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Health Economic Value of Blood in Kenya, Ghana and Ivory Coast: The Case of Maternal Bleeding

Valeur économique du sang pour la santé au Kenya, au Ghana et en Côte d'Ivoire : le cas de l'hémorragie maternelle

Owusu-Ofori S[1], Sekongo YM[2], Rajab JA[3], Asamoah-Akuoko L[4], Magutu V[5], Bah A[6], Lamotte M[7], Dierick K[6]

[1] Komfo Anokye Teaching Hospital, Ghana
[2] Centre National de Transfusion Sanguine, Abidjan, Ivory Coast
[3] Haematology & Blood Transfusion Unit University of Nairobi, Kenya
[4] National Blood Service, Ghana
[5] Haematology & Blood Transfusion Unit, University, Nairobi, Kenya
[6] Terumo Blood and Cell Technologies, Zaventem, Belgium
[7] IQVIA, Zaventem, Belgium

Corresponding Author:
Dierick Koenraad.
Terumo Blood and Cell Technologies
Ikaroslaan 41
Zaventem, Belgium
koenraad.dierick@terumobct.com

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ABSTRACT

Background: In sub-Saharan Africa, severe bleeding accounts for up to 44% of maternal deaths, and the need for blood products far outstrips supply.

Aims and objectives: We aimed to map the causes and consequences of blood shortage in Kenya, Ghana and Ivory Coast and estimate the health economic impact of overcoming blood shortages resulting in maternal bleeding.

Methods: We conducted a targeted literature review to evaluate the impact of blood shortage on maternal mortality rates due to post-partum haemorrhage (PPH). Clinical experts from the selected countries were included as an additional source of information. Using a *de novo* budget impact model, costs associated with severe maternal bleeding were compared with investment costs to adequately manage maternal bleeding.

Results: Of the estimated 4 000 941 births/year, 118 428 will be confronted with severe PPH requiring blood transfusion. The estimated total yearly value of life years lost for the three countries combined would be 57 104 042 USD. The total cost to provide adequate blood supply (13 units/patient) was 33 781 945 USD, meaning that blood transfusion in PPH results in 23 322 097 USD saved with savings starting from the first year onwards in Kenya and Ghana, and from the second year onwards in Ivory Coast.

Conclusion: In Kenya, Ghana and Ivory Coast, an increased investment in blood supply would likely provide large cost savings in less than two years.

RÉSUMÉ

Contexte : En Afrique subsaharienne, les hémorragies sévères représentent jusqu'à 44 % des décès maternels, et le besoin en produits sanguins dépasse de loin l'offre.

Buts et objectifs : Nous avons cherché à cartographier les causes et les conséquences des pénuries de sang au Kenya, au Ghana et en Côte d'Ivoire et à estimer l'impact économique sur la santé de la résolution des pénuries de sang entraînant des saignements maternels.

Méthodes : Nous avons effectué une revue ciblée de la littérature pour évaluer l'impact de la pénurie de sang sur les taux de mortalité maternelle due à l'hémorragie du post-partum (HPP). Des experts cliniques des pays sélectionnés ont été inclus comme source d'information supplémentaire. À l'aide d'un modèle d'impact budgétaire de novo, les coûts associés aux saignements maternels graves ont été comparés aux coûts d'investissement pour gérer correctement les saignements maternels.

Résultats : Sur les 4 000 941 naissances/an estimées, 118 428 seront confrontées à une HPP sévère nécessitant une transfusion sanguine. La valeur annuelle totale estimée des années de vie perdues pour les trois pays combinés serait de 57 104 042 USD. Le coût total pour fournir un approvisionnement en sang adéquat (13 unités/patient) était de 33 781 945 USD, ce qui signifie que la transfusion sanguine dans l'HPP permet d'économiser 23 322 097 USD avec des économies à partir de la première année au Kenya et au Ghana, et à partir de la seconde à partir d'un an en Côte d'Ivoire.

Conclusion : Au Kenya, au Ghana et en Côte d'Ivoire, un investissement accru dans l'approvisionnement en sang permettrait probablement de réaliser d'importantes économies en moins de deux ans.

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INTRODUCTION

Blood transfusion is an essential component of the healthcare system of every country. Maintaining access to and availability of safe blood is crucial for patients requiring blood transfusion and can be lifesaving.

In 2013, the most recent year for which global data are available, an estimated 112.5 million blood units were donated worldwide. Of these, 5.6 million blood units were collected in 46 African countries, accounting for only 4% of global donations, although these countries are inhabited by approximately 13% of the global population.[1] In developed countries, blood transfusions are used mainly in patients with chronic medical conditions such as cancer or blood disorders as well as in supportive care in cardiovascular and transplant surgery, and in the management of trauma; most recipients of blood are aged 75 years or older.[2] By contrast, in developing countries, a large percentage of blood recipients are children with blood disorders, especially severe anaemia secondary to malaria.[1,3] Blood is also frequently needed for the management of complications of pregnancy and childbirth.[2] Among the latter, haemorrhage accounted for 27.1% of global maternal deaths between 2003 and 2009, more than 99% of them occurring in developing countries.[4] In the sub-Saharan region of Africa, severe bleeding is estimated to account for up to 44% of maternal deaths, and the need for blood products far outstrips supply.[3] In the World Health Organisation (WHO) African region, blood requirements were estimated at about 8 million units in 2010, but only approximately 3.5 million units were collected, with an average yearly blood donation rate of 4.3 units/1 000 population. Considering the WHO guideline of collecting at least 10 units per 1 000 population, this constituted a shortage of nearly 4.7 million units of blood annually.[3] Contributing factors include a lack of structured blood supply chains and blood donor programmes, limited access to healthcare, particularly in rural areas, and limited supplies of test kits for blood screening.[2,5] Examples of African countries struggling to match blood supply to blood demand include Kenya,[6-10] Ghana[11-15] and Ivory Coast.[16-19]

Although the link between the blood supply and morbidity and mortality within a country is well understood,[20-23] to date, there is a paucity of data regarding the impact of increased blood supply on healthcare performance in Kenya, Ghana and Ivory Coast. More specifically, only a few studies in the African region have evaluated predictors of survival of patients requiring acute massive transfusion (e.g. due to maternal bleeding) or regular transfusion (e.g. due to chronic anaemia).[9,24] To address this data gap, we conducted a targeted literature review to understand the impact of blood availability on the health outcomes of patients in Kenya, Ghana and Ivory Coast. We assessed the health economic impact of blood shortages on maternal bleeding and constructed a *de novo* budget impact model to compare the costs associated with severe maternal bleeding (i.e. post-partum haemorrhage [PPH]) versus the cost of investment to adequately manage maternal bleeding.

