

# A systematic review of indications when and how a military Walking Blood Bank could bridge blood product unavailability

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**Background** - Blood supply problems in remote areas are well known. To overcome this shortage, many countries have developed innovative Walking Blood Bank (WBB) protocols. However, no common standards have yet been set for their use and common actions. Given that these procedures involve a certain risk, it would be interesting to analyse the activating criteria that lead to using this unusual protocol. Thus, this review aimed to identify indications for a WBB and the common risk mitigation measures.

**Material and methods** - This PRISMA-compliant review only included studies published from 1985 to 25<sup>th</sup> of January 2023 that describe adult male military casualties requiring blood transfused locally using a walking blood transfusion protocol. All relevant data (i.e., activation and contextual factors and risk mitigation measures) were tabulated to retrieve information from the selected military studies.

**Results** - Our results indicated that activation criteria were homogeneous across the 12 reviewed studies. Whole blood was collected from a WBB when there was a shortage of blood products and when platelets were needed. In the literature reviewed, the main risks associated with such a protocol, namely hemolytic adverse events and transfusion transmitted diseases, are mitigated by the use of typing and screening measures if they are reported. However, there is less consistency in the implementation of those risk mitigation measures.

**Discussion** - This unusual protocol needs to be integrated into the medical support plan until conventional transfusion support can take over, and should include on-site blood collection from a donor, whether a WBB or an emergency donor panel. The benefits of such a protocol outweigh the risks in a life-threatening situation, especially since these risks can be anticipated and minimised by planning to pre-screen all potential donors before their deployment. Finally, educating and training the staff who must implement this unusual procedure can also improve the safety and survival rate of future patients.

**Keywords:** *Walking Blood Bank, whole blood, emergency donor panel, indications, risk mitigation measures.*

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## INTRODUCTION

Over the last decade, transfusion medicine has evolved towards fractionated whole blood components such as red blood cells, platelets, or plasma, to improve the efficiency of storage and use in a standard hospital environment<sup>1</sup>. However, in austere environment (e.g., combat zones), military medical support must also provide the most appropriate product for the treatment of shock and coagulopathies, as hemorrhage remains a major cause of death among combat casualties<sup>2</sup>. Nevertheless, logistical constraints limit access and/or storage of these blood products<sup>3</sup>. The medical support system has been forced to adapt by developing innovative solutions that improve combat casualty care (e.g., DCR)<sup>4</sup>. They have therefore developed techniques, such as walking blood bank (WBB) protocol, to sufficiently access blood anywhere to support combat casualties until their evacuation<sup>5</sup> and thereby increase their survival rate<sup>6</sup>. A WBB is a pool of donors available "on call" to donate whole blood (WB) in the event of an emergency<sup>7</sup>. These donors are among those deployed and consent to be registered as prospective donors prior to deployment<sup>8</sup>.

In addition to its essential role in increasing the survival rate of hemorrhagic patients, WB also offers biological advantages by providing all the blood components in a single transfusion to counteract the lethal triad observed in hemorrhage patients<sup>9,10</sup>. Essential blood components are often in short supply on the battlefield, especially platelets. Due to their short shelf life –between 5 and 7 days depending on the country– platelets are usually unavailable. This is why the use of WB, which contains platelets, can be essential for the treatment of certain hemorrhagic patients in extreme environments. Whole blood transfusion seems to be the only accessible solution in logistically challenging situations. This solution would address the need for platelets and logistical issues<sup>9</sup>. Any disadvantages that may arise seems far outweighed by the benefits of such a transfusion<sup>11</sup>. While risks will always exist, we can control and mitigate them. The literature shows that if the donor is pre-screened and a clear protocol is followed<sup>11</sup>, WB transfusion from a WBB is safe and effective. WBB implementation currently appears to rely on several different protocol-driven techniques<sup>11</sup>.

There is no existing interoperable protocol for the use of WBB even within the NATO coalition based on different national regulations.

