (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
13. 11 not 12

PubMed;

#1. Search ((("Blood Component Transfusion"[Mesh]) OR "Exchange Transfusion, Whole Blood"[Mesh]) OR "Plasma Exchange"[Mesh]) OR "Blood Transfusion"[Mesh:NoExp]

#2. Search transfusion[tiab]

#3. Search #1 OR #2

#4. Search ("africa south of the sahara"[MeSH Terms] OR "africa, central"[MeSH Terms] OR "cameroon"[MeSH Terms] OR "central african republic"[MeSH Terms] OR "chad"[MeSH Terms] OR "congo"[MeSH Terms] OR "democratic republic of the congo"[MeSH Terms] OR "equatorial guinea"[MeSH Terms] OR "gabon"[MeSH Terms] OR "africa, eastern"[MeSH Terms] OR "burundi"[MeSH Terms] OR "djibouti"[MeSH Terms] OR "eritrea"[MeSH Terms] OR "ethiopia"[MeSH Terms] OR "kenya"[MeSH Terms] OR "rwanda"[MeSH Terms] OR "somalia"[MeSH Terms] OR "sudan"[MeSH Terms] OR "tanzania"[MeSH Terms] OR "uganda"[MeSH Terms] OR "africa, southern"[MeSH Terms] OR "angola"[MeSH Terms] OR "botswana"[MeSH Terms] OR "lesotho"[MeSH Terms] OR "malawi"[MeSH Terms] OR "mozambique"[MeSH Terms] OR "namibia"[MeSH Terms] OR "south africa"[MeSH Terms] OR "swaziland"[MeSH Terms] OR "zambia"[MeSH Terms] OR "zimbabwe"[MeSH Terms] OR "africa, western"[MeSH Terms] OR "benin"[MeSH Terms] OR "burkina faso"[MeSH Terms] OR "cape verde"[MeSH Terms] OR "Cote d'Ivoire"[MeSH] OR "gambia"[MeSH Terms] OR "ghana"[MeSH Terms] OR "guinea"[MeSH Terms] OR "guinea-bissau"[MeSH Terms] OR "liberia"[MeSH Terms] OR "mali"[MeSH Terms] OR "mauritania"[MeSH

Terms] OR "niger"[MeSH Terms] OR "nigeria"[MeSH Terms] OR "senegal"[MeSH Terms] OR "sierra leone"[MeSH Terms] OR "togo"[MeSH Terms] OR sub-Sahara[tiab] OR sahara[tiab] OR central africa[tiab] OR Cameroon[tiab] OR Central African Republic[tiab] OR Chad[tiab] OR Congo[tiab] OR "Democratic Republic of the Congo"[tiab] OR Equatorial Guinea[tiab] OR Gabon[tiab] OR Eastern africa[tiab] OR Burundi[tiab] OR Djibouti[tiab] OR Eritrea[tiab] OR Ethiopia[tiab] OR Kenya[tiab] OR Rwanda[tiab] OR Somalia[tiab] OR Sudan[tiab] OR Tanzania[tiab] OR Uganda[tiab] OR Southern africa[tiab] OR Angola[tiab] OR Botswana[tiab] OR Lesotho[tiab] OR Malawi[tiab] OR Mozambique[tiab] OR Namibia[tiab] OR South Africa[tiab] OR Swaziland[tiab] OR Zambia[tiab] OR Zimbabwe[tiab] OR Western africa[tiab] OR Benin[tiab] OR Burkina Faso[tiab] OR Cape Verde[tiab] OR "Cote d'Ivoire"[tiab] OR Gambia[tiab] OR Ghana[tiab] OR Guinea[tiab] OR Guinea-Bissau[tiab] OR Liberia[tiab] OR Mali[tiab] OR Mauritania[tiab] OR Niger[tiab] OR Nigeria[tiab] OR Senegal[tiab] OR Sierra Leone[tiab] OR Togo[tiab] OR Ivory Coast[tiab] OR central africa[Ad] OR Cameroon[Ad] OR Central African Republic[Ad] OR Chad[Ad] OR Congo[Ad] OR Democratic Republic of the Congo[Ad] OR Equatorial Guinea[Ad] OR Gabon[Ad] OR Eastern africa[Ad] OR Burundi[Ad] OR Djibouti[Ad] OR Eritrea[Ad] OR Ethiopia[Ad] OR Kenya[ad] OR Rwanda[Ad] OR Somalia[Ad] OR Sudan[Ad] OR Tanzania[Ad] OR Uganda[Ad] OR Southern africa[Ad] OR Angola[Ad] OR Botswana[Ad] OR Lesotho[Ad] OR Malawi[Ad] OR Mozambique[Ad] OR Namibia[Ad] OR South Africa[Ad] OR Swaziland[Ad] OR Zambia[ad] OR Zimbabwe[Ad] OR west africa[ad] OR Benin[ad] OR Burkina Faso[Ad] OR Cape Verde[Ad] OR "Cote d'Ivoire"[Ad] OR Gambia[Ad] OR Ghana[ad] OR Guinea[Ad] OR Guinea-Bissau[Ad] OR Liberia[ad] OR Mali[Ad] OR Mauritania[Ad] OR Niger[Ad] OR Nigeria[Ad] OR Senegal[Ad] OR Sierra Leone[Ad] OR Togo[Ad] OR Ivory Coast[Ad])

