Adult Massive Transfusion Protocol (MTP) Audit Report

Final Report

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EXECUTIVE SUMMARY

Massive Transfusion Protocols (MTPs) were originally designed in order to provide red cells and plasma components rapidly in a situation where transfusion guided by laboratory tests is not possible due to the rapidity of haemorrhage. MTPs have been implemented in most major hospitals in New Zealand in recent years. Local audits have been undertaken in Auckland and Wellington but there has been no New Zealand-wide audit.

The aim of the audit was to ascertain compliance with the hospital MTP algorithm as well as ascertain the settings in which the MTPs were being activated. The audit was conducted in Waitemata, Auckland, Counties Manukau, Waikato, MidCentral, Capital & Coast, Canterbury and Southern District Health Boards (DHBs). Data was collected from the New Zealand Blood Service eProgesa computer system, the local DHB laboratory information system, staff involved with the activation and a review of clinical notes.

The audit covered the period 1/7/2015 to 30/6/2016 and included 353 MTP activations with 6-84 MTPs audited per DHB. A small proportion of MTP activations did not require any blood and only 60% of MTPs used the initial two to three emergency units ("box 0" or "first response") in the protocol, with variation by site and department. The 'first response' units were included in the MTP to allow time for more in-depth assessment of the patient prior to launching into the more expensive MTP boxes. The proportion of activations with no blood used and the proportion of activations that did not proceed past box one, are indicative of the potential for greater use of the 'first response' units.

There was little difference between MTPs in Delivery Suites, Emergency Departments, Intensive Care Units or Theatres once the total number of units was accounted for, other than cryoprecipitate. Consistent with concerns that pregnant women's fibrinogen is physiologically higher initially, there is greater emphasis on fibrinogen replacement in obstetrics.

Component ratios overall were 0.79 fresh frozen plasma (FFP) per red cell, 0.09 NZ platelet adult therapeutic doses and 0.31 NZ cryoprecipitate units per red cell. Although these ratios are lower than that described as ideal in the literature, the results of laboratory testing were reassuring. Haemoglobin and platelets were well maintained. The median INR/PR and APTT rose with successive boxes, with INR/PR peaking after box 3 with a median of 1.25 and APTT showing a median of 41 seconds after box 4. Fibrinogen showed most variation initially, but was in excess of 1g/L in 93% of measurements. pH was the most consistently abnormal of the laboratory results audited, albeit stably so, with a median of 7.26 overall and medians for each box between 7.23 and 7.28. Ionised calcium showed a possible trend towards falling and potassium towards rising over the number of boxes used, but neither showed a strong correlation coefficient.

The median interval between boxes being issued was 22 minutes. Similarly, the median time between a box being issued and samples being sent for laboratory analysis was 28 minutes. This is consistent with the MTP which recommends that samples should be sent every 30 minutes. Viscoelastography (TEG or ROTEM) was used in 26% of patients, with one DHB's auditor not accessing viscoelastography results and one DHB not using viscoelastography at all at that time.

On average, nineteen components were transfused per patient with six returned and three being discarded. There was wide variation between DHBs.

Only46% of patients received tranexamic acid despite wide recommendation for its use. Factor VIIa was used in only five patients (1.4%), consistent with published studies showing little benefit to the use of factor VIIa in haemorrhage other than possibly as a last resort option.

Survival was 89%, 86%, 76% at cessation of the MTP, 24 hours and 30 days respectively. There was no statistical difference across the eight DHBs.

In general, the audit showed good compliance with the Massive Transfusion Protocol and consistency with international experience.

It is recommended that

1. hospitals should review their systems around MTP activations to ensure
    a. traceability of components
    b. timely notification of cessation of MTPs
    c. transfusion observations are performed, notably respiratory rates, a key component of transfusion Early Warning Systems (EWS)
2. blood banks and hospitals together should look at ways to reduce wastage, e.g. moving to extended life plasma.
3. as the use of tranexamic acid appears low, hospitals should review whether this is an issue of lack of use or poor documentation.
4. despite the lack of evidence for 1:1:1 component ratios relative to 1:1:2, consideration should be given to whether the MTP is fit for achieving these ratios and whether clinical practice is responding to international guidance on the higher use of FFP in massive transfusion.
5. tranexamic acid should be given early with even short delays reducing the benefit of treatment.

INTRODUCTION

Following the seminal publication on massive transfusion and component ratios[1], notwithstanding the associated debate[2,3], there has been significant interest in getting component ratios correct and ensuring rapid delivery of these components. Massive Transfusion Protocols (MTPs) were originally designed for use in the trauma setting[4,5], mostly in Emergency Departments, in order to provide red cells and plasma components rapidly. In many areas MTPs are now also utilised for other significant bleeding occurrences e.g. for post-partum haemorrhage or aneurysm repair[6,7].

