





# Systematic reviews on platelet transfusions: Is there unnecessary duplication of effort? A scoping review

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## Abstract

**Background and Objectives:** Platelet transfusions are used across multiple patient populations to prevent and correct bleeding. This scoping review aimed to map the currently available systematic reviews (SRs) and evidence-based guidelines in the field of platelet transfusion.

**Materials and Methods:** A systematic literature search was conducted in seven databases for SRs on effectiveness (including dose and timing, transfusion trigger and ratio to other blood products), production modalities and decision support related to platelet transfusion. The following data were charted: methodological features of the SR, population, concept and context features, outcomes reported, study design and number of studies included. Results were synthesized in interactive evidence maps.

**Results:** We identified 110 SRs. The majority focused on clinical effectiveness, including prophylactic or therapeutic transfusions compared to no platelet transfusion (34 SRs), prophylactic compared to therapeutic-only transfusion (8 SRs), dose, timing (11 SRs) and threshold for platelet transfusion (15 SRs) and the ratio of platelet transfusion to other blood products in massive transfusion (14 SRs). Furthermore, we included 34 SRs on decision support, of which 26 evaluated viscoelastic testing. Finally, we identified 22 SRs on platelet production modalities, including derivation (4 SRs), pathogen inactivation (6 SRs), leucodepletion (4 SRs) and ABO/human leucocyte antigen matching (5 SRs). The SRs were mapped according to concept and clinical context.

**Conclusion:** An interactive evidence map of SRs and evidence-based guidelines in the field of platelet transfusion has been developed and identified multiple reviews. This work serves as a tool for researchers looking for evidence gaps, thereby both supporting research and avoiding unnecessary duplication.

## Keywords

decision support, haemostasis, platelet apheresis, platelet transfusion, scoping review, thrombocytopenia, viscoelastic

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**Highlights**

- This scoping review identified a total of 110 systematic reviews (SRs) and mapped them in interactive evidence maps according to clinical context and concept.
- Several areas, for example, platelet transfusion in intracerebral haemorrhage and the ratio of blood products in massive transfusion and viscoelastic testing to guide platelet transfusion, are served by multiple overlapping SRs.
- Scoping reviews can be a tool to avoid research waste. This work provides a comprehensive overview of the available research in the field of platelet transfusion.

**INTRODUCTION**

Platelets are the second most commonly transfused cellular blood component. Platelets are involved in haemostasis, but also have other roles [1]. Thrombocytopenia, or disorders of platelet function, may result in bleeding, which can be life-threatening [2]. Thrombocytopenia is often defined by a platelet count  $<100$  to  $150 \times 10^9/L$ , whereas severe thrombocytopenia is defined by a platelet count  $<50 \times 10^9/L$  [2, 3]. Thrombocytopenia can occur due to increased use (e.g. in severe bleeding), decreased production (e.g., haematological disorders) or immune-mediated destruction of platelets (e.g., neonatal alloimmune thrombocytopenia). Therefore, platelets are widely used across multiple clinical settings in hospitalized patients [4, 5], and can be administered either therapeutically, to stop bleeding, or prophylactically, to prevent bleeding [6]. Platelet transfusions are most often used in patients with haematological malignancies, undergoing cardiac surgery or before procedures in intensive care settings [7]. The increased demand and limited supply of platelet products show that judicious use of platelet transfusions is crucial.

Several methods for preparing platelets, platelet dosing, platelet transfusion threshold and platelet product specifications have been investigated in studies [8–14]. This demonstrates the importance of considering the best available evidence on the effectiveness and cost-effectiveness of procedures, collected in systematic reviews (SRs), to guide the development of evidence-based guidelines for clinical practice [15]. A current overview of existing SRs and topics for which no SR is as yet published is not available. Therefore, the aim of this scoping review is to develop an evidence map informing future SRs in the field of platelet transfusion.

**MATERIALS AND METHODS**

A completed (Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA])-Scoping Reviews reporting checklist can be found in Appendix S1. A concise methods section is presented below, and a full version can be found in Appendix S2.

**Selection criteria**

We included patients of any age eligible for platelet transfusion. We included any SR of controlled research, with an explicit methods

section, in the field of platelet transfusion, in any clinical context, without language restrictions. We included SRs comparing the effectiveness of platelet transfusion to no platelet transfusion, prophylactic to therapeutic platelet transfusion, different doses and timings of platelet transfusion, different ratios of platelets to other blood products in major transfusion and different production modalities for platelet transfusions, decision support systems for platelet transfusion and the impact of platelets on refractoriness or alloimmunization.

