

Massive Transfusion Protocols cause Significant Blood Unit Wastage: A Systematic Review and Meta-Analysis

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ABSTRACT

Massive Transfusion Protocols (MTP) are activated when a patient is actively bleeding to allow the blood bank to prioritise blood components ordered for this patient. However, as many units are issued out in quick succession for the MTP patient, wastage can occur. This could be due to over activation of the MTP, failing to promptly notify the blood bank to deactivate the MTP, or miscommunication between clinical and blood banking staff. The aim of this systematic review was to explore the relationship between different unit types that are wasted during an MTP, with a hypothesis that units requiring thawing-Fresh Frozen Plasma (FFP) and cryoprecipitate-would be more likely to be wasted.

The highest wastage rates in an MTP were found to be in Platelets (10.0%), Cryoprecipitate (10.0%) and FFP (9.9%), whereas red cell waste was the lowest at (1.3%). Platelets, FFP and Cryoprecipitate were found to be wasted at a higher rate than red cells, with statistically significant results. The hypothesis that thawed units lead to higher rates of waste was partially supported.

FFP that is converted to extended life plasma if it is not transfused immediately leads to lower wastage rates. Proper storage and prompt return of unused units to the blood bank allows the unit to be reissued to another patient.

Keywords: Blood wastage; Extended life plasma; Overactivation; Life-threatening haemorrhage

INTRODUCTION

MTP is a standardised emergency procedure for rapid transfusions of blood components for life-threatening haemorrhage [1-3]. MTP is most consistently defined as administering 10 or more units of Packed Red Blood Cells (PRBCs) within 24 hours, or greater than 5 units of PRBCs within four hours [4]. Prompt activation and implementation of an MTP is essential to prevent the development of hypothermia, acidosis and coagulopathy, collectively known as the "lethal triad". The development of the lethal triad is known to increase the risk of mortality [3,5]. MTPs are designed to facilitate immediate communication and coordination between the blood bank and medical staff. The protocol ensures blood components are rapidly delivered in predetermined ratios. MTP criteria and blood component ratios. While the use of MTPs has been effective in reducing the impact of haemorrhage, the protocol's rigorous demands and the urgent ordering of blood products, frequently result in over-ordering of units and overactivation of protocol, subsequently causing waste of blood components [6].

Hospitals design their own criteria for activation of an MTP, which may be based on a variety of factors. Rapidly assessing and identifying a critically haemorrhaging patient and swift activation of an MTP as well as notifying the blood bank is significant in increasing the chances of the patient's survival [7]. A doctor is usually responsible for initiating the activation of an MTP. However, in Weykamp, the level I trauma centre the paper investigates automatically activates for some trauma patients if certain criteria are met [8].

There is much literature exploring the effectiveness of various ratios of red cells to plasma to platelets. The most widely accepted ratio is 1:1:1 as this has been found to be most beneficial for bleeding patients [9]. The use of plasma and platelets in an MTP serves to aid in correcting coagulopathy in the bleeding patient [10,11]. Transfusing multiple units of red cells alone leads to dilution of coagulation factors and platelets (dilutional coagulopathy), hence the need for a more balanced regimen of products including FFP, platelets and cryoprecipitate when transfusing a large number of units [11].

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Prevention of blood wastage in an MTP

Blood collected from a donor is a scarce and valuable resource that is collected from an individual who has chosen to donate with the desire to selflessly help someone in need. Toprak found the most common reasons leading to the wastage of blood components were due to expired units, failing to return unused units to the blood bank in time and patients refusing transfusion [12]. The study also found that MTP activation led to wastage due to overactivation of the MTP for patients that did not warrant activation, as well as failing to deactivate the MTP promptly [12]. It was also identified that thawed products-FFP and cryoprecipitate had the highest wastage rates and it was emphasised that overuse of the MTP led to waste of thawed products [12].

As large quantities of blood components are issued rapidly during an MTP, this can lead to wastage as units returned to the blood bank do not meet appropriate storage or temperature requirements and therefore must be discarded [13]. The MTP was designed to facilitate effective communication between clinical and laboratory staff in order to prevent wastage of blood [14].

