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Review Article

Clinical Effectiveness and Safety of Pathogen-Reduction Technologies for Platelets and Plasma: A Systematic Review

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Abstract:
Pathogen-reduction technologies (PRTs) methods for platelet and plasma are increasingly being relied on to inactivate a broad spectrum of pathogens to ensure safety in transfusion. However, there is continuing debate about the impact of such technology on clinical effectiveness, bleeding outcomes, and transfusion-related adverse events.
Objective: This systematic review evaluated the clinical effectiveness and safety of PRT-treated platelets and plasma using studies published between 2015 and 2025.
Methods: Following PRISMA 2020 guidelines, major databases including PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched for studies published between 2015 and 2025. Eligible studies included human studies, platelet and/or plasma products that have been treated with specific PRT technology. A total of 1256 records were identified. Findings were synthesized narratively and presented descriptively.
Results: Fifteen qualifying studies utilizing pathogen-reduced platelets and plasma from various areas were included. In randomized trials, platelets treated with PRT consistently exhibited decreased CCI at both 1 hour and 24 hours compared to conventional platelets, with certain studies indicating greater platelet use. Even though the platelet increments were lower, most trials did not report any significant rise in WHO grade ≥2 clinical bleeding, and the hemostatic efficacy was still satisfactory. Safety outcomes were relatively good: datasets showed that transfusion-reaction rates were low (<1%) and major adverse events were not so common. PRT systems showed strong pathogen-inactivation abilities, including the ability to effectively inactivate clinically important viruses such as hepatitis viruses, dengue, and Japanese encephalitis virus. Different technologies had different results, and UVC-based systems sometimes showed smaller increases after transfusions.
Conclusion: Platelets and plasma treated with PRT are still clinically useful and very safe. They also greatly lower the risk of infections that can be spread by transfusions. Even though there are fewer laboratory increments and more platelet use, these changes don't seem to affect clinical hemostasis. Strengthening implementation methods, inventory planning, and hemovigilance systems alongside continuing evaluation of performance will enable safer transfusion procedures and safeguard vulnerable patient groups globally.

Keywords: Pathogen-Reduction Technologies (PRT); Platelets; Plasma; Transfusion Safety; Clinical Effectiveness; Pathogen Inactivation

Introduction

Blood transfusion is essential in healthcare for the day-to-day use of blood products in surgeries, trauma cases, cancer treatment, childbirth, and many other medical conditions. The bigger, long-pursued goal of blood and blood component transfusion is to achieve pathogen reduced platelet component through proven pathogen reduction technologies. Platelets and plasma are two of the most commonly transfused blood components. The World Health Organization recently reported transfusion of more than 25 million platelet units and 35 million plasma units each year across the globe (Kanagasabai et al., 2021). These blood components are critical for preventing or controlling bleeding (Metcalf et al., 2025). Even so, implicit in this is the need to ensure safe and available products for patients. However, it is important to note that every transfusion still carries the risk of transmitting infections.

Historically, safe blood components are only focused on a combination of donor screening, education, blood screening for selected pathogens. This still remains a norm in many regions of the world with some advancements in testing methods to ensure safe blood (levy et al., 2018; Metcalf et al., 2025). Despite these advancement in testing methods, about 1 in every 2,000–3,000 platelet units according to the National Institute of Health, may still become contaminated with bacteria, and/or viruses like HIV, hepatitis B, and hepatitis C (Haas et al., 2019). This remains an ongoing concern especially in regions with weaker blood-safety systems.

Worldwide, transfusion-transmitted infections exhibit a higher prevalence in low- and middle-income countries. From the World Health Organization (WHO) reports, we see that high-income countries contribute more than 40% of the world's blood donations, despite representing less than 20% of the global population (Jacobs et al., 2024). In numerous resource-constrained environments, including regions within Africa and Asia, screening methodologies remain underdeveloped. For instance, bacterial contamination rates in platelets have been reported to reach as high as 1–3% in certain African hospital studies, in contrast to 0.01–0.2% in Europe and North America. Plasma contamination rates are reduced but remain considerable, particularly for viruses that might not be identified during the "window period" of infection (White et al., 2020; Cardoso et al., 2023).

To address these dangers, pathogen-reduction technologies (PRTs) were created. These systems employ chemicals or light-based mechanisms to inactivate bacteria, viruses, and parasites in blood components. The most widely utilized PRT systems now are amotosalen-UVA, riboflavin-UV, and methylene blue. These methods have been used widely in Europe, where several nations treat approximately 100% of their platelet units using PRT. In contrast, PRT usage is currently restricted in many countries of Africa, Asia, and Latin America, mostly due to cost, equipment limitations, and uncertainty regarding therapeutic effects.

Several studies have demonstrated that PRT can minimize bacterial contamination dramatically by up to 99.9% for various technologies and lower the risk of transfusion-transmitted illnesses (LaFontaine et al., 2021). However, there are still worries regarding whether these treated components operate as effectively as untreated ones. Some clinical trials reveal somewhat decreased platelet count increases or reduced clotting activity after PRT therapy. Other findings reveal comparable bleeding results and similar fatality rates when comparing pathogen-reduced components with regular ones. Because of these varied outcomes, the global medical community still argues how useful and safe PRTs genuinely are in real clinical practice.

Although various trials and regional reviews are already ongoing, there is scarcity of systematic reviews that integrate information on both the clinical benefit and safety of pathogen-reduced platelets and plasma. We also found out that many research originate from high-income nations, and just a handful contain data from low-resource countries where the demand for safer blood is highest. Also, there are significant discrepancies in study designs, sample sizes, technology employed, and end measures, making it challenging to compare results directly.

Current Study

With this review, we seek to address these gaps by bringing together evidence on the clinical outcomes and safety of pathogen-reduction technologies for platelets and plasma. In this review, we will summarize global and regional evidence on how well pathogen-reduced platelets and plasma perform clinically. This review also aims to evaluate the safety of PRTs, including transfusion reactions and adverse events as it pertains to patient safety. Also, we aim to compare pathogen-reduced components with standard blood components across different countries and technologies. Consequently, integrating findings from around the world, this review will help provide a clearer and more complete understanding of the effectiveness and safety of pathogen-reduction systems, supporting better decision-making in transfusion medicine.