The aim of this review is to identify situations where the benefits exceed the risks of resorting to a military WBB by focusing on these two questions:

1. What military context leads to the activation of a WBB (when/where)? and
2. What measures can be taken to minimize the inherent risk of such an implementation on the battlefield?

## MATERIALS AND METHODS

This systematic review was conducted according to Preferred Reporting Items in Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

### Literature search and screening criteria

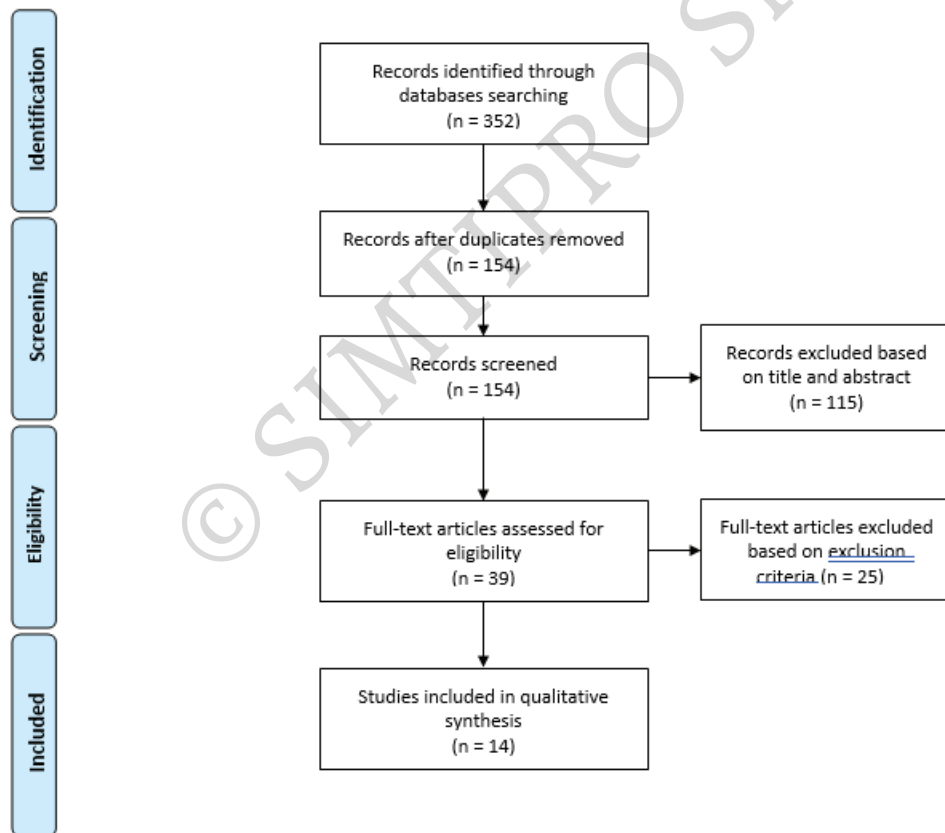
PubMed and Scopus databases were searched using the following keywords: "Walking blood bank"; "Walking AND blood AND bank"; "Emergency whole blood"; "Buddy transfusion"; "Blood far forward"; "Walking donor"; "Emergency donor panel" and "Warm fresh whole blood". All articles published from 1985 (after HIV appearance in blood transfusion) until 25<sup>th</sup> of January 2023 were considered.

### Selection of studies (exclusion and inclusion criteria)

First, the lead investigator identified relevant studies by reviewing the abstracts according to the inclusion and exclusion criteria. In addition, two authors independently assessed all the full texts, and then the full list of eligible studies was agreed by all the authors. The exclusion and inclusion criteria for study selection are described in **Table I**. Studies were included if they described male military adults who were injured and required transfusion of blood collected in the field according to a WBB protocol. Our research focused specifically on adult male military patients, who make up over 95% of our deployable at-risk-population. Furthermore, studies in women tend to reflect transfusion in a perinatal setting, which is not representative of managing bleeding patients in the military. Moreover, studies reporting field-tested protocols and information on at least two of the three outcomes of interest (see **Table I**) may be considered even if they did not include patients. A flowchart illustrating the selection procedure is presented in **Figure 1**.

