

Accepted Manuscript

Chapter 12: Improving Blood Transfusion Services

Tara Tancred, Imelda Bates

PII: S1521-6934(19)30052-5

DOI: <https://doi.org/10.1016/j.bpobgyn.2019.05.007>

Reference: YBEOG 1936

To appear in: *Best Practice & Research Clinical Obstetrics & Gynaecology*

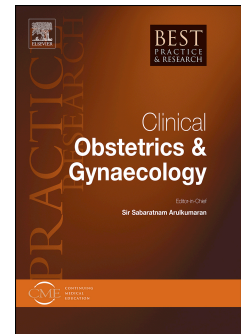
Received Date: 4 February 2019

Revised Date: 1 May 2019

Accepted Date: 2 May 2019

Please cite this article as: Tancred T, Bates I, Chapter 12: Improving Blood Transfusion Services, *Best Practice & Research Clinical Obstetrics & Gynaecology*, <https://doi.org/10.1016/j.bpobgyn.2019.05.007>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Chapter 12: Improving Blood Transfusion Services

Tara Tancred*, Imelda Bates

International Public Health, Liverpool School of Tropical Medicine, UK

*Corresponding author: tara.tancred@lstmed.ac.uk

Abstract

Postpartum haemorrhage contributes to 25% of maternal deaths worldwide, rising to 40% in Sub-Saharan Africa. Treatment of postpartum haemorrhage—particularly for anaemic women—requires timely, quality blood transfusions. There are a number of barriers to the provision of transfusion services, especially in low- and middle-income settings where the need is the greatest. These include unavailability of blood, unsafe blood, poor uptake of labour and delivery care, difficulties getting blood to transfusing facilities, and poor documentation of patient information. Examples of innovative and practical solutions to overcome these barriers are highlighted.

Keywords: postpartum hemorrhage, anemia, blood transfusion, innovation, LMICs

ESTABLISHING THE NEED FOR BLOOD TRANSFUSIONS FOR THE TREATMENT OF POSTPARTUM HAEMORRHAGE

USE OF BLOOD IN HIGH-INCOME AND LOW-INCOME SETTINGS

Blood and blood components have been recognised since 2013 as essential medicines. That is, items that are needed to meet the priority health needs of a population (1). The World Health Organization recommends that:

1. There should be a centralised, nationally-coordinated blood transfusion service.
2. Donations should only come from voluntary, non-remunerated donors from low-risk populations.
3. All donated blood must be tested for transfusion-transmitted infections, blood grouping, and compatibility.
4. Unnecessary transfusions must be reduced whenever possible through the effective clinical use of blood and the use of alternatives (2).

There are markedly different uses of blood in higher- and lower-income settings. In high-income countries, blood transfusions are most commonly used for supportive care in heart and transplant surgeries, to treat massive trauma, or for therapeutic use in oncology. In these settings, 79% of transfusions are given to people over the age of 60. However, in low- and middle-income countries (LMICs), two-thirds of blood transfusions are given to anaemic children under the age of five, followed by use in the treatment of maternal complications, the most common of which is postpartum haemorrhage (PPH) (3). In Sub-Saharan Africa in particular, specific factors place considerable strain on the blood supply, including a high prevalence of anaemia, malaria, and poor transfusion medicine infrastructure (4).

Overall, a usage rate of 32 units of blood per 1000 persons is reported in high-income countries, 12.5 units in upper middle income countries, 5.38 units in lower-middle income countries, and 3.41 units in low-income countries (5, 6). These data suggest that there is a significant under-utilisation of blood in LMICs (3).

BURDEN OF POSTPARTUM HAEMORRHAGE

Severe PPH (5–7) (see Chapter XX) is highly likely to require a blood transfusion to manage potential complications of blood loss. A review in 2012 found that, worldwide, 10.8% of women giving birth experienced PPH, with the highest concentration of these women residing in Africa, where 25.7% of women giving birth experienced PPH. Only 2.8% of women experienced a blood loss of more than 1000 ml, the highest burden again concentrated in the African region, where it impacted 5.1% of women (8). When a woman experiences severe PPH and is in need of a blood transfusion, death can occur within two hours. Therefore timely access to blood transfusion is of utmost importance (7).

BURDEN OF ANAEMIA

Globally, an estimated 50% of pregnant women are affected by anaemia (6), the majority of whom are found in South Asia and Central and West Africa (9). The prevalence of anaemia among pregnant women in low- and middle-income countries ranges from 25% to 65% (10). There is a relationship between anaemia and PPH. Women with anaemia are not only more likely to have PPH, but they are much more likely to have an adverse clinical outcome from even much smaller volumes of blood loss (6). For example, one study in India found that 35% of pregnant women had moderate-to-severe anaemia. Women with severe anaemia were at 9.45 increased odds of experiencing PPH. These odds increased 17-fold for women with

moderate-to-severe anaemia who had their labour induced, and 19-fold for those with anaemia and infection (11).

Anaemia therefore presents a double burden by increasing both the likelihood and severity of PPH that necessitate a blood transfusion. Unfortunately, anaemia and PPH are both concentrated in LMICs where access to timely, quality blood transfusion services is limited (9).

THE IMPORTANCE OF COMPREHENSIVE EMERGENCY OBSTETRIC CARE FACILITIES

There are many different mechanical and medical interventions that can be carried out in order to manage PPH (see Chapter XX). However, where these fail, a blood transfusion may become necessary to save a woman's life (13–15). As part of this life-saving package of care, emergency obstetric care is a key strategy for reducing maternal mortality (16). Blood transfusions, however, are a key requirement for comprehensive, but not basic, facilities that offer emergency obstetric care (Table 1).