#5. Search #3 AND #4

AIM;

1. transfusion AND (instance:"ghl") AND (db:("AIM"))

Appendix 2: The protocol_ Blood utilization in sub-Saharan Africa: a systematic review of current data

Introduction

The demand for blood transfusion in sub-Saharan Africa (SSA) from severe anemia conditions such as malarial anemia, obstetric hemorrhage, trauma, and sickle cell anemia far exceeds the current supply, with a shortfall of about 50%.[1] It has been postulated that the human population growth in the region, coupled with other factors such as weak and unsustainable donor recruitment and retention systems are likely to further worsen the blood demand situation in the region.[1,2] Although the main determinant of transfusion demand is the anemia burden which stands at 60% in sub-Saharan Africa,[3] to larger extent, blood utilization also is an important factor.

Data on the current use of blood products for transfusion in sub-Saharan Africa is scarce, although estimates for the common indications for transfusion have been made. It is estimated that about 80% of all blood transfusions in SSA are given to three disease conditions, namely; Malaria, obstetric hemorrhage and accident related indications.[1]

Evidence on the use of blood products in SSA is important both for informing best practices for appropriate use of blood, and for forecasting future demand for blood. Both of these two factors are very important to transfusion and the health care system in SSA. In the first place, because the demand-supply deficits of blood continue to plague the region and would require more prudent measures to ensure adequate blood supply. And secondly, the rapid changing dynamics in population growth and increase in life expectancy on one side[4] versus uneven economic growth and varying disease epidemiology. Concerning the latter; there have been notable improvements in the epidemiology of some infectious diseases in the region such as the case of the promising impact of malaria elimination, [5,6] yet several other emerging health concerns such as Cancers and other Non-Communicable Diseases (NCDs) are on the increase.[7,8] These driving forces among other factors will have unprecedented impact on the demand and use of blood products in SSA.

There is therefore need to generate evidence on this subject that can aid future projections for transfusion needs and their implications on transfusion and health care services in the region. No prior review on this topic could be found.

Aim: To review the current data on blood utilization in sub- Saharan Africa.

Research question: What proportion of available blood products is used for transfusion for the different anemia related disease conditions in sub-Saharan African health facilities.

"*PICO*" criteria:

- P; population = sub- Saharan Africa health facilities

- I; intervention or exposure = Transfusion
- C; Comparison groups = Not applicable
- O; Outcome = Blood utilization

Our intervention of interest will include: Transfusion with any of the following blood products, at any dose, and for all indications;

a) Packed Red blood cells (RBCs)
b) Whole blood (WB)
c) Platelets (PLTs)
d) Fresh frozen plasma (FFP)

The outcome; The proportion of blood products used (during the specified time period; with enough information about numbers or percentages) for different diseases.

Study population / setting will include: Health facilities (all levels) such as district hospitals, referral hospitals (both public and private) in sub-Saharan Africa. sub-Saharan Africa includes all the 54 countries in Africa, excluding Algeria, Egypt, Libya, Morocco & Tunisia.

Blood utilization: This will include all anemia related disease conditions specified, for which transfusions are given; whether broad or narrow, such as; Obstetrics and gynecology, pediatrics, trauma/accident/injuries, surgical, cancers or sickle cell anemia.

Target evidence / study design: Cross sectional studies and cohorts.

Methods:

a) Inclusion criteria for studies:

- Cross-sectional and cohort studies; both prospective and retrospective
- Clinical trials can be included
- Studies specifically designed to report on one or more categories of disease conditions using up one or more specified blood product(s).
- Studies reporting on transfusion with any one or more of the following products, namely; Red blood cells (RBCs), Whole blood (WB), Platelets, Plasma or Fresh frozen plasma.
- Studies conducted in any one or more sub- Saharan African countries,
- Studies published after 1st January 2000
- Studies conducted at a specified level of H/facility; such as general Hospital, referral hospital etc.
- Duration of the study must be specified
- Conference abstracts reporting on blood products use
- Studies published in English or French.

b) Exclusion criteria:

- Studies whose observation period is < 1 month
- Case reports and case series

c) The search stategy:

- Electronic searches
- MEDLINE, through PubMED
- EMBASE
- Systematic “snow balling”; by looking at the reference lists of selected articles using **Scopus** citation database (backward searching)
- In MEDILE; look up the articles that show up in “related articles”

d) **The search terms:**

P: (sub-Saharan Africa) OR Angola) OR Benin) OR Botswana) OR Burkina Faso) OR Burundi) OR Cameroon) OR Cape Verde) OR Central African Republic) OR Chad) OR Comoros) OR Congo) OR Democratic Republic of Congo) OR Djibouti) OR Equatorial Guinea) OR Eritrea) OR Ethiopia) OR Gabon) OR Gambia) OR Ghana) OR Guinea) OR Guinea-Bissau) OR Ivory Coast) OR Kenya) OR Lesotho) OR Liberia) OR Madagascar) OR Malawi) OR Mali) OR Mauritania) OR Mauritius) OR Mozambique) OR Namibia) OR Niger) OR Nigeria) OR Réunion) OR