**Table I - Exclusion and inclusion criteria for military study selection**

		Inclusion criteria	Exclusion criteria
<b>Screening</b>	<b>Language</b>	<b>Papers written in English</b>	<b>Papers written in all other languages</b>
	Study design	Prospective (including feasibility studies) or retrospective studies in international peer-reviewed journal	Unpublished material, communication, letter to the editor, reviews, and conference abstract
	Publication year	Papers published from 1986 onwards	Papers published up to 1985 to include the ITT related risk
	Participants	Military males adults if patients are involved	Females and children
<b>Eligibility</b>	Outcomes	At least 2 of 3: <ul style="list-style-type: none"> <li>• indication of resorting to a Walking Blood Bank</li> <li>• donor safety</li> <li>• recipient/patient safety</li> </ul>	Analysis of donor, patient, or use of the Walking Blood Bank apart
	Setting	Military setting	Civilian setting



**Figure 1 - PRISMA flowchart illustrating the entire selection process, from the literature search to the selection of studies of interest based on the inclusion and exclusion criteria**

The screening process allows the rejection of duplicates and papers that do not meet the inclusion criteria based on titles and abstracts (i.e., language, year of publication, study design and participants). The eligibility process involves full-text analysis of the remaining papers based on specific outcome criteria, namely the setting and reporting of at least 2 of the following 3 aspects: activation criteria, donor safety or/and patient safety.

**Data extraction and analysis**

The data were extracted by the lead author and checked by a second author to ensure accuracy. Disagreements were discussed and decision was taken by a third author. The literature review was divided into two steps: activation indicators and risk mitigation measures.

To retrieve information from the selected studies, several tables were created. All relevant data regarding the activation factors of a WBB are compiled in **Table II**. The following contextual factors were determined:

1. availability of a blood bank and type of product in stock,
2. type of patient injury,
3. type of emergency situation (i.e., massive transfusion, mass casualty, remote, or combinations of the above).

In addition, this table also included the activation criteria of the WBB as well as information on the type of WB used (i.e.: cold-stored WB or fresh warm WB).

All the mitigating and protective measures implemented in each study to minimize the risk associated with the use of a WBB were summarized in **Tables III to V**. These countermeasures were grouped into two categories: donor-related and patient-related. The latter were likely to occur at two different times, before deployment and on-site during blood collection. Information on donor-related activities is provided as follows:

1. donor screening before deployment and
2. donor screening at blood collection.

**Table II - Summary of the indications of activation of a Walking Blood Bank**

Authors	Basic situation			Walking blood bank activation	
	Blood bank product available?	Type of Injuries	Situation	Activation indicator	WB used
Lewis et al., 2020	Yes (CSWB + Full CT)	Blast injury, hemorrhage	Mass casualties, massive transfusion	Depletion of CSWB/evacuation impossible or delayed	FWB
Miller et al., 2018	Yes (frozen pRBC + FFP)	No specific injury described: Helicopter crash	Mass casualties, massive transfusion	Platelets needed/severe coagulopathy	FWB
Bassett et al., 2016	Yes (Full CT)	Traumatic amputations, blast injury, shrapnel injury	Massive transfusion	Combat injured patients likely to require massive transfusion (benefits from early activation)	FWB
Strandenes et al., 2015	No (no blood bank available)	No specific injury described: Feasibility study for Norwegian frigate conducting antipiracy operations	Remote situation	Planning	CSWB for banking
Garcia Hejl et al., 2015	Yes (pRBC, FDP)	No specific injury described: Feasibility study	Mass casualties, massive transfusion	Platelets needed/severe coagulopathy	FWB
Hrezo and Clark, 2003	No	Rectal bleeding	Remote situation	Shortage of blood products	FWB
Gaspary et al., 2020	Yes (CSWB + Full CT)	No specific injury described: feasibility study	Mass casualties, massive transfusion	Shortage of blood products (CS LTOWB serve to start massive transfusion until FWB become available from the WBB)	FWB
Hakre et al., 2013	Not reported	IED Blast	Mass Casualties, massive transfusion + remote situation	Shortage of blood products	FWB
Malsby et al., 2005	Not reported	Gunshot wound	Massive transfusion + remote situation	Shortage of blood products	FWB
Liu et al., 2014	Yes (RBC, FFP, PLT)	No specific injury described: Hit by a ship cable	Massive transfusion	To correct coagulopathy when all other blood products failed	FWB
Gaddy et al., 2021	No (any products available at POI)	Gunshot wound	Remote situation	Absence of blood products (transfusion after extraction before evacuation, POI)	FWB
Song et al., 2021	Yes (CSWB)	Blast injury	Remote situation	No access to stored blood product at the POI: Delay for evacuation	FWB