Methodology

Study Design

This was a systematic review done in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. These guidelines provided a clear and organized process from identifying studies to selecting those that met our study criteria. Because our goal was to examine the clinical effectiveness and safety of pathogen-reduction technologies (PRTs) used for platelets and plasma, we framed our research question using the Population–Concept–Context (PCC) approach. This framework was chosen because it is suitable for descriptive (Parums, 2021), outcome-based, and technology-focused reviews. In this review, the concept centered on the use of validated pathogen-reduction technologies such as amotosalen-UVA, riboflavin-UV, methylene blue, or solvent-detergent systems; and the context covered all healthcare settings globally, including hospitals, transfusion centers, and regional blood services. The methodology for this study was prepared before the search process began. The evaluation followed the registered plan unless revisions were necessary, and these would be stated properly.

Eligibility Criteria

A stringent inclusion criterion was employed to guarantee that only relevant and scientifically valuable papers were included. Studies were eligible if they involved human participants who received pathogen-reduced platelets or plasma and reported clinical outcomes such as corrected count increment (CCI), bleeding episodes, transfusion reactions, or other safety-related findings. We included observational studies, prospective or retrospective cohorts, whether they are randomized or non-randomized clinical trials, and comparative studies that evaluated treated versus standard blood components. Only studies published in English between 2015 and 2025 were considered, as this time range reflects the period when modern pathogen-reduction technologies became widely available and clinically used. We excluded reviews, editorials, case reports, and conference abstracts without extractable data to avoid very small sample sizes that could bias interpretation. Animal studies and reports with duplicated or overlapping datasets were removed, retaining only the most complete or recent publication from each research group. These criteria allowed us to maintain a high level of quality and relevance across all included studies.

Information Sources and Search Strategy

A comprehensive search strategy was developed to identify all studies relevant to the clinical use of pathogen-reduction technologies for platelets and plasma. We searched several major databases, including PubMed/MEDLINE, Embase, Scopus, Web of Science Core Collection, and the Cochrane Library. We also searched Google Scholar to identify grey literature such as institutional reports or academic theses, and we reviewed clinical-trial registries like ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform for completed or ongoing studies. The final database search was conducted on 1 June 2025. To reduce the risk of missing key studies, a manual screening of the reference lists of included articles and relevant review papers was done, and we performed forward citation tracking to identify additional studies that may have cited the included publications.

In our search strategy we combined controlled vocabulary terms such as MeSH terms with keywords related to pathogen reduction and clinical outcomes. A representative search string used in PubMed included: “pathogen reduction,” “pathogen inactivation,” “amotosalen,” “riboflavin,” “methylene blue,” or “solvent detergent.” These were combined with search terms like “platelets,” “platelet concentrate,” “plasma,” or “fresh frozen plasma”. Additional search terms were: “clinical effectiveness,” “clinical outcome,” “safety,” and “transfusion reaction” Search strings were adapted for each database based on specific indexing requirements. Filters were applied where available to restrict results to human studies and English-language publications, and to select results within the specified time range. Together, these methods helped us get a broad and systematic coverage of the available literature.

Study Selection

All retrieved records were exported into EndNote for deduplication. After duplicates were removed, two reviewers independently screened the titles and abstracts to identify studies that were potentially eligible. Articles that appeared relevant were then assessed in full text using the established inclusion and exclusion criteria. The two reviewers compared their decisions, and any disagreements were resolved through discussion or by consulting a third reviewer when necessary. Reasons for excluding studies at the full-text stage were carefully documented to maintain transparency. The selection process is presented in a PRISMA 2020 flow diagram, which shows the number of studies identified, screened, assessed for eligibility, and included in the final synthesis.

Data Extraction and Management

A structured data extraction form was developed using Microsoft Excel and tested on a small sample of studies to ensure clarity and consistency. Two reviewers independently extracted information

from the included studies. Extracted data included study characteristics (author, year, country, design, setting, and sample size), we then extracted characteristics of the pathogen-reduction technology used, and details about the clinical and safety outcomes reported. Specific outcomes included corrected count increment (CCI), eventual bleeding events, transfusion reactions, adverse events, hospitalization outcomes, and mortality where available. When studies compared pathogen-reduced products with standard components, data for both groups were extracted separately. After extraction, the two reviewers compared their entries and resolved any discrepancies by consensus. This dual-extraction method helped reduce bias and improve data accuracy.

Quality Appraisal

To assess methodological quality and risk of bias, we used the Joanna Briggs Institute (JBI) Critical Appraisal Tools, which are appropriate for a lot of study designs, including cohort studies, clinical trials, and cross-sectional studies. Two reviewers independently evaluated each study using the tool that matched its design. The appraisal considered factors such as the appropriateness of the sampling frame, the reliability of outcome measurement, handling of confounding variables, and the suitability of the analytical methods used. Each criterion was rated as "yes," "no," or "unclear." Disagreements were resolved through discussion or with help from a third reviewer. Studies were then classified as having low, moderate, or high risk of bias. Summary ratings are presented in a table to support interpretation of the findings.

Data Synthesis

Given the expected differences across studies such as variations in PRT systems, study designs, outcome measures, and clinical settings we conducted a narrative synthesis rather than a statistical meta-analysis (Hilton, 2024). We first summarized the characteristics of the included studies to highlight sources of heterogeneity. Clinical effectiveness outcomes, such as platelet count increments, bleeding events, and transfusion success, were described and compared across studies. Safety outcomes, including febrile reactions, allergic responses, and other adverse events, were also synthesized narratively. When two or more studies reported similar measures (for example, CCI or bleeding rates), we presented ranges and median values to aid comparison without masking important methodological differences. A meta-analysis wasn't done because the studies were heterogenous, for example, they used different PRT systems, storage methods, patient groups, and definitions of bleeding outcomes. These differences made it unsafe to combine the results, as it could lead to misleading conclusions. Findings are presented in structured tables to enhance clarity and support a transparent interpretation of the evidence.

Ethical Considerations

This review relies totally on already published studies from reputable journals for data synthesis. Therefore, no institutional ethical approval was required. However, care was taken to ensure chosen studies stated ethical approval by relevant ethics committee or institution where applicable with consent statement. This systematic review ultimately adhered to standards of transparency, accountability, reproducibility and research integrity.