Rwanda) OR (Sao tome and principe) OR Senegal) OR Seychelles) OR Sierra Leone) OR Somalia) OR South Africa) OR South Sudan) OR Sudan) OR Swaziland) OR Tanzania) OR Togo) OR Uganda) OR Western Sahara) OR Zambia) OR Zimbabwe)

AND

I: (Transfusion) OR Blood transfusion) OR Erythrocyte transfusion) OR Blood component transfusion)

AND

C: N/A

AND

O : (Blood products) AND blood use) OR Blood utilization)

e) Removal of duplicates

- Duplicates in search results from MEDLINE and EMBASE will be removed using endnote software

f) Study selection screening:

- Duplicate screening will be done; two researchers screening each paper
- Screen titles and abstracts of all articles, then
- Read the full text of the articles in the initial screen

g) Data abstraction and management

The following data will be extracted to an excel data sheet:

- Author, year of publication,
- Study setting, country,
- Level of health facility,
- Study design,
- Study period,
- Number of study participants, & their characteristics
- Type and numbers of blood products reported,
- Disease conditions treated
- Outcome variable; the proportions of blood products utilized for the different disease categories.

h) Statistical analysis and data synthesis strategy

- A qualitative synthesis of the evidence will be done
- Quantitative analysis will be done using Prism software (GraphPad).
- Summary estimates will be grouped for the different disease conditions
- We will estimate the number of blood products (and the 95% CI)

- The relative ratios of; WB to packed RBCs, those of FFP to (WB + packed RBCs) and PLTs to (WB + packed RBCs) will be computed, as a measure of the current use of component therapy in SSA
- We shall attempt to examine trends from the year 2000 to 2018, by spliting the data into into categories; 2000 – 2009 and 2009 – 2018

i) Management of bias

- We will minimize selection bias; specifically selective outcome reporting, by contacting the authors of the different studies for details on the data and clarifications,
- Regarding information bias, we will do double data abstraction. One researcher will abstract the data initially. A second researcher will then check these data for accuracy.

