Transfusion Medicine Reviews 34 (2020) 94–100

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage:
https://www.journals.elsevier.com/transfusion-medicine-reviews/

Selection of Blood, Blood Components, and Blood Products as Essential Medicines in 105 Low- and Middle-Income Countries

Washington T. Samukange, MSc [a,b], Helga Gardarsdottir, PhD [a], Hubert G.M. Leufkens, PhD [a], Aukje K. Mantel-Teeuwisse, PhD [a,*]

[a] Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht University, Utrecht, the Netherlands
[b] Paul Ehrlich Institut, Langen, Germany

ARTICLE INFO

Available online 9 November 2019

Keywords:
blood and blood products
selection of essential medicines
low- and middle-income countries

ABSTRACT

Blood products of human origin are essential treatment options for several diseases, for example, hemophilia. We studied the alignment of national essential medicines lists (NEMLs) of low- and middle-income countries (LMICs) with the World Health Organization (WHO) Model List for the selection of blood products of human origin. The most recent versions of NEMLs from all LMICs were studied for the inclusion of blood products of human origin (blood and blood components, plasma products, and immunoglobulins). Data obtained from 105 NEMLs were compared to the 2017 WHO Model List. The median number of blood products of human origin on the NEMLs was 4 (range: 0-10). Immunoglobulins were most frequently included (73%). Blood and blood components were the least selected products (15%). The uptake of plasma products was around 50%. Nine countries did not have any blood products of human origin on their NEMLs. Some NEMLs included blood products not listed on the WHO Model List (albumin, hepatitis A immunoglobulin, and cryoprecipitate). We observed variation in selection according to WHO region, income level, and year of NEML update. Alignment of NEMLs with the WHO Model List varied greatly for different groups of blood products, ranging from good uptake for immunoglobulins, reasonable uptake for plasma products, to poor uptake for blood and blood components. This heterogeneity in selection and inclusion of blood products of human origin on NEMLs may be partly explained as being due to specific country characteristics, but some of it may not be explained. Policy makers need to rely on evidence in making decisions about which blood products to select, include, and remove on their NEMLs.

Contents

* Corresponding author at: Aukje K. Mantel-Teeuwise, Utrecht Institute for Pharmaceutical Sciences (UIPS), Faculty of Science, Utrecht University, Utrecht, the Netherlands.
E-mail address: A.K.Mantel@uu.nl (A.K. Mantel-Teeuwisse).

https://doi.org/10.1016/j.tmrv.2019.10.005

Blood is a vital health care resource used in a broad range of clinical services. Red cell transfusion, in particular, has a therapeutic index that exceeds that of many common medications and is generally credited with saving millions of lives [1]. Worldwide access to this life-saving intervention is limited to relatively few [2]. For example, around 5 million units of blood are collected annually in Africa, and this accounts for only 4% of the global blood donations, although this region is home to around 13% of the global population [3]. Furthermore, the annual demand for safe blood in Africa is estimated to be more than 8 million units, meaning that around 50% of the demand is being met, with a similar trend being observed in South East Asia [3].

To underscore the essential role of plasma, plasma used in transfusion, and plasma-derived medicinal products (PDMPs), the 19th World Health Organization (WHO) Expert Committee on the Selection and Use of Essential Medicines considered and approved an application to add blood and blood components (whole blood, red blood cells, platelets, and fresh frozen plasma) to the core list of the WHO Model List of Essential Medicines in 2013 [4]. Essential medicines (EMs) are defined by WHO as those medicinal products that satisfy the health care needs of the majority of the population [5]. For selection as an EM, due regard to disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness is made. To be added to the WHO EM list, any person or organization can submit an application to the WHO Secretariat, and the expert committee will make a decision based on the criteria described above. EMs are intended to be available within the context of functioning health systems at all times, in adequate amounts, in the appropriate dosage forms, with assured quality, and at a price the individual and the community can afford [5].

The purpose of adding blood and blood products to the EM list was meant to provide a boost for the awareness of the global need for blood and of blood's vital role in public health [6]. By developing its Model List of EMs, the WHO aims to help countries prioritize and select the medicines to include in their national essential medicines lists (NEMLs) [6]. In many countries, this list forms the basis of national drug policies, helps to define the minimum medicine needs for a basic health system, and forms the basis for standard treatment guidelines and procurement of medicines, especially in low- and middle-income countries (LMICs) [5,6].