Table 1. Basic emergency and comprehensive emergency obstetric care components (17)

Basic emergency obstetric care	Comprehensive emergency obstetric care
Intravenous or intramuscular antibiotics	All components of basic emergency obstetric care
Intravenous or intramuscular uterotonic drugs for the active management of the third stage of labour and prevention of PPH	Provision of caesarean section
Intravenous or intramuscular anticonvulsants for the management of pre-eclampsia/eclampsia	Provision of blood transfusions
Manual removal of the placenta	
Manual removal of retained products of conception	
Assisted vaginal delivery (e.g. vacuum	

extraction or forceps delivery)	
Resuscitation of newborn baby using a bag and mask	

The most frequent use of blood for obstetric complications is for the treatment of PPH but transfusions are also needed to prevent deaths from antenatal haemorrhage and complications of abortion, ectopic pregnancy, and ruptured uterus (17).

Comprehensive emergency obstetric care is typically offered at district or regional hospitals though not all facilities are able to provide blood transfusions. (Table 2) (18).

Table 2. Examples of distribution of transfusing facilities between hospitals and non-hospitals in a selection of low- and middle-income countries (18)

Country	Percentage hospitals providing transfusions	Percentage non-hospitals providing transfusions
Benin	81%	0%
Kenya	75%	11%
Mali	33%	12%
Mozambique	100%	29%
Uganda	97%	1%
Bangladesh	97%	0%
India	9–56%	0%
Nepal	31%	1%

The reasons for this include poor infrastructure, inability to adhere to regulations, lack of staff capacity, shortages of reagents and screening supplies, and inadequate laboratory support (18).

These findings highlight the need for more equitable access to timely transfusion and for effective referral systems (7). Expansion of comprehensive emergency obstetric care capacity across settings has been recognised as important. In particular, improving the ability and supply of specialists, provision of caesarean kits, and provision of blood transfusion services

that are free to the user have been some priority areas of improvement identified by practitioners (19).

THE IMPACT OF BLOOD TRANSFUSION ON MORTALITY DUE TO POSTPARTUM HAEMORRHAGE

There has been a slow decline in maternal mortality ratios, and globally, 99% of maternal deaths are concentrated in LMICs. Nearly two-thirds of these deaths occur in Sub-Saharan Africa alone, or about 201,000 maternal deaths per year (20). PPH is the most common cause of maternal mortality worldwide, contributing to 25% of maternal deaths, and up to 40% of maternal deaths in Sub-Saharan Africa (21). Globally, 68% of maternal deaths occur in the postpartum period (22).

Lack of blood for transfusion is responsible for unnecessary deaths from PPH. Studies of maternal haemorrhage deaths in Sub-Saharan Africa found that 26% (16–72%) of deaths were due to a lack of blood (7). A confidential enquiry into maternal deaths in South Africa found that for 35% of maternal deaths, problems including transport between facilities, lack of access to intensive care, lack of blood, and unavailability of staff were implicated (23). In another study from Uganda, lack of blood transfusions was a key missing signal function across facilities, increasing the odds of maternal death 13.7-fold (24). Globally, up to 150,000 maternal deaths could be prevented through access to safe blood (25).

While the exact need for blood for PPH in Sub-Saharan Africa has not been calculated, a rough estimation based on crude birth rates, current population levels, and the prevalence of anaemia and severe PPH, suggests that 1,850,000–9,000,000 blood transfusions might

reasonably be expected for the management of PPH alone (4). This value may well exceed the total amount of blood (i.e. 5.6 million units) donated annually in Sub-Saharan Africa (3).

CHALLENGES AND POTENTIAL SOLUTIONS FOR ENSURING EFFECTIVE BLOOD TRANSFUSION SERVICES FOR POSTPARTUM HAEMORRHAGE

In LMICs in particular, women do not consistently receive the blood transfusions they need, when they need them, for PPH. There are a number of reasons for this lack of timely provision of safe blood, including a lack of reagents and transfusing supplies, lack of trained staff, high background prevalence of transfusion-transmitted infections and screening tests with insufficient sensitivity, inadequate blood bank storage facilities, transportation and referral barriers, high costs of blood, and poor implementation of existing national blood policies (7, 26-29).

BLOOD DONATION

The rate of donation of blood is 33.1/1000 people in high-income settings, 11.7 in middle-income settings, and 4.6 in low-income settings. Overall, despite having 48% of the world's population, donors from LMICs contribute only 24% of the global blood supply (3).

Globally, people's perspective about blood donation are different. In LMICs, there tend to be misconceptions about the purpose and safety of blood donation, but high levels of pro-social motivation (30, 31). As a result of cultural barriers, misconceptions, high rates of donor ineligibility, and poor donation infrastructure, sufficient numbers of blood donations are chronically lacking, producing serious inequalities in the availability of blood.

In many LMICs, transfusion services are hospital-led. If a woman experiences PPH and needs blood, it is often the responsibility of the family to find a "replacement donor" to

replace the blood used to treat the woman, sometimes having to pay the donor. These replacement donations will be screened by the hospital for infections, and undergo grouping, and compatibility testing. Unfortunately, this system prone to delays, as well as inconvenience and potential hardship for families (32). The alternative to the hospital-based model is the centralised model, in which blood transfusion services are centralised, typically at the national level. Here, blood donation is organised through recruitment campaigns and targets voluntary, non-remunerated donors. Ideally, these donors become repeat donors, who have the best safety profile among blood donors, due to regular testing (21, 33). A centralised system benefits from quality assurance systems and more sophisticated tests than are available in hospitals (29). While the centralised model had its advantages, and is preferable in well-resourced contexts, it is very difficult to operationalise within LMICs. In these settings, the cost of a centralised blood service is often prohibitive, due to the added costs of donor recruitment campaigns, dedicated collection teams, vehicles, cold chain maintenance, quality assurance mechanisms, and regular distribution of blood to distant facilities (29, 32, 34). A unit of blood from the centralised model may cost 4–8 times as much as a unit of blood from a hospital-based model (32).