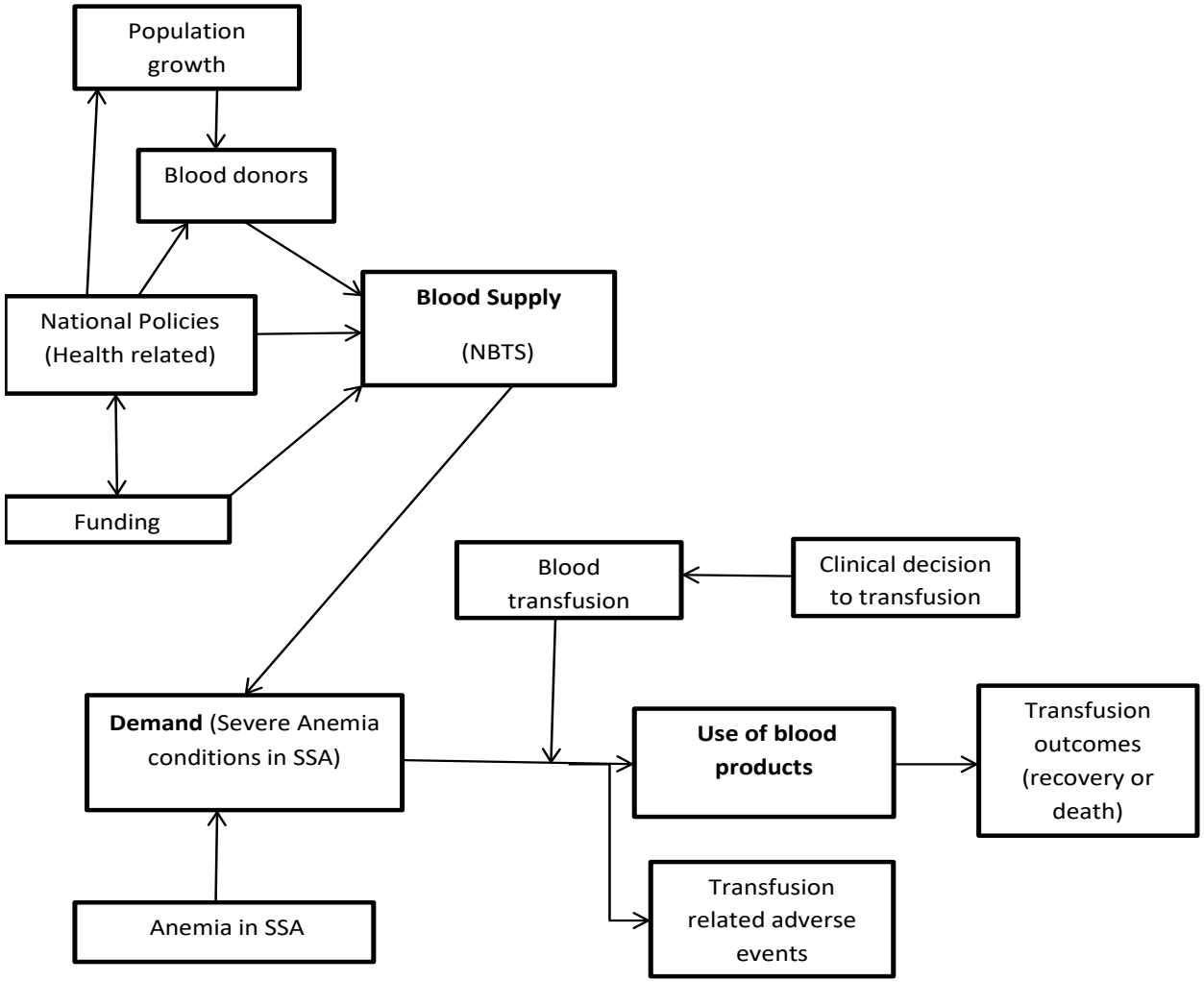
j) Timelines for the review

- Protocol development; May –June 2018
- Electronic search ; June 2018
- Screening and data abstraction : July 2018
- Data analysis, synthesis and manuscript writing: Aug. 2018
- Manuscript submission: Sept. 2018

k) **Limitations:**

The proportions reported in the papers could be based on a sizable percentage of blood products available for an entire nation; which does not tell us anything about the absolute amount of blood available. For this reason therefore, we will focus on proportions, as the absolute numbers of blood products are beyond the scope of this current review.

l) **Analytical framework:**



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Appendix 3.1: A summary of 37 studies reporting blood utilization in sub-Saharan Africa (SSA)

Author	Country	Year of study	Study duration (Months)	Study design	Study setting	Level of H/facility	Number of H/-Facilities	Blood components reported on	Patients transfused	Number of Blood products used	Patient type transfused
Akinola et al (2010) [37]	Nigeria	2007	3	Retrospective	Urban	Tertiary	1	not specified	41	89	C/section births
Akoko et al (2015) [43]	Tanzania	2013	8	Prospective	Urban	Tertiary	1	not specified	105	153	Elective -Surgical
Anorlu et al (2003) [32]	Nigeria	1995	36	Retrospective	Urban	Tertiary	1	not specified	231	623	Obstetrics only
Arewa et al (2009) [13]	Nigeria	2004	12	Prospective	Urban	Tertiary	1	4	682	772	General
Bugge et al (2013) [14]	Malawi	2010	1	Prospective	Rural	Secondary	1	1	104	104	General

Butler et al (2015) [7]	Uganda	2014	3	Prospective	Urban	Tertiary	1	4	3,662	6,330	General
Chalya et al (2016) [44]	Tanzania	2013-2014	12	Retrospective	Urban	Tertiary	1	not specified	256	342	Elective major-operations
Drammeh et al (2017) [12]	Tanzania	2013	4	Prospective	Mixed	Mixed	Many	4	14,698	16,728	General
Hume et al (2016) [45]	Uganda	2014	6	Prospective	Urban	Tertiary	1	1	50	323	Cancer patients
Imarengiaye et al (2006) [38]	Nigeria	1998-2002	48	Retrospective	Urban	Tertiary	1	1	60	130	C/section births
Lawson-Ananissoh et al (2015) [49]	Togo	2013	12	Retrospective	Urban	Tertiary	1	2	136	140	Hepato-Gastroenterology
Mafirakureva et al (2015) [11]	Zimbabwe	2012	12	Retrospective	Urban	Tertiary	4	5	1,793	4,249	General
Magoha et al	Kenya	1997	3	Prospective	Urban	Tertiary	1	1	63	67	Elective, Surgical

(2001) [47]											
Mbanya et al (2001) [15]	Cameroon	1994-1998	60	Retrospective	Urban	Tertiary	1	1	26,973	26,982	General
Mosha et al (2009) [23]	Tanzania	2007	3	Prospective	Rural	Secondary	2	1	160	166	Pediatrics
Mueller et al (2012) [24]	DRC	2009-2010	5	Prospective	Rural	Secondary	1	2	657	657	Pediatrics
Murray et al (2011) [25]	South Africa	2008	12	Retrospective	Urban	Tertiary	1	3	42	450	Pediatric oncology
Natukunda et al (2010) [16]	Uganda	2008	12	Retrospective	Rural	Tertiary	1	3	1,674	2,777	General
Obed et al (2010) [48]	Nigeria	1998-2005	96	Prospective	Urban	Tertiary	1	1	1,221	1,221	Obs & Gyn
Ogunlesi et al, (2016) [26]	Nigeria	2013-2014	16	Prospective	Urban	Secondary	1	1	79	133	Pediatrics
Ogunlesi et al	Nigeria	2008	12	Retrospective	Urban	Tertiary	1	3	112	251	Newborns