Several studies have described the alignment of NEMLs and the WHO Model List for at least 5 different medicines or disease areas such as oncology medicines [7] and diabetes [8]. In the current study, we evaluated the level of alignment between NEMLs and WHO's 2017 Model Lists of EMs by determining the degree of inclusion of blood products of human origin in NEMLs in LMICs as our main aim. Secondly, we evaluated the correlations between the numbers of blood, blood components, and blood products included in the national medicines lists and several country characteristics.

Methods

Data Collection and Classification

The latest available NEMLs from all LMICs across all WHO regions were obtained from publicly available sources including the WHO Web site and WHO country offices (April 2018). The latest available update of the NEML was included in the analysis for each country (https://www.who.int/selection_medicines/country_lists/en/). The 2017 WHO EMs Model List was used as the reference list. Medicines were included in this study if they were classified as "blood products of human origin." The available NEMLs on the WHO Web site are updated annually according to the latest received NEML from the countries. The 10 medicines shown in Table 1 were listed as blood products of human origin in the 2017 WHO Model List. In addition, we identified all blood products of human origin included in the NEMLs but not in the WHO Model List.

Translations were obtained for the NEMLs that used the Cyrillic alphabet and/or were not in English, that is, those of the Russian Federation, Kyrgyzstan, Macedonia (Republic of Macedonia), and Serbia. The translators were all native speakers and were given the list of medicines in Table 1 to search from the non-English NEMLs. No distinction was made on the basis of the form and strength of any blood and blood product.

For each country, data on annual per-capita government health expenditure were obtained from WHO's Global Observatory (https://www.who.int/gho/en). Information on per-capita gross national income (GNI) used was based on the Atlas method and obtained from the World Bank (https://data.worldbank.org/indicator/NY.GNP.PCAP.PP.CD).

Data Analysis

We report the proportions of countries that included, on their NEMLs, each of the blood products of human origin on the 2017 WHO Model List according to classifications shown in Table 1. We also report the median numbers and interquartile ranges for the number of medicines included in the NEMLs by World Bank income group and by WHO region. The frequency of countries including "other medicines" that are blood products of human origin not included in the WHO Model List on their NEMLs was also identified, and the median occurrence by World Bank income group and by WHO region was calculated. Additionally, we analyze the data stratified by WHO regions and World Bank income group. We also sort the data according to the NEMLs updated between 2013 and 2018.

Nonparametric tests were used to assess differences in the median number of included essential blood and blood products in NEMLs. The Mann-Whitney test was used to investigate and compare the differences between number of blood products of human origin on NEMLs updated before 2013 vs those updated in 2013 or thereafter (2013 being the first year of inclusion of blood components on the WHO

Table 1
Essential blood products of human origin on the 2017 WHO 20th Essential Model List

Product	WHO 20th EML 2017	
Blood and blood components	Fresh-frozen plasma	
	Platelets	
	Red blood cells	
	Whole blood	
Immunologicals	Sera and immunoglobulins	Anti-D immunoglobulin (human)
		Anti-rabies immunoglobulin (human)
		Anti-tetanus immunoglobulin (human)
Plasma-derived medicines	Human immunoglobulins	Normal immunoglobulin
	Blood coagulation factors	Coagulation factor VIII
		Coagulation factor IX

Table 2
Countries included in the study and year that the latest national essential medicines list was issued, 2018