In practice, many LMIC countries have adopted an approach that combines the centralised model's lower-risk donors and quality assurance systems, while supporting hospitals to collect and maintain their own blood stores (29, 34). Funding to support transfusion services, especially the hospital-based model, is scarce, since traditionally, the use of replacement donors has been discouraged. Funders may even tie their funds to conditions such as the exclusive use of voluntary, non-remunerated donors (4), even though donations from the replacement system provide a substantial proportion of the blood supply. Only 11 countries in Sub-Saharan Africa, for example, have managed to achieve 100% of blood donations from

voluntary, non-remunerated donors, and overall, only 67% of donations come from voluntary non-remunerated donors (3, 35). Globally, 83.3% of donations are voluntary, non-remunerated donations, 16.4% are family or replacement donations, and 0.3% are paid donations (3). There are efforts, however, to increase numbers of voluntary, non-remunerated blood donations, particularly among adults with the lowest risk profiles (Box 1).

Box 1. Improving repeat, voluntary, non-remunerated blood donation in LMICs: “Pledge 25” clubs *Pledge 25 clubs—sometimes called post-school donor clubs—are an Africa-wide initiative supported by the Africa Society for Blood Transfusion and the Global Blood Fund that started in Zimbabwe in 1994 (36). It targets young adults and members pledge to donate 25 units of blood before the age of 30. Members also make a commitment to adhering to a healthy, low-risk lifestyle (37). These clubs seek to create the safest donor profile possible, and have been successful across various contexts. For example, in Zimbabwe in 2010, almost 26% of blood donors throughout the country—which is one of the few in Africa to maintain a 100% voluntary, non-remunerated volunteer base—were from Pledge 25 clubs (36).*

Low availability of blood donors and inadequate cold chain maintenance and pathogen testing also contributes to low blood stocks (29). Stockouts of blood may occur in both hospitals and central blood banks, regardless of the donation model used. For example, in Uganda, an audit of large hospitals providing critical care found that only 66% of requests for transfusions were fulfilled. Among the 34% who did not receive the transfusion required, for two thirds of them, the hospital blood bank ran out of blood, and for the remaining third, the national blood bank did not have enough blood (38). Innovative technologies are being used in some high-income countries to maintain adequate blood stocks (Box 2).

Box 2. Using an innovative technology to encourage blood donation in the UK’s National Health Service

In the UK, an estimated 200,000 new donors are needed each year. To underline the life-saving capacity of blood transfusions and its importance in healthcare, the National Health Service in the UK launched a new campaign. A large billboard is in front of a group of people, who have been given stickers on their arms where a needle might go if they were donating blood. Using a smartphone app, they can watch as their arm gets a needle and some tape and their blood starts to flow. On the billboard, they can see directly their blood filling a bag for a recipient. The impact of the transfusion is clear, as the ill recipient gets better and better before their eyes. The recipients used in the campaign are not just actors, they are people who have been saved through blood transfusions. The campaign has not yet been evaluated, but is anticipated to prompt an increase in blood donation (39).

SCREENING BLOOD

The high population prevalence of infections and weak infrastructure for screening and documentation, means that transfusion-transmitted infections are of concern in LMICs (3). In Sub-Saharan Africa, 1.3% of blood units were estimated to be reactive to HIV, 4.2% to Hepatitis B virus, 1.0% for Hepatitis C virus, and 0.8% for syphilis (3, 35). Here, pregnant women and children under the age of five are at the greatest risk of acquiring such infections, as they are the largest recipients of blood donations (29).

The use of rapid tests has been promoted, especially in LMICs, but they have variable sensitivity and need to be validated to the settings in which they are to be used (40, 41). Ideally, tests for the most common transfusion-transmittable infections, such as HIV, Hepatitis B virus, and Hepatitis C virus, should be highly sensitive to reduce the risk of transmitting infection to blood recipients (42). Nucleic acid testing provides maximum sensitivity, but is prohibitively expensive for LMICs (29), so efforts to improve the sensitivity and use of rapid diagnostic tests are important (41). There are some promising examples of such innovation emerging (Box 3).

Box 3. Use of compact microfluidics technology to test for transfusion-transmittable infections
Despite the preference for centralised blood banking models, in many LMICs, out of necessity, hospital-based collection and testing of blood persist. Low cost, durable, sensitive tests are therefore needed to ensure the highest safety of blood possible, given many restraining factors. A portable, point-of care system is being introduced by an American company called Daktari Diagnostics. This system uses microfluidic devices that require only a small amount of blood. Tests for HIV and Hepatitis C virus can be performed at the same time, capturing key cellular indicators and counting the virus, giving an estimate of viral load within 30 minutes.

Microfluidic devices are low-cost, have low power consumption, and have fast sampling and processing. A sensitive, cost-effective test may prove a reasonable substitute for less effective rapid tests in many LMICs (43).

Stockouts of testing kits for transfusion-transmittable infections are common in LMICs, having been reported by 20 countries in Africa, and 15 other countries across all regions except Europe (3). Globally, 13 countries (six in Africa, three in the Americas, three in the Western Pacific, and one in the Eastern Mediterranean) have reported being unable to test for

one or more of the four key transfusion-transmittable infections: HIV, Hepatitis B virus, Hepatitis C virus, and syphilis. Globally, HIV testing rates for blood for transfusion range from 91.5% to 99.7%, Hepatitis B virus testing from 26.8% to 98.5%, Hepatitis C virus from 17.5% to 99%, and syphilis from 66% to 98.4% (3).