Current practices

MTPs have evolved to balance rapid blood product delivery with efforts to minimise wastage. The activation of MTP occurs through procedures initiated by clinicians when faced with severe haemorrhage. Effective communication between the clinicians and the blood bank is lead to the timely delivery of blood units. Paganini emphasises the need for regularly updating and revising MTP protocols to ensure they are serving the hospital as effectively as possible and thus minimising wastage [13]. During an MTP, the issuing of blood products is distributed in specific standardised ratios that align with the organisation's protocols. Thromboelastography (TEG) and Rotational Thromboelastometry (ROTEM) are widely used tools that provide real-time assessments of a patient's coagulopathy [15]. Real-time assessments allow clinicians to order blood units specifically tailored to the patient's individual needs, guiding a targeted transfusion and reducing unnecessary blood unit wastage [16]. Effective communication between clinical teams and the blood bank is essential to ensure the timely deactivation of the protocol. However, studies have shown that timely deactivation remains a challenge, with some institutions reporting low rates of protocol termination within recommended timeframes [2]. This delay in deactivation can lead to unnecessary preparation and potential wastage of blood products.

There is much existing literature on MTPs in trauma and non-trauma patients, ratio of blood components administered, patient mortality and coagulopathy. There is a need for further exploration of the relationship between MTPs and its role in blood wastage.

Research question and hypothesis

The Patient, Intervention, Outcome and Comparison (PICO) framework was applied to this study. In patients who are massively haemorrhaging (patient) who have an MTP activation (intervention), does blood wastage (outcome) vary by type of unit issued (comparison) [17]. In addition, it is hypothesised that during an MTP, FFP and cryoprecipitate has a higher rate of wastage compared to red cells and platelets due to thawing requirements.

MATERIALS AND METHODS

Study design

This study was conducted using the Preferred Reporting Items

for Systematic-Reviews and Meta-Analysis (PRISMA) to search for appropriate articles related to blood wastage in an MTP [18]. This methodology was used to perform database searches to gather articles from databases, which were narrowed down to address the specific research question.

Search strategy

In order to identify relevant papers for this meta-analysis, four databases were used: Scopus, Embase, PubMed and Ebsco. The search terms used were "massive transfusion protocol" with "activation", "massive blood transfusion" and "massive transfusion protocol". Search terms such as "MTP" and "haemorrhage" were found to obtain far too many generic results and were therefore not utilised. There was no time restriction applied to the results from the searches. Refer Figure 1 to the search strategy process.

Eligibility criteria

The studies found in the database searches were screened based on title and abstract. An eligibility criteria was applied that excluded results that were not journal articles, not in English, no full text available and not having suitable data for meta-analysis. The final six studies included in the meta-analysis and systematic review relate to MTPs and observe blood wastage as a result of them.

Data extraction

Data was extracted from the six studies included in order to perform the meta-analysis. The total number of units issued out was included, as well as red cell waste, FFP waste, platelet waste and cryoprecipitate waste that occurs during an MTP. Data was also extracted relating to the number of units that had to be discarded and thus wasted, out of the total number of the units that were returned to the blood bank [19].

Statistical analysis

In order to produce the forest plots for this meta-analysis, the open meta-analyst software was used. One arm proportion was used to analyse the data on red cell waste in an MTP, FFP waste, platelet waste as well as cryoprecipitate waste. As well as a one arm proportion on the number of units that were wasted after being returned to the blood bank. For all forest plots produced, the arcsine transformed proportion was utilised, along with binary random effects analysis method and maximum likelihood method.

Additionally, Data extracted from the included studies compared the number of blood units wasted to those requested for PRBC, Platelet concentrates (PLT) and FFP components. The association between increased blood unit wastage was evaluated using Odds Ratios (ORs) with 95% CI. To estimate effect sizes, a binary random-effects model utilisingthe maximum likelihood approach was employed, reporting results as ORs with 95% CI and assessing heterogeneity across studies. The heterogeneity was evaluated using the Mantel-Haenszel method (I² test), with a significance level of (Figure 1) $p \le 0.05$. This analysis was performed using Review Manager (Rev Man) software (Version 5.4, The Cochrane Collaboration, 2020) to assess the association of blood unit wastage among the different blood components [20].