AIMS AND OBJECTIVES

The objectives of this study were to 1) map the causes and consequences of the shortages of blood and blood components in Kenya, Ghana and Ivory Coast; 2) summarise the impact of blood shortage on socio-economic outcomes and mortality (with specific focus on the maternal mortality due to severe maternal bleeding, i.e. PPH) and assess the health economic impact of increased blood collections on the burden of maternal bleeding.

MATERIALS AND METHODS

Study design

This study focused on three sub-Saharan African countries: Kenya, Ghana and Ivory Coast, to cover both West and East coast of Africa. These countries were selected based on the origin and expertise of the clinical experts involved in the study design. The study consisted of four steps:

1. The incidence and consequences of maternal bleeding were identified by means of a targeted literature review, including epidemiological data, consisting of two main parts. The first part (Search 1) included an initial PubMed search to define the scope of the problem (i.e. blood shortage as a cause of maternal bleeding) in the target countries, and the second part (Search 2 and Search 3) included additional searches using both PubMed and grey literature search, to assess the health economic impact of the problem.
2. As few publications on these topics were identified following the literature search, clinical experts from the selected countries provided additional information. Each expert holds a senior position in the central blood service organisation in one of the three countries of interest and is directly involved in blood donor care, blood collection, blood availability, and clinical transfusion practice.
3. Next, the costs associated with the treatment of severe maternal bleeding were mapped by means of targeted literature search (Search 4) and input of the clinical experts.
4. Finally, a *de novo* budget impact model was created to compare the costs associated with consequences of severe maternal bleeding (i.e. the cost of a life lost according to WHO and European Commission guidelines) versus the cost of investment in blood supply (Search 5).

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Search strategy and eligibility criteria

The first part of the literature search (Search 1) was performed using PubMed to identify articles evaluating the impact of blood shortage on healthcare performances in Kenya, Ghana and Ivory Coast, published between 1980 and 2019 (with majority of the articles published between 2010 and 2019) in English or French (articles in French were considered only if the abstract was available in English). All articles that included any information on blood supply or maternal bleeding were considered. The following search terms were applied separately and in combination with the names of countries of investigation (Kenya, Ghana and Ivory Coast): blood, availability, supply, demand, donation, transfusion, shortage, maternal, haemorrhage, hemorrhage, bleeding, pregnancy, collection (**Supplementary file 1**).

The second step included additional targeted searches aiming at finding information on the health economic impact of blood shortage and maternal bleeding in each country, i.e. articles that described blood transfusion performed in maternal bleeding (Search 2), and articles that provided guidelines for the treatment of maternal bleeding (Search 3), using PubMed and Google Scholar to identify relevant grey literature. The search string included in **Supplementary file 1** in combination with 'Kenya', 'Ghana' or 'Ivory Coast' was applied.

The search term applied in Search 4 was "cost of blood transfusion" in combination with the name of each country of investigation (Kenya, Ghana and Ivory Coast). In Search 5, the search terms included the variables identified in Search 1, 2 and 3 (i.e. average life expectation, age of delivery, female employment rate, modal income and cost of blood transfusion) combined with the country names. Sources from local or global authorities (ministries of health, WHO) and sources coming from non-governmental organisations were considered more trustworthy than sources coming from commercial organisations.

Budget impact model

The objective of the budget impact model was to understand the net economic return upon achieving a sufficient blood availability for treating severe PPH. In our literature review, we identified that blood shortages exist and that not all women suffering from PPH have access to blood transfusion. Hence, our model compared the current state with the situation where enough blood would be available.

The health economic model was based on the previously published methodology for estimating the present value of lifetime earnings.[25] A *de novo* budget impact modelling was combined with the estimation of the value of a life lost, including sensitivity analysis, as recommended by the *International Society for Pharmacoeconomics and Outcomes Research* guidelines.[26] Variables for the budget impact model were identified from the literature research (Search 1, 2 and 3).

Budget impact modelling is a frequently applied technique in health economics; moreover, it has also been applied within the blood transfusion environment.[27-32]

To estimate the number of lives lost due to PPH in the three countries of interest, we used the *de novo* budget model. In our estimations, we applied a top-down approach starting from PPH incidence to estimate the total mortality figure. Based on the shortage of blood in the region and the information provided by the clinical experts, it was assumed that 75% of women would not have blood transfusion available and 25% would have access to lifesaving blood transfusion.[33]

RESULTS

Literature and data selection

The initial PubMed search (Search 1) yielded 703 publications; 327 of those publications related to Kenya, 312 to Ghana (One reference [113] included data for both Ghana and Kenya) and 65 to Ivory Coast. After initial abstract screening, 649 were excluded as they did not address the topics of blood supply or maternal bleeding in the target countries. Hence, 54 publications were retained that directly discussed the impact of blood availability on patient health outcomes (**Figure 1 and Table 1A**).

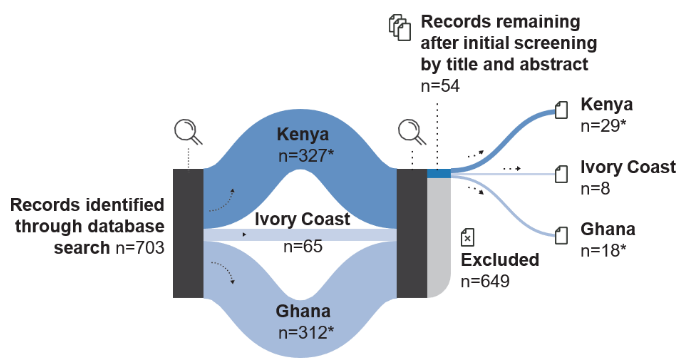

Figure 1. Flowchart of the initial literature search (Search 1)
n, number.
* One reference, Drammeh et al [113], included data for Kenya and Ghana and was therefore counted for both countries.