MTPs have been implemented in most major hospitals in New Zealand over recent years. Auckland District Health Board (DHB) commenced in 2009, with Capital & Coast DHB and Canterbury DHB shortly after in early 2010.

Waikato, MidCentral, Counties-Manukau and Waitemata DHBs followed. The last site to commence using the MTP was Southern DHB in 2014. Many of the smaller DHBs throughout New Zealand have adapted the standard MTP template to meet differing regional issues such as minimal (or no) platelet supplies. Local audits have been undertaken at Auckland and Capital & Coast District Health Boards but there has been no New Zealand-wide audit.

AIM

The aim of this audit was to

- Ascertain the compliance to the scheduled MTP when activated, including
    - Did the patient receive 2-3 units Whole Blood Plasma Reduced (WBPR) or Red Blood Cells (RBC) (O RhD Negative or Group specific) prior to activation?
    - How many MTP boxes were issued?
    - What components were transfused, returned and/or wasted?
    - Were the appropriate lab tests performed and documented?
    - Were other drugs/blood products/recombinants used e.g. Tranexamic acid, Factor VIIa?
    - Were there any differences in the use of the protocols between ED, Theatre and Delivery Suite patients?
    - What was the patient outcome (end of MTP, 24hrs post MTP and 30 days post MTP)?
- Obtain the “indication” of the MTP activation.

DEFINITION

For the purpose of this audit, “Massive Transfusion Protocol activation” was defined as any time the official DHB Adult MTP was activated within the eight audited hospitals during 2015/2016 financial year.

METHOD

The New Zealand Blood Service (NZBS) Transfusion Nurse Specialists (TNS) in the six main centres (Auckland, Waikato, MidCentral, Capital & Coast, Canterbury and Southern DHBs) and the Clinical Nurse Specialists – Transfusion (CNS) in Counties Manukau and Waitemata DHB collected all adult MTP episodes concurrent to activation in their largest hospital during the one year audit period.

Data collected for each episode included:

- Patient demographics: age, gender, weight (if available), NHI number
- Clinical specialty
- Laboratory data: Haemoglobin, Platelet count, Coagulation studies, viscoelastography (if used)

- Transfusion data: date, time and number of red cells, fresh frozen plasma, platelets and cryoprecipitate units transfused.
- Number of MTP "boxes" issued, time collected
- Date and time of activation and of deactivation, duration of activation and profession of activator/deactivator
- Blood components issued and transfused in the 24 hours pre and post MTP activation/deactivation, and whether cell salvage was used
- Recombinant/non-recombinant products or medications used
- Clinical data: patient's indication for the MTP activation, location of activation, medications
- Component wastage
- Documentation of MTP activation and components issued locatable in the patient records

The data was collected from the NZBS eProgesa computer system, the local DHB laboratory information system, blood bank scientists/technicians, clinicians and a review of clinical notes. The cases were also discussed with relevant DHB staff and Blood Bank scientists where necessary.

LIMITATIONS

The activation of the MTP is the responsibility of a medical practitioner in the departments involved, and should be based on the clinical condition of the patient as the case unfolded. Therefore, the audit report does not make judgement on the medical decision to activate the MTP other than to note the haemodynamic parameters at the time of activation of the MTP.

ANALYSIS and REPORTING

The data was collated in a web-based PostgreSQL database with restricted access, located on a secure NZBS webserver. Only the TNS collecting the data and the TMS overseeing the audit had access to any individual patient details. Identifying data was kept to a minimum, restricted to NHI, age and gender. The results presented in this report have been further anonymised.

The data was analysed by the TNSs, CNSs and TMS using PGAdmin III, R and Excel. A draft report was circulated to the Hospital transfusion Committee chairs of the participating DHBs for comment with changes incorporated into this final report.

RESULTS

Demographics

The audit covered the period 1/7/2015 to 30/6/2016 and included 353 MTP activations. The distribution across the eight participating DHBs is shown in table 1. The majority of MTP activations took place in theatres and emergency departments. Both genders showed a peak in the 61 – 70 year age range but women also showed a peak in the 21-30 year age range (figure 1).