Results

Study Selection

The database and manual searches yielded 1,256 records (Databases = 1,078, Registers = 131, and Google Scholar = 47). After removing 994 records due to 369 duplicates, 580 unrelated matches with keywords, and 45 language restricted studies, 262 unique titles and abstracts were left and screened. The titles and abstracts of these records were carefully screened to remove studies that were not directly relevant to pathogen-reduction technologies (PRTs), did not focus on platelets or plasma, or did not report clinical outcomes. This step led to the exclusion of 20 studies. This is seen in Figure 1. 242 full texts were assessed for retrieval, of which 202 were not retrieved due to accessibility oe subscription issues. Then remaining 38 articles were assessed for eligibility, and 23 were excluded because they had no clinical outcomes data (n = 11), were in-vitro studies (n = 6), had very small samples (n = 5), or used an overlapping dataset (n = 1). After this careful screening, a total of 15 studies met all inclusion criteria and were included in the final synthesis. These studies included a mix of randomized controlled trials, observational cohorts, and hemovigilance reports, representing a variety of clinical settings. The full process of selection is shown in the PRISMA 2020 flow diagram in figure 1, which summarizes how studies were identified, screened, and included. 15 studies were finally included in the narrative synthesis (figure 1).

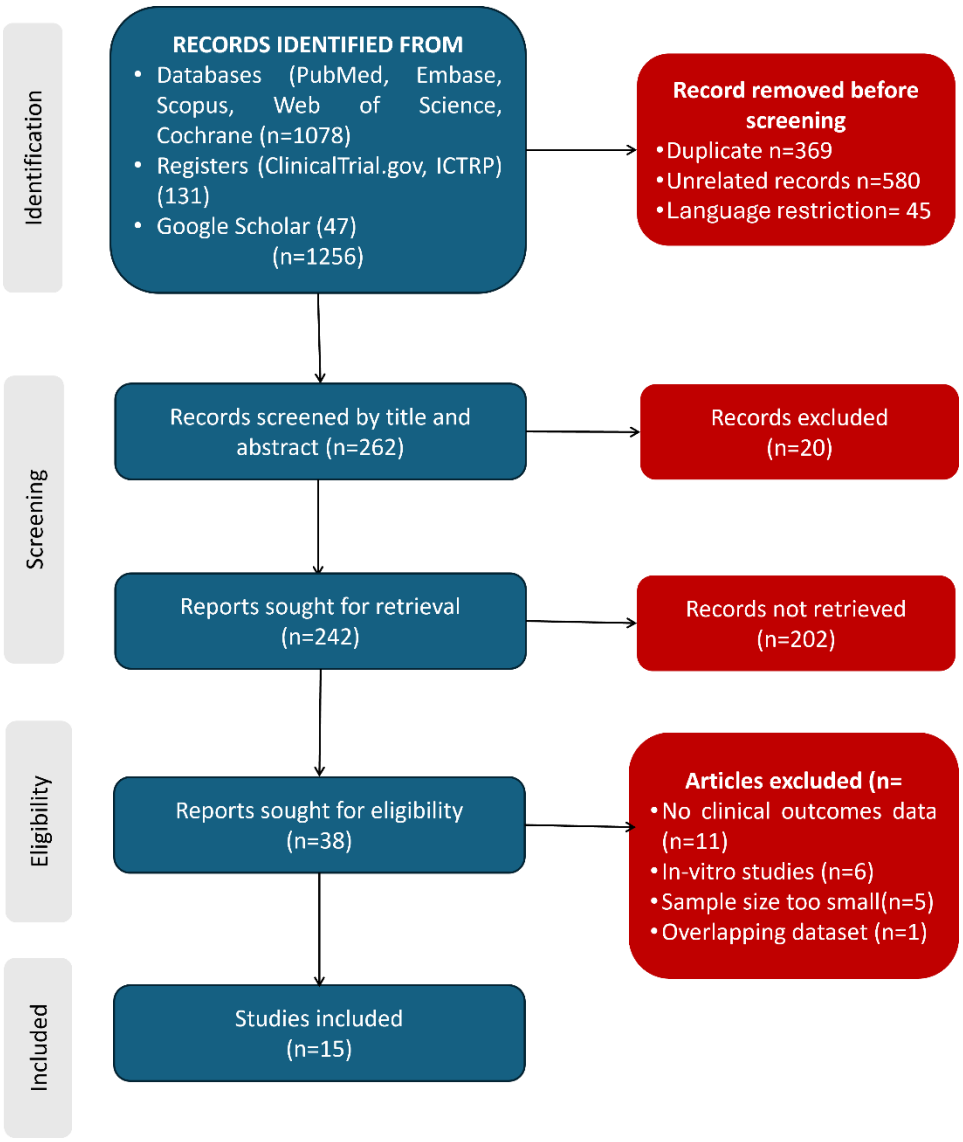

Figure 1. PRISMA 2020 flow diagram illustrating the identification, screening, eligibility assessment, and inclusion of studies in the review.

Study Characteristics

The fifteen studies in this review were done between 2015 and 2025. The studies came from many parts of the world, like Europe, North America, Asia, and Latin America. Many European studies, like the ones by Garban et al., (2018), Rebulla et al., (2017), and Brixner et al., (2021), came from countries that have used pathogen-reduction technology for some time. They mostly used the INTERCEPT® and Mirasol® systems. Their research methods were strong, with big clinical trials and many hospitals taking part.

Studies from North America, like Schulz et al., (2019), also used good clinical methods. Some of them focused more on how to start using the systems, how they work for children, or how patients respond early during treatment. We found out that some studies were very large and followed thousands of blood transfusions, like the ones by Knutson et al., (2015) and Piotrowski et al., (2018). These helped to check how safe the systems are in real life. Other studies were small, like Drawz (2015), which tested count changes in less than 30 patients. Because of this, the number of people in the studies was very different. Some had more than 500 patients or more than 10,000 transfusions, while a few special studies had less than 50 people, especially studies with children or patients with weak immune systems.