Income group	Region	Number	Total
Low income	Africa	21	24
	Benin 2009, Burkina Faso 2014, Burundi 2012, Central African Republic 2009, Chad 2007, DR Congo 2010, Eriteria 2010, Ethiopia 2015, Guinea 2012, Liberia 2017, Malawi 2015, Mali 2008, Mozambique 2017, Rwanda 2015, Senegal 2013, Sierra Leone 2010, Somalia 2014, Tanzania 2017, Togo 2012, Uganda 2016, Zimbabwe 2015		
	Americas	1	
	Haiti 2012		
	Eastern Mediterranean	1	
	Afghanistan 2014		
	South East Asia	1	
	Nepal 2016		
Low-middle income	Africa	11	43
	Angola 2008, Cabo Verde 2009, Congo Republic 2013, Côte d'Ivoire 2014, Ghana 2017, Kenya 2016, Maurutania 2008, Nigeria 2010, Sudan 2014, Eswatini 2012, Zambia 2013		
	Americas	5	
	Bolivia 2013, El Salvador 2010, Guatemala 2013, Honduras 2011, Nicaragua 2013		
	Eastern Mediterranean	6	
	Djibouti 2007, Jordan 2011, Morocco 2012, Syrian Arab Republic 2014, Tunisia 2008, Yemen Republic 2009		
	Europe	5	
	Armenia 2010, Georgia 2007, Krygyz Republic 2009, Moldova 2009,Tajikistan 2009		
	South East Asia	7	
	Indonesia 2011, Vietnam 2008, Bangladesh 2017, India 2015, Pakistan 2016,Sri Lanka 2014, Timor-Leste 2015		
	Western Pacific	9	
	Cambodia 2012, Bhutan 2016, Lao PDR 2016, Myanmar 2010, Papua New Guinea 2012, Philippines 2008, Solomon Islands 2017, Kiribati 2009, Vanuatu 2007,		
Upper-middle income	Africa	4	38
	Algeria 2007, Botswana 2012, Namibia 2016, South Africa 2015		
	Americas	15	
	Belize 2011, Brazil 2017, Colombia 2011, Costa Rica 2014, Cuba 2012, Dominica 2015, Ecuador 2009, Guyana 2010, Jamaica 2015, Mexico 2009, Panama 2017, Paraguay 2009, Peru 2012, St. Vincent and the Grenadines 2010, Suriname 2014		
	Eastern Mediterranean	3	
	Iran 2014, Iraq 2010, Lebanon 2014		
	Europe	7	
	Bulgaria 2018, Croatia 2010, Macedonia FYR 2010, Montenegro 2011, Russian Federation 2012, Serbia 2010, Turkey 2018		
	South East Asia	2	
	Maldives 2011, Thailand 2012		
	Western Pacific	7	
	China 2012, Fiji 2015, Malaysia 2016, Marshall Islands 2007, Nauru 2010, Tonga 2007, Tuvalu 2008		

Model List), and the Kruskal-Wallis test for comparison between the number of blood products of human origin and geographic regions, and income groups. Correlations between the total numbers of blood products listed and per-capita GNI and current health expenditure per capita were evaluated using the Pearson correlation coefficients (r). All statistical analyses were conducted using SigmaPlot software, version 13, and Excel (Microsoft, Redmond, WA).

Results

Using the World Bank database, a total of 139 countries met the criteria for LMICs in March 2018. Thirty-four countries were excluded from this study because either the NEMLs could not be translated (Belarus, Mongolia, Ukraine, and Uzbekistan) or were unavailable from the public sources used at time of data collection (n = 23, April 2018) or NEMLs were dated before 2007 (n = 7). The latter was done because WHO periodically encourages countries to update their NEMLs. Eventually, 105 LMICs' NEMLs (Table 2) were included in the analysis. Of the countries studied, 24 were low income (23%), 43 were lower-middle income (41%), and 38 were higher-middle income (36%). The median year of release of the most recently available national medicines list was 2012 with a range (min-max) from 2007 to 2018. Forty-five (43%) countries studied had updated their NEMLs since the addition of blood and blood components to the WHO Model List in 2013.

The median number of blood products of human origin included in the NEMLs was 4 out of the 10 blood products included on the WHO Model List. Only 38 countries (36%) had included at least 6 of the 10 listed essential blood products on their NEMLs, and 6 countries (6%) had all 10 essential medicines on their NEMLs (Figure 1). Nine countries (Algeria, Angola, Colombia, Kiribati, Marshall Islands, Vanuatu, Solomon Islands, Somalia, and Tuvalu) did not have any essential blood and blood products on their NEMLs.

Overall, blood and blood components were the least included essential medicines on the NEMLs studied, available in less than 15% of the countries studied (Figure 2). Uptake of plasma-derived medicines such as human normal immunoglobulin, coagulation factor VIII, and factor IX was reasonable at around 50%. Immunoglobulins were the most widely selected blood and blood product, with all 3 products, namely, human anti-D immunoglobulin, human antirabies immunoglobulin, and human antitetanus immunoglobulin, available in more than 70% of the country lists studied, especially in low-income countries. Some differences in selections of blood products of human origin were observed when the data were stratified according to WHO regions (see Supplementary Figures S1A and B). Restricting the analysis to NEMLs updated after 2013 did yield similar results (see Supplementary Figure S2).