**Search strategy and study selection**

We searched for SRs on 5 May 2021, without applying date limits, in PubMed, Embase, Web of Science, Cumulated Index to Nursing and Allied Health Literature, Cochrane Database of Systematic Reviews, Transfusion Evidence Library and International Prospective Register of Systematic Reviews (PROSPERO).

Studies were assessed for eligibility by two independent reviewers at the title and abstract and full-text levels. Discrepancies were resolved by discussion or consulting a third reviewer. We screened the reference lists and the first 20 ‘similar articles’ in PubMed of included studies for additional eligible studies.

**Data charting, synthesis and presentation**

Data charting from eligible SRs was done by two independent reviewers. We analysed data by population, concept, outcome type, methodological features, patient age and outdatedness. Data are presented in interactive evidence maps using EPPI-Mapper v2.1.0 [16].

**RESULTS****Search results**

A total of 9199 records were identified from the database searches, leading to a total of 5583 unique records that were reviewed. Following exclusions, 169 records, reporting on 110 unique SRs, were included, 13 of which were identified through screening of reference lists and ‘similar articles’ in PubMed of included records (Appendix S3). Multiple records reporting on the same topic area were

noted, including previous versions of the SRs, protocols and PROSPERO registrations and conference abstracts. The eligibility of another 48 records, reporting on 40 SRs, could not be ascertained due to a lack of information (mainly review protocols and conference abstracts of ongoing SRs). These records have an 'awaiting classification' status and may be assessed for eligibility again in future updates of this scoping review (Appendix S4). An overview of studies not meeting eligibility criteria can be found in Appendix S5.

## Characteristics of the included SRs

An interactive evidence map describing the characteristics of the included SRs can be accessed online through this link: <https://www.cebap.org/storage/cebap/20220110-eppimap-studydesign.html>. A static overview is included in this article as Figure 1. A detailed overview of charted characteristics can be found in Appendix S6.

Of the 110 included SRs, 11 were SRs embedded in evidence-based guideline projects [9, 17–26], and three were overviews of reviews concerning the management of traumatic brain injury [27, 28] or trauma-induced coagulopathy [29]. The remainder were SRs of primary research, either experimental studies, observational studies or both. The majority of SRs were conducted in the United Kingdom (20%), Canada (19%) and the United States (18%).

## Populations studied

Nine SRs included studies on intensive care unit (ICU) patients, of which one specifically included dengue patients. Fifty-three SRs focused on emergency care patients, including spontaneous or traumatic brain injury patients or patients defined as 'trauma' or 'massive bleeding' patients. Furthermore, 31 SRs included studies conducted in a haematological or oncological setting. Eighteen SRs studied general oncology/haematology patients, five SRs focused on haematopoietic stem cell transplant patients, nine SRs on hypoproliferative bone marrow disorders, three SRs on thrombotic or immune thrombocytopenia purpura, one SR on disseminated intravascular coagulation, two SRs on heparin-induced thrombocytopenia and five SRs on foetal/neonatal alloimmune thrombocytopenia. Thirty-seven SRs concerned surgery patients, 19 of which concerned cardiac surgery patients, eight concerned liver surgery patients, five concerned patients undergoing minor procedures and 16 concerned other or unspecified elective surgery patients. Finally, three SRs included studies with healthy volunteers, and the context of studies included in four SRs was classified as 'other'.

Four SRs specifically focused on the paediatric population, and a further five investigated platelet transfusion in foetal/neonatal alloimmune thrombocytopenia. The remainder either did not specify or specifically included studies in an adult population. The interactive evidence map, segmented by population age, can be accessed through this link <https://www.cebap.org/storage/cebap/20220110-eppimap-age.html>; a static overview can be found in Figure 2.