The studies looked at different pathogen-reduction systems. The most common one was Amotosalen-UVA platelets (INTERCEPT®). This was seen in Garban (2018) and Rebulla (2017). Riboflavin-UV (Mirasol®) was also used in many studies, including randomized trials and observational studies like those by van der Meer (2018), Drawz et al., (2015), and Piotrowski et al., (2018). Some studies checked UV-C treated platelets, like the German trial by Brixner et

al., (2021). Other studies looked at plasma treatment systems like methylene blue and solvent-detergent plasma, as described in Arroyo (2020).

The nature of patients' population also differed. The patients in the studies were from different groups. From review, we saw that many studies included adult patients with cancer and blood-related conditions needing platelet transfusions. Other studies included both medical and surgical patients (Bahar et al., 2020) and children (Schulz et al., 2019). Most studies compared pathogen-reduced blood products with normal, untreated ones. This made it easy to see the differences in how the platelets worked, how much bleeding happened, and how safe they were.

Table 1: Characteristics of included Studies (2015-2025)

Study	Country / Region	Study design	PRT technology	Component(s)	Sample size / transfusions reported	Patient population	Comparator	Main purpose
Knutson et al., (2015)	Multinational (21 centres, 11 countries)	Prospective active hemovigilance cohort	Amotosalen + UVA (INTERCEPT)	Platelets	19,175 transfusions (≈4,067 patients reported in cohort)	Routine transfusion recipients (varied)	Historical/expected rates	Safety / hemovigilance
Drawz et al., (2015)	Multi-centre/International (authors from Europe/US/Latin)	Observational (routine use)	Riboflavin + UV (MIRASOL)	Platelets in PAS	19 patients transfused (small transfusion series reported)	Hematologic patients	Standard platelets historical	CCI / transfusion response
Rebulla et al., (2017)	Italy (multicentre)	Randomized controlled trials (two parallel non-inferiority RCTs)	INTERCEPT (amotosalen–UVA) & MIRASOL (riboflavin–UV)	Platelets (in PAS)	424 evaluable patients (trial stopped early; planned 828)	Onco-hematology patients	Untreated standard platelets	Clinical effectiveness / bleeding
Piotrowski et al., (2018)	Europe (multiple centres: Poland, Spain, Lithuania, Greece, Luxembourg, Austria, Belgium)	Passive hemovigilance	Riboflavin + UV (MIRASOL)	Platelets, plasma	Regional hemovigilance reports (aggregated)	Routine transfusion recipients	Historical rates	Safety surveillance
van der Meer et al., (2018)	Netherlands / Canada (multicentre)	Randomized non-inferiority trial	Riboflavin + UV (MIRASOL)	Platelets	469 patients randomized contributing 567 transfusion-periods	Hematologic malignancy patients with thrombocytopenia	Standard plasma-stored platelets	Hemostatic efficacy / bleeding

Garban et al., (2018)	France (13 tertiary hospitals)	Randomized, 3-arm non-inferiority clinical trial	Amotosalen + UVA (INTERCEPT)	Platelets	790 evaluable patients	Thrombocytopenic patients with hematologic malignancy	Platelets in plasma & platelets in additive solution	Hemostatic efficacy / WHO bleeding
Schulz et al., (2019)	USA (single large tertiary centre)	Quality-assurance / comparative review during transition	INTERCEPT (amotosalen–UVA) (FDA-approved PR platelets)	Platelets	Transfusion counts by subgroup (NICU n=91/145; infants n=125/254; PED n=644/673 transfusions)	Neonates, infants, children	Conventional platelets during transition	Utilization & short-term safety
Bahar et al., (2020)	International / adult centres	Observational hemovigilance	INTERCEPT / MIRASOL (centre dependent)	Platelets	Large centre transfusion datasets (reported in paper)	Adult patients	Standard platelets	Utilization / transfusion reactions
Arroyo et al., (2020)	Spain (multi-centre comparison)	Comparative clinical study	Methylene blue + visible light (MB plasma)	Fresh-frozen plasma	Number of TPE episodes compared (MBP vs QP groups)	Patients with TTP	Quarantine FFP (QP)	Therapeutic efficacy in TTP
Brixner et al., (2021)	Europe (multicentre)	Randomized, double-blind non-inferiority trial	UVC (Theraflex-type)	Platelets	~170 patients (study reported 171 eligible)	Hematologic-oncology thrombocytopenic patients	Untreated platelets	1-hr CCI non-inferiority
Jimenez-Marco et al., (2021)	Spain / Europe	Implementation & cohort reports (experience papers)	Riboflavin + UV (MIRASOL)	Platelets & plasma	Routine production & hemovigilance numbers (centre reports)	Routine transfusion recipients (incl neonates)	Historical controls	Implementation, safety, production data
Ladaique et al., (2023)	France	Single-centre observational experience	Amotosalen + UVA (INTERCEPT)	Platelets	Number of AML patients transfused reported (centre series)	AML patients undergoing chemo	Conventional platelets historical	Therapeutic efficacy in AML

Pedraza et al., (2024)	Honduras / Central America	Before-after implementation study	Amotosalen + UVA (INTERCEPT)	Platelets	Centre platelet availability / inventory data reported	National platelet supply users	Pre-implementation data	Availability & system impact in LMIC
Łętowska et al., (2016)	Warsaw region (Poland)	Hemovigilance survey (2009–2013)	MIRASOL (riboflavin + UV)	Platelets & plasma	Regional transfusion counts reported	Routine recipients	Historical rates	Safety / reaction rates
Rustanti et al., (2020)	Indonesia (Asia)	Laboratory-based experimental virology study	Riboflavin + UV (Mirasol® system	Platelet concentrate	multiple platelet units tested against viral spiking assays	inactivation experiment	No comparator platelets; effectiveness benchmarked against viral concentration before/after PRT	To evaluate the ability of PRT to inactivate Japanese Encephalitis Virus

Clinical Effectiveness

Across all the studies, the results were mostly the same. Platelets that went through pathogen-reduction treatment (PRT) showed lower lab results after transfusion. This was seen in the 1-hour and 24-hour corrected count increment (CCI). The strongest evidence came from big randomized trials like Rebulla et al., (2017), van der Meer et al., (2018), and Brixner et al., (2021). In these studies, the PRT platelets gave lower increases than normal platelets. Smaller studies, like Drawz (2015), also showed the same pattern. These results happened because the PRT process causes small changes in how the platelets look and work.