The category “other medicines” was created for medicines encountered on NEMLs which fit the description of “blood products of human origin” but are not listed on the WHO EML. These included albumin, fibrinogen, cryoprecipitate, factor VII, factor X, plasma protein, and the anti–hepatitis A immunoglobulin. Albumin was selected in more country NEMLs than the other non-WHO EM listed blood products of human origin, with selection in more than half (53%) of the countries studied (Figure 3). Albumin was included in more NEMLs in the Eastern

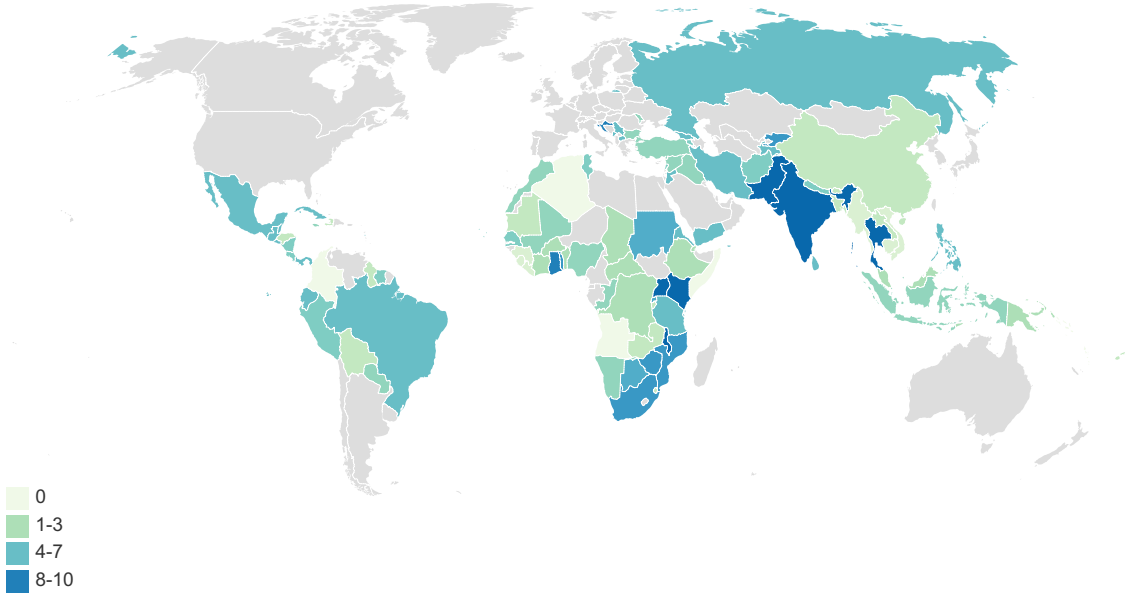

Fig. 1. Number of selected essential blood products of human origin found on NEMLs in 105 LMICs.

Mediterranean, Europe, and Americas than in the other regions (see Supplementary Figure S1B). The appearance of other products, namely, plasma protein, factor X, factor VII, fibrinogen, anti–hepatitis B immunoglobulin, and cryoprecipitate, was relatively low (Figure 3).

The number of essential blood and blood products on NEMLs differed significantly across the WHO regions ($P = .002$), with countries from the European region having higher numbers of products compared to countries from the Western Pacific region. No considerable differences in number of essential blood and blood products included in NEMLs across the World Bank income groups were observed; a median of 3.5 (min-max: 0-10) was included in low-income countries, 4 (min-max: 0-10) in lower-middle-income countries, and 5 (min-max: 0-10) in upper-middle-income countries ($P = .635$). The correlation between the total number of essential blood products of human origin listed and per-capita GNI was weak and not statistically significant ($P = .288$, $r = 0.107$). The number of blood products on NEMLs updated in and after 2013 was significantly different to that observed on NEMLs updated before 2013 ($P = .045$). Additionally, no correlation was observed between the current government health expenditure and the total number of essential blood products ($P = .563$, $r = 0.058$).

A third of the countries from the African region included at least 1 blood and blood component as an essential medicine in comparison to countries in the Americas and the Eastern Mediterranean regions which did not include any blood and blood component on their