RESULTS

Study selection

A total of 6331 results were obtained from the four databases and 3211

duplicates were excluded. From this point, 2668 results were excluded during a title and abstract screening. To narrow down further, articles were excluded due to not being relevant to the research question, not being in English, not including data in a format usable for metaanalysis, as well as for no full text being found. Two additional studies were added through manual searches. Finally, six papers were included in this meta-analysis. Refer to Figure 1 for the PRISMA flowchart that outlines this process.

Study characteristics

A summary of the six studies used in this meta-analysis and systematic review are shown in (Table1). The studies took place over a variety of countries, the study period ranged from 2013 to 2022 and all studies used a retrospective study design. The total number of units issued, total number of MTP activations, the total percentage of units discarded in an MTP is shown, as well as if the FFP was converted to extended life plasma at that hospital. Finally, the parameters measured for the meta-analysis are shown [21].

Study quality assessment

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) was used to assess the quality and strength of the studies selected for this systematic review and meta-analysis [22]. The quality of each study was assessed by categorising these criteria as either "Yes" or "No." Conradi et al, did not state the limitations of the study, further weakening its overall quality assessment [20]. The STROBE checklist revealed that one study did not have an abstract that outlined the findings of the study. It was also found that one study did not discuss limitations of their results or methodology. The studies selected were of fairly high methodological quality overall (Tables 2 and 3).



 Table 1: Summary of studies included in meta-analysis of blood wastage during MTPs. The data extracted from these six studies to be used in meta-analysis is presented in Table 2.

Study	Year	Country	Study Period	Study Design	Total number of units issued	Number of MTP activations	Percentage of units wasted	FFP converted to extended life plasma	Parameter measured
Chong et al.[19]	2022	Singapore	2013 - 2018	Retrospective	323	26	1.50%	Yes	Red cell, FFP, platelet and cryoprecipitate waste

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Conradi et al.[20]	2013	Germany	2012	Retrospective	877	69	23.49%	No	Red cell, FFP and platelet waste
Dunbar et al. [2]	2017	USA	2015 - 2016	Retrospective	6139	-	1.97%	Yes	Red cell, FFP, platelet and cryoprecipitate waste
Khan et al. [11]	2013	London	2007 - 2009	Retrospective	1757	40	5.46%	Yes	Red cell, FFP, platelet and cryoprecipitate waste
Paganini et al. [13]	2021	USA	2015 - 2018	Retrospective	6459	134	4.61%	No	Red cell, FFP and platelet waste
McDaniel et al. [23]	2013	USA	2011	Retrospective	1911	52	2.88%	No	Red cell, FFP and platelet waste

Table 2: Summary of results showing wastage during an MTP broken down by type of blood component.

Study	Year	Total units issued	Red cell waste from units issued	FFP waste from units issued	Platelet waste from units issued	Cryoprecipitate waste from units issued
Chong et al. [19]	2022	323	2/168	3/77	0/43	0/35
Conradi et al. [20]	2013	877	8/507	194/338	4/32	-
Dunbar et al. [2]	2017	6139	51/3110	47/2816	5/83	18/130
Khan et al. [11]	2013	1757	8/1119	54/404	16/116	18/118
Paganini et al. [13]	2021	6459	81/3668	119/2074	98/717	-
McDaniel et al. [23]	2013	1911	6/922	9/660	40/329	-

Table 3: STROBE checklist to assess the quality of studies used in the meta-analysis.

		Title and Abstract	Introduction		Methods		Results	Disc	ussion
Study	Year	Abstract summarises what was found	States objectives and hypothesis	Key elements of study design	Eligibility criteria of participants	Addresses potential sources of bias	Reports number of outcome events	Summarises key results	Discusses limitations of the study
Chong et al. [19]	2022	Y	Y	Y	Y	Y	Y	Y	Y
Conradi et al. [20]	2013	Ν	Y	Y	Y	Y	Y	Y	N
Dunbar et al. [2]	2017	Y	Y	Y	Y	Y	Y	Y	Y
Khan et al. [11]	2013	Y	Y	Y	Y	Y	Y	Y	Y
Paganini et al. [13]		Y	Y	Y	Y	Y	Y	Y	Y
McDaniel et al. [23]	2013	Y	Y	Y	Y	Y	Y	Y	Y

Note: Y-Authors assessing the quality of studies; N-Authors not involving the quality of studies.