DHB	n	% male	median age	Delivery Suite	ED	ICU	Theatre	Other
Auckland	76	51%	47	5%	34%	8%	50%	3%
Canterbury	57	63%	53	0%	30%	11%	56%	4%
Capital & Coast	53	57%	62	13%	36%	6%	38%	8%
Counties Manukau	84	50%	39.5	4%	31%	6%	50%	10%
MidCentral	6	33%	53.5	0%	50%	0%	50%	0%
Southern	14	71%	62.5	0%	43%	14%	29%	14%
Waikato	45	58%	56	9%	42%	7%	40%	2%
Waitemata	18	61%	63.5	0%	6%	11%	78%	6%
Overall	353	55%	52.5	5%	33%	8%	48%	6%

Table 1: *Number and demographics of audit cases per DHB*

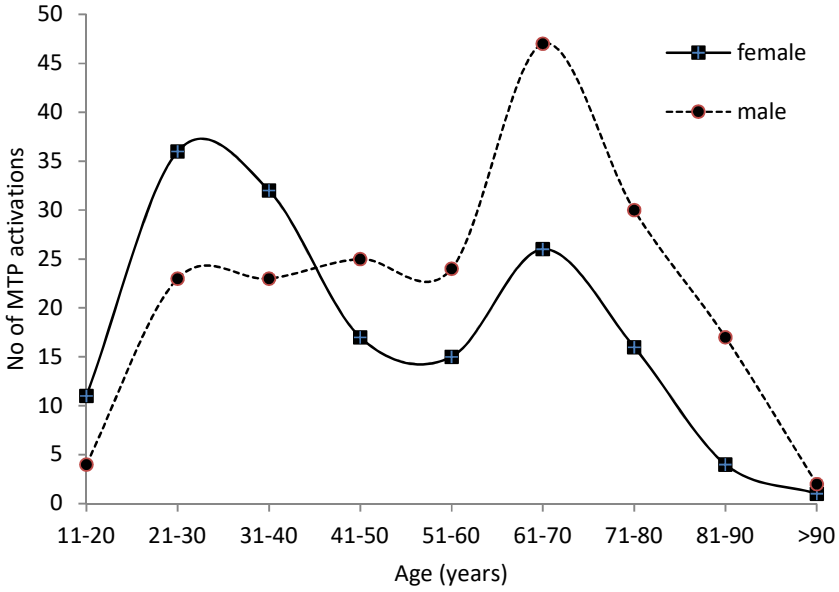


Figure 1: *Age of patients in MTP audit by gender*

The commonest clinical specialty involved in massive transfusions were surgery (including general surgery and vascular surgery), emergency medicine and obstetrics (table 2).

Specialty	n	%
General surgery	150	42%
Emergency	55	16%
O & G	35	10%
Vascular	31	9%
Cardiothoracic	14	4%
Gastroenterology	14	4%
Other surgical	28	8%
Other	26	7%
Overall	353	

Table 2: *MTP activations by specialty*

Trauma, post-operative bleeding, specifically abdominal aortic aneurysms (ruptures and repairs), post-partum haemorrhages and gastrointestinal haemorrhage accounted for 86% of MTP activations (table 3).

DHB	AAA±repair	APH	GI bleed	Post-op	PPH	Surgical	Trauma	Other	n
Auckland	12%	1%	9%	13%	12%	1%	32%	20%	76
Canterbury	14%	2%	16%	21%	12%	2%	25%	9%	57
Capital & Coast	26%	2%	13%	26%	6%	0%	19%	8%	53
Counties Manukau	7%	1%	14%	24%	18%	0%	20%	15%	84
MidCentral	50%	0%	0%	0%	0%	0%	33%	17%	6
Southern	29%	0%	29%	7%	0%	0%	36%	0%	14
Waikato	11%	0%	13%	13%	7%	0%	42%	13%	45
Waitemata	0%	0%	67%	11%	17%	0%	0%	6%	18
Overall	14%	1%	16%	18%	12%	1%	26%	13%	353

Table 3: *MTP activations by source of bleeding*

Half of MTP activations took place in the nine hours between 11 am and 8 pm (figure 2), more than double that occurring in the same number of hours overnight (11pm – 8 am). This is likely to be a reflection of the proportion of cases being activated in theatre (table 1). In three instances, the blood bank was managing two MTPs simultaneously (two in Auckland, one in Wellington). All six were activated around the middle of the day, between 10:45 and 12:30.