Search 2 and Search 3 yielded 37 additional articles (**Table 1B**). Search 4, performed to identify articles reporting guidelines for constructing the health economic model, yielded two references, while Search 5, aimed to identify sources of data to populate the model, resulted in 15 references.

Absolute shortage of blood units

The WHO estimates that resource-limited countries will begin to meet clinical demand for blood if at least 10 whole blood units per 1 000 inhabitants are collected annually.[3] While neither Kenya,

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Table 1A: Literature search results (Search 1)

Author, publication year	Study location	Study dates	Ref
Search 1: Extent and consequences of blood shortages on maternal bleeding in target countries			
Nabwera HM et al., 2016	Kenya	May 2005–Apr 2007	6
Oduor M, 2009	Kenya	1980s–2009	7
Osoro AA et al., 2013	Kenya	Jan 2009–Jun 2010	8
Riviello ED et al., 2015	Kenya	2004–2010	9
Thomas J et al., 2017	Kenya	Sep 2013–Mar 2016	10
Kiguli S et al., 2015	Kenya, Tanzania and Uganda	Jan 2009–Jan 2011	24
NP	Kenya	Apr 2004–Sep 2004	105
Bartonjo G et al., 2019	Kenya	Nov 2011–Jan 2012	39
Basavaraju SV et al., 2010	Kenya	Aug 2007–Dec 2007	103
Brown H et al., 2016	Kenya	Jan 2013–May 2015	62
Desai M et al., 2013	Kenya	2003–2008	74
Drammeh B et al., 2019	Ghana, Kenya, Malawi, Mozambique, Nigeria, Rwanda and Tanzania	Feb–Sep 2017	113
Kimani D et al., 2011	Kenya	Aug 2007–Dec 2007	36
Burke TF et al., 2017	Kenya, Senegal, Sierra Leone and Tanzania	Sep 2012–Sep 2016	73
Lackritz EM et al., 1997	Kenya	Mar 1991–Sep 1991	114
Lackritz EM et al., 1993	Kenya	Sep 1990–Jul 1991	37
Makokha AE, 1991	Kenya	1978–1987	82
Moore A et al., 2001	Kenya	Apr 1994–Jul 1994	115
Ngugi PM et al., 2007	Kenya	Jun 2004–May 2005	116
Onyango CG et al., 2018	Kenya	Nov 2015–Oct 2016	35
Otieno T et al., 2004	Kenya	NP	117
Pedro R et al., 2010	Kenya	Jan 2002–Dec 2009	59
Ramanathan A et al., 2018	Kenya and Sierra Leone	Sep 2012–Dec 2015	76
Riang'a RM et al., 2017	Kenya	Apr 2015–Aug 2015	118
Saidi H et al., 2014	Kenya	2009–2010	119
Wakaria EN et al., 2017	Kenya	Jan 2013–Feb 2015	106
Wamamba D et al., 2017	Kenya	2015	42
Zucker JR et al., 1994	Kenya	Dec 1990–Jul 1991	120
Guerriero C et al., 2010	Kenya, South Africa, Tanzania and Botswana	NA	44
Adu-poku F et al., 2020	Ghana	2015-2016	121
Adusi-Poku Y et al., 2015	Ghana	Jan 2012–Dec 2012	11
Gething PW et al., 2012	Ghana	NA	12
Mohammed S et al., 2018	Ghana	Jan 2018–Feb 2018	13
Owusu-Sarpong A et al., 2017	Ghana	Jan 2012–Dec 2012	14
Stanton CK et al., 2013	Ghana	Apr 2011–Nov 2012	15
NP	Ghana, Nigeria and Sierra Leone	NP	122
Allain JP et al., 2009	Ghana	2004–2007	40
Allain JP et al., 2008	Ghana	2003–2007	109
Commey JO et al., 1995	Ghana	1991	123
Fofie C et al., 2010	Ghana	Jan 2007–Dec 2008	80
Geelhoed D et al., 2006	Ghana	Jan 1999–Jan 2000	58
Kubio C et al., 2012	Ghana	2007–2009	41
Martey JO et al., 1993	Ghana	1981–1989	77
Owusu-Ofori AK et al., 2013	Ghana	2010	43
Owusu-Ofori S et al., 2010	Ghana	2002–2008	124
Pantoja T et al., 2016	Ghana	All	70
Hensher M et al., 2000	Ivory Coast, Zimbabwe and Mozambique	NP	17
Kouao MD et al., 2012	Ivory Coast	Jan 2006–Dec 2008	18
Tagny CT et al., 2009	Burkina Faso, Cameroon, Congo, Ivory Coast, Mali, Niger and Rwanda	2006-2007	125
Tagny CT et al., 2009	Burkina Faso, Cameroon, Congo, Ivory Coast, Mali, Niger and Rwanda	2007	19
Berardi JC et al., 1989	Ivory Coast	1980 versus 1985	126
Schutz R et al., 1993	Ivory Coast	Feb 1991–Nov 1991	38
Prata N et al., 2005	Ivory Coast, Tanzania	Aug 2003–July 2004	79
Thonneau PF et al., 2004	Ivory Coast	May 1999-Oct 1999	78

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Table 1B: Literature search results (Searches 2—5)