GETTING BLOOD TO WOMEN WHO NEED IT, WHEN THEY NEED IT

In many settings, especially those with large rural populations and a high prevalence of home births, a significant barrier exists in terms of getting women to facilities, and eventually, to a facility that has the capacity to provide a blood transfusion. Referral systems linking to higher-level facilities are often inadequate or absent (44). Helping women in LMICs adequately prepare for birth during pregnancy by identifying a blood donor, identifying a facility give birth in, and arranging resources for transportation, are critical for preventing delays and achieving better outcomes for women with PPH (45). Community sensitisation and mobilisation can be helpful in terms of helping to get women who need blood to facilities where transfusions are available (Box 4).

Box 4. Mobilising communities for increased uptake of skilled attendance at birth
Options, a UK-based non-governmental organisation, worked from 2015–2018 on a “Maternal and Newborn Improvement” programme, with the central aim of increasing skilled attendance at birth. At the conclusion of the intervention period, skilled birth attendance increased from 41% to 84%. There were a number of activities that were carried out to achieve this result. One was the retraining of traditional birth attendants as birth companions, who could confirm a woman was in labour and be with her on her way to the hospital and throughout labour and childbirth. Another was the provision of vouchers that could be used to subsidise the cost of motorcycle transport—the most common method of transportation, especially in rural settings. One-third of women arriving at facilities for birth had done so using these vouchers. A third area of intervention was around the introduction of a performance-based financing scheme in health facilities to improve the quality of care. Finally, facilities were also equipped with solar power, to prevent blackouts (46).

Rapid transfer of blood to remote facilities, rather than transferring women to higher-level facilities, has also gained momentum recently through the use of drones (Box 5).

Box 5. Use of drones for the transport of blood

Drones may have the capacity to deliver blood over long distances. A study by Amukele and colleagues found that blood samples flown for three hours (258 km) in a cooling box, experienced only minor differences in glucose and potassium levels, suggesting the overall feasibility of drone transport of blood, albeit with stringent environmental controls (47).

The Ministry of Health in Rwanda has capitalised on drone technology to reduce deaths due to PPH. Staff in three district hospitals—located in remote, mountainous areas that are difficult to reach via road—can use their phones to order blood by drones. In Rwanda, a centralised blood banking system exists, but barriers in getting blood to peripheral facilities have been largely overcome through drone technology (48).

DOCUMENTATION OF PATIENT DATA

Patient documentation in higher-income settings is generally robust, and often electronic.

However, the use of electronic health records is far from ubiquitous, and in many LMIC health systems, inconsistently applied or unavailable (49), with severe implications for blood transfusion.

In LMICs, there may be additional barriers to the correct documentation of patient data. For example, some patients may have inconsistent spelling of their name, they may not know their birthdates, and most records are hand-written. Staff may therefore struggle to identify the correct blood transfusion recipient and to administer the blood due to lack of training. Systems for monitoring and documentation of vital signs and adverse events during and after transfusion are scarce in LMICs. This puts women with PPH at particular risk, since for them, transfusions are often administered in an acute emergency, and correct documentation is critically important to prevent unnecessary transfusion-related complications and deaths (4). Innovations to improve the documentation of patient information, including details critical for blood transfusions, are increasingly available (Box 6).

Box 6. Mobile storage of personal health information

Mobile technologies are increasing rapidly worldwide, including in LMICs. In Benin, prompted by the unnecessary death of a patient during childbirth who could not remember her blood type—and for whom such information was not documented—Dr. Vena Ahouansou created a technology company that uses tech to store and transfer medical information. People use their mobile phones to register for an application that logs key personal medical information, including blood type. The company then places the information into a QR code that can be made into a bracelet (\$4 USD), or added as a patch on a mobile phone or other personal item (\$2 USD). Once the patch or the bracelet is scanned by users of the application, the necessary medical information

of that person appears (50). Such technology could be coopted by blood transfusion services for providers to both store and access critical patient information.

DECIDING WHEN TO PERFORM A BLOOD TRANSFUSION FOR POSTPARTUM HAEMORRHAGE

Before the correct treatment can be given, it is essential that a prompt and accurate diagnosis of PPH can be made (44). Often, particularly in LMICs, providers estimate blood loss visually, which can underestimate postpartum blood loss by 33–50% (6). Gold standards like the use of photospectrometry and estimation of blood loss through calibrated bags are much more accurate, and while common in high-income settings, are little-used in LMICs. In these settings, clinicians have to rely on monitoring of the patient's vital signs, blood test results, and timely diagnosis of the cause of haemorrhage to determine the best course of action to minimise morbidity and mortality (6). There are emerging opportunities, however, to better diagnose the severity of PPH to determine if a blood transfusion is required (Box 7).

Box 7. Bedside fibrinogen testing to determine the severity of PPH and need for transfusion

Due to problems surrounding accurate diagnosis of PPH in LMICs, other markers have been suggested as reliable indicators of severe PPH. For example, clotting factors like fibrinogen decrease rapidly, early on in PPH, exacerbating bleeding. Judging the speed of the fall of fibrinogen may be an important marker of severity, and can be assessed with a bedside test (12). A bedside test—ROTEM—highlighted the possibility of assigning cut-off values, based on ROTEM parameters, to determine a transfusion threshold value, thus minimising the unnecessary use of transfusions for PPH management (51). What remains is research into lower-cost diagnostic devices, like ROTEM, for application in LMICs.