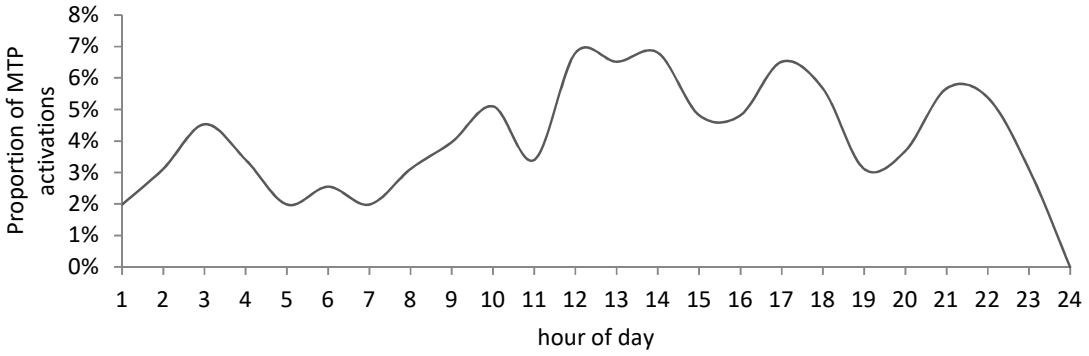


Figure 2: *Time of MTP activations*

Looking at shifts, there was a degree of variation between DHBs with Southern and Waitemata showing more activations in the evening shift than the day shift but all others showing most MTPs during the day shift.

DHB	0 - 8 hr	9 - 16 hr	17 - 24 hr	n
Auckland	28%	51%	21%	76
Canterbury	30%	51%	19%	57
Capital and Coast	15%	60%	25%	53
Counties Manukau	31%	44%	25%	84
MidCentral	17%	50%	33%	6
Southern	21%	36%	43%	14
Waikato	20%	42%	38%	45
Waitemata	11%	44%	44%	18
Overall	25%	49%	27%	353

Table 4: *Distribution of MTP activations by shift and DHB*

Consultants and registrars made 82% of MTP activations (table 5), consistent with expectations that the decision to activate the MTP should be taken by medical staff of some seniority. Three exceptions were noted (asterisks in table 5): Dunedin Hospital, where the switchboard operator notifies Blood Bank as part of a formalised notification chain used for all emergencies; Palmerston North where after hours notifications are made via switchboard; and Auckland where almost 22% of activations were notified by nurses, presumably under the direction of a consultant or registrar.

DHB	Consultant	Registrar	RMO	Midwife	RN	Other	n
Auckland	47%	21%	1%	3%	22%	5%	76
Canterbury	46%	44%	5%	0%	4%	2%	57
Capital and Coast	36%	49%	0%	6%	8%	2%	53
Counties Manukau	49%	45%	1%	1%	2%	1%	84
MidCentral	50%	17%	0%	0%	0%	33%	6
Southern	7%	7%	0%	0%	0%	86%	14
Waikato	71%	20%	0%	0%	0%	9%	45
Waitemata	89%	0%	0%	0%	6%	6%	18
Overall	50%	33%	1%	2%	7%	7%	353

Table 5: *Distribution of MTP activation notifications by profession and DHB (* see text above)*

A small proportion of MTP activations did not require any blood support (figure 3). Not all sites used the initial three emergency units ('first response') in the protocol (tables 6 & 7). Table 7 looks specifically at ED and theatre as these two locations account for 82% of MTP activations. The 'first response' units of were included in the MTP to allow time for more in-depth assessment of the patient prior to launching into the more expensive MTP boxes. The proportion of activations with no blood used and the proportion that do not proceed past box one, are indicative of the potential for greater use of the 'first response' units.

DHB	'First response' units used
Auckland	42%
Canterbury	72%
Capital and Coast	66%
Counties Manukau	44%
MidCentral	67%
Southern	79%
Waikato	96%
Waitemata	50%
Overall	60%

Table 6: *Use of 'first response' units by DHB*

DHB	ED	Theatre
Auckland	50%	32%
Canterbury	76%	72%
Capital and Coast	63%	70%
Counties Manukau	85%	29%
MidCentral	67%	67%
Southern	100%	75%
Waikato	100%	100%
Waitemata	100%	43%
Overall	75%	53%