Author, publication year	Study location	Study dates	Ref
Search 2: Extent and consequences of blood shortages on maternal bleeding in target countries or sub-Saharan Africa			
Diane MK et al., 2014	Ivory Coast	1992	16
Abera B et al., 2017	Ethiopia	May 2016–June 2016	104
Allain JP, 2011	Sub-Saharan Africa	NP	102
Aneke JC et al., 2017	Nigeria	All	127
Bates I et al., 2008	Africa	1970–2006	48
Barro L et al., 2018	Sub-Saharan Africa	NA	107
Bonnet MP et al., 2016	NP	NP	99
Bullough CH, 1981	Malawi	1977	128
Royal College of Obstetricians & Gynaecologists	NA	NA	83
Kanagasabai U et al., 2018	Sub-Saharan Africa	2014–2016	34
Osei EN et al., 2013	Ghana	2011–2012	129
Oyakhire GK, 1980	Nigeria	1976–1977	130
Pavord S et al., 2015	NA	NA	63
Spiegel DA et al., 2017	Sierra Leone, Uganda, Mauritania, Benin, Zambia, Burkina Faso, Democratic Republic of Congo and Togo	2010, 2012 or 2013	131
Taye Makuria A et al., 2017	Ethiopia	NA	23
Zawde D et al., 1991	Ethiopia	NP	132
National Council for Population and Development	Kenya	2015	49
Muchemi OM et al, 2016	Kenya	2008-2012	50
Owolabi O et al, 2020	Kenya	2018	51
WHO, 2011	Kenya	2011	52
Asamoah BO, 2011	Ghana	2000-2005	53
Der EM et al, 2013	Ghana	2004-2008	54
Agence de presse Africaine, 2020	Ivory Coast	2020	55
Merdad L, Ali MM, 2018	Sub-Saharan Africa	1990-2014	56
Unicef, 2012	Ivory Coast	2012	57
Search 3: Guidelines and recommendations for the treatment of maternal bleeding			
International Federation of Gynecology and Obstetrics (FIGO), 2018	Worldwide	1990–2015	60
Anderson JM et al., 2007	NA	NA	61
Erhabor O et al., 2011	Sub-Saharan Africa	NA	133
Field SP et al., 2007	Sub-Saharan Africa	NA	134
Ford JB et al., 2011	Australia	2003–2011	66
Jansen AJ et al., 2005	NA	NA	81
Kent A, 2010	Worldwide	NA	135
Ramler PI et al., 2017	Netherlands	2004–2006	64
Sheldon WR et al., 2014	Africa, Asia, Latin America/Caribbean and Middle East	May 2010–Dec 2011	68
Smith JR, 2018	Worldwide	NA	65
Weeks A, 2014	NA	NA	69
Yiadom MYAB, 2018	Worldwide	NA	136
Search 4: Guidelines for the health economic model			
Max WR et al., 2004	USA	2000	25
Mauskopf JA et al., 2007	NA	2007	26
Search 5: Data to populate the model			
Balki M et al., 2008	Canada	2000–2005	137
Kuma HHS et al., 2015	Nigeria	NP	100
Prick BW et al., 2016	The Netherlands	2000–2008	84
World Health Organisation, 2016	Worldwide	2011, 2012 or 2013	1
Central Intelligence Agency, 2019	Worldwide	NA	94
The World Bank, 2019	Ghana	2019	88
The World Bank, 2019	Worldwide	2019	95
CEIC, 2019	Kenya	2008–2019	96
Global Press Journal, 2017	Kenya, Ghana, Rwanda, Zambia, Uganda, Cameroon, Zimbabwe, Nigeria and Democratic Republic of Congo	NP	101
UNICEF, 2019	Kenya	2019	87
Knoema, 2019	Ghana	2019	86
NUMBEO, 2019	Kenya	2019	138
NUMBEO, 2019	Ghana	2019	97
NUMBEO, 2019	Ivory Coast	2019	98
World Population Review, 2019	Ivory Coast	2019	89

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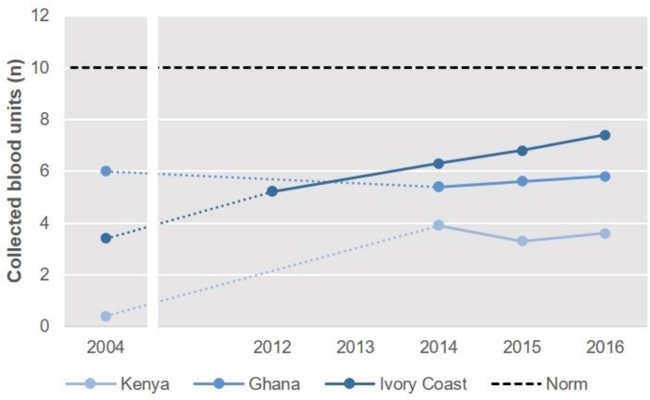

Figure 2. Blood collections per 1 000 inhabitants (2004–2016)*
*Based on Kanagasabai et al [34]: data for 2004 and 2014–2016, and Diane et al [16]: data for 2012

Ghana, nor Ivory Coast achieve this threshold, improvement was seen in Kenya (up to 2014) and Ivory Coast in the last years (**Figure 2**).[16,34]

Failure throughout the entire blood supply chain

The reasons contributing to the gap between blood demand and blood availability in Kenya, Ghana and Ivory Coast are listed in **Table 2**, based on the literature.

Based on the above findings, the literature review and insights from the clinical experts within the countries of investigation, it can be concluded that the local blood value chain fails to meet international guidelines across-the-board.

Table 2: Main reasons for the gap between blood demand and blood availability in Kenya, Ghana and Ivory Coast

Reason for gap between blood demand and blood availability	Country	Ref
Insufficient financial resources for the organisation and management of the blood supply chain	Kenya, Ghana, Ivory Coast	17,19,102,109
Missing healthcare infrastructure (blood collection centres, storage, collection devices and disposables, and blood testing) at the point of blood collections, as well as missing healthcare infrastructure at the point of blood	Ghana, Ivory Coast	12,19
Higher levels of transfusion transmittable infections	Kenya, Ghana, Ivory Coast	16,19,35,121
Missing local blood transfusion guidelines and non-adherence to international recommendations	Ivory Coast	19
Lack of information on the availability of blood versus demand (at a centre level)	Ivory Coast	16,19
Difficulties in distribution of blood products	Ivory Coast	107,125
Shortage of repeat/non-remunerated blood donors	Kenya, Ghana, Ivory Coast	16,18,41,103
Difficulties in the collection, distribution and application of blood due to lack of well-trained personnel in transfusion medicine	Kenya, Ghana, Ivory Coast	16,19,106,113
Cultural counterarguments for the collection and transfusion of blood	Ghana, Ivory Coast	109,125
Shortages of specific blood types	Ivory Coast	16,19
Large differences between rural and urban healthcare infrastructure	Kenya, Ghana, Ivory Coast	12,19,102
Misuse of the scarce available units of blood (blood transfusions provided to patients who do not have the highest need)	Ghana, Ivory Coast	19,129

Burden of transfusion transmittable infection

In addition to blood shortage, safety of the available blood constitutes another major challenge in the three countries of interest. The blood may be contaminated with human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), syphilis, malaria and other transfusion transmittable infections (TTIs), which further complicates the organisation of a stable blood supply chain, and impacts the blood collection costs, as contaminated blood units have to be discarded.[16,19,34,35]

Across the investigated countries, the published TTI prevalence ranged from 1.2%–20.0% for HIV,[35-39] 3.1%–7.5% for HBV,[35,39-42] 3.2%–6.1% for HCV,[35,39-41] 1.0%–4.7% for syphilis,[35,39-42] and 0.6%–50.0% for malaria.[39,43] However, large variations were found per country, region, blood collection service and hospital type. Furthermore, the blood-borne infection screening policies may differ among the countries; in particular, screening for malaria is not mandated in non-endemic regions.