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Meta-analysis by unit type wasted in a MTP

Red cell waste during an MTP: A forest plot was created representing the rate of red cell wasted from the total number of red cells issued in an MTP (Figure 2A). The one-arm proportion of red cell waste was statistically significant and shows a wastage rate of 1.3% (95% CI (0.009, 0.019); p<0.001. The forest plot is shown to have a high degree of heterogeneity (I2=74.04, p<0.001).

FFP waste during an MTP: A forest plot was created representing the rate of FFP units wasted from the total number of FFP units issued in an MTP (Figure 2B). The one-arm proportion of FFP waste was statistically significant and shows a wastage rate of 9.9% (95% CI (0.013, 0.252); P=0.002. The forest plot is shown to have a high degree of heterogeneity (I2=99.56, p<0.001).

Platelet waste during an MTP: A forest plot was created representing the rate of platelets wasted from the total number of platelets issued in an MTP (Figure 2C). The one-arm proportion of platelet waste was statistically significant and showed a wastage rate of 10% (95% CI (0.065, 0.142); p<0.001. The forest plot is shown to have a high degree of heterogeneity (I2=72.40, p=0.005).

Cryoprecipitate waste during an MTP: A forest plot was created representing the rate of cryoprecipitate wasted from the total number of cryoprecipitate units issued in an MTP (Figure 2D). The one-arm proportion of cryoprecipitate waste was statistically significant and shows a wastage rate of 10.0% (95% CI (0.038, 0.186); p<0.001. The forest plot is shown to have a high degree of heterogeneity (I2=75.5, p=0.009) (Figure 2).

Meta-analysis comparing units wasted in an MTP/Red cell waste compared to platelet waste in an MTP: A forest plot was created representing the red cell wastage in an MTP compared with platelet wastage (Figure 3A). The two-arm proportion was statistically significant showing platelets had a higher rate of wastage than red cells (95% CI (0.06, 0.21); p<0.00001. The forest plot is shown to have a moderate to high degree of heterogeneity (I2=68, p=0.008).

Red cell waste compared to cryoprecipitate waste in an MTP: A forest plot was created representing the red cell wastage in an MTP compared with cryoprecipitate wastage (Figure 3B). The two-arm proportion was statistically significant showing cryoprecipitate had a higher rate of wastage than red cells (95% CI (0.03, 0.25); p<0.00001. The forest plot is shown to have a moderate degree of heterogeneity (I2=67, P=0.05).

Cryoprecipitate waste compared to platelet waste in an MTP: A forest plot was created representing the cryoprecipitate wastage in an MTP compared with platelet wastage (Figure 3C). The two-arm proportion was not statistically significant between cryoprecipitate and platelet wastage (95% CI (0.30, 1.40); p=0.27. The forest plot is shown to have a low degree of heterogeneity (I2=36, p=0.21) (Figure 3).

Red cell waste compared to FFP waste in an MTP: A forest plot was created representing the red cell wastage in an MTP compared with FFP wastage (Figure 4A). The two-arm proportion was statistically significant showing FFP had a higher rate of wastage than red cells (95% CI (0.05, 0.64); p=0.009. The forest plot is shown to have a high degree of heterogeneity (I2=97, p<0.00001).

FFP waste compared to platelet waste in an MTP: A forest plot was created representing the FFP wastage in an MTP compared with platelet wastage (Figure 4B). The two-arm proportion was not statistically significant between FFP and platelet wastage (95% CI (0.52, 4.10); p=0.47. The forest plot is shown to have a high degree of heterogeneity (I2=92, p<0.00001).