(2011) [40]											
Orish et al (2016) [27]	Ghana	2010	36	Retrospective	Urban	Tertiary	1	not specified	141	141	Pediatrics
Lawani et al (2013) [33]	Nigeria	2012	12	Prospective	not clear	Tertiary	1	2	151	253	Obstetrics only
Osei et al (2013) [34]	Ghana	2011	3	Prospective	Urban	Tertiary	1	3	519	1001	Obs & Gyn
Oseni et al (2008) [28]	Nigeria	?	12	Prospective	Urban	Tertiary	1	1	106	106	Pediatrics
Ozumba et al (2009) [39]	Nigeria	2000	36	Retrospective	Urban	Tertiary	1	not specified	117	212	C/section births
Pam et al (2009) [41]	Nigeria	2000-2001	9	Prospective	Urban	Tertiary	1	2	62	84	Newborns
Pitman et al (2015) [8]	Namibia	2007	48	Mixed	Mixed	Mixed	many	3	39,313	91,207	General
Raban et al	South	2009-	60	Retrospective	Urban	Tertiary	1	1	113	142	Newborns,

(2015) [42]	Africa	2013									Bleeding
Salverda et al (2017) [29]	South Africa	2009-2014	66	Retrospective	Urban	Tertiary	1	1	144	144	Pediatric trauma
Sonnekus et al (2014) [46]	South Africa	2012	3	Retrospective	Urban	Tertiary	1	1	148	174	General, Thrombocytopenic & bleeding
Thomas et al (2017) [30]	Kenya	2013-2016	31	Retrospective	Mixed	Mixed	10	2	2,352	2,352	Pediatrics
Tobi et al (2014) [17]	Nigeria	2011-2013	24	Retrospective	Urban	Tertiary	1	3	191	424	ICU patients
Traore et al (2011) [18]	Mali	2006	6	Prospective	Rural	Secondary	1	1	134	230	General
Tsima et al (2016) [35]	Botswana	2014	8	Retrospective	Rural	nixed	4	4	71	117	Post-abortion only
Ughasoro et al (2013) [31]	Nigeria	2011	12	Retrospective	Urban	Tertiary	1	4	95	238	Pediatrics

Vandenberg et al (2016) [36]	South Africa	2013	5	Retrospective	Urban	Tertiary	3	1	234	234	Obstetrics only
Totals									**96,690**	**159,746**	

Appendix 3.2: A summary of studies on general patient populations combined to evaluate blood utilization in SSA

			Number of blood products used for each diagnostic category											
Author	Patients transfu-sed	Blood products used	Pediatric malaria	Other malaria	Obstetric hemorrh-age & others	Other bleeding	Cancers	Other NCDs & organ disorders; e.g Diabetes	HIV-related	Other infec-tions	SCA	Trauma (& burns)	Surge-ry (Non-trauma)	Other medical condition / unknown anemia
§ Arewa et al (2009) [13]	682	772	0 *	0 *	0 *	242	0 *	89	0 *	0 *	0 *	0 *	158	283
§ Bugge et al (2013) [14]	104	104	55	4	18	0 *	0 *	0 *	3	0 *	0 *	0 *	4	20
§ Butler et al (2015) [7]	3,662	6,330	125	0 *	788	130	2,122	306	350	61	437	422	395	1,194
Drammeh et	14,698	0 †	0 *	0 *	0	0	0	0	0	0	0	0	0	0

al (2017) [12]														
Mafirakureva et al (2015) [11]	1,793	0 †	0 *	0 *	0 †	0 *	0 †	0 †	0 *	0 †	0 *	0 †	0 *	0 †
§ Mbanya et al (2001) [15]	26,973	26,982	6,628	0 *	4,855	4,999	0 *	0 *	0 *	2,432	6,080	0 *	0 *	1,987
§ Natukunda et al (2010) [16]	1,674	2,777	556	362	261	562	217	118	0 *	533	11	63	55	39
Pitman et al (2015) [8]	39,313	0 †	0 *	0 *	0 †	0 †	0 *	0 †	0 †	0 †	0 *	0 *	0 *	0 †
Tobi et al (2014) [17]	191	0 ‡	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *
§ Traore et al (2011) [18]	134	230	0 *	0 *	123	0 *	0 *	0 *	0 *	0 *	0 *	0 *	0 *	107
Totals	89,224	37,195	7,365	366	6,045	5933	2,339	513	353	3,026	6,528	485	612	3,630

*value not reported in the original study, †value not included in this analysis, ‡products had no diagnosis category reported on, not included in the primary outcome analysis, §the six studies used to determine the primary outcome.

Appendix 3.3: A summary of blood utilization among pediatric only studies

		Number of blood products used for each diagnostic category					
Author	Overall No. of products used	Malaria	SCA	Sepsis, Pneumonia & other infections	Cancers	Malnutrition	Other conditions (Organ disorder, HIV, trauma)
Mosha et al (2009) [23]	166	157	-	1	-	1	1
Mueller et al (2012) [24]	657	565	-	115	-	31	-
Murray et al (2011) [25]	450	0	-	-	450	-	-
Ogunlesi et al (2016) [26]	133	75	19	-	-	-	-
Orish et al (2016) [27]	141	83	-	-	-	-	58

Oseni et al (2008) [28]	106	94	-	10	-	-	4
Salverda et al (2017) [29]	144	-		-	-	-	144
Thomas et al (2017) [30]	2,352	1,811	329	-	-	188	118
Ughasoro et al (2013) [31]	238	25	28	36	75	13	37
Totals	4,387	2,810	376	162	525	233	362