REDUCING THE NEED FOR BLOOD TRANSFUSIONS

While blood transfusions can and do save lives, ensuring that blood transfusions are used only when absolutely necessary is important for a number of reasons. Firstly, blood transfusions can be dangerous and should only be used as a last resort. The estimated in-hospital case fatality rate following blood transfusions across health facilities in Africa is 6–20% (21). Secondly, blood transfusions are expensive. For example, in Sub-Saharan Africa, the cost per unit of blood transfused can be more than 80 USD for a unit of whole blood, and 95 USD for red cell concentrates (52). These values are found within the context of an

average expenditure per capita on health of 30 USD in LMICs (53). Unnecessary blood transfusions can result in considerable wasted resources. For example, in Mexico, 47.8% of blood transfusions carried out in one hospital between 1 January and 30 June 2015 did not have adequate clinical indication, costing the hospital an estimated \$861,000 USD per year (54). For obstetric bleeding, uterotonics like oxytocin, ergometrine, and misoprostol, especially in combination, can stop haemorrhage and may be more cost-effective than providing a blood transfusion (55). An alternative to allogenic blood transfusions is the use of autologous transfusions—using the recipient’s own blood—which have been suggested by some authors for possible treatment of PPH. Autologous blood transfusions have been used safely in obstetrics, particularly for treatment of ectopic pregnancies. This approach is possible, even in low- and middle-income countries. For example, in Benin, over 200 procedures of autologous blood transfusion for treatment of ectopic pregnancy were carried out, using a Tanguieta funnel. This perforated funnel is placed inside the peritoneal cavity, where it collects blood. The blood is filtered and aspirated into prepared transfusion bags, where it can be reinfused into the patient. A similar approach of retrieval, filtering, and reinfusion may be possible for the management of postpartum haemorrhage (25). However, there are limited data around this approach, and a need for more research. An additional approach, specifically for women at risk of haemorrhage who undergo a caesarean section, is intraoperative cell salvage (Box 8).

Box 8. The use of intraoperative cell salvage during caesarean section when women are at high risk of haemorrhage

During a caesarean section, blood is lost. To minimise the use of donated blood—which is a finite resource—between June 2013 and April 2016, Khan and colleagues worked across 26 UK obstetric units, carrying out intraoperative cell salvage for women at risk of haemorrhage undergoing caesarean section amongst a 1498 women as part of a randomised controlled trial. The control group had 1492 women, who received routine care. The rate of transfusion was slightly lower (2.5% compared to 3.5% in the control group) for the intervention group undergoing cell salvage (OR 0.65, $p = 0.056$), with the strongest effect for emergency caesarean sections (OR 0.58, 95% CI 0.34 to 0.99). Fetomaternal haemorrhage was higher in the intervention group when the woman was rhesus-D negative and the baby was rhesus-D positive (OR 5.63, 95% CI 1.43 to 22.14), highlighting the need for adherence to anti-D prophylaxis protocols to minimise risk. Overall, there was modest evidence of the applicability of cell salvage to minimise the use of allogenic blood transfusion (56). More

research into the applicability of this approach, particularly in low- and middle-income countries where allogenic blood transfusion may not be an option, or itself carries life-threatening risks, would be valuable.

TREATMENT OF ANAEMIA

There is a close relationship between anaemia, PPH, and severe maternal outcomes, so the prevention, early diagnosis, and treatment of anaemia and its causes can reduce unnecessary blood transfusions (57). In LMICs, anaemia diagnosis is often based solely on clinical symptoms, leading in some instances to the inappropriate use of blood transfusion. In addition to exposing the patient to unnecessary risks, this may not be a cost-effective approach since a haemoglobin test is around 40 times cheaper than a unit of blood (29).

Mobile technologies are emerging as a possible solution to the sensitive diagnosis of anaemia (Box 9).

Box 9. Use of smartphone technology for rapid, sensitive anaemia testing

In the case of PPH, screening for anaemia is important. New technology that can be used to rapidly and accurately test a woman's blood for anaemia, has been introduced. Using a smartphone-based imaging cytometry platform, the density of red and white blood cells and haemoglobin concentration can be captured. A separate optical attachment to the phone takes the image, which is then processed immediately on a phone application, giving a rapid analysis, on par with a much more expensive benchtop haematology analyser. Results can be stored on the phone or sent to a central server, where they can be utilised to provide remote diagnosis if a skilled technical person is not on-hand (58).

Interventions like supplementation of iron and folic acid during antenatal care, malaria prevention and treatment in malaria-endemic areas and treatment of helminth infection in helminth-endemic areas can substantially reduce anaemia, and are cost-effective and relatively easy to implement (59, 60). An example from paediatric care indicates that, barring instances of congestive heart failure, giving children iron treatment, as opposed to transfusion for iron-deficiency anaemia, offers better recovery (61).

QUALITY ASSURANCE AND HAEMOVIGILANCE

In 155 (87%) countries, including 44 (96%) from Africa, there are specific standards around the collection, testing, processing, storage, and distribution of blood and blood components (3). However, in LMICs, there are a myriad of barriers preventing implementation of these standards (62). Therefore, low-cost interventions like quality improvement, which can aid the implementation of pre-existing standards of care around all aspects of blood transfusion, may be beneficial, particularly in such contexts (Box 10).

Box 10. Standards-based audit to improve the quality of blood transfusion services

Standards-based audit (sometimes called “clinical audit” or “criterion-based audit”) is a problem-solving approach frequently applied in clinical settings to improve the quality of care (63). Standards around blood transfusion are widespread, particularly in Africa (3). Applying standards-based audit, facility-based audit teams select a standard of care that they are not meeting (for example, routine screening of all blood donations for HIV, Hepatitis B and C, and syphilis). They collect some data to understand the extent of the problem, and then design and implement solutions to address the problem. After a period of implementation, a second measurement to determine progress will be carried out. Teams can work on as many standards of care as they are able to. Over time, the cumulative impact of this quality improvement approach can be marked (64). Quality improvement that relies on local solutions to local problems, is felt to be particularly appropriate for LMICs, where resource constraints are pronounced (65).