Table 7: *Use of 'first response' units in ED and Theatre by DHB*

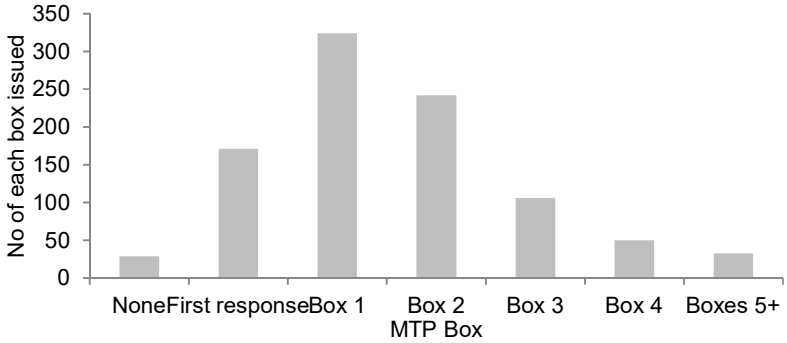


Figure 3: *Number of each MTP box issued*

The MTP only achieved the 1:1 ratio of FFP: red cells at Capital & Coast DHB, although Counties Manukau came close (table 8). Unusually, Auckland DHB has a higher ratio (0.84) when looking at components issued, but it drops to 0.66 when returned components are considered. There was no difference when looking at the overall ratio for all DHBs for all MTPs vs those that extended beyond Box 1 (p=0.60). Note that when looking at the platelet ratio that each New Zealand unit is an adult therapeutic dose, equivalent to four whole-blood derived units. 0.31 units of cryoprecipitate (approx. 0.4g) were transfused per red cell.

DHB	n	Whole blood *	Red cells	FFP	Platelets	Cryoprecipitate	FFP per RBC	platelets per RBC
Auckland	76	70	452	277	65	174	0.66	0.12
Canterbury	57	25	379	290	28	98	0.78	0.07
Capital and Coast	53	26	233	241	31	89	1.03	0.12
Counties Manukau	84	0	423	391	39	154	0.92	0.09
MidCentral	6	0	46	31	0	9	0.67	0.00
Southern	14	0	73	49	4	18	0.67	0.05
Waikato	45	7	370	256	29	112	0.70	0.08
Waitemata	18	0	70	46	5	14	0.66	0.07
Overall	353	128	2046	1581	201	668	0.79	0.09

Table 8: *Components transfused by DHB (*whole blood includes whole blood plasma reduced)*

Delivery Suites had a slightly higher ratio of cryoprecipitate use compared with other groups, despite fewer units issued per MTP and a lower FFP to red cell ratio (table 9). The latter observation is possibly due to fewer boxes used with a mean of seven components transfused vs 14 for the other locations. Of interest, Dunedin Hospital has a massive obstetric bleed (MOB) protocol (call for help, management plan and release of first response red cells) which operates as a precursor protocol to the MTP. During the year of audit, no MTP activations for post-partum haemorrhage were activated with all MOB calls resulting in cessation of the bleed before a MTP was indicated.

		Components transfused per MTP					Components per red cell		
Location	n	Whole blood	Red cells	FFP	Platelets	Cryo	FFP	Platelets	Cryo
DS	18	0.1	3.4	1.8	0.2	1.6	0.5	0.0	0.5
ED	117	0.6	5.5	4.1	0.4	1.6	0.7	0.1	0.3
ICU	27	0.2	5.7	4.3	0.7	1.6	0.8	0.1	0.3
Theatre	172	0.1	4.8	3.8	0.4	1.2	0.8	0.1	0.3

Table 9: *Components transfused per MTP and component ratios for Delivery Suite (DS), Emergency Department (ED), Intensive Care Unit (ICU) and Theatre*

Records for the administration of tranexamic acid (TXA) were found in 46% of MTP activations (table 10). This was given early in the MTP (mean of 10 minutes after activation; median 13 minutes after activation) (figure 4). The percentage use of TXA appears low and there is concern from a number of DHBs whether this represented non-use. It was acknowledged that documentation is compromised by the different systems in use so it is possible that the low rate reflects difficulty accessing this documentation.

DHB	n	% Receiving TXA
Auckland	76	58%
Canterbury	57	9%
Capital and Coast	53	34%
Counties Manukau	84	69%
MidCentral	6	17%
Southern	14	71%
Waikato	45	47%
Waitemata	18	39%
Overall	353	46%

Table 10: *Proportion of patients receiving tranexamic acid (TXA) by DHB*

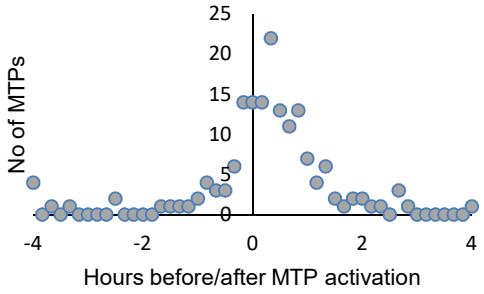


Figure 4: *Timing of TXA in relation to MTP activation*

DHB	FVIIa	Calcium	Other	n
Auckland	1%	80%	8%	76
Canterbury	0%	5%	2%	57
Capital and Coast	6%	15%	13%	53
Counties Manukau	1%	48%	6%	84
MidCentral	0%	33%	0%	6
Southern	0%	21%	29%	14
Waikato	0%	58%	13%	45
Waitemata	0%	44%	11%	18
Overall	1%	43%	9%	353