Even though the lab numbers were lower, most studies said there was no big increase in patient bleeding. For example, Garban (2018) found that bleeding of WHO grade 2 or more happened at almost the same rate in both PRT and normal platelet groups. Van der Meer et al., (2018) also showed that bleeding was not worse in the PRT group in their main analysis, although there were some small differences in another analysis. Some studies show that PRT-treated platelets may need to be given more often, but they still protect patients from serious bleeding just like normal platelets. Studies on plasma PRT, like Arroyo et al., (2020), also showed similar patient results when compared with regular plasma.

Some studies also looked at how many transfusions patients needed. A few studies, found that patients receiving pathogen-reduced platelets required slightly more transfusions. However, other studies found no meaningful differences. Importantly, none of the studies reported higher rates of severe bleeding in the PRT groups.

Table 2: Count Increment (CCI) and Platelet Recovery Outcomes Across Included Studies

Study	**Component**	**PRT system**	**Sample / transfusions**	**Main clinical-effectiveness outcome (summary)**	**Notes**
Knutson et al., (2015)	Platelets	Amotosalen-UVA (INTERCEPT)	~19,175 transfusions	Clinical effectiveness adequate for routine transfusion use; no signal of increased	Large safety dataset; focus on hemovigilance rather than controlled CCI comparisons.

				bleeding vs historical expectations.	
Drawz et al., (2015)	Platelets (PAS)	Riboflavin-UV (MIRASOL)	19 patients (small series)	CCI and clinical response acceptable in small series; limited power.	Intended as clinical CCI/practical use report.
Rebulla et al., (2017)	Platelets	INTERCEPT & MIRASOL	~424 evaluable patients	Lower post-transfusion CCIs reported for PRT platelets, but bleeding outcomes similar to standard platelets.	Trial stopped early; underpowered for some endpoints — interpret with caution.
Piotrowski et al., (2018)	Platelets & plasma	Riboflavin-UV (MIRASOL)	Regional aggregated transfusions	Routine use observations: low rates of serious bleeding events and no new safety signals.	Surveillance/registry data; descriptive.
van der Meer et al., (2018)	Platelets	Riboflavin-UV (MIRASOL)	469 patients randomized	Non-inferior for clinical bleeding outcomes despite small reductions in laboratory platelet increments.	Well-conducted RCT; supports clinical effectiveness.
Garban et al., (2018)	Platelets	Amotosalen-UVA (INTERCEPT)	~790 evaluable	No clinically important increase in bleeding; PRT platelets met non-inferiority margins for clinical endpoints in the trial.	Large oncology population; meaningful clinical endpoint data.
Schulz et al., (2019)	Platelets	Amotosalen-UVA (INTERCEPT)	Multiple pediatric transfusions reported	Utilization patterns stable; no increase in severe bleeding; safety acceptable in neonates/children.	Institutional QA report; paediatric focus.
Bahar et al., (2020)	Platelets	INTERCEPT / MIRASOL (centres)	Large centre datasets	Clinical hemostasis maintained; no signal of worse bleeding; some centres reported small increase in platelet usage.	Implementation/usage focused.
Arroyo et al., (2020)	Plasma	Methylene blue + visible light	Number of TPE episodes (reported)	Methylene-blue plasma effective for therapeutic plasma exchange (TTP) with comparable clinical responses to quarantine FFP.	Clinical outcome focus (TTP).
Brixner et al., (2021)	Platelets	UVC (Theraflex-type)	~171 patients	1-hr CCI non-inferiority tested; overall clinical bleeding similar	RCT supports clinical viability of UVC PRT for platelets.

				between groups though CCIs modestly lower in PRT arm.	
Jimenez-Marco et al., (2021)	Platelets & plasma	Riboflavin-UV (MIRASOL)	~9,673 platelet transfusions (centre)	Implementation maintained clinical service with few reported bleeding complications; operational metrics improved.	Large centre experience; real-world effectiveness and logistics.
Ladaique et al., (2023)	Platelets	Amotosalen-UVA (INTERCEPT)	AML patient transfusion series	Clinical efficacy adequate for AML transfusions; no excess bleeding; transfusion support maintained.	Real-world oncology data.
Pedraza et al., (2024)	Platelets	Amotosalen-UVA (INTERCEPT)	National / centre inventory data	Implementation improved platelet availability and provided clinically acceptable products; no large safety signals reported.	LMIC implementation benefits emphasised.
Łętowska et al., (2016)	Platelets & plasma	Riboflavin-UV (MIRASOL)	Regional counts reported	Safety and clinical effectiveness consistent with existing practice; hemovigilance rates comparable to historic controls.	Surveillance data.
Rustanti et al., (2020)	Plasma & platelets (spiked units)	Methylene blue (plasma); UVC (platelets)	Spiked units, lab study	Demonstrated strong inactivation of Japanese encephalitis virus (JEV) in treated products — supports PRT efficacy against Asian endemic virus.	Laboratory pathogen-inactivation study — not clinical patient outcomes.

Safety Outcomes

The safety results from the studies were mostly very good. Big hemovigilance reports, like the INTERCEPT study by Knutson et al. (2015), showed that transfusion reactions were very rare. Less than 1% of transfusions had any quick reaction, and serious reactions happened in fewer than 0.1%. Other studies from Europe and North America like Piotrowski et al. (2018), Schulz et al. (2019), and Bahar et al. (2020) also showed that after using pathogen-reduced blood products, the number of febrile, allergic, and other reactions stayed the same or even became lower.

Another important part of safety is preventing infections from blood transfusion. Many studies showed that PRT systems are very strong in killing germs. Lab studies like Rustanti et al. (2020) proved that the systems can remove dangerous viruses, including Japanese encephalitis virus, which is important in places where such viruses exist. Plasma PRT systems, like methylene blue treatment, also showed very good ability to kill viruses and bacteria, making blood transfusion safer. A few studies reported some small concerns, like slightly higher platelet use or a small increase in refractoriness with some PRT systems. For example, Brixner et al. (2021) found that UVC-treated platelets had higher transfusion failure compared to normal platelets. But these issues did not lead to more serious problems for patients. Overall, the evidence shows that pathogen-reduced blood products are very safe and give strong protection against infection risks.