FFP waste compared to cryoprecipitate waste in an MTP: A forest plot was created representing the FFP wastage in an MTP compared with cryoprecipitate wastage (Figure 4C). The two-arm proportion was not statistically significant between FFP and cryoprecipitate wastage (95% CI (0.07, 3.43); p=0.48. The forest plot is shown to have a significant degree of heterogeneity (I2=94, p<0.00001) (Figure 4).



(A) Platelet vs Red Cell Waste

	PRBC Wastage		PLT Wastage			Odds ratio	Odds ratio			Risk of Bias							
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Rand	om, 95% Cl	AE	зс	D	Е	FG	i			
Chong et al., 2022 [19]	2	168	0	43	3.8%	1.31 [0.06 , 27.71]		-	? 1	•	?	• •	• •	,			
Conradi et al., 2013 [20]	8	507	4	32	13.7%	0.11 [0.03 , 0.40]			? 1	•) 🥐	•	• •)			
Dunbar et al., 2017 [2]	51	3110	5	83	17.7%	0.26 [0.10 , 0.67]			? 1	•	, ?	•	• •)			
Khan et al., 2013 [11]	8	1119	16	116	18.8%	0.05 [0.02 , 0.11]			? 1) 🥐	•	• •)			
McDaniel et al., 2013 [23]	6	922	40	329	18.9%	0.05 [0.02 , 0.11]			? 1) 🥐	•	• •)			
Paganini et al., 2021 [13]	81	3668	98	717	27.0%	0.14 [0.10 , 0.19]	-		? 1	•	•	•	• •				
Total		9494		1320	100.0%	0.11 [0.06 , 0.21]	•										
Total events:	156		163				Ŧ										
Test for overall effect: Z = 6	6.75 (P < 0.	00001)					0 01 01	1 10 10	0								
Test for subgroup differenc	es: Not app	olicable					PLT Wastage	PRBC Wastag	e								
Heterogeneity: Tau ² = 0.37	; Chi ² = 15.	48, df = 5	5 (P = 0.00	8); l² = 68	3%		-	-									

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

(B) Cryoprecipitate vs Red Cell Waste

	PRBC W	astage	CRYO W	astage		Odds ratio	Odds	ratio		R	isk	of E	Bias	5	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rando	om, 95% Cl	Α	в	С	D	Е	F	G
Chong et al., 2022 [19]	2	168	0	35	9.9%	1.07 [0.05 , 22.69]]		?	?	•	?	•	÷	•
Dunbar et al., 2017 [2]	51	3110	18	130	48.7%	0.10 [0.06 , 0.18]	∣ –∎– ∣		?	?	•	?	÷	÷	Ŧ
Khan et al., 2013 [11]	8	1119	18	118	41.4%	0.04 [0.02 , 0.09]	」 _■_ │		?	?	•	?	÷	÷	÷
Total		4397		283	100.0%	0.09 [0.03 , 0.25]	•								
Total events:	61		36												
Test for overall effect: Z	= 4.49 (P <	0.00001)				0.01 0.1 1	10 100							
Test for subgroup differe	nces: Not a	applicable					CRYO Wastage	PRBC Wastage							
Heterogeneity: Tau ² = 0.	52; Chi² = 6	6.06, df =	2 (P = 0.0	5); l² = 67	7%										

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

(C) Cryoprecipitate vs Platelet Waste

	PLT Wa	stage	CRYO W	astage		Odds ratio	Odds ratio		F	₹isl	c of	Bia	s	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	Α	в	С	D	Е	F	G
Chong et al., 2022 [19]	0	43	0	35		Not estimable		?	?	•	?	•	•	•
Dunbar et al., 2017 [2]	5	83	18	130	39.2%	0.40 [0.14 , 1.12]		?	?	•	?	•	•	•
Khan et al., 2013 [11]	16	116	18	118	60.8%	0.89 [0.43 , 1.84]		?	?	•	?	Ŧ	•	•
Total		242		283	100.0%	0.65 [0.30 , 1.40]	•							
Total events:	21		36											
Test for overall effect: Z	= 1.10 (P =	: 0.27)					0.01 0.1 1 10 100	,						
Test for subgroup differe	ences: Not a	applicable	e				CRYO Wastage PLT Wastage							
Heterogeneity: Tau ² = 0.	.12; Chi² =	1.55, df =	1 (P = 0.2	1); I² = 3	6%									
Risk of bias legend														
(A) Random sequence g	generation	selection	bias)											
(B) Allocation concealm	ent (selecti	on bias)												
(C) Blinding of participar	nts and per	sonnel (p	erformanc	e bias)										
(D) Blinding of outcome	assessmer	nt (detect	ion bias)											
(E) Incomplete outcome	data (attrit	ion bias)												
(E) Coloctive reporting (renewing bi	>												