In high-income countries, 99.6% of donations were screened, following quality assurance processes, compared to 97% in upper-middle income countries, 81% in lower-middle income countries, and 66% in low-income countries. In LMICs, hospitals play an important role in transfusion services, owing to an absence of robust, centralised blood banking and distribution systems (32). However hospitals may have an underdeveloped transfusion infrastructure and lack transfusion policies, monitoring and evaluation systems, named persons responsible for the oversight of the quality of blood transfusions, and robust documentation processes (66).

Haemovigilance is the monitoring and evaluation of any adverse events that are due to blood transfusion. These findings are very important in the continual improvement of blood transfusion services. However, only 39% of countries globally reported having such a system in place, including 77% of countries in Europe, and only 14% of countries in the Americas.

FINANCING BLOOD SERVICES

Investment in blood transfusion services in low-resources settings is often insufficient to establish and sustain safe and adequate national blood supplies (3). In Sub-Saharan Africa, 78% of countries reported reliance on external, and therefore likely unsustainable, support. For example, between 2011–2014, PEPFAR gave \$437 million USD to 14 countries across Sub-Saharan Africa and the Caribbean. While this funding contributed to an increase in blood collections by 19%, without this funding, these gains may recede (21). Only 16% of countries reported any kind of cost recovery, which is the model used to finance 67% of blood transfusion services in Europe (3).

ACKNOWLEDGEMENT

This work was completed without any dedicated funding.

CONFLICTS OF INTEREST

The authors have no conflicting interests.

PRACTICE POINTS

- Preventing and managing anaemia in pregnant women should be prioritised to reduce the risks of poor outcomes from PPH and to minimise the use of blood or blood components.
- Women should be encouraged to give birth with a skilled attendant present, who should be trained to recognise severe anaemia as a risk factor for PPH.
- Effective active management of the third stage of labour, the use of uterotonics, uterine massage, and other methods should be used to the greatest extent possible to manage PPH. Blood transfusion should be used as a last resort.

RESEARCH AGENDA

- Implementation research around strategies to reduce the number of women entering third stage of labour with significant anaemia
- Better methods of diagnosing PPH and high-risk women in LMICs to avoid unnecessary blood transfusions, and to ensure that blood transfusions do occur when needed
- Further research around alternatives to allogenic blood transfusion, such as autologous blood transfusions, or intraoperative cell salvage, particularly in resource-constrained settings
- Ongoing research into low-cost, high-sensitivity blood tests to reduce the risks of transfusion-transmitted infections

- Overall health policy and systems research to promote health systems strengthening, particularly around establishment of referral infrastructure and financing for transfusion services.

REFERENCES

1. World Health Organization. WHO Model List of Essential Medicines. Geneva: World Health Organization; 2017.
2. World Health Organization. Aide Memoire for National Blood Programmes. Geneva: World Health Organization; 2002.
- *3. World Health Organization. Global Status Report on Blood Safety and Availability. Geneva: World Health Organization; 2017.
4. Lund TC, Hume H, Allain JP, McCullough J, Dzik W. The blood supply in Sub-Saharan Africa: Needs, challenges, and solutions. *Transfusion and Apheresis Science*. 2013;49(3):416-21.
5. Bonnar J. Massive obstetric haemorrhage. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2000;14(1):1-18.
6. Rath WH. Postpartum hemorrhage—update on problems of definitions and diagnosis. *Acta obstetrica et gynecologica Scandinavica*. 2011;90(5):421-8.
- *7. Bates I, Chapotera GK, McKew S, van den Broek N. Maternal mortality in sub-Saharan Africa: the contribution of ineffective blood transfusion services. *BJOG*. 2008;115(11):1331-9.
8. Calvert C, Thomas SL, Ronsmans C, Wagner KS, Adler AJ, Filippi V. Identifying regional variation in the prevalence of postpartum haemorrhage: a systematic review and meta-analysis. *PLoS One*. 2012;7(7):e41114.
9. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995-2011: a systematic analysis of population-representative data. *Lancet Glob Health*. 2013;1(1):e16-25.
10. World Bank Group. Prevalence of anaemia among pregnant women (%): World Health Organization, Global Health Observatory Data Repository; 2019 [Available from: <https://data.worldbank.org/indicator/SH.PR.G.ANEM>].
11. Nair M, Choudhury MK, Choudhury SS, Kakoty SD, Sarma UC, Webster P, et al. Association between maternal anaemia and pregnancy outcomes: a cohort study in Assam, India. *BMJ Glob Health*. 2016;1(1):e000026.
12. Weeks A. The prevention and treatment of postpartum haemorrhage: what do we know, and where do we go to next? *BJOG*. 2015;122(2):202-10.
13. Lalonde A, International Federation of G, Obstetrics. Prevention and treatment of postpartum hemorrhage in low-resource settings. *Int J Gynaecol Obstet*. 2012;117(2):108-18.
14. Ahonen J, Stefanovic V, Lassila R. Management of post-partum haemorrhage. *Acta Anaesthesiol Scand*. 2010;54(10):1164-78.
15. Bonnet MP, Benhamou D. Management of postpartum haemorrhage. *F1000Res*. 2016;5.
16. Paxton A, Maine D, Freedman L, Fry D, Lobis S. The evidence for emergency obstetric care. *Int J Gynaecol Obstet*. 2005;88(2):181-93.