Table 11: *Other pharmaceuticals*

Factor VIIa was rarely given across all DHBs audited (table 11). Calcium administration showed significant variation from 5% in Canterbury to 81% in Auckland. Other drugs included adrenaline/noradrenaline (n = 5), ergometrics & prostaglandins (6), potassium chloride (1), mannitol (1), metaraminol (1), omeprazole (1), prothrombinex (7), vitamin K (2). It is possible that the use of

other pharmaceutical measures may not have been completely captured due to incomplete documentation at the time of clinical review.

Despite concerns about the amount of extra-cellular potassium in red cell components, there appeared to be no significant correlation (R^2 <0.06) between serum potassium level and the time from MTP activation or the number of red cells issued (figures 5a and 5b). It was not possible, due to the design of the audit, to look at the age of red cells and potassium levels.

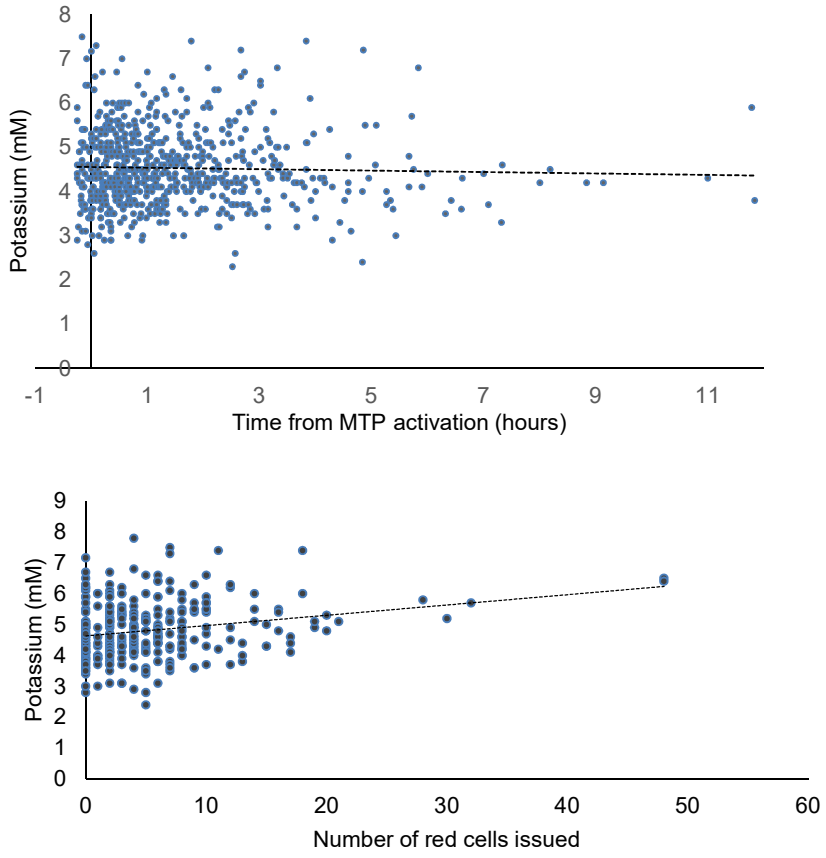


Figure 5 (a & b): *Potassium concentration relative to time and number of red cells transfused*

The median duration of MTPs was 59 minutes (mean 88 minutes) with a range of 0-12.25 hours (figure 6).

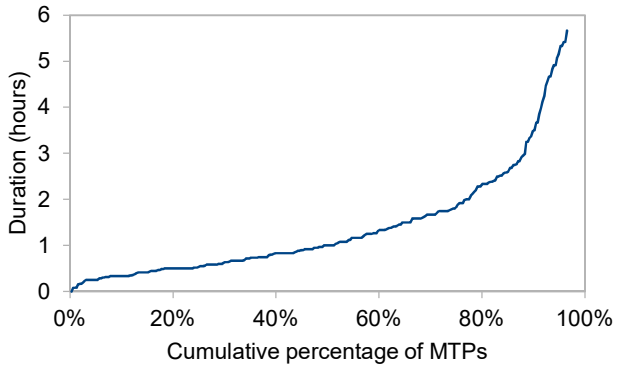


Figure 6: *Duration of MTPs*

The median interval between boxes being issued was 22 minutes (figure 7 – note logarithmic y-axis and boxes showing upper and lower quartiles). Similarly, the median time between a box being issued and samples being sent for laboratory analysis was 28 minutes (figure 8). This is consistent with the MTP which recommends that samples should be sent every 30 minutes.