## Concept studied

Fifty-eight SRs addressed the clinical effectiveness of platelet transfusions. Thirty-four SRs investigated the effectiveness of platelet transfusions compared to no platelet transfusions to prevent or treat bleeding, while eight compared prophylactic to therapeutic-only platelet transfusions. Eleven SRs focused on the dose and timing of platelet transfusions, and 15 included studies on platelet transfusion thresholds in prophylactic platelet transfusion. Finally, 14 SRs included studies comparing the ratio of platelets to other blood products in massive transfusion. Thirty-four SRs looked at decision support systems to guide platelet transfusions. Twenty-six SRs focused on point-of-care viscoelastic testing (thromboelastography and/or rotational thromboelastometry), while eight looked at other decision supports, mainly the use of formal transfusion protocols. Twenty-two SRs were identified that included information on platelet production modalities. Seven SRs included studies on the impact of platelet storage duration, while two searched for studies on the storage temperature of platelets. Four SRs included studies on derivation methods of platelets (whole blood derived vs. apheresis derived), six SRs concentrated on pathogen inactivation of platelets and four SRs assessed leucodepletion. Finally, five SRs investigated the clinical impact of platelet matching by ABO type or human leucocyte antigen cross-matching.

## Outcomes reported

Regarding outcome types included, 76 SRs reported a death-related outcome (e.g. 30-day mortality), 69 SRs reported morbidity (e.g., bleeding, re-operation due to bleeding), 62 SRs reported outcomes related to transfusion (e.g., number of blood products used, transfusion requirement, transfusion interval), 33 SRs reported a haematological outcome (e.g., platelet count increment), 37 SRs reported length of stay outcomes (e.g., length of hospital stay or ICU stay), 48 SRs reported at least one adverse event (e.g., acute transfusion reactions), 7 SRs reported an economic outcome (e.g., costs associated) and 13 SRs reported an outcome that did not fit in any of the prior categories (e.g., quality of life).

## Methodological features

The included SRs differed from each other in terms of methodological features. Only 66 SRs had a clearly defined research question, including elements of a population, intervention, control and outcomes question. The vast majority searched more than one database, but 15 SRs searched only in PubMed/Medline. A formal quality appraisal of included studies was conducted in 80 SRs, and 33 also assessed the certainty of the body of evidence, all but one, using the grading of recommendations, assessment, development and evaluation methodology [15]. Fifty-two of the included SRs were published before 2017, while 58 were published in 2017 or later. For the SRs supporting an



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**FIGURE 1** Evidence map illustrating the number of identified systematic reviews, mapped by clinical context and concept, segmented by study design included

evidence-based clinical practice guideline, eight were published in 2017 or later, and only three were from before 2017.

Regarding the outdatedness of the searches, 36 SRs had a search date less than 5 years old, while 69 SRs had a search date older than 5 years old, and therefore, considered outdated. The search data of five SRs were not sufficiently reported to assess outdatedness. An interactive evidence map segmenting the SRs by outdatedness can be accessed via <https://www.cebap.org/storage/cebap/20220714-eppimap-outdatedness.html>; a static version is shown in Figure 3.