CSWB: cold stored whole blood; pRBC: packed red blood cells; FDP: freeze-dried plasma; CT: components therapy; FFP: fresh frozen plasma; RBC: red blood cells; PLT: platelets; POI: point of injury; IED: improvised explosive device; CS LTOWB: cold stored low titer O whole blood; FWB: fresh whole blood; WB: whole blood.

This distinction was made because fully equipped laboratories and remotely accessible laboratories differ greatly in terms of resources, procedures, availability, as well as the sensitivity and specificity of the tests used. The blood grouping, the type of screening

(i.e., infectious disease screening using questionnaire, nucleic acid testing, serology, or rapid test) and the virus tested were reported if mentioned. Donor screening included questionnaires and/or tests, and we considered both as one. The tests might differ depending on national

**Table III - Summary of the “typing” risk mitigation measure**

Authors	Type of WB	Pre-deployment	At collection
Lewis <i>et al.</i> , 2020	Type sp. & LTOWB	Not detailed	Not reported
Miller <i>et al.</i> , 2018	Type sp.	Only a 10% sample of on board personal	Confirmation
Bassett <i>et al.</i> , 2016	Not reported	Refer to CPG	Refer to CPG
Strandenes <i>et al.</i> , 2015	LTOWB + AWB	National standard procedure for regular donor in civilian health care: Grouping + titer	Confirmation (rapid test)
Garcia Hejl <i>et al.</i> , 2015	Type sp.	No reported	Type
Hrezo and Clark, 2003	Type sp.	Only a 10% sample of population	Type + Crossmatch
Gaspary <i>et al.</i> , 2020	LTOWB	Not reported	Samples collected on site and send back to homeland for titer analysis
Hakre <i>et al.</i> , 2013	OWB + AWB	Not reported	Not reported
Malsby <i>et al.</i> , 2005	OWB	Not detailed	Not reported
Liu <i>et al.</i> , 2014	Not reported	Not reported	Not reported
Gaddy <i>et al.</i> , 2021	Type sp. LTOWB prehospital	Yes: blood ID card	Confirmation by rapid test required but not executed due to tactical limitations - use of blood ID card
Song <i>et al.</i> , 2021	LTOWB	Not reported	Not reported

WB: whole blood; Type sp.: ABO type specific; LTOWB: low titer O whole blood; OWB: O whole blood; AWB: A whole blood; LTOWB: low titer O whole blood; CPG: clinical practice guidelines; ID: identification.