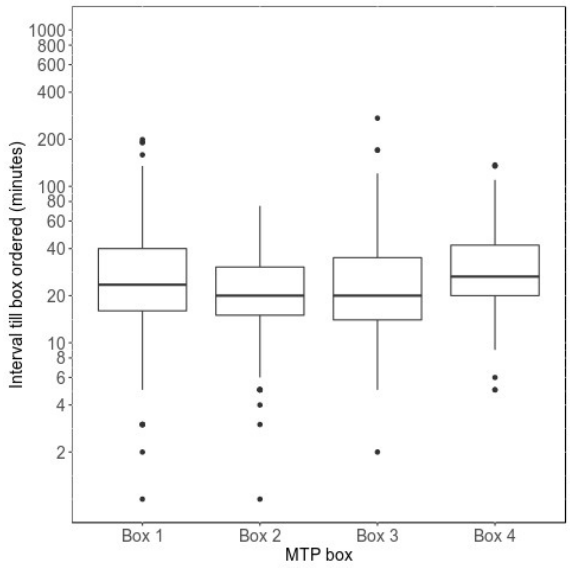


Figure 7: Interval *between boxes*

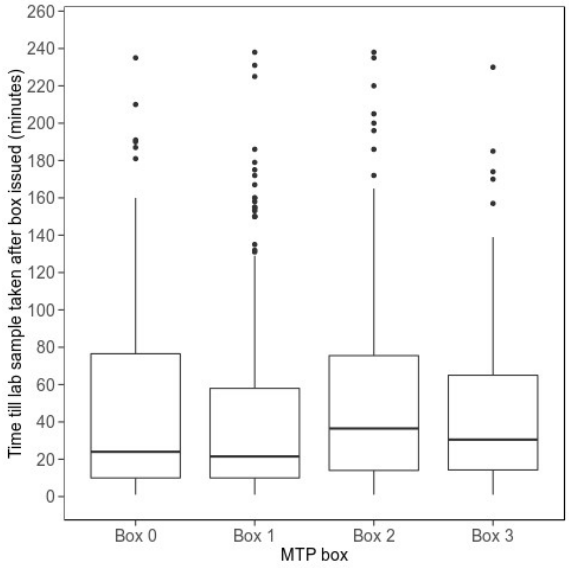
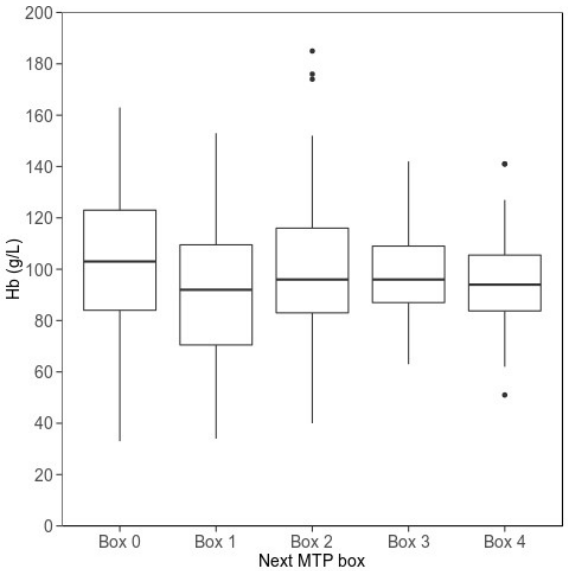
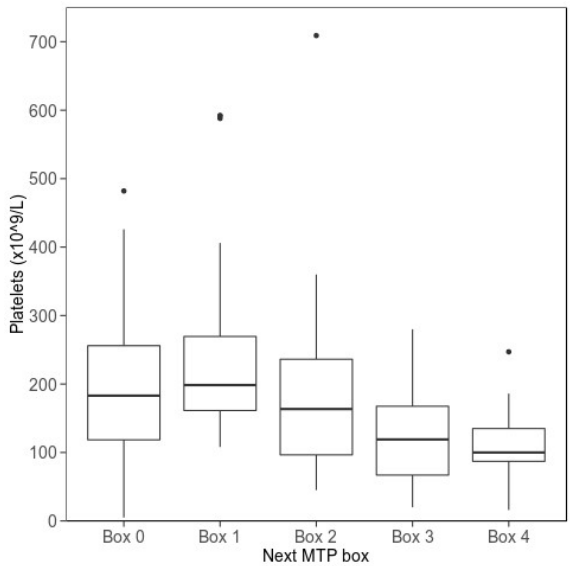