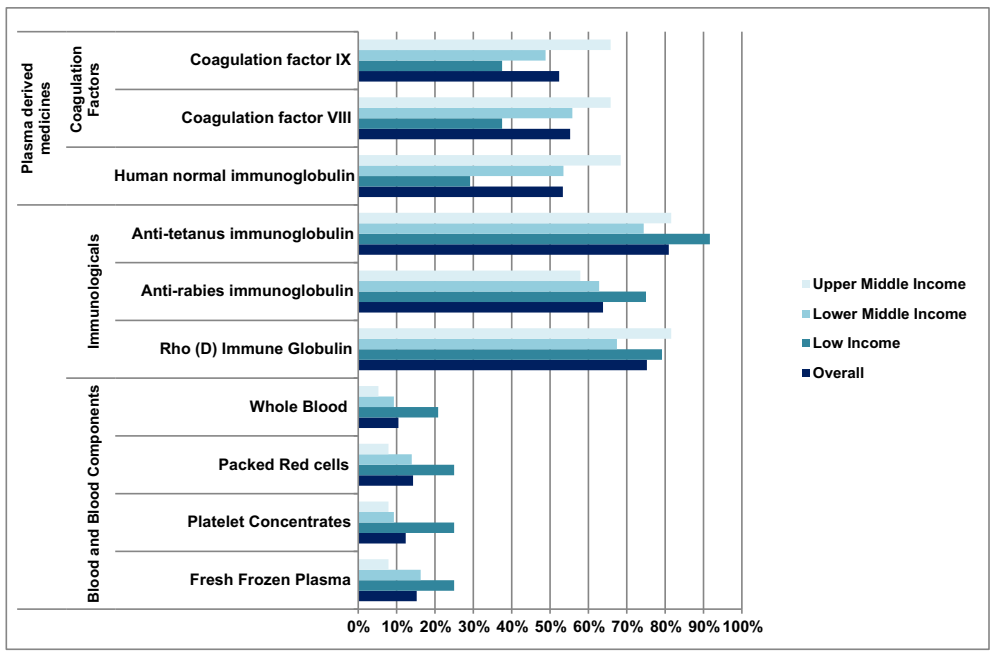

Fig. 2. Overall inclusion blood products of human origin in 105 NEMLs and by income region. Low income, n = 24; lower middle income, n = 43; and upper middle income, n = 38.

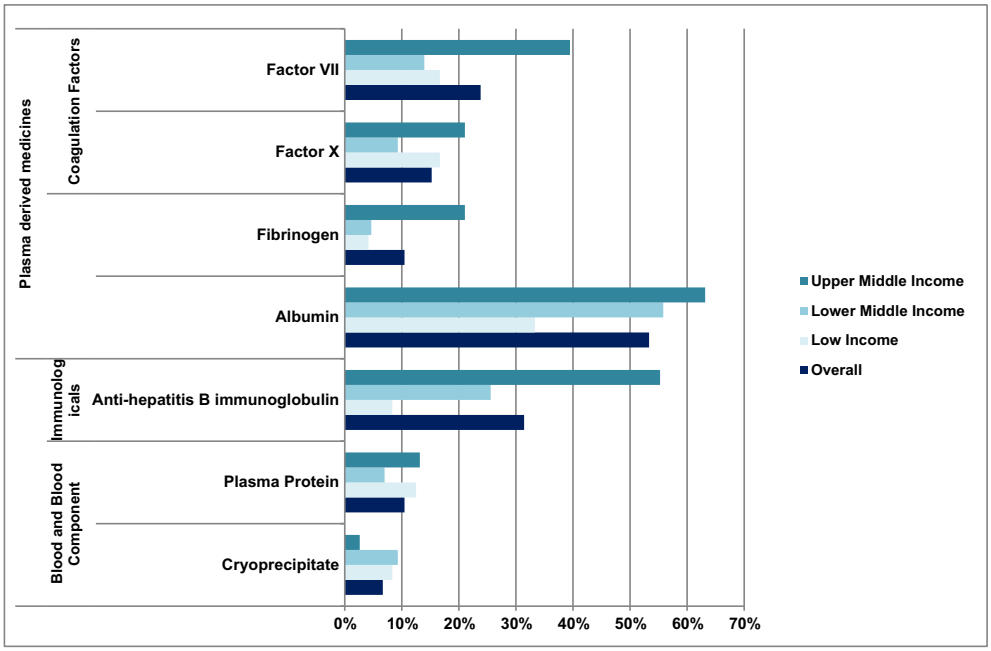

Fig. 3. Overall inclusion "other medicines" in 105 NEMLs and by income region. Low income, n = 24; lower middle income, n = 43; and upper middle income, n = 38.

NEMLs. Blood and blood components were listed in 25% of low-income countries, which was higher than in any other income regions, but differences were not significant ($P = .138$). Out of 45 countries who updated their NEMLs after the 2013 addition of blood and blood components to the WHO Model List, only 10 had included blood and blood components as essential medicines.