**Table IV - Summary of the “screening” risk mitigation measure**

Authors	Pre-deployment	At collection
Lewis <i>et al.</i> , 2020	Not detailed	Not reported
Miller <i>et al.</i> , 2018	Only a 10% sample of on board personal HBV - HCV - Syphilis - malaria	Rapid tests
Bassett <i>et al.</i> , 2016	Refer to CPG	Refer to CPG
Strandenes <i>et al.</i> , 2015	National standard procedure for regular donor in civilian health care	Combined rapid test
Garcia Hejl <i>et al.</i> , 2015	No reported	Questionnaire Rapid tests HIV, HCV + complete HBV vaccination
Hrezo and Clark, 2003	Only a 10% sample of population. Questionnaire Serologic tests: HIV, HCV, HBV, HTLV	Rapid testing
Gaspary <i>et al.</i> , 2020	Recommended JTS CPG but not executed	Rapid testing
Hakre <i>et al.</i> , 2013	Questionnaire Screening (90 days): HIV, HCV, HBV, Syphilis, HTLV, West Nile virus (sample back to the US). Complete HBV vaccination.	Rapid tests: HIV, HCV, HBV
Malsby <i>et al.</i> , 2005	Not detailed	Not reported
Liu <i>et al.</i> , 2014	Not reported	Not reported
Gaddy <i>et al.</i> , 2021	Not reported	Not reported
Song <i>et al.</i> , 2021	Not reported	Not reported

HBV: hepatitis B virus; HCV: hepatitis C virus; CPG: clinical practice guidelines; HIV: human immunodeficiency virus; HTLV: human T-lymphotropic virus; JTS: Joint Trauma system; TTD: transfusion transmitted diseases.

**Table V** - Summary of the patients' follow-up parameters

Authors	Patient follow-up/Measured indicators
Lewis <i>et al.</i> , 2020	TACO - Surgery - Recovery
Miller <i>et al.</i> , 2018	HR - Blood Pressure - pH - Lactate - Hb - PLT count
Bassett <i>et al.</i> , 2016	pH - BE - Hb. 30 days follow-up: survival + transfusion reaction/blood borne pathogens transfer - OR time - time to transfer
Strandenes <i>et al.</i> , 2015	Not reported
Garcia Hejl <i>et al.</i> , 2015	Sample for immunoassays infectious agents: HTLV, HIV, HBV, Syphilis + Nucleic Acid Testing: HIV, HCV, HBV
Hrezo and Clark, 2003	Blood count - PT/PTT - Hb - HR - BP - sO <sub>2</sub> . Sample for future serologic testing. 48 h follow-up - Surgery
Gaspary <i>et al.</i> , 2020	Sample back for pre-screening to add donor to register
Hakre <i>et al.</i> , 2013	Transfusion associated adverse events. TTD's: HTLV - WBC - Temperature
Malsby <i>et al.</i> , 2005	Pulse - BP - Surgery. Follow-up 4 weeks
Liu <i>et al.</i> , 2014	Temperature - HR - Respiratory rate - BP - Hb - PT- INR - PTT - PLT count - Calcium level - Surgery - Acute lung injury - Respiratory distresses
Gaddy <i>et al.</i> , 2021	sO <sub>2</sub> - BP - HR - Respiration - Pulse - Glasgow score - Surgery
Song <i>et al.</i> , 2021	Survival - Surgery

TACO: transfusion-associated circulatory overload; HR: heart rate; Hb: hemoglobin; PLT: platelets; BE: base excess; OR: operating room; HTLV: human T lymphotropic virus; HIV: human immunodeficiency virus; HBV: hepatitis B virus; PT/PTT: prothrombin time/partial thromboplastin time; BP: blood pressure; sO<sub>2</sub>: oxygen saturation; TTD: transfusion transmitted disease; WBC: white blood cells; INR: international normalized ratio.

requirements. Regarding the risk associated with the product, a distinction was made between the studies using only O WB and using type-specific blood or both depending on the situations. The tables also listed if the authors did consider the titer of hemolysins (low or not) in the product. All medical and related laboratory parameters helping to assess the patient's status were reported in the tables. Finally, the data concerning the patient's follow-up after transfusion were also included when available.

### Assessment of the quality of evidence

The quality of evidence was assessed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to rate the reliability of evidence from each included study. This was assessed by the lead author and independently verified by two others.