Table 3: Safety outcomes and clinical effectiveness reported in included studies

Study	PRT system	Key safety findings (summary)	Serious adverse events (SAE) reported	Notes on infection/sepsis reduction
Knutson et al., (2015)	INTERCEPT	Low overall transfusion-reaction rates; no new safety signal	No signal of increased SAE attributable to PRT	Hemovigilance shows reductions in bacterial septic transfusion events vs historical expectations.
Drawz et al., (2015)	MIRASOL	Small series: no increase in febrile/allergic reactions	NR (small sample)	Not powered to show infection-rate changes.
Rebulla et al., (2017)	INTERCEPT & MIRASOL	Adverse reaction rates similar between PRT and control arms	No excess SAE linked to PRT	Noted fewer bacterial contamination events in PRT groups (laboratory/processing findings).
Piotrowsk et al., (2018)	MIRASOL	Hemovigilance: no emergent safety concerns	Rare SAEs; none attributable specifically to PRT	Surveillance supports safety in routine use.
van der Meer et al., (2018)	MIRASOL	Similar transfusion-reaction profile; no excess febrile or allergic events	No increase in SAE reported	Clinical safety supported by non-inferiority design.
Garban et al., (2018)	INTERCEPT	Comparable AE rates across arms; no increased risk	No PRT-related SAE signal	Large RCT with formal safety monitoring.
Schulz et al., (2019)	INTERCEPT	Pediatric QA: no increase in serious transfusion reactions; febrile rates similar	No notable SAE increase	Pediatrics: PRT safe for neonatal/infant use per centre report.
Bahar et al., (2020)	INTERCEPT / MIRASOL	Routine safety acceptable; some centres reported fewer febrile/septic reactions	NR (aggregated data)	Some evidence that bacterial contamination/sepsis reduced after PRT adoption.
Arroyo et al., (2020)	Methylene blue plasma	Low adverse-reaction rates; clinically effective in TPE	No excess SAE	MB plasma historically associated with low AE rates; study supports equivalence.
Brixner et al., (2021)	UVC	AE profile similar to control; serious reactions rare	No significant SAE signal	UVC PRT safety acceptable in RCT setting.
Jimenez-Marco et al., (2021)	MIRASOL	Implementation safety: low transfusion reactions; hemovigilance compatible with safety expectations	Rare SAEs; none attributable to PRT	Real-world safety across many transfusions.
Ladaique et al., (2023)	INTERCEPT	No increase in adverse events in AML cohort	NR (single-centre data)	Clinically safe in oncology setting.
Pedraza et al., (2024)	INTERCEPT	Implementation in LMIC: no surge in adverse reactions; improved availability	NR (implementation data)	Focus on operational safety; no new safety signals reported.

Łętowska et al., (2016)	MIRASOL	Hemovigilance: transfusion-reaction rates comparable to pre-PRT era	No PRT-specific SAEs identified	Supports routine safety.
Rustanti et al., (2020)	MB (plasma) & UVC (platelets)	Lab study — not applicable to clinical transfusion reactions	Not applicable	Demonstrated viral inactivation capability (JEV) — safety inference implies reduced transfusion-transmitted infection risk.

Quality Appraisal of Included Studies

The overall quality of the fifteen studies was generally good. Most of the randomized controlled trials—like Garban et al. (2018), Rebulla et al. (2017), van der Meer et al. (2018), and Brixner et al. (2021)—showed strong and well-organized methods. These trials clearly explained how they chose participants, how they randomized them, what treatments they used, and how they checked their results. They also had low risk of bias in important areas like hiding the allocation and blinding the people who checked the lab results. Even though doctors and patients could not be blinded because of how PRT treatment works, the reporting of outcomes was still clear and consistent. The hemovigilance and observational studies also showed good quality, especially the big datasets from Knutson et al. (2015), Piotrowski et al. (2018), Bahar et al. (2020), and Pedraza et al. (2024). These studies followed thousands of transfusions, which made their safety results stronger and more reliable. But because observational studies depend on normal hospital records and not on controlled trial settings, they can have some confounding factors. Still, their large sample sizes and real-life usefulness made them valuable for understanding how PRT works in practice. Smaller studies like Drawz et al. (2015) and laboratory studies like Rustanti et al. (2020) had some limits because they used small sample sizes and did not include many patient outcomes. Even so, they provided useful information about platelet quality and how well the systems kill viruses. Plasma-focused studies like Arroyo et al. (2020) also showed good methods and clearly defined their outcomes.

Table 4: Study Design and Preliminary risk of bias from studies

Study	Design	Preliminary risk of bias (overall)	Rationale (brief)
Knutson et al., (2015)	Prospective hemovigilance cohort	Moderate	Large real-world dataset; observational—subject to reporting variation and no randomized comparator.
Drawz et al., (2015)	Small observational series	High (for clinical-effectiveness inference)	Small sample; limited power; observational.
Rebulla et al., (2017)	Randomized parallel trials	Low–Moderate	RCT design reduces bias, but early stopping and limited power for some endpoints raises concerns.
Piotrowsk et al., (2018)	Passive hemovigilance	Moderate	Passive reporting may undercapture events; good for safety signals but limited causal inference.
van der Meer et al., (2018)	Randomized non-inferiority RCT	Low	Well-designed RCT with appropriate endpoints; good internal validity.
Garban et al., (2018)	Randomized 3-arm RCT	Low	Large multicentre RCT with robust methods for clinical endpoints.
Schulz et al., (2019)	Before–after QA (paediatrics)	Moderate	Institutional QA design; subject to temporal confounding and local practice changes.
Bahar et al., (2020)	Observational hemovigilance	Moderate	Real-world data but observational limitations.
Arroyo et al., (2020)	Comparative clinical (TPE context)	Moderate	Clinical comparative design; may not be randomized.