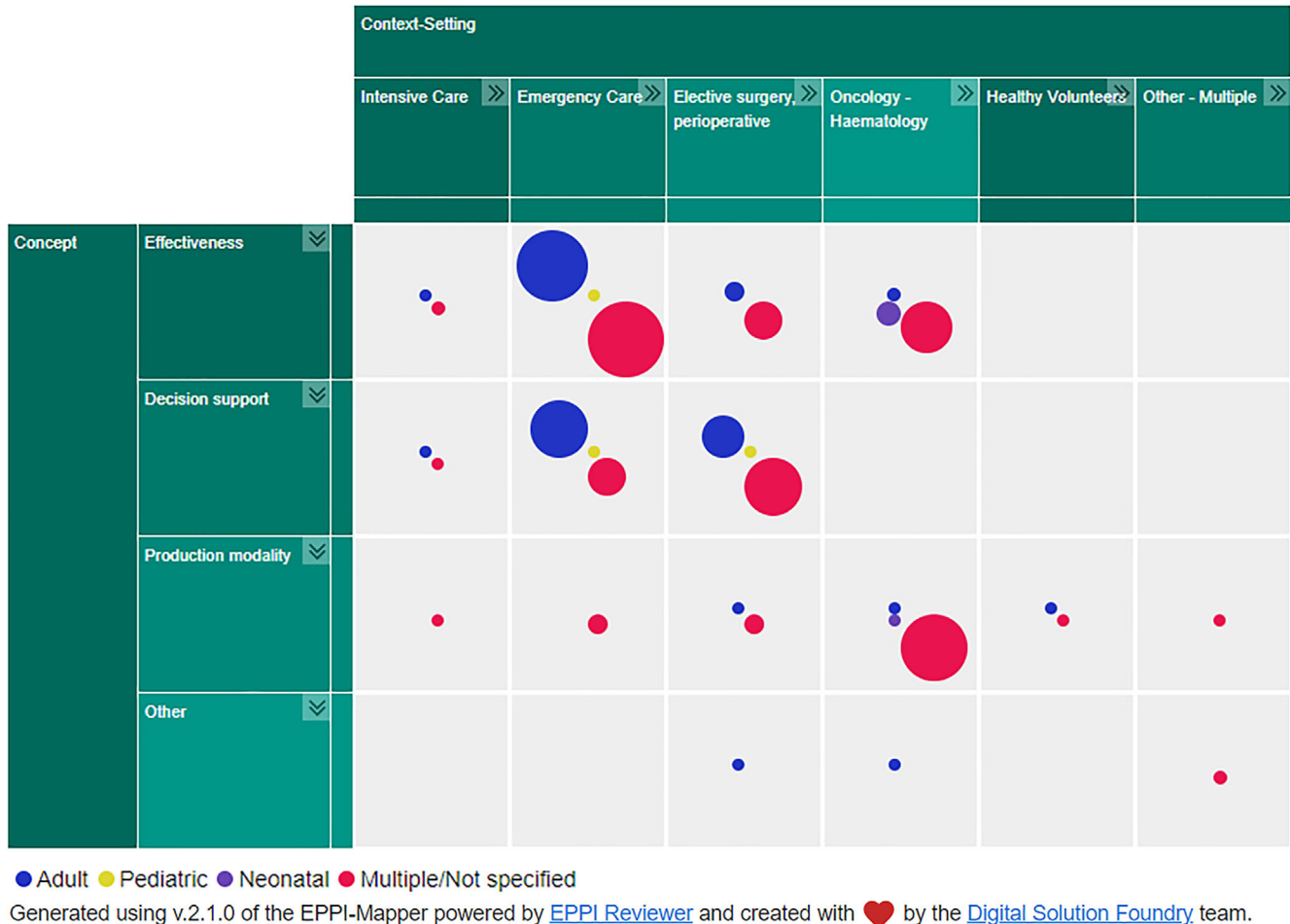
## DISCUSSION

This scoping review mapped the currently available SRs in the field of platelet transfusion. It not only provides an overview of the evidence but is also an important reference for clinician education. Moreover, it promotes new research by identifying research gaps and redundancy. We have identified 110 SRs. The high number of reviews, many published in the last few years, raises important questions as to which reviews should be accessed by busy clinicians. We labelled 40 SRs as

‘awaiting’ classification, which demonstrates that this is clearly an active and ongoing field of research.

About a third of the identified SRs had a search date less than 5 years old, which has been suggested to be a relevant cut-off for considering a SR as up-to-date [30]. If resources allow, the interactive versions of our evidence maps that are online available will be updated regularly. Future updates of the evidence map resulting from this project will likely have an important impact on the completeness of this overview.

It is clear that some areas of research are better served by SRs than others. This may correspond to the amount of underlying primary research available, the need to combine studies in meta-analyses when sample sizes are small or when outcomes are infrequent, or in areas of controversy. Several indications, for example, the use of viscoelastic testing to guide transfusion in cardiac surgery or the effectiveness of therapeutic platelet transfusion in traumatic brain injury, are covered by several overlapping SRs. This demonstrates the added value of a scoping review, which can serve as a tool to minimize future redundancy. Chalmers and Glasziou highlighted that many trials are conducted and reported without reference to existing literature,



**FIGURE 2** Evidence map illustrating the number of identified systematic reviews, mapped by clinical context and concept, segmented by age category

thereby potentially leading to studies answering already solved research questions [31]. Our scoping review identified a similar concept for SRs. In addition, several authors demonstrated that the number of published SRs and meta-analyses had grown steadily over the years [32, 33]. In order to avoid overlap and duplication in evidence syntheses, an initial consideration of whether a new SR is actually needed should be the first step in the set-up of a potential new SR protocol. Scoping reviews and evidence gap maps might be useful tools to answer this need [34, 35], especially if they include a search in the international prospective register for SRs, PROSPERO, for ongoing SRs [36].