(F) Selective reporting (reporting bias)

(G) Other bias

Figure 3: Forest plots of 2-way proportion meta-analyses comparing Note: A) Red cell and FFP waste in an MTP; B) FFP and platelet waste; C) Cryoprecipitate and FFP waste during an MTP.

(A) FFP vs Red Cell Waste

	PRBC W	/astage	FFP Wa	stage		Odds ratio	Odds ratio		F	Risk	of	Bia	S	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	Α	в	С	D	Е	F	G
Chong et al., 2022 [19]	2	168	3	77	13.5%	0.30 [0.05 , 1.82]	ı —•-	?	?	•	?	•	•	•
Conradi et al., 2013 [20]	8	507	194	338	17.2%	0.01 [0.01 , 0.02]	←	?	?	•	?	Ŧ	•	•
Dunbar et al., 2017 [2]	51	3110	47	2816	17.9%	0.98 [0.66 , 1.46]	Ⅰ +	?	?	•	?	Ŧ	•	•
Khan et al., 2013 [11]	8	1119	54	404	17.1%	0.05 [0.02 , 0.10]	·	?	?	•	?	Ŧ	•	•
McDaniel et al., 2013 [23]	6	922	9	660	16.3%	0.47 [0.17 , 1.34]	∣ _∎-	?	?	•	?	Ŧ	•	•
Paganini et al., 2021 [13]	81	3668	119	2074	18.0%	0.37 [0.28 , 0.49]	•	?	?	•	•	Ŧ	•	•
Total		9494		6369	100.0%	0.17 [0.05 , 0.64]								
Total events:	156		426				-							
Test for overall effect: Z = 2	2.63 (P = 0.	009)					0.01 0.1 1 10 1	4						
Test for subgroup differenc	es: Not app	olicable					FFP Wastage PRBC Wasta	age						
Heterogeneity: Tau ² = 2.45	; Chi² = 14	5.65, df =	5 (P < 0.0	0001); l²	= 97%									
Risk of bias legend														

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

(B) FFP vs Platelet Waste

	PLT Wa	stage	FFP Wa	stage		Odds ratio	Odds ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	ABCDEFG
Chong et al., 2022 [19]	0	43	3	77	7.6%	0.24 [0.01 , 4.85]]	? ? 🖨 ? 🖶 🖶
Conradi et al., 2013 [20]	4	32	194	338	16.8%	0.11 [0.04 , 0.31]	ı — •	?? \varTheta ? 🗣 🗣
Dunbar et al., 2017 [2]	5	83	47	2816	17.5%	3.78 [1.46 , 9.76]] –	?? \varTheta ? 🗣 🗣
Khan et al., 2013 [11]	16	116	54	404	19.2%	1.04 [0.57 , 1.89]	i 🔶	?? \varTheta ? 🗣 🗣 🗣
McDaniel et al., 2013 [23]	40	329	9	660	18.6%	10.01 [4.79 , 20.90]	i –	?? 🗣 ? 🗣 🗣 🖨
Paganini et al., 2021 [13]	98	717	119	2074	20.2%	2.60 [1.96 , 3.45]	i +	?? 🕈 🕈 🗣 🗣
Total		1320		6369	100.0%	1.46 [0.52 , 4.10]	•	
Total events:	163		426				-	
Test for overall effect: Z = 0).72 (P = 0.	47)						100
Test for subgroup differenc	es: Not app	olicable					FFP Wastage PLT Wastage	
Heterogeneity: Tau ² = 1.35	; Chi ² = 59.	03, df = 5	5 (P < 0.00	001); l² =	92%			