The listing of plasma-derived medicines as essential medicines was more frequent in upper-middle-income countries than in lower-middle-income countries (Figure 2). The numbers of plasma-derived essential medicines that appeared on national medicines lists differed considerably across World Bank income groups ($P = .011$). Human normal immunoglobulin was poorly represented in the African region and in low-income countries, with only 40% of African countries and less than 30% of low-income countries including this essential medicine. The inclusion of all 3 plasma-derived medicines on the NEMLs in upper-middle-income countries was more than 66%.

In upper-middle-income countries, albumin appeared in 63% of the NEMLs, whereas anti–hepatitis B immunoglobulin was listed in more than 55% of the NEMLs. The appearance of albumin on NEMLs did not differ significantly across the income regions ($P = .068$), whereas for the anti–hepatitis B immunoglobulin, a significant difference was observed between the low-income and upper-middle-income groups ($P = .002$).

Discussion

We noted that there was a good uptake in NEMLs of immunoglobulins (60%-70%) in NEMLs, particularly tetanus and rabies in low-income countries, and a reasonable uptake of plasma products (40%-50%) and a poor uptake of blood and blood components (10%-20%). Moreover, we also observed a number of blood products of human origin on NEMLs which are not on the WHO Model List, namely, albumin, fibrinogen and plasma proteins, coagulation factors VII and X, anti–hepatitis B immunoglobulin, and cryoprecipitate. The overall median number of blood products of human origin (medicines) included in NEMLs that aligned with the 2017 WHO Model List was 4. Nine countries did not have any blood product on their NEMLs.

The recently added blood and blood components were listed on NEMLs of fewer countries when compared with plasma-derived medicines which have been on the WHO EM list for decades. [9] The selection of blood and blood components in NEMLs was suboptimal, a finding previously reported for selection of essential medicines for oncology [7]. Despite the significant progress made in the addition and listing of blood and blood components in the Model List, this study has revealed that subsequent translation of this addition to country NEMLs is much lower than anticipated at the time of inclusion of blood components on the WHO Model List in 2013. There has not been an immediate response by governments and policymakers in LMICs to add whole blood, packed red cells, platelets, and fresh frozen plasma to their NEMLs. A possible reason for the absence of blood and blood components on NEMLs in the majority of countries in this study is that this class of blood products may not be classified as a medicine under current legislation [10]. Some countries in our study such as Bulgaria, Croatia, and Serbia define *blood* as either a substance of human origin or tissue [10]. Any subsequent change in definitions may have far-reaching implications in these countries which include regulatory oversight and associated cost implications. Elsewhere in Africa and South East Asia, legal definitions for blood for transfusion as a medicinal product or substance of human origin are not adequately articulated in legal texts [3]. Regardless, in the African region, there were more countries with blood and blood components on their NEMLs when compared with the other WHO regions.

Antirabies and antitetanus immunoglobulins were well represented and available in more than of the NEMLs studied. The selection of immunologicals differed significantly across the WHO regions in line with previously reported epidemiological circumstances in those regions [11]. Several studies noted a high burden of rabies [12,13] and tetanus [14,15] in, for example, India, Pakistan, and Nigeria, countries where we also observed a high selection for immunoglobulins. The influence of burden of disease as well as income levels of countries has been widely reported to affect the selection of medicines listed in a country's NEML [11,16]. This selection process may to a large extent be a result of policymakers being reasonably informed about their national health care priorities [7].

The burden of primary immune disease and hemophilia for which plasma-derived medicines are the most important, if not the only treatment option, is low or either relatively unknown in sub-Saharan African countries [17]. Upper-middle-income countries such as Brazil and regions where primary immune diseases and hemophilia were more frequently reported in literature appeared to select more essential plasma-derived medicines on their NEMLs [18,19]. The African and Western Pacific regions had the lowest median number of plasma-derived medicines with 1 (range: 0-3) and 0.5 (range: 0-3), respectively.

Essential plasma-derived medicines are imported at considerable cost and remain very expensive, which may lead to inadequate access in low-income countries [20]. The observations made in this study regarding the noninclusion of plasma-derived medicines in low-income countries' NEMLs could contribute to the widely reported unequal access to essential orphan medicines (for patients of hemophilia and primary immune diseases) in sub-Saharan Africa and Asia when compared with upper-middle- and high-income countries [20,21].