Appendix 3.4: A summary of blood utilization among obstetrics and gynecology only studies

		Number of blood products used for each diagnostic category						
Author	Blood products used	APH	PPH & other post-delivery complications, e.g sepsis	Cesarean sections	Cancers	Abortions	Ectopic preg. & ruptured uterus	Others (causes of anemias)
Anorlu et al (2003) [32]	623	-	63	350	-	-	104	106
Lawani et al (2013) [33]	253	29	224	-	-	-	-	-
Osei et al (2013) [34]	1001	158	237	39	168	108	128	148

Tsima et al (2016) [35]	117	-	-	-	-	117	-	-
Vandenberg et al (2016) [36]	234	-	-	96	-	-	-	138
Totals	2,228	187	524	485	168	225	232	392

Appendix 3.5: A summary of blood utilization among cesarean sections only studies

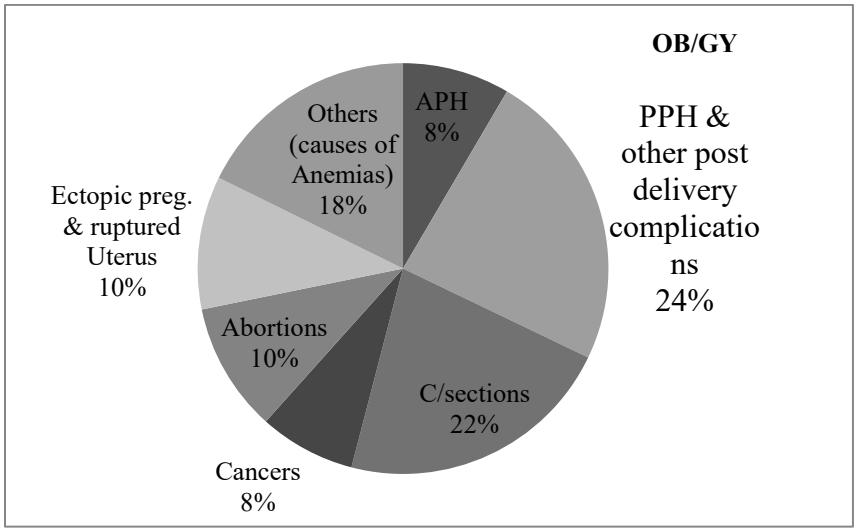
		Number of blood products used for each diagnostic category					
Author	Blood products used	Placenta Previa	Obstructed Labor	Malpresenation	PET & Fetal conditions	Previous C/Section	Others
Akinola et al (2010) [37 *]	89	-	-	-	-	-	-
Imarengiaye et al (2006) [38]	130	19	9	4	14	7	7
Ozumba et al (2009) [39]	212	28	35	12	9	24	9
Totals	431	47	44	16	23	31	16

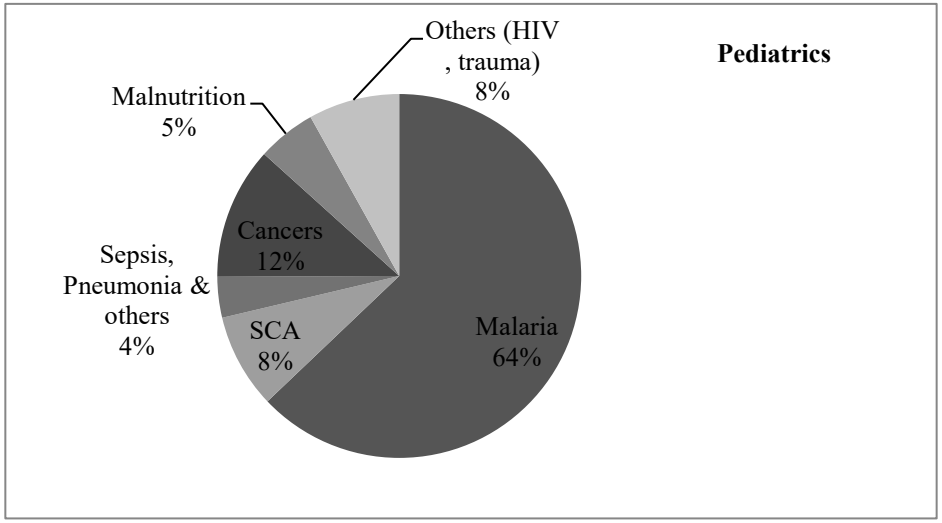
*This study only reported cesarean sections as being emergence (70/89) or elective (19/89)