Risk of bias legend

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(D) Blinding of outcome assessment (detection bias)

(E) Incomplete outcome data (attrition bias)

(F) Selective reporting (reporting bias)

(G) Other bias

(C) Cryoprecipitate vs FFP Waste

	FFP Wa	stage	CRYO W	/astage		Odds ratio	Odds ratio		R	lisk	of	Bia	s	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl	Α	в	С	D	Е	F	G
Chong et al., 2022 [19]	3	77	0	35	20.7%	3.34 [0.17 , 66.33]		?	?	•	?	•	÷	•
Dunbar et al., 2017 [2]	47	2816	18	130	39.6%	0.11 [0.06 , 0.19]		?	?	•	?	•	•	•
Khan et al., 2013 [11]	54	404	18	118	39.6%	0.86 [0.48 , 1.53]	-	?	?	•	?	•	÷	•
Total		3297		283	100.0%	0.50 [0.07 , 3.43]								
Total events:	104		36											
Test for overall effect: Z	= 0.71 (P =	0.48)					0.01 0.1 1 10 100							
Test for subgroup differe	nces: Not a	applicable	9				CRYO Wastage FFP Wastage							
Heterogeneity: Tau ² = 2.	37; Chi² = 3	30.93, df	= 2 (P < 0	.00001); I	² = 94%									
Risk of bias legend														
(A) Random sequence g	eneration (selection	bias)											
(B) Allocation concealme	ent (selectio	on bias)												
(C) Blinding of participar	nts and pers	sonnel (p	erformanc	e bias)										
(D) Blinding of outcome	assessmer	nt (detecti	ion bias)											
(E) Incomplete outcome	data (attriti	ion bias)												
(F) Selective reporting (r	eporting bi	as)												

(F) Selective reporting (re
 (G) Other bias

Figure 4: Forest plots of 2 way proportion meta-analyses comparing Note: A) Red cell and platelet waste in an MTP; B) Red cell and cryoprecipitate waste; C) Cryoprecipitate and platelet waste during an MTP.

DISCUSSION

The hypothesis that red cells and platelets would have lower wastage rates compared with FFP and cryoprecipitate in an MTP was partially supported. This reasoning was due to FFP and cryoprecipitate products having short expiry times once they have been thawed.

One arm proportions revealed that red cell wastage (1.3%) was lower than platelet wastage (10.0%), FFP wastage (9.9%) and cryoprecipitate wastage (10.0%). When two arm proportions were carried out, platelets, FFP and cryoprecipitate were found to have higher wastage rates than red cells. However, all other two way proportions between units were not statistically significant [23].

Thawed blood components and wastage

FFP and cryoprecipitate is administered in an MTP to replace lost coagulation factors and fibrinogen in order to correct coagulopathy and stabilise the bleeding patient. FFP and cryoprecipitate are products that must be thawed before use, as they are frozen after collection. Thawed FFP can be stored and used for critically bleeding patients and some hospitals even keep pre-thawed FFP on hand for MTP situations [24]. In the study by Dunbar thawed FFP is stored and used within 5 days or it must be discarded, whereas thawed cryoprecipitate must be used within 4-6 hours or it must be discarded [2].

Balvers et al., found that FFP wastage was higher during MTP activation compared to FFP issued out to trauma patients before a massive transfusion protocol was implemented [24]. They acted upon this finding and increased the expiry time of thawed FFP from three days to seven days. This led to a 25% reduction in FFP waste during an MTP. They asserted that the levels of coagulation factors in the product was still adequate within this seven-day timeframe. However, von Heymann et al., found that factor VIII and other coagulation factor levels significantly decreased in thawed FFP after 6 days, but found no decrease in fibrinogen levels after 6 days [25].

Three of the six studies included in the meta-analyses did not convert thawed plasma to extended life plasma [13,20,23]. Conradi et al., is the outlier in the one arm meta-analysis of FFP waste [20]. This study also had a far higher FFP wastage rate than the other studies, as all thawed plasma units returned to the blood bank were discarded. This may have also contributed to the extremely high degree of heterogeneity in the meta-analysis (I2=99.56, p<0.001).