Our study found several blood products that are not included on the WHO Model List. These include previously listed and now deleted albumin (2000), fibrinogen, and plasma proteins (1983). In addition, coagulation factors VII and X, anti–hepatitis B immunoglobulin, and cryoprecipitate were present on some NEMLs. Albumin was represented in more than half of the NEMLs. The deletion of albumin from the WHO Model List was a result of a review by the Cochrane Collaboration which indicated the possibility of previously unrecognized hazards and lack of evidence of efficacy of albumin compared with alternatives [22]. This highlights the need for reliance on evidence in decision making about the selection of medicines on NEMLs in the countries involved [23]. This type of listing, without consulting the WHO Model EM List, may lead to countries investing in medicines that offer inadequate overall benefit and may have potential harm [23].

An important observation was the inclusion of cryoprecipitate in 7% of the NEMLs. This blood component is currently not on WHO Model EM list. Cryoprecipitate is available as therapy for hemophilia A, von Willebrand disease, and major hemorrhage [24,25]. Compared to blood coagulation factors and fibrinogen, cryoprecipitate provides a cheaper alternative therapy [24,25] for the small population of hemophilia patients in low-income countries such as Kenya and Zimbabwe [18], where this product is a treatment option. Systematic reviews to compare the effectiveness of fibrinogen and cryoprecipitate have not been able to make a recommendation, and no mortality difference was observed [26]. The same argument made to list orphan medicines such as coagulation factors VIII and IX on the EML can be used to support the listing of cryoprecipitate as an essential medicine in view of its cheaper production costs. However, a big concern about the safety of use of cryoprecipitate over potential transmission of blood borne pathogens remains, mostly in Europe [27].

Although this study included the large majority of LMICs, the results we present here should not be interpreted on their own. We selected the 2017 WHO Model List as the reference list for this study because it was the most recent available WHO Model List following the 2013 inclusion of blood and blood components to the Model List. Essential blood products of human origin are selected and provided in varying settings in LMICs. The results of this study should be considered with caution because there are several limitations. The cross-sectional nature as opposed to a longitudinal study design did not allow for the evaluation of direct access to essential blood and blood products in the countries. Although the lists we used are considered valid at the time of data collection, there are possibilities of missing recent updates. The direct measurement of access and availability of blood products of human origin has not been studied so far in LMICs and would be an important next step.

Conclusion

Selection of essential blood, blood components, and blood products was explored in this study as a prerequisite of access to this specific and important group of essential medicines which is often neglected by policy makers. The level of uptake of blood products of human origin on NEMLs is a crucial first step in making these medicines available. This study provides evidence that selection of blood products, especially blood and blood components, is suboptimal in LMICs, which may impact patients' access to these treatment options. The selection and inclusion of blood products of human origin in NEMLs are highly heterogeneous, and part of this might be justified as due to specific country characteristics, but some of it may not be explained. Policymakers need to rely on evidence in making decisions about which medicines to select, include, or remove on their NEMLs. More importantly, governments should regularly update their NEMLs.

Contributors

AKMT, HG, and WS were involved in the conception of the study. WS did the data collection and analysis and wrote the first draft of the manuscript. All authors contributed to study design, interpretation of results, and editing of the manuscript.

Declaration of Interest

We declare no competing interests.

Acknowledgments

The authors wish to thank Ivana Škrnjug, Alexandru Rusu, and Boyan Todorov for help in translating some of the NEMLs from non-English languages. We thank Dr Micha Nübling for carefully reading the manuscript.

This research was supported by the German Federal Ministry of Health's Global Health Protection Programme based on a decision by the German Bundestag.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tmrv.2019.10.005.

References

[1] Klein HG. Should blood be an essential medicine? N Engl J Med 2013;368(3):199–201.
[2] Lancet T. Improving blood safety worldwide. The Lancet 2007;370(9585):361.
[3] World Health Organization. Global status report on blood safety and availability. Geneva. Switzerland: World Health Organization; 2016; 2017.
[4] World Health Organization. The selection and use of essential medicines: report of the WHO Expert Committee, 2013 (including the 18th WHO model list of essential medicines and the 4th WHO model list of essential medicines for children). Geneva: World Health Organization; 2014.
[5] Robertson J, Magrini N, Barr R, Forte G, Ondari C. Medicines for cancers in children: the WHO model for selection of essential medicines. Pediatr Blood Cancer 2015;62(10):1689–93.
[6] Robertson J, Barr R, Shulman LN, Forte GB, Magrini N. Essential medicines for cancer: WHO recommendations and national priorities. Bull World Health Organ 2016;94(10):735–42.
[7] Bazargani YT. Boer A de, Schellens JHM, Leufkens HGM, Mantel-Teeuwisse AK. Selection of oncology medicines in low- and middle-income countries. Ann Oncol 2014;25(1):270–6.
[8] Bazargani YT. Boer A de, Leufkens HGM, Mantel-Teeuwisse AK. Selection of essential medicines for diabetes in low and middle income countries: a survey of 32 national essential medicines lists. PLoS ONE 2014;9(9):e106072.
[9] Persaud N, Jiang M, Shaikh R, Bali A, Oronsaye E, Woods H, et al. Comparison of essential medicines lists in 137 countries. Bull World Health Organ 2019;97(6):394–404C.