Health economic assessment of blood shortage: the case of maternal bleeding

Shortages of blood supplies in Kenya, Ghana and Ivory Coast directly contribute to the overall mortality and morbidity figures.[10,44] In the three countries of interest, the maternal mortality ratio ranged from 308 to 617 per 100 000 live births in 2017.[45-47] Based on the available literature data, among all maternal deaths, the percentage of maternal deaths due to haemorrhage in these countries ranges from 24%–57% in Kenya,[48-52] 12%–48% in Ghana[48,53,54] and 33%–42% in Ivory Coast.[55-57] Moreover, blood shortage contributes to the increased foetal mortality as well.[48,58,59]

Severe post-partum haemorrhage

PPH is defined as blood loss of >500 mL after vaginal or >1 000 mL after Caesarean delivery, a bleeding rate in excess of 150 mL per minute and/or haemodynamic changes suggestive of excessive blood loss.[60-64] All pregnancies ≥20 weeks' gestation are at risk for PPH and its sequelae.[65] Blood shortage contributes to the mortality due to PPH, and the majority of deaths occur in resource-poor settings where home-deliveries are common and treatment options, including blood transfusion, are not readily available.[66-70]

Of all maternal deaths, over 90% occur in low-resourced countries and the leading cause of death is PPH.[60,63,71] PPH is estimated to be the cause of approximately 35% of maternal deaths worldwide.[72] Based on our literature search, in Kenya, Ghana and Ivory Coast, PPH accounts for 2.6%–34%,[73-76] 3.2%–27%,[14,53,58,77] and 1.1%–37%,[78,79] of the maternal mortality rates, respectively.

Lives lost due to PPH

Based on the literature, in a theoretical birth cohort of 100 000 births a year, 21.8% (21 830) women would experience PPH,[68,69,80-82] of

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which 3.0% (2 960) are likely to be severe.[61,68,69,83,84]

In our model, we included a mortality rate of 3.0% (or 22 cases out of 100 000) within the transfused cohort as confirmed by the local experts. Considering that 75.0% of severe PPH cases will not get transfused (2 220 cases), and that the mortality risk without transfusion is 6.5 times higher than with blood transfusion, this results in the mortality rate of 19.5% (433 cases per 100 000). Considering the above data, PPH would result in a total of 455 (22+433 cases) maternal deaths per 100 000 births within the sub-Saharan African region. Literature also suggests that 50 in 100 000 women with severe PPH would not be saved even with massive blood transfusion.[60,62,68,69,77] Hence, in a cohort of 100 000 births, there would be 433 maternal deaths (0.43%) due to PPH, of which 50 could not have been saved, resulting in 383 (88.5%) cases that are potentially avoidable with massive blood transfusion (**Figure 3A**). Therefore, based on our model calculations, the estimated numbers of maternal deaths due to PPH are 9 611 in Kenya (**Figure 3B**), 3 619 in Ghana (**Figure 3C**) and 4 090 in Ivory Coast (**Figure 3D**); of those, 8 503, 3 202 and 3 618, respectively, are potentially avoidable with massive blood transfusion (**Table 3**).