## RESULTS

### Search results

The literature search identified 352 records, of which 154 were assessed for eligibility after removing 198 duplicates. Based on title, abstract and article type, 115 studies were also excluded according to the inclusion and exclusion criteria defined in **Table I**. There was also one study exclusion on language grounds. The lead investigator identified 39 relevant studies through a review of abstracts against the exclusion criteria. Twelve papers agreed by all authors were included

in the review<sup>12-23</sup>. A summary of the results of the literature search is shown in **Figure 1**.

### Quality of evidence

Nine of the 12 included articles were case reports and series<sup>12,13,16-22</sup>. Therefore, they were all graded "very low" according to the GRADE system. There were also three prospective observational studies<sup>14,15,23</sup>. They were all graded as "low" quality according to the GRADE system. Clustering by repeat authors did not appear to be an area of potential bias. These low-quality gradings were mainly due to the observational design of all studies, putting them at risk of bias, imprecision, inconsistency and indirectness. There was no disagreement between the reviewers with regard to the risk of bias and the GRADE rating.

### Analysing results

#### Activation indicators of a WBB

Based on the situations considered (see **Table II**), the literature review identified four studies that only referred to a remote environment to support the use of a WBB<sup>17,21-23</sup>. Another reported having the WBB protocol ready to provide blood during an event combining remote situations, mass casualty and massive transfusion<sup>18</sup>. The remaining studies supported the activation of the WBB, either for massive transfusions<sup>16-20</sup>, or for a combination of mass casualties and massive transfusions<sup>12-15</sup>, or for a combination of massive transfusions and remote situations<sup>19</sup>.

Accordingly, apart from the study by Strandenes and colleagues<sup>23</sup>, all studies justified the use of a WBB as a response to shortages of blood products, and/or delays in evacuation (see **Table II**)<sup>12,13,22,14-21</sup>. Shortages were either contextual or caused by the depletion of available supplies due to acute point-in-time demand<sup>12,17-19,22</sup>. Some of the authors also pointed out the shortage of a specific blood component: blood platelets<sup>13,14,20</sup>. As platelets were often scarce on the battlefield, they could only be obtained from WB. Whole blood has made the difference in the stabilisation and recovery of coagulopathic patients with certain types of injuries resulting in bleeding casualties<sup>13,14,20</sup>.

All 9 retrospective studies described hemorrhagic patients with either uncontrollable bleeding or coagulopathy due to various traumatic injuries as the cause of injury leading to activation of a WBB (see **Table II**)<sup>12,13,16-22</sup>. Among the remaining three prospective studies, two studies evaluated the feasibility of setting up a WBB and the supply potential generated by implementing the protocol<sup>14,15</sup>, while the third one described the protocol they used to collect and bank WB from a pool of identified donors to anticipate potential needs on board<sup>23</sup>. It was also the only study to specify the use of cold-stored WB as a means of accessing and maintaining a “blood bank” without having home blood<sup>23</sup>.

### **Risk mitigation measures of a WBB**

#### **Linked to the donor**

Two measures are reported to be used to limit donor-related risks, namely blood typing (**Table III**) and donor screening (**Table IV**). Both can be performed in early pre-deployment planning and/or on-site at the time of collection.

Across studies, blood typing prior to deployment and its confirmation at the time of collection were often combined with the aim of establishing a registry of potential donors and their blood groups that could be confirmed at the time of collection<sup>13,16,17,21,23</sup>. Three studies focusing on patient or donor screening failed to report pre-deployment or on-site blood group typing<sup>18,20,22</sup>. The study by Song and colleagues reported on the use of a donor registry, but did not provide any details on the potential risk reduction measures that were taken either prior to deployment or at the time of collection<sup>22</sup>. Nevertheless, it seemed to be a relatively important measure as most authors reported

it, even though the protocols were quite different, and the lack of reporting did not mean that it was not done. The use of WB from only O donor, rather than type-specific or compatible blood, was reported in only 3 studies<sup>15,19,22</sup>. Furthermore, two studies did not even address this issue and did not specify the product used<sup>16,20</sup>.