[10] The European Parliament and the Council of the EU. Directive 2002/98/EC of the European Parliament and of the council: setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood componentsand amending Directive 2001/83/EC. In: Official Journal of the European Council; 2003; 30–40.
[11] Mahmić-Kaknjo M, Jeličić-Kadić A, Utrobičić A, Chan K, Bero L, Marušić A. Essential medicines availability is still suboptimal in many countries: a scoping review. J Clin Epidemiol 2018;98:41–52.
[12] Fooks AR, Cliquet F, Finke S, Freuling C, Hemachudha T, Mani RS, et al. Rabies. Nat Rev Dis Primers 2017;3:17091.
[13] Taylor LH, Nel LH. Global epidemiology of canine rabies: past, present, and future prospects. Vet Med (Auckl) 2015;6:361–71.
[14] Thwaites CL, Loan HT. Eradication of tetanus. Br Med Bull 2015;116:69–77.
[15] Thwaites CL, Beeching NJ, Newton CR. Maternal and neonatal tetanus. The Lancet 2015;385(9965):362–70.
[16] Bazargani YT, Ugurlu M. Boer A de, Leufkens HGM, Mantel-Teeuwisse AK. Selection of essential medicines for the prevention and treatment of cardiovascular diseases in low and middle income countries. BMC Cardiovasc Disord 2018;18(1):126.
[17] Naidoo R, Ungerer L, Cooper M, Pienaar S, Eley BS. Primary immunodeficiencies: a 27-year review at a tertiary paediatric hospital in Cape Town, South Africa J Clin Immunol 2011;31(1):99–105.
[18] Stonebraker JS, Bolton-Maggs PHB, Soucie JM, Walker I. Brooker M. A study of variations in the reported haemophilia A prevalence around the world. Haemophilia 2010;16(1):20–32.
[19] Errante PR, Franco JL, Espinosa-Rosales FJ, Sorensen R, Condino-Neto A. Advances in primary immunodeficiency diseases in Latin America: epidemiology, research, and perspectives. Ann N Y Acad Sci 2012;1250:62–72.
[20] Strengers PFW, Klein HG. Plasma is a strategic resource. Transfusion 2016;56(12):3133–7.
[21] Farrugia A, Cassar J. Plasma-derived medicines: access and usage issues. Blood Transfus 2012;10(3):273–8.
[22] Roberts I, Blackhall K, Alderson P, Bunn F, Schierhout G. Human albumin solution for resuscitation and volume expansion in critically ill patients. Cochrane Database Syst Rev 2011;11:CD001208.
[23] Jeličić Kadić A, Žanić M, Škaričić N, Marušić A. Using the WHO essential medicines list to assess the appropriateness of insurance coverage decisions: a case study of the Croatian national medicine reimbursement list. PLoS ONE 2014;9(10):e111474.
[24] Novak A, Stanworth SJ, Curry N. Do we still need cryoprecipitate? Cryoprecipitate and fibrinogen concentrate as treatments for major hemorrhage—how do they compare? Expert Rev Hematol 2018;11(5):351–60.
[25] Wong H, Curry N. Do we need cryoprecipitate in the era of fibrinogen concentrate and other specific factor replacement options? VOXS 2018;13(1):23–8.
[26] Jensen NHL, Stensballe J, Afshari A. Comparing efficacy and safety of fibrinogen concentrate to cryoprecipitate in bleeding patients: a systematic review. Acta Anaesthesiol Scand 2016;60(8):1033–42.
[27] Nascimento B, Goodnough LT, Levy JH. Cryoprecipitate therapy. Br J Anaesth 2014;113(6):922–34.