17. World Health Organization, UNFPA, UNICEF, Averting Maternal Death and Disability (AMDD). Monitoring emergency obstetric care: a handbook. Geneva: World Health Organization; 2009.
18. Bailey P, Paxton A, Lobis S, Fry D. The availability of life-saving obstetric services in developing countries: an in-depth look at the signal functions for emergency obstetric care. *Int J Gynaecol Obstet.* 2006;93(3):285-91.
19. Sharma G, Mathai M, Dickson KE, Weeks A, Hofmeyr GJ, Lavender T, et al. Quality care during labour and birth: a multi-country analysis of health system bottlenecks and potential solutions. *BMC pregnancy and childbirth.* 2015;15(2):S2.
20. World Health Organization, Unicef, UNFPA, World Bank Group, United Nations. Trends in maternal mortality: 1990-2015: estimates from WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division. Geneva: World Health Organization; 2015. Report No.: 9241565144.
- *21. Hassal O, Bates I, B Mb. Chapter 19: Blood Transfusion in Resource-Limited Settings. In: Ryan E, Hill D, Solomon T, Aronson N, Endy T, editors. *Hunters Tropical Medicine and Emerging Infectious Diseases.* 10th ed. London: Elsevier; 2019 (in press).
- *22. Merdad L, Ali MM. Timing of maternal death: Levels, trends, and ecological correlates using sibling data from 34 sub-Saharan African countries. *PLoS One.* 2018;13(1):e0189416.
23. Moodley J, Pattinson RC, Fawcus S, Schoon M, Moran N, Shweni P. The confidential enquiry into maternal deaths in South Africa: a case study. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2014;121:53-60.
24. Mbonye AK, Asimwe JB, Kabarangira J, Nanda G, Orinda V. Emergency obstetric care as the priority intervention to reduce maternal mortality in Uganda. *Int J Gynaecol Obstet.* 2007;96(3):220-5.
25. Schantz-Dunn J, Nawal M. The use of blood in obstetrics and gynecology in the developing world. *Reviews in obstetrics and gynecology.* 2011;4(2):86.
26. Allain JP, Owusu-Ofori S, Bates I. Blood transfusion in sub-Saharan Africa. *Transfusion Alternatives in Transfusion Medicine.* 2004;6(1):16-23.
- *27. Roberts DJ, Field S, Delaney M, Bates I. Problems and approaches for blood transfusion in the developing countries. *Hematology/oncology clinics of North America.* 2016;30(2):477-95.
28. Tagny CT, Diarra A, Yahaya R, Hakizimana M, Nguessan A, Mbensa G, et al. Characteristics of blood donors and donated blood in sub-Saharan Francophone Africa. *Journal of Transfusion.* 2009;49(8):1592-9.
- *29. Roberts D, Kitchen A, Field S, Bates I, Allain J, Delaney M. Chapter 24: Blood Transfusion in a Global Context. In: Murphy M, Pamphilon D, editors. *Practical Transfusion Medicine.* Third ed. Oxford: Wiley-Blackwell; 2009.
30. Asamoah-Akuoko L, Hassall OW, Bates I, Ullum H. Blood donors' perceptions, motivators and deterrents in Sub-Saharan Africa - a scoping review of evidence. *Br J Haematol.* 2017;177(6):864-77.
31. Zanin TZ, Hersey DP, Cone DC, Agrawal P. Tapping into a vital resource: Understanding the motivators and barriers to blood donation in Sub-Saharan Africa. *Afr J Emerg Med.* 2016;6(2):70-9.
- *32. Bates I, Manyasi G, Medina Lara A. Reducing replacement donors in Sub-Saharan Africa: challenges and affordability. *Transfus Med.* 2007;17(6):434-42.
33. Choudhury N, Tulsiani S, Desai P, Shah R, Mathur A, Harimoorthy V. Serial follow-up of repeat voluntary blood donors reactive for anti-HCV ELISA. *Asian J Transfus Sci.* 2011;5(1):26-31.

- *34. Gallaher JR, Mulima G, Kopp D, Shores CG, Charles AG. Consequences of centralised blood bank policies in sub-Saharan Africa. *The Lancet Global Health*. 2017;5(2):e131-e2.
35. Loua A, Nikiema J, Kasilo O, Tagny C. Blood safety and availability in the WHO African region. *Globla Surgery*. 2018;4(3):1–7.
36. Muchokwani E. Unlocking the potential for blood adequacy in Africa. Harare: Global Blood Fund; 2018.
37. Global Blood Fund, Africa Society for Blood Transfusion. For post-school blood donors: Pledge 25 Club 2019 [Available from: <https://pledge25.club/>].
38. Okong P, Byamugisha J, Mirembe F, Byaruhanga R, Bergstrom S. Audit of severe maternal morbidity in Uganda--implications for quality of obstetric care. *Acta Obstet Gynecol Scand*. 2006;85(7):797-804.
39. NHS Blood and Transplant. Innovative technology used to attrct new donors 2019 [Available from: <https://www.blood.co.uk/news-and-campaigns/innovative-technology-used-to-attract-new-donors/>].
40. Garraud O, Amorim Filho L, Laperche S, Tayou-Tagny C, Pozzetto B. The infectious risks in blood transfusion as of today—a no black and white situation. *La Presse Médicale*. 2016;45(7-8):e303-e11.
41. Pruett CR, Vermeulen M, Zacharias P, Ingram C, Tayou Tagny C, Bloch EM. The use of rapid diagnostic tests for transfusion infectious screening in Africa: a literature review. *Transfus Med Rev*. 2015;29(1):35-44.
42. Pirozzolo JJ, LeMay DC. Blood-borne infections. *Clinics in sports medicine*. 2007;26(3):425-31.
43. Summerton A, Churchill N. Daktari Diagnostics takes on health care challenges, one device at a time: Center for the Protection of Intellectual Property; 2018 [Available from: <https://medium.com/innovate4health/daktari-diagnostics-takes-on-africas-healthcare-challenges-one-diagnostic-device-at-a-time-90d898fa9b49>].
- *44. Geller S, Adams M, Kelly P, Kodkany B, Derman R. Postpartum hemorrhage in resource-poor settings. *International Journal of Gynecology and Obstetrics*. 2006;92(3):202-11.
45. World Health Organization, The Partnership for Maternal Newborn & Child Health. Opportunities for Africa's newborns. Cape Town: Mills Litho; 2006.
46. Options UK. Key innovations to increase access to quality maternal health care 2019 [Available from: <https://options.co.uk/news/key-innovations-to-increase-access-to-quality-maternal-health-care>].
47. Amukele TK, Hernandez J, Snozek CLH, Wyatt RG, Douglas M, Amini R, et al. Drone Transport of Chemistry and Hematology Samples Over Long Distances. *Am J Clin Pathol*. 2017;148(5):427-35.
48. Cheney C. Scaling up efforts in blood donation innovation: Devex; 2018 [Available from: <https://www.devex.com/news/scaling-up-efforts-in-blood-donation-innovation-93791>].
49. Stone C. A glimpse at EHR implementation around the world: the lessons the US can learn Chicago, IL: HIMSS Foundation; 2014.
50. Schenker J. How tech is helping tackle Africa's healthcare challenges: The Innovator; 2018 [Available from: <https://innovator.news/how-tech-is-tackling-africas-healthcare-challenges-130f065b3d8a>].
51. Huissoud C, Carrabin N, Audibert F, Levrat A, Massignon D, Berland M, et al. Bedside assessment of fibrinogen level in postpartum haemorrhage by thrombelastometry. *BJOG*. 2009;116(8):1097-102.
52. Tull K. Blood costs in Zimbabwe: K4D Helpdesk Report 246. Brighton, UK: Institute of Development Studies; 2017.