Brixner et al., (2021)	Randomized non-inferiority RCT	Low–Moderate	RCT quality good; sample size moderate.
Jimenez-Marco et al., (2021)	Implementation cohort	Moderate	Strong implementation data; observational evidence.
Ladaique et al., (2023)	Single-centre observational	Moderate	Single-centre limits generalizability.
Pedraza et al., (2024)	Before–after implementation (LMIC)	Moderate	Good implementation value; potential confounding by cointerventions.
Łętowska et al., (2016)	Hemovigilance survey	Moderate	Surveillance data; limited causal inferences.
Rustanti et al., (2020)	Laboratory inactivation study	High (for clinical outcomes)	Robust lab data on pathogen inactivation but not clinical patient outcomes.

Regional Findings and Patterns

The studies showed some differences between regions because transfusion systems, common infections, and available PRT technologies are not the same everywhere. European countries provided the highest number of strong randomized trials, including work by Garban et al. (2018), Rebulla et al. (2017), and Brixner et al. (2021). These countries already use PRT widely, so their studies were able to check bleeding outcomes, platelet use, and detailed blood results in a more advanced way. European research also looked at newer PRT methods, like UV-C platelets, giving special information about how these systems perform.

North American studies, including Knutson et al. (2015), Piotrowski et al. (2018), and Schulz et al. (2019), mostly provided large safety reports and post-implementation reviews. These hemovigilance datasets gave very strong evidence that transfusion reactions remained very low after PRT was introduced. While European studies focused more on how well the treatments work, North American findings showed what happens in real-life hospital practice across large groups of patients.

Latin American research, shown by Arroyo et al. (2020), added information about plasma PRT and how transfusions work in areas with different infection problems. This helped the global understanding of how PRT plasma performs in places with fewer resources and different disease risks.

Asia was represented by Rustanti et al. (2020), which studied how well PRT kills viruses in platelets. This study did not involve giving platelets to patients, but it was very important for the region because it tested the technology against Japanese encephalitis virus—an infection that is common there. This showed that PRT can be useful in places facing viral threats that are not usually seen in Europe or North America.

Discussion and Limitations

This systematic review assessed the clinical efficacy and safety of pathogen-reduction technologies (PRTs) utilized for platelets and plasma across publications published between 2015 and 2025. The findings from the 15 included studies show a generally consistent pattern: most PRT systems reduce laboratory measures of platelet recovery such as the corrected count increment (CCI), yet clinical outcomes such as bleeding control and safety remain largely comparable to standard blood components. At the same time, other studies have documented variations in platelet consumption and operational needs following PRT deployment. Together, these data reveal a wide picture of how PRT performs in real clinical practice and how it affects patients, transfusion services, and national blood systems. Although PRTs make transfusions safer, using them can create practical challenges. Studies like those by Rebulla et al. and Brixner et al. found that some UVC systems led to increased platelet use and higher rates of refractoriness. This can add pressure on platelet supplies, increase workload, and raise overall costs. These issues are especially important for low- and middle-income countries, where resources and infrastructure are often limited. Because of this, the operational impact of PRTs should be interpreted with caution.

Overall, the randomized studies agreed that PRT-treated platelets give lower 1-hour and 24-hour corrected count increments (CCI) compared to untreated platelets. This was shown in many important studies, including Garban et al. (2018), Rebulla et al. (2017), van der Meer et al. (2018), and Brixner et al. (2021).

These studies consistently showed that treated platelets, whether processed with amotosalen-UVA, riboflavin-UV, or UVC light had smaller increases after transfusion. This lower increase is thought to happen because the PRT process puts stress on the platelets and

causes some changes in their structure. However, it is important to note that the amount of decrease was not the same for all PRT systems. Some systems had smaller effects than others. In this work, photochemical PRT systems such as amotosalen-UVA and riboflavin-UV, which rely on additive molecules, are explicitly distinguished from photophysical UVC systems that operate without chemical photosensitizers; this distinction may explain the differing outcomes observed in the Brixner et al. UVC trial. Despite the reduced CCI values, the trials did not discover notable variations in clinical hemostasis, showing that platelet function is conserved sufficiently to maintain acceptable bleeding control.

Clinical bleeding outcomes comprised a significant aspect of the study assessments. Most of the high-quality randomized trials reported no significant increase in WHO grade ≥2 hemorrhage in patients receiving PRT-treated platelets. For example, Garban et al. (2018) observed identical rates of clinically significant bleeding across intervention and control groups in the EFFIPAP study. Likewise, van der Meer et al. (2018) found that in intention-to-treat analysis, pathogen-reduced platelets were non-inferior to untreated platelets in avoiding moderate to severe bleeding. Findings from systematic reviews such as Estcourt et al. (2017) and Pati et al. (2022) further reinforced this finding, revealing that although PRT platelets lower laboratory increases, they do not significantly impair clinical bleeding outcomes. Therefore, it can be claimed that, across various trials and circumstances, PRT maintains hemostatic effectiveness at a clinically acceptable level.

Safety outcomes were also comparable across research. Hemovigilance systems, particularly large observational datasets such as the one described by Knutson et al. (2015), demonstrated relatively low transfusion-reaction rates using PRT platelets. In their research, the rate of acute transfusion responses was just 0.6%, with significant adverse effects (<0.1%) seldom ascribed to transfusion. Similar outcomes were observed in observational and post-implementation studies in diverse locations, including those by Piotrowski et al. (2018), Schulz et al. (2019), and Bahar et al. (2020). These trials observed constant rates of febrile, allergic, and other transfusion responses despite shifting to pathogen-reduced components. In addition, PRTs offer a substantial advantage by essentially preventing many transfusion-transmitted infections, a benefit confirmed both clinically and in laboratory investigations such as Rustanti et al. (2020). Because of this, PRTs continue to be considered as a major safety enhancer, especially in circumstances where the danger of infection transmission is considerable.