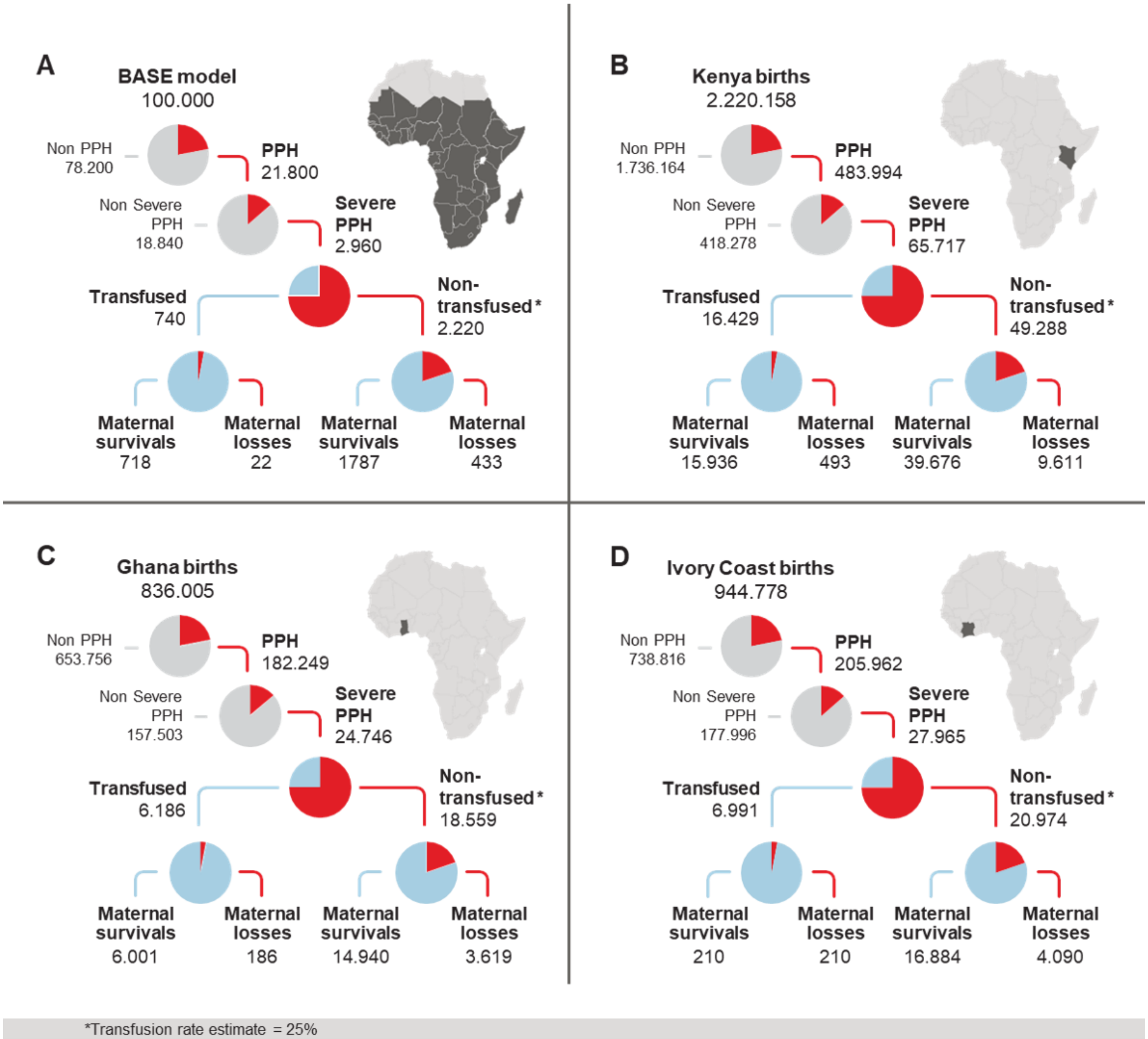

Figure 3. Estimation of number of lives lost due to PPH and shortage of blood in A) the sub-Saharan African region, B) Kenya, C) Ghana and D) Ivory Coast
PPH, post-partum haemorrhage.

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Table 3. *Economic impact of blood transfusion in PPH*

	Kenya	Ghana	Ivory Coast	Total or Average
Yearly births, n **(A)**	2 220 158[87]	836 005[86]	944 778[85]	4 000 941
PPH related mortality, % **(B)**	0.43[60,62,68,69,77]			
PPH-related mortality (cases), n **(B)**	9 613	3 619	4 090	17 324
Deaths avoidable by transfusion, n **(C)**	8 503	3 202	3 618	15 323
Female life expectancy, years **(D)**	69[90-93]	63[88]	54[89]	64*
Median age at delivery, years **(E)**	20.3[94]	22.3[94]	27.0[94]	22*
Life years lost **(F)** (= D-E)	49	41	27	42*
Total life years lost **(G)** (=C*F)	415 382	130 317	97 699	643 398
Female employment rate, % **(H)**	64[95]	64[95]	48[95]	60*
Yearly value of a life lost (USD) **(I)**	6 979	6 259	3 626	6 037*
Total value of life years lost due to avoidable PPH deaths (USD) **(J)** (= G*H*I)	1 855 326 710	522 019 809	170 044 014	2 547 390 533
Yearly value of life years lost (USD) **(K)** (= J/F)	37 980 076	12 826 040	6 297 926	57 104 042
Blood units required for massive blood transfusion, n **(L)**	13[9,64,80,99,100]			
Cost of collection, test, storage of a unit of blood (USD) **(M)**	100[101]			
Cost of providing blood to the patient (USD) **(N)**	50			
Total cost of blood transfusion per unit **(O)** (= N+M)	150			
Total cost of required PPH blood transfusion per year (USD) **(P) (= B*O*L)**	18 745 904	7 058 808	7 977 233	33 781 945
Net economic impact of blood transfusion (USD) (Q) (= K-P)	19 234 172	**5 767 231**	**-1 679 307**	23 322 097

n, number; PPH, post-partum haemorrhage; USD, United States dollar.
* weighted average in function of the yearly births per country

Economic impact of increased blood transfusion on maternal bleeding

Applying a simplified and undiscounted human capital method,[25] we estimated the net economic benefit of blood transfusion in PPH for Kenya, Ghana and Ivory Coast. The model was constructed as follows (see **Table 3**):

(A) Considering the births per year in the countries of investigation,[85-87]

(B) Not all PPH cases will be severe and result in a life lost; based on the above-mentioned calculation, we considered 0.43% of PPH cases to be fatal due to blood shortage.[60,62,68,69,77]

(C) Not all deaths due to PPH are avoidable; an estimated 0.05% of births cannot be saved with massive blood transfusion during severe PPH,[60,62,68,69,77] giving a transfusion save rate **(C')** of 383 per 100 000 births.

(D) Life expectancy varies between the countries of investigation.[88-93] In combination with the assumed age at delivery of 20–27 years[94] **(E)**, this results in the amount of life years lost per woman **(F = D-E)** who dies of severe PPH.

(G = F*C) The total life years lost per country is calculated based on the amount of life years lost per woman **(F)**, multiplied with the avoidable deaths **(C)**.

(H) The first parameter used in the evaluation of the financial impact of life years lost was the labour rate (proportion of females who are employed). Female employment rates in the countries of investigation varied between 48% and 64%.[95]

(I) The financial value of a single life year lost was the yearly net income of an individual in the country of investigation.[96-98] Combining the employment rate **(H)** with the yearly value of a life lost **(I)** by multiplying these returns **(I')** which represents the employment adjusted value of a life **(J = G*I*H).** The total value of life years lost due to severe PPH was estimated as the total amount of avoidable life years lost **(G)** multiplied with the yearly net income of an individual **(I)** and adjusted for the labour rate. We estimated that the total value of life years lost for Kenya, Ghana and Ivory Coast combined is close to 2.5 billion US dollars (USD) over a period of 40 years.

(K) To assess the yearly financial impact of severe PPH, the total value of life years lost **(J)** is divided by the life years lost per woman that dies due to severe PPH **(F)**. This step is necessary to compare the yearly investments to collect, manage and transfuse a unit of blood with the yearly cost of a life lost.