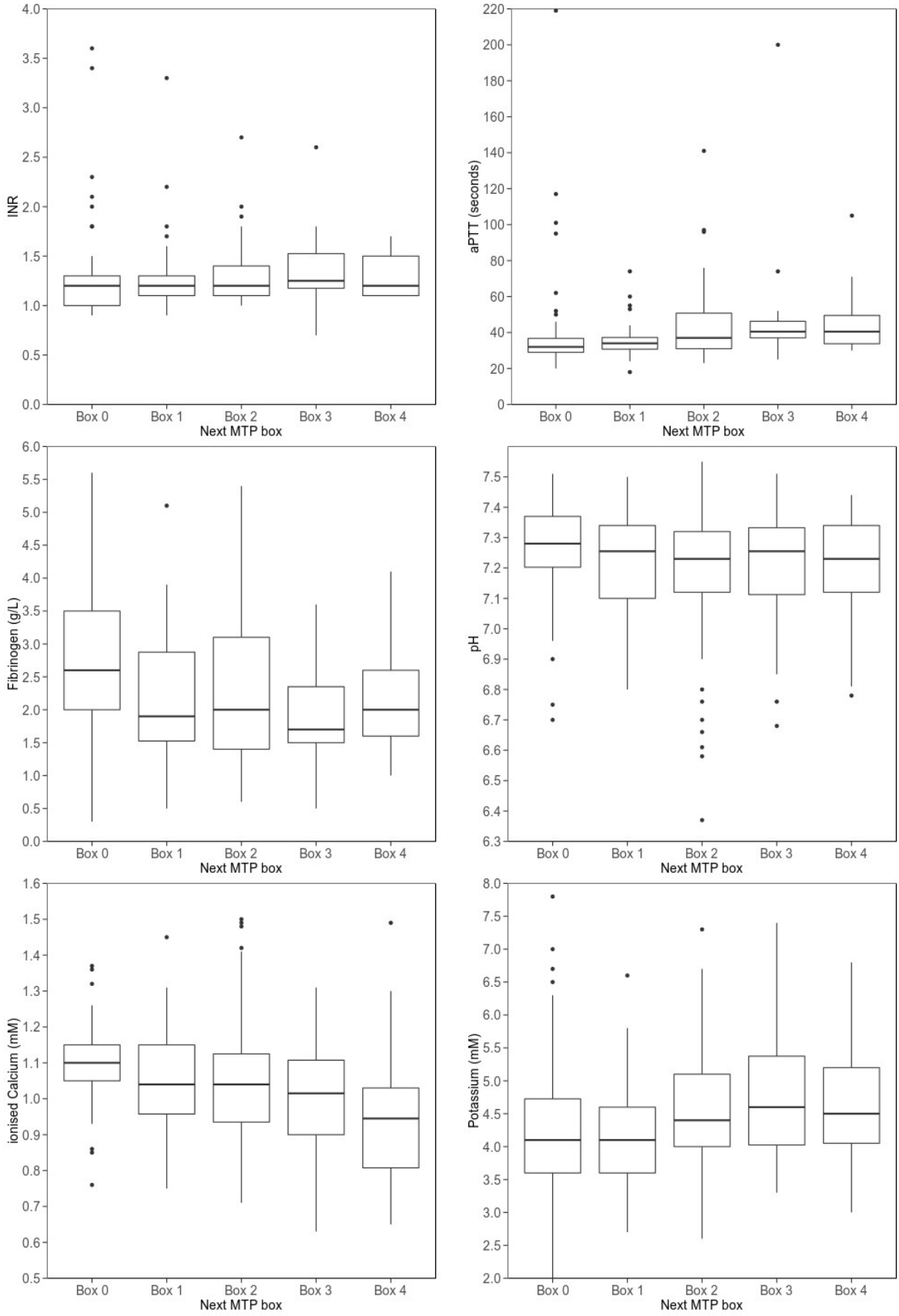
Figure 8: *Time to send lab samples after each box*

The laboratory values (figures 9a–h), while displaying an expected degree of spread, showed median (solid bar) values that were reassuring for patient management. Haemoglobin was well maintained, frequently higher than the target value of 90g/L of goal-directed transfusion. Platelets fell with time but only 4% of results were below 50 x 10^9/L. Both haemoglobin and platelets converged with subsequent boxes, indicating a good mix of products to bring up low results while not transfusing excessively.