53. World Health Organization. WHO Global Health Expenditure Atlas. Geneva: World Health Organization; 2014.
54. Cázares-Benito M, Cázares-Tamez R, Pérez-Chávez F, Díaz-Olachea C, Ramos-García A, Díaz-Chuc E, et al. Impact on costs related to inadequate indication of blood transfusion. *Medicina Universitaria*. 2016;18(72):148-52.
55. Gallos ID, Williams HM, Price MJ, Merriel A, Gee H, Lissauer D, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. *Cochrane Database Syst Rev*. 2018;4:CD011689.
56. Khan KS, Moore P, Wilson M, Hooper R, Allard S, Wrench I, et al. A randomised controlled trial and economic evaluation of intraoperative cell salvage during caesarean section in women at risk of haemorrhage: the SALVO (cell SALvage in Obstetrics) trial. *Health Technol Assess*. 2018;22(2):1–88.
57. World Health Organization. The Clinical Uses of Blood Handbook. Geneva: World Health Organization; 2002.
58. Zhu H, Sencan I, Wong J, Dimitrov S, Tseng D, Nagashima K, et al. Cost-effective and rapid blood analysis on a cell-phone. *Lab Chip*. 2013;13(7):1282-8.
59. Casey GJ, Sartori D, Horton SE, Phuc TQ, Phu LB, Thach DT, et al. Weekly iron-folic acid supplementation with regular deworming is cost-effective in preventing anaemia in women of reproductive age in Vietnam. *PLoS One*. 2011;6(9):e23723.
60. Ouedraogo S, Koura GK, Bodeau-Livinec F, Accrombessi MM, Massougbodji A, Cot M. Maternal anemia in pregnancy: assessing the effect of routine preventive measures in a malaria-endemic area. *Am J Trop Med Hyg*. 2013;88(2):292-300.
61. Ozdemir N. Iron deficiency anemia from diagnosis to treatment in children. *Turk Pediatri Ars*. 2015;50(1):11-9.
- *62. Roberts DJ, Field S, Delaney M, Bates I. Problems and approaches for blood transfusion in the developing countries. *Hematology/Oncology Clinics*. 2016;30(2):477-95.
63. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, et al. Audit and feedback: effects on professional practice and healthcare outcomes. *Cochrane Database Syst Rev*. 2012(6):CD000259.
64. Umar N, Litaker D, Terris DD. Toward more sustainable health care quality improvement in developing countries: the "little steps" approach. *Quality management in health care*. 2009;18(4):295-304.
65. Smits HL, Leatherman S, Berwick DM. Quality improvement in the developing world. *International journal for quality in health care : journal of the International Society for Quality in Health Care / ISQua*. 2002;14(6):439-40.
66. Kajja I. Appropriate clinical use of blood in Uganda. *ISBT Science Series*. 2013;8(1):214-6.

SUMMARY

There are many barriers, and some innovative solutions, to the provision of timely, quality blood transfusions for the management of PPH. The challenges are particularly pronounced in LMICs, where the highest prevalence of both anaemia and PPH are found. The need for innovation to increase repeat, voluntary donation from low-risk donors, including converting replacement donors into regular donors, are critically important. Centralised models of blood banking, while desirable, may be unaffordable and impractical in LMICs. There are exciting new technologies that could improve the sensitivity of point-of-use testing, such as the use of mobile technologies or microfluidic chips, and of linking patient information to transfusions using mobile technologies. Blood may be provided faster to women with PPH through ensuring better referral processes, adequate supplies at health facilities, and transportation of blood and blood components to remote regions using drones. Improving the way that PPH is diagnosed, to fully understand if and when blood transfusions are necessary, may help to eliminate risky, costly blood transfusions. Technologies like bedside fibrinogen tests may assist in assessing the severity of PPH, and the need for blood transfusions. Alternatives to allogenic blood transfusion, such as autologous blood transfusion or intraoperative cell salvage, may also be life-saving options, particularly where there are barriers around the timely provision of blood transfusion. Finally, improving the effectiveness and safety of blood transfusions through hospital-based quality improvement activities has great potential to enact the standards of care for blood transfusions for PPH that exist across LMICs, but that are poorly implemented. Overall, health systems strengthening and context-sensitive cost-recovery financing mechanisms for blood transfusion services are essential for the sustainability of high quality blood services that will benefit all those needing transfusions, including women with PPH.