Platelet wastage

It was found that platelets had a statistically significant higher rate of wastage compared to red cells in an MTP. Platelet waste was found to have a high wastage rate overall compared to FFP and cryoprecipitate. This finding was unexpected and was not consistent with the hypothesis. Paganini et al., supported this finding and also found platelets had the highest rate of wastage compared to red cells and FFP in an MTP [13]. Their study attributed the high platelet waste to the units not being immediately transfused after being received. However, in the majority of literature available on the topic of MTP and blood component waste, FFP is found to have the highest discard rate of any unit type as was the case in the other six studies used in this meta-analysis.

Discarded units upon return to the blood bank

When units are issued in an MTP, they may be returned and used for another patient-provided they are received in the appropriate condition. A reason for the return of units to the blood bank in an MTP is the patient's death, which is the cause in 4.9% of returned units [21]. Units may also be returned if they are no longer clinically required, a large proportion (50.7%) of patients in an MTP did not even receive a transfusion in the study by Conradi et al., [20].

Units can be issued to another patient if they are returned to the blood bank within 30 minutes of being issued out. However, they must also meet temperature requirements of red cells and FFP being under 10 degrees Celsius and platelets being within 20 to 24 degrees [19]. If the units do not meet this criteria, they are discarded. However, some hospitals have a criteria of red cells remaining between 1 and 6 degrees to be accepted back into the blood bank and utilise a temperature monitoring device to ensure the unit remains within that range [2]. The hospitals included in Dunbar saw units of red cells and thawed plasma issued out in a cooler where they maintain temperature for up to 12 hours, whereas platelets and cryoprecipitate are issued at room temperature [2]. Any units kept by the patient's bedside in anticipation of transfusion during the MTP are discarded if returned to the blood bank. This demonstrates the strict criteria units must meet if they are to be returned, which unfortunately leads to a high wastage rate upon return.

Causes of blood component waste in an MTP

It has been suggested that over activation of MTP was a major cause of wastage in blood products and for stricter criteria to be applied when making the decision to call an MTP [20,24-26]. Another cause of wastage in an MTP was found to be a delay in clinical staff notifying the blood bank that the MTP had been deactivated [13]. It was also attributed to poor communication between the clinical staff and laboratory blood bank staff.

CONCLUSION

Massive transfusion protocol inevitably leads to some wastage of units in order to provide the bleeding patient with sufficient blood components as quickly as possible. This study found FFP, cryoprecipitate and platelets to have the highest wastage rates during an MTP. It was also found that FFP, platelets and cryoprecipitate had a significantly higher wastage rate than red cells. The need for hospitals to be prepared for an MTP leads to precautionary measures such as having precious pre-thawed group AB plasma on hand, which could potentially be wasted due to its short shelf life. Measures such as conversion of thawed FFP into extended life plasma can help to reduce wastage rates. To keep wastage at a minimum in the future, it is worth it for hospitals to consider if the activation criteria for the MTP is suitable in order to prevent over activation. As well as ensuring prompt deactivation of the MTP is communicated to blood bank staff, so the staff refrain from thawing more units. Future research direction should explore the relationship between wastage rates during an MTP compared to wastage rates in units issued out routinely.

LIMITATIONS

All the studies used in this meta-analysis were retrospective, therefore possible sources of bias may be present surrounding how the data was selected to be used in these studies. The data used in these studies also relies on accurate reporting and documentation within hospitals around the number of units issued and wasted, which may be another significant source of error. Several of the meta-analyses had a high degree of heterogeneity, which is a reflection of the limited number of studies used in those meta-analyses as well as small sample sizes. This reduces the reliability of the data in being able to predict a statistically significant relationship in unit wastage.

Another limitation is hospitals having different policies on criteria for activation of the MTP, which may lead to varied rates of MTP activation. Different hospital policies on whether a unit that has been returned to the blood bank can be accepted or must be discarded is another variable that cannot be controlled between hospitals included in the meta-analysis.

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CONFLICT OF INTEREST

None to report.

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DATA AVAILABILITY STATEMENT

Data are available upon request.

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