For donor screening risk mitigation measures (i.e., tests or questionnaires), all details provided by authors are shown in **Table IV**. Eight studies reported pre-deployment screening as part of the donor registry planning in the preparedness phase<sup>12,13,15-19,23</sup> and seven at the time of collection<sup>13-18,23</sup>. Six studies performed pre-deployment and on-site screening<sup>13,15-18,23</sup>. Two studies did not report on-site testing but did report pre-deployment testing<sup>12,13,16-19</sup>, and one reported on-site testing but did not report pre-deployment testing<sup>14</sup>. Despite this, only two studies reported no screening at least once during the process<sup>20,21</sup>. In their study, Song and colleagues did not report any screening before or at the time of collection, but specified that the protocol was to “call” donors from a registry<sup>22</sup>.

#### **Linked to the patients**

It was not possible to identify only one or even a few important parameters for patient follow-up, as all authors used different parameters (see **Table V**), except for the prospective study by Strandenes et al, which used no parameters for follow-up<sup>23</sup>. From a transfusion perspective, the parameters reported in these studies can be divided into two main types:

1. the medical parameters, where the most commonly reported were blood pressure, heart rate, survival rate, surgery, transfusion reactions and laboratory parameters reflecting the status of the patient (e.g.: hemoglobin or pH, lactate)<sup>12,13,16,17,19-22</sup> and
2. adverse events related to TTDs or screening on sample return to the home country<sup>14-18</sup>.

Patient follow-up for potential TTDs was reported in five studies<sup>14-18</sup>. Hakre and colleagues focused their analysis on one patient's seroconversion following an on-site walking blood transfusion<sup>18</sup>.

### **DISCUSSION**

This review aimed to identify activation criteria for military WBB as well as the risk mitigation measures associated with their use.

Our first research question investigated the rationale for its application. Two main trends have been identified in the literature to justify the use of WBB protocols:

1. access to blood products in case of shortage (i.e., logistical indication of activation)<sup>12,15-23</sup> and
2. access to blood products for the treatment of a hemorrhagic patient when a required specific component is not available (i.e., clinical indication of activation)<sup>13,14,20</sup>.

All but two of the studies<sup>21,23</sup> reported on the use of fresh WB to overcome the shortage of blood products<sup>12-22</sup>. Gaddy *et al.* reported collecting blood for a casualty during a combat assault and withdrawing it at the site of injury. There was no shortage of blood, but blood was not immediately available on site<sup>21</sup>. Strandenes and colleagues, however, chose a different strategy, collecting blood to build up an emergency bank<sup>23</sup>. These two different strategies are equally acceptable and can be chosen according to the initial situation: collecting to meet a specific need based on a shortage or creating a bank based on an absence. Yet, both strategies are named differently: one is called a “Walking Blood Bank” while the other is called an “Emergency Donor Panel” (EDP). The NATO Blood Panel recently discussed this difference<sup>24</sup>. It was decided that the WBB refers to WB collected for banking. In contrast, the emergency donor panel refers to a pool of pre-screened donors who are ready to give blood for immediate use without banking<sup>24</sup>. One may notice that this distinction is not yet clear in the literature. Therefore, to ensure that all studies were included, we decided to extend our search to the most used terms in the literature. Furthermore, all authors reported using this protocol to avoid overwhelming their designated transfusion system for highly demanding patients presenting with uncontrolled bleeding leading to massive transfusion or hemorrhagic shock. As previously reported in the literature, WB is an essential resource for DCR, e.g., at sea, it offers operational flexibility as the use of component therapy, the ratio “1:1 RBC”: FFP” is not always and everywhere sustainable<sup>23</sup>. Our analysis led us to the same conclusion. The use of FWB collected on site could become, in exceptional situations, the only solution to access blood and save lives. While this review focuses only on the military setting, it was also used in isolated and large geographical areas presenting blood supply

challenges comparable to military theatres (e.g.,<sup>25-28</sup>). The Norwegian Preparedness Plan is the more developed and published model for using WBB/EDP in the civil world when geography or supply is difficult to secure<sup>27</sup>.