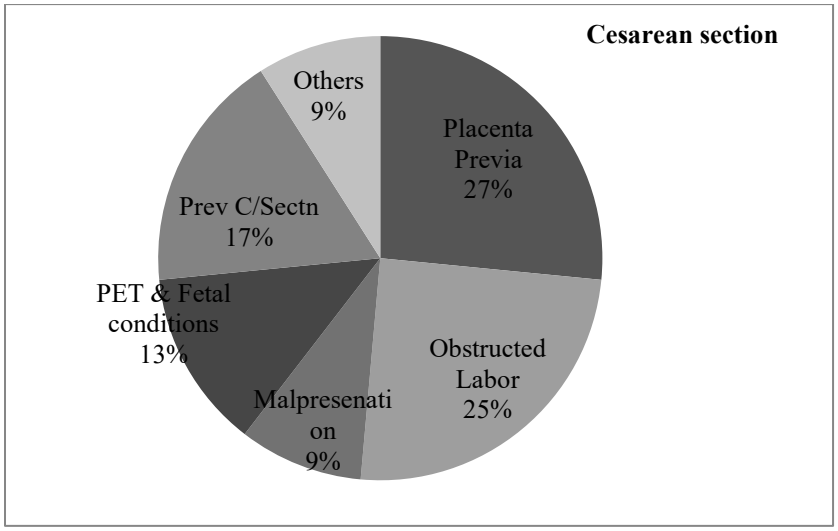
Appendix 3.6: A summary of blood utilization among newborn only studies

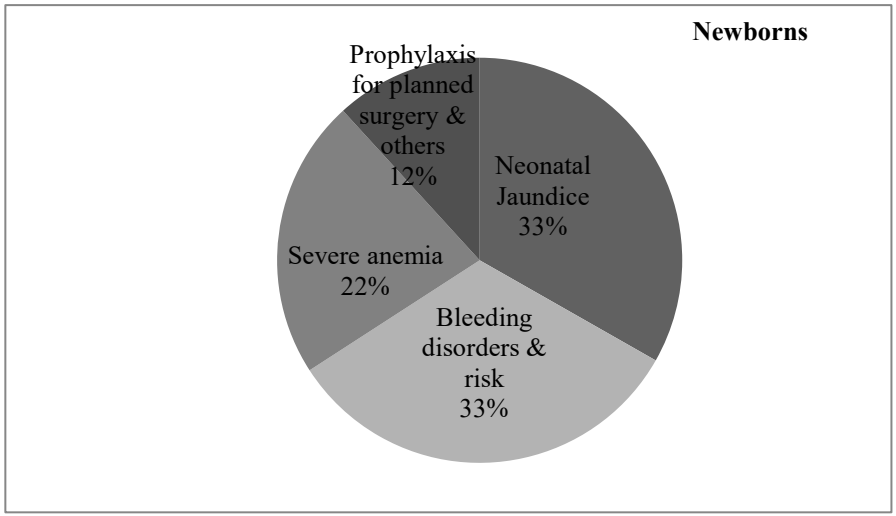
	Blood product used				**Diagnostic category**			
Author	RBCs (#)	WB (#)	FFP (#)	No. of blood products used	Neonatal Jaundice	Bleeding disorders & risk of bleeding	Severe anemia	Prophylaxis for planned surgery & others
Ogunlesi et al (2011) [40]	115	130	6	251	62	5	42	2
Pam et al (2009) [41]	30	54	0	84	48	3	32	1
Raban et al (2015) [42]	0	0	142	142	-	100	-	36
Total	145	184	148	477	110	108	74	39

Appendix 3.7: Blood utilization in pediatrics, obstetrics and gynecology (OB/GY), cesarean section births and newborns









Appendix 3.8: A summary of studies on the utilization of platelets or autologous whole blood

				Blood products used for each diagnostic category					
Blood product	Author	Total # products	Patient type	Leukemia	Lymphomas, other cancers	Marrow failure	Surgery	Obstetrics	Gynecology
Platelets	Hume et al (2016) [45]	323	Oncology	36	10	3	-	-	-
	Sonnekus et al (2014) [46] *	174	General, bleeding	-	-	69	13	-	-
Autologous blood	Magoha et al (2001) [47]	67	Elective, surgical	-	-		67	-	-
	Obed et al (2010) [48]	1,221	Obstetrics & Gynecology	-	-	-	-	625	596