(L) The first driver to estimate the cost of blood transfusion is the number of units of blood transfused. For severe PPH, massive blood transfusion is required. Our literature search indicated that the

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average number of units of blood transfused during massive blood transfusion is 13.[9,64,80,99,100]

(M) Secondly, for the countries of interest and confirmed with the local experts, the cost to collect, test and store a unit of blood was considered to be 100 USD,[101]

(N) and the cost of providing a unit of blood to the patient was considered to be 50 USD.[101]

(O) As a consequence, the total cost of providing a unit of blood was 150 USD **(O = N+M)**.

(P) Not only women who survive severe PPH are transfused, and women who have been transfused and do not survive should be also considered. Hence, the total cost of required PPH blood transfusion per year is **(P = B*O*L).**

(Q) To come to an evaluation of the net economic benefit of blood transfusion in case of severe PPH, we compared the yearly value of life years lost **(K)** with the total cost of required PPH blood transfusion **(P) (Q = K-P).**

Our economic evaluation showed that there are an estimated 4 000 941 births per year in the above-mentioned countries. In 17 324 cases, the mother will be confronted with severe PPH that will require blood transfusion. Not all of them will get appropriate blood transfusion, and we estimated that the total yearly value of life years lost for the three countries combined would be 57 104 042 USD. The total expected cost to provide enough blood transfusion (13 units) to these patients would be 33 781 945 USD.

Having blood transfusion available to treat PPH results in cost savings in Kenya and Ghana within the first year. In Ivory Coast, in the first year, there are additional costs, mainly due to the lower level of income per inhabitant, the higher median age at delivery and hence, the lower average life expectancy. However, as from the second year, cost savings can be expected also for this country (**Figure 4**). Hence, local governments would need less than two years to have cost savings on the investment in blood availability.

Sensitivity analysis and simplification

Details of the calculation of the net economic impact of blood transfusion in PPH are included in Supplementary material (**Supplementary file 2**).

To assess the uncertainty in these calculations, a sensitivity analysis was performed that included variations in the following variables: female employment rates **(H)**, value of a life year lost per year **(I)**, number of blood units required for massive blood transfusion **(L)**, total cost of blood transfusions per unit **(M)**. These variables were altered in the previous calculations to assess the reliability of the outcomes.

Running the sensitivity analysis, we found that net economic return may vary depending on the assumption. Keeping all other parameters equal (ceteris paribus), we found a breakeven point with an employment rate at 37% which is substantially lower than the 60% that we included in our calculation. We also found that as from a yearly value of a life lost of 3 661 USD, cost savings can be expected. For the blood units required, none of the tested scenarios resulted in additional costs. When the number of blood units required per patient with severe PPH is 21 or higher, which is substantially above the 13 units included in our calculations, the operation is cost neutral. Lastly, we checked the sensitivity of the model to the cost of a blood unit. As from a cost of blood above 247 USD per unit (instead of the 150 USD used in the base case), providing blood transfusion was no longer cost-saving (**Table 4**).

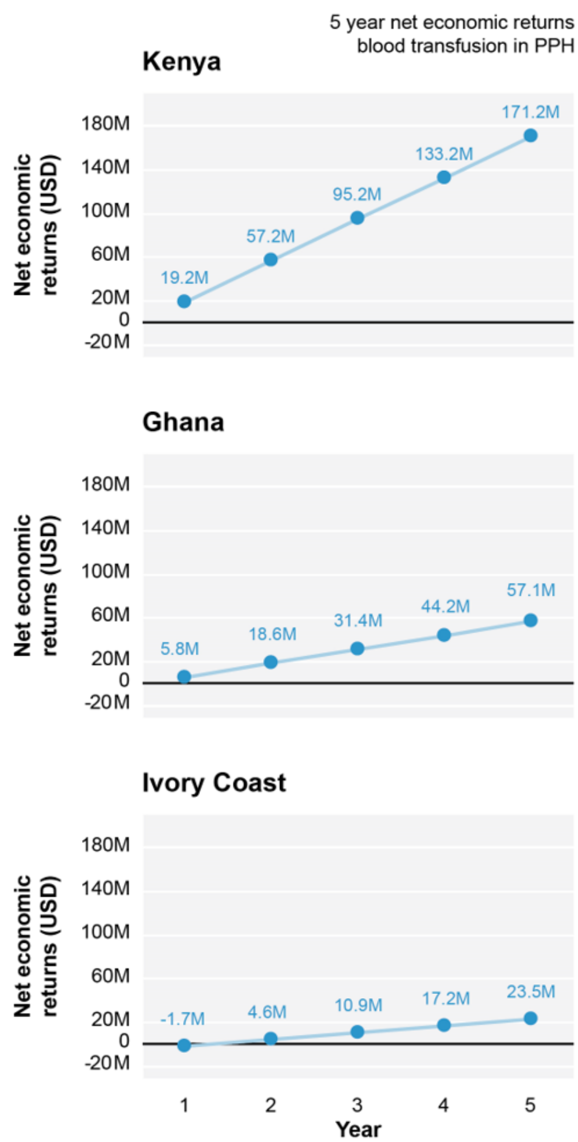

Figure 4. 5-year cost savings for blood transfusion in PPH
PPH, post-partum haemorrhage; USD, United States dollar.

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Table 4. *Source variables of sensitivity analysis*

	Sensitivity range	Net economic return (-/+) USD	Break even point
Female employment rate (H)	5%	-29 157 281	37%
	64%	25 413 749	
Yearly value of a life lost (USD) (I)	1 500	-1 994 013 381	3 661
	120 000	76 952 546	
Blood units required (L)	7	37 509 171	21
	19	6 325 837	
Cost of blood per unit (USD) (O)	75	38 808 476	247
	300	-11 864 441	

USD, United States Dollar

DISCUSSION

The available literature data suggest that in Kenya, Ghana and Ivory Coast, there is an absolute shortage of safe blood originating from the failures in certain aspects of the blood supply chain. The existing gap between demand for blood and blood supply results in the delay in initiating, or not providing potentially lifesaving transfusions.[9,10,37] One of the main reasons is the shortage of donors.[16,18,41,102,103] This might be linked to both operational difficulties, including lack of specialised centres or blood collection points,[7,12,19,41] cultural aspects related to personal beliefs or fears of being tested,[16,19,102,104] or educational challenges including the lack of trained personnel, clear guidelines and effective management of the blood supply.[9,16,19,37,105]