Finally, some authors reported choosing to use FWB in order to obtain a clinical advantage<sup>20</sup>, as FWB offers a better survival rate in hemorrhagic shock<sup>29</sup>. However, it is still a highly controversial topic as the purported benefits of FWB are still not clearly evidence based<sup>30,31</sup>.

Concerning our second research question, while the awareness of risk is common to all articles, the protocols differ in their implementation regarding the use of risk mitigation measures, both in terms of the type of test and the timing of its implementation. Our review showed that risks related to both donors and products need to be considered. It is well established in the literature that FWBs should come from pre-screened donors to reduce the higher risk of TTD<sup>29</sup>. However, in our review, even if both TTD screening and blood typing are considered to reduce the risk, the techniques used, and the timing of the interventions varied widely and did not allow standardization of practice. There are two main explanations for this. The first one would be the national regulation, which is quite specific to each country. Therefore, because all requirements and protocols are different (Germany, USA, UK, Canada)<sup>32</sup>, interoperability in the use of WBB cannot be adopted by all NATO members. As it also depends on the prevalence in the home country, there are no standards for TTD screening<sup>29</sup>. The second one relates to the bias inherent to the design. Most of the reviewed studies were case studies. This implies that the data used are those that are available a posteriori and some of the data may be missing without necessarily indicating that the procedure such as testing was not carried out. Furthermore, it is also possible that some information is missing because the authors choose to omit reporting some data and not because the full test was not carried out. Not reporting did not mean that it did not happen. Regarding the product used, it would be more convenient in terms of the risk of transfusion reactions to use only O donors. However, our results do not reflect this. Most authors reported using ABO type specific WB, but unfortunately did not rationalise their choice<sup>12-14,17,18,21,23</sup>. Indeed, O donors represent approximately 45% of the



Caucasian population, whereas A donors represent approximately 45% of the same population. By limiting the sample to O donors, an important part of the donor pool is excluded. This may be important for obtaining sufficient resources. Nonetheless, this presupposes that the typing has been determined pre-deployment or at the time of donation. In addition, some authors report also considering the hemolysin titer in O WB<sup>12,15,21-23</sup>. However, there is no consensus on titer determination, either from a technical point of view or from a cut-off point of view. Therefore, not every nation would consider a donor as a low titre donor using the same levels. This is part of the limitation of the use of low titers in an international setting<sup>33</sup>. This would lead to complications in communication, monitoring and interoperability decisions. Finally, patient outcomes were also considered in the studies reviewed, but there was no evidence of a consensus on these and their reporting was inconsistent. Nevertheless, all efforts should be made to assess patients' stability according to the resources available.

## CONCLUSIONS

A blood collection protocol, whether a WBB or an emergency donor panel, must be part of the transfusion support concept because it provides access to resources that are otherwise inaccessible. Obviously, this will only be implemented in exceptional situations due to the associated risk. Most stakeholders are aware of these risks, which, if mitigated, are outweighed by benefits. Therefore, measures are taken to prevent, monitor and minimize the risks entailed by such protocol. To ensure a comprehensive selection of donors for the registry, it is essential to include this comprehensive protocol in the medical support planning process of operation. The key to success are donors, their education and regular follow-up. Based on this review, there is a clear need for such a protocol in the military operational setting, but it can also be applied in the civilian world, particularly in remote locations. However, it must be part of the country's preparedness plan to ensure the best possible care for patients.

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## AUTHORS' CONTRIBUTIONS

JD proposed the research question, performed the literature search, the data extraction and analysis, assessed the quality and drafted the manuscript. ED checked the accuracy of the literature search, participated to the analysis, independently verified the quality assessment, contributed to the writing of the manuscript. FT checked the accuracy of the literature search, participated to the analysis, independently verified the quality assessment, resolved discrepancies between JD and ED during data extraction and revised the manuscript. VD is responsible for the supervision and revised the manuscript. All Authors contributed to the final manuscript and approved its final version. JD is guarantor.

*The Authors declare no conflicts of interest.*

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