*In this study, 84/174 records had missing diagnosis

Fig. 1. Study-selection flow chart

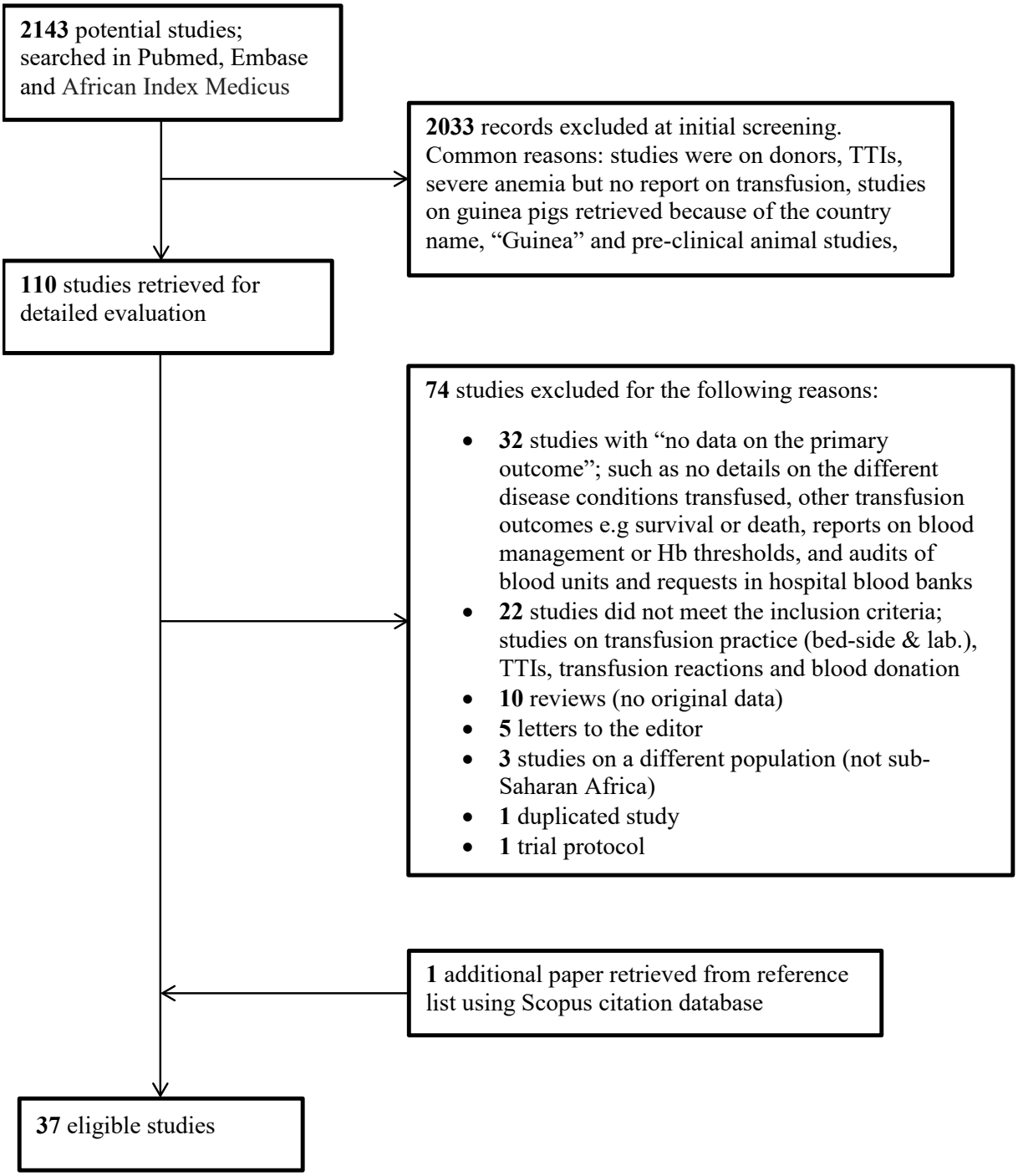


Fig. 2. The geographical location and relative sample size of the 37 studies included

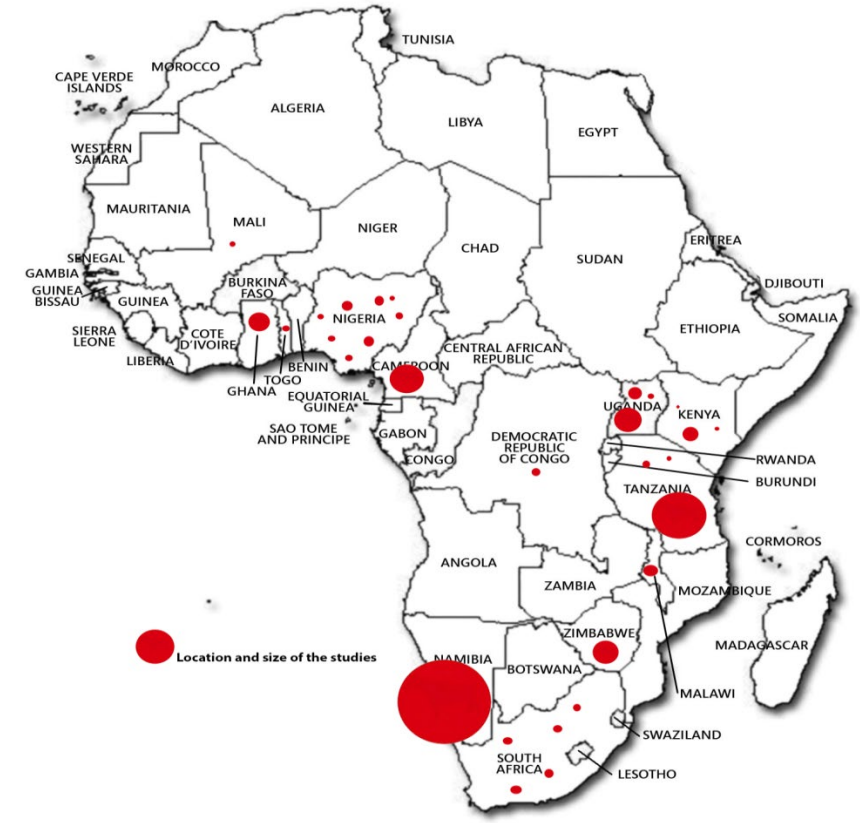


Fig. 3. Blood utilization by diagnostic categories in sub-Saharan Africa