Blood safety is another critical challenge in the developing countries, where many blood collection centres struggle with chronic shortage of necessary kits and equipment for appropriate testing for TTI while, contrary to the countries of the developed world, infectious diseases are widespread across the sub-Saharan Africa.[7,16,18,19,102] The availability of safe donors is crucial for the performance of the blood value chain. In a sub-Saharan Africa review, lack of donors and the unwillingness of available kinsmen and friends to donate were present among factors that contributed to establishing a direct association between maternal deaths and lack of blood transfusions.[48] Local governments and authorities in Kenya, Ghana and Ivory Coast, along with a strong support of international governmental and non-governmental organisations, have taken the initiatives within the last decades to improve the availability of safe blood; however, there is still room for improvement.[6,19,34,81,106-108] Additionally, the scarce financial resources for blood transfusion services, including testing, prevents effective implementation of the international guidelines and requirements for blood safety, highlighting the need for further funding.[17,19,109-111] Consequently, the delay or non-compliance to the appropriate use of blood transfusions leads to higher morbidity and mortality ratios within the countries of investigation compared to countries with sufficient safe blood supply.[48,110,112] For anaemic patients (often children and pregnant women) who do not receive a blood transfusion on time, the risk for death could be over twice as high versus their peers who do receive their blood transfusion appropriately.[10,16] Worldwide, an estimated 800 women die every day from preventable causes related to pregnancy or childbirth, among which untreated haemorrhage is a major contributor.[60,61,63,99] Maternal deaths from haemorrhage are rampant because once bleeding starts, death can occur in around 2 hours compared with 10 hours for eclampsia and 72 hours for obstructed labour.[20] Our literature search suggests that in Kenya, Ghana and Ivory Coast, maternal mortality ratios range from 308 to 617 per 100 000 live births, with nearly 30% of deaths attributable to the blood shortage.[45-48] In Kenya, Ghana and Ivory Coast, up to approximately 40% of maternal mortality could be attributed to PPH.[79]

Ultimately, this comes with a substantial negative impact on the economic output for the countries of investigation. Our research suggests that an increased investment in the safe blood supply chain in Kenya, Ghana and Ivory Coast is likely to provide large positive economic and societal returns in less than two years. Even considering the relatively low-income levels, the cost of saved lives outweighs the investments in the supply of blood with cost savings.

The strengths of this study include robustness of the data, which are based on the literature search, the novelty of the *de novo* budget impact model, as, to our knowledge, estimating the value of a life lost related to blood transfusion has not been performed before, and its generalisability as, although focused on the maternal bleeding in this study, it could be used for other assessments where blood transfusion is needed, e.g. surgery, trauma, leukaemia or sickle cell disease, and for other countries with different blood availability situation. This study is not free of limitations, including the model calculation, as we faced some difficulties in collecting the accurate data on e.g. the female employment rate, particularly in rural areas, salaries, and percentages of transfused patients. Moreover, other costs, such as cost of educating people to donate blood, cost of additional donation centres that could facilitate blood availability, and cost related to transport, logistics, storage at remote locations are not considered in the model.

In addition, the assumption that in the three countries of interest, 75%

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of women would not have blood transfusion available and 25% would have access to lifesaving blood transfusion, is supported solely by data and experience of the clinical experts from Ivory Coast, while such supportive evidence is lacking for Kenya and Ghana; due to lack of other data supportive of this assumption, further research is needed to identify the capacity of these countries to provide blood transfusion services. Finally, maternal mortality rates due to PPH likely vary depending on region, i.e. rural versus urban areas, and the level of care i.e. primary versus tertiary/quaternary facilities,

CONCLUSION

Our research suggests that in Kenya, Ghana and Ivory Coast, there is an absolute shortage of safe blood originating from the weaknesses in the blood supply chain, despite the considerable efforts to improve access to safe and adequate blood supplies. In the context of maternal deaths, the shortage of blood directly contributes to high maternal mortality from PPH in these countries. Furthermore, an expansion of the investment in blood safety value chain in these countries is likely to provide large positive economic returns in terms of preventing fatal PPH in less than two years.

Disclosures

Shirley Owusu-Ofori reports personal fees from Terumo Blood and Cell Techonologies outside the submitted work. Aicha Bah and Koenraad Dierick were employees of Terumo Blood and Cell Technologies at the time of the study conduct and publication development. Lucy Asamoah-Akuoko, Yassongui Mamadou Sekongo, Jamilla Rajab, Valerie Magutu and Mark Lamotte have nothing to disclose.

Author contributions

All authors were involved in the data collection and interpretation, reviewed and approved the manuscript prior to submission.

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SUPPLEMENTARY FILES

Supplementary file 1. PubMed search strategy

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "hemorrhage"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "blood shortage"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "blood supply"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "Blood Availability"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "Blood donation"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "Blood demand"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "Blood transfusion"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "Maternal bleeding"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "pregnancy"[Title/Abstract]

("Kenya"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "ivory coast"[Title/Abstract] OR "Africa"[Title/Abstract]) AND "collection"[Title/Abstract]

Supplementary file 2. Sensitivity analysis and simplification

The net economic impact of blood transfusion in PPH can be calculated using the following equation:

$$\boldsymbol{Q = [I' * C] - P}$$

where

$\boldsymbol{Q}$ = Net economic impact of blood transfusion in PPH

$\boldsymbol{I'}$ = Employment adjusted value of a life

$\boldsymbol{C}$ = Number of avoidable deaths

$\boldsymbol{P}$ = Total cost of required PPH-associated blood transfusion per year

The above-mentioned mathematical expression can be further expanded into:

$$\boldsymbol{Q = [H * I * A * C'] - [M * L * B]}$$

where

$\boldsymbol{H}$ = Employment rate

$\boldsymbol{I}$ = Value of a life year lost per year

$\boldsymbol{A}$ = Number of births per year

$\boldsymbol{C'}$ = Transfusion save rate

$\boldsymbol{M}$ = Cost of collection, test, storage of a blood unit

$\boldsymbol{L}$ = Blood units required for massive blood transfusion

$\boldsymbol{B}$ = PPH-related mortality (cases)

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