Although most data agreed well, considerable variance and outliers were detected. In certain studies, notably per-protocol analysis, non-inferiority margins for bleeding outcomes were not satisfied. For example, the per-protocol arm of the van der Meer et al. (2018) study indicated slightly greater bleeding levels in the PRT group, even though the intention-to-treat analysis fulfilled non-inferiority criteria. Similarly, Rebulla et al. (2017) showed greater platelet utilization and smaller increments utilizing both amotosalen and riboflavin systems. These data demonstrate that while PRT is typically beneficial, some technologies or patient subgroups may exhibit lower effectiveness that must be monitored. Another area of difference involves platelet usage: numerous trials showed that patients receiving PRT platelets required more frequent transfusions or higher numbers of units, with some studies indicating increases of up to 50% (Brixner et al., 2021). This implies that while PRT provides safety, it may raise operational demands and resource consumption in blood banks. The observed increase in platelet utilization following PRT adoption suggests that hospitals transitioning to 100% PRT may need to reinforce inventory management processes, including maintaining adequate buffer stocks to prevent supply strain

Differences across PRT technology also contributed to variances in outcomes. Amotosalen-UVA and riboflavin-based systems have been the most intensively investigated, with fairly consistent effects across varied populations. In contrast, newer systems like UVC-based PRT exhibited somewhat increased rates of refractoriness (repeated inadequate post-transfusion platelet increment despite adequate dosing) and transfusion failure (inability of a platelet unit to achieve the expected rise in platelet count under standard clinical conditions) in certain instances (Brixner et al., 2021). Plasma-specific PRT approaches, such as the methylene blue system examined by Arroyo et al. (2020), revealed clinical efficacy equivalent to conventional plasma, albeit some previous studies reported minor decreases in coagulation factors. These technological variations underscore the need of selecting PRT systems based on the demands and capabilities of the blood service or clinical setting.

The consequences of these discoveries are substantial for blood banks and transfusion programs. The most essential advantage of PRT usage is better blood safety, notably in reducing transfusion-transmitted illnesses from known and developing pathogens. This is particularly useful in nations where screening infrastructure is poor or when donor populations have increased infection risks. However, deployment of PRT may also lead to greater platelet consumption, which might strain inventories and raise

expenses. Blood banks must plan for these logistical problems while acknowledging the long-term safety advantages. Furthermore, certain PRT systems offer prolonged storage, such as 7-day shelf life for platelets, which can enhance supply management and minimize waste (Pedraza et al., 2024). Thus, PRT can both improve and challenge blood systems, depending on how resources are utilized.

For national blood safety programs, PRT provides an extra protection beyond regular testing procedures. It decreases reliance on donor deferral procedures, mitigates risk from developing diseases, and adds consistency to transfusion safety even during outbreaks. Hemovigilance data across multiple locations indicate PRT as a viable strategy for minimizing bacterial contamination occurrences and enhancing patient protection (Knutson et al., 2015; Piotrowski et al., 2018). These benefits may assist drive policy and long-term planning for transfusion services, especially in impoverished nations or high-risk contexts.

Patients also stand to gain from the usage of PRT-treated blood components. Despite decreased laboratory increments, clinical results stay steady, and the chance of obtaining a safer product is substantially higher. Patients with weaker immune systems, such as those undergoing cancer therapy or stem cell transplantation, are particularly safeguarded by PRT's capacity to inactivate viruses, germs, and parasites. Although certain patients may require more frequent transfusions due to lesser increments, the overall risk profile remains extremely favorable, and this trade-off is frequently acceptable in practical practice.

Study Limitations

This systematic review has significant limitations that should be noted. First, the included research differed in design, sample size, and population characteristics. Randomized controlled trials exhibited excellent internal validity, however numerous observational and hemovigilance studies lacked randomization and blinding, which may add bias. Second, discrepancies across PRT technology make direct comparison problematic. Systems such as amotosalen-UVA, riboflavin-UV, and UVC employ distinct pathways, and their efficacy differs between results.

Another problem is that several research focused mostly on laboratory markers rather than clinically significant bleeding events. Similarly, not many trials disclosed precise safety data such as particular transfusion-reaction subtypes or long-term outcomes. There were also geographical disparities, since some locations have more advanced blood screening methods, while others rely largely on PRT due to increased infection dangers. Although the review includes data from the Asian region, most of the evidence is derived from laboratory inactivation studies, and clinical outcome data from Asian patient populations remain limited; thus, clinical generalizability for this region should be interpreted cautiously

Lastly, publication bias may be present because most research come from well-resourced environments, and some unfavorable findings may remain unreported. These criteria should be addressed when assessing the generalizability of the findings.

Conclusion

This systematic analysis investigated the clinical efficacy and safety of pathogen-reduction technologies (PRTs) utilized for platelets and plasma across studies published from 2015 to 2025. The overall findings suggest that although PRT-treated platelets regularly offer reduced laboratory increments—specifically lowered corrected count increment (CCI) values—they nonetheless demonstrate appropriate clinical hemostatic efficacy in most patients. Clinical bleeding outcomes, notably WHO grade ≥2 hemorrhage, were typically comparable between PRT and traditional platelets in the majority of randomized trials and observational studies. Furthermore, PRT-treated plasma also maintained excellent therapeutic responses across diverse clinical applications.

Safety findings were extremely positive across all examined trials. Transfusion responses were modest, and significant adverse outcomes were infrequent. Large hemovigilance datasets supported the good safety profile of PRT components, while laboratory investigations indicated robust inactivation of a wide spectrum of pathogens. This makes PRT an important technique for boosting transfusion safety, especially in locations with high infectious disease burden or limited screening capabilities. However, problems were also discovered. Several studies found greater platelet consumption and, in certain situations, higher transfusion failure rates related with specific PRT methods. These outcomes can boost operational expenses and impose additional strain on blood bank inventory. Technology-specific variances also exist, as certain newer systems (e.g., UVC-based PRT) demonstrated somewhat worse performance in selected outcomes. Given the heterogeneity in PRT technologies, study designs, and outcome reporting, the conclusions of this review should be interpreted cautiously, and future comparative trials are needed to better define technology-specific performance

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Authors' Contributions:
Oluchi Okechukwu conceived the study, coordinated the systematic review process, and drafted the main sections of the manuscript. Oluchi Okechukwu and Chidinma Gab-Obinna contributed to the study design and literature screening. Adepeju Kafayat Olowookere and Christopher Bijabdo Jato performed data extraction and quality appraisal of included studies. Richard Afriyie Osei and Dorcas Okayo Okoroafor contributed to data synthesis and interpretation of findings. Lawrence John Ajutor and Tobi David Farinde assisted with database searching and reference management. All authors critically reviewed, edited, and approved the final manuscript.
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