Our approach has several advantages. First, we used elaborate search methods and a rigorous methodology [37], thereby aiming to obtain as complete an overview of the state-of-the-art in platelet transfusion as possible. Furthermore, our approach to visually display the identified SRs in interactive maps has the advantage of usability, whereby users can quickly scan the existing evidence for their topic of interest using the different filtering options available. Finally, our work directly demonstrates the research gaps in this field and can thereby inform future reviewers and researchers as to where useful work may be undertaken. When looking at the outcomes reported in

the SRs, it is clear that few existing SRs pay attention to economic aspects related to platelet transfusion and production modalities or quality of life. Five of the seven SRs, including an economic outcome, focus on decision support systems [38-42], and two on platelet dose [9, 43]. The few SRs that defined quality of life as an outcome of interest actually did not identify any primary research study reporting this outcome [2, 6, 12, 39, 43-48]. Although a minority of SRs report at least one adverse event, no SR was identified with platelet transfusion-related adverse events as the main focus, despite the fact that platelets are regularly associated with adverse events and carry a higher risk of bacterial contamination than other blood products [49, 50]. Other potential research gaps may include prophylactic versus therapeutic-only platelet transfusion in the paediatric patient population [51], cardiac surgery or critical illness.

Limitations include an initial scope that included alternatives to platelet transfusion (e.g., tranexamic acid). Second, our scoping review is secondary research. It does not show whether there are primary research studies available in a given field of work. Finally, given that we have conducted a scoping review, the purpose of this exercise is to map the existing evidence and not a formal critical appraisal and evaluation of effectiveness.



● Up to date ● Outdated ● Unclear

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**FIGURE 3** Evidence map illustrating the number of identified systematic reviews, mapped by clinical context and concept, segmented by outdatedness

In conclusion, we have mapped the currently available secondary research in the field of platelet transfusion using a rigorous scoping review methodology. This work serves both clinicians, researchers and guideline developers in search for a quick and clear overview regarding the state-of-the-art in themes related to platelet transfusion, from clinical effectiveness to production modalities and decision support.

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does the mentioning of trade names or commercial products constitute endorsement or recommendation of use.

**CONFLICT OF INTEREST**

*Relevant financial conflicts of interest directly related to this review:* Bert Avau, Dorien O, Koen Veys, Hans Van Remoortel, Jørgen Georgsen, Nadine Shehata, Simon J. Stanworth, Emmy De Buck, Veerle Compernelle and Philippe Vandekerckhove declared not having any relevant direct financial conflict of interest. Susan Nahiriak declared to have received travel reimbursements from the Canadian Blood Services for travel to Scientific Research Advisory Committee, which occasionally discusses International Collaboration for Transfusion Medicine Guidelines (ICTMG) projects.

*Relevant financial conflicts of interest not directly related to this review:* Bert Avau, Dorien O, Koen Veys, Hans Van Remoortel, Emmy De Buck, Veerle Compernelle and Philippe Vandekerckhove are employees of Belgian Red Cross-Flanders, which is responsible for supplying adequate quantities of safe blood products to hospitals in Flanders and Brussels on a continuous basis and is funded by the Ministry of Social Affairs. Belgian Red Cross-Flanders received a grant from the European Blood Alliance to conduct this review.



Nadine Shehata reported having received personal fees from the ICTMG for the development of the ICTMG platelet guideline. Simon J. Stanworth declared being an employee of the NHSBT, a blood service supplier for England, which manufactures platelets and having received grants for the conduct of trials of platelets in neonates and platelets and tranexamic acid in haematological cancers. Jørgen Georgsen and Susan Nahirniak declared not having any other relevant financial conflicts of interest.

*Relevant intellectual conflicts of interest:* Bert Avau, Dorien O, Koen Veys, Hans Van Remoortel, Jørgen Georgsen, Emmy De Buck, Veerle Comperolle and Philippe Vandekerckhove declared not having any intellectual conflict of interest. Simon J. Stanworth declared having authored multiple systematic reviews (SRs) on the use of platelets and tranexamic acid in haematology—none within the last three years and being involved in a new guideline on platelets and plasma in critically ill children. Simon J. Stanworth and Susan Nahirniak declared being the co-chair of the platelet guideline revision working group of the ICTMG. Nadine Shehata declared having been a co-author on previous SRs and a guideline on platelet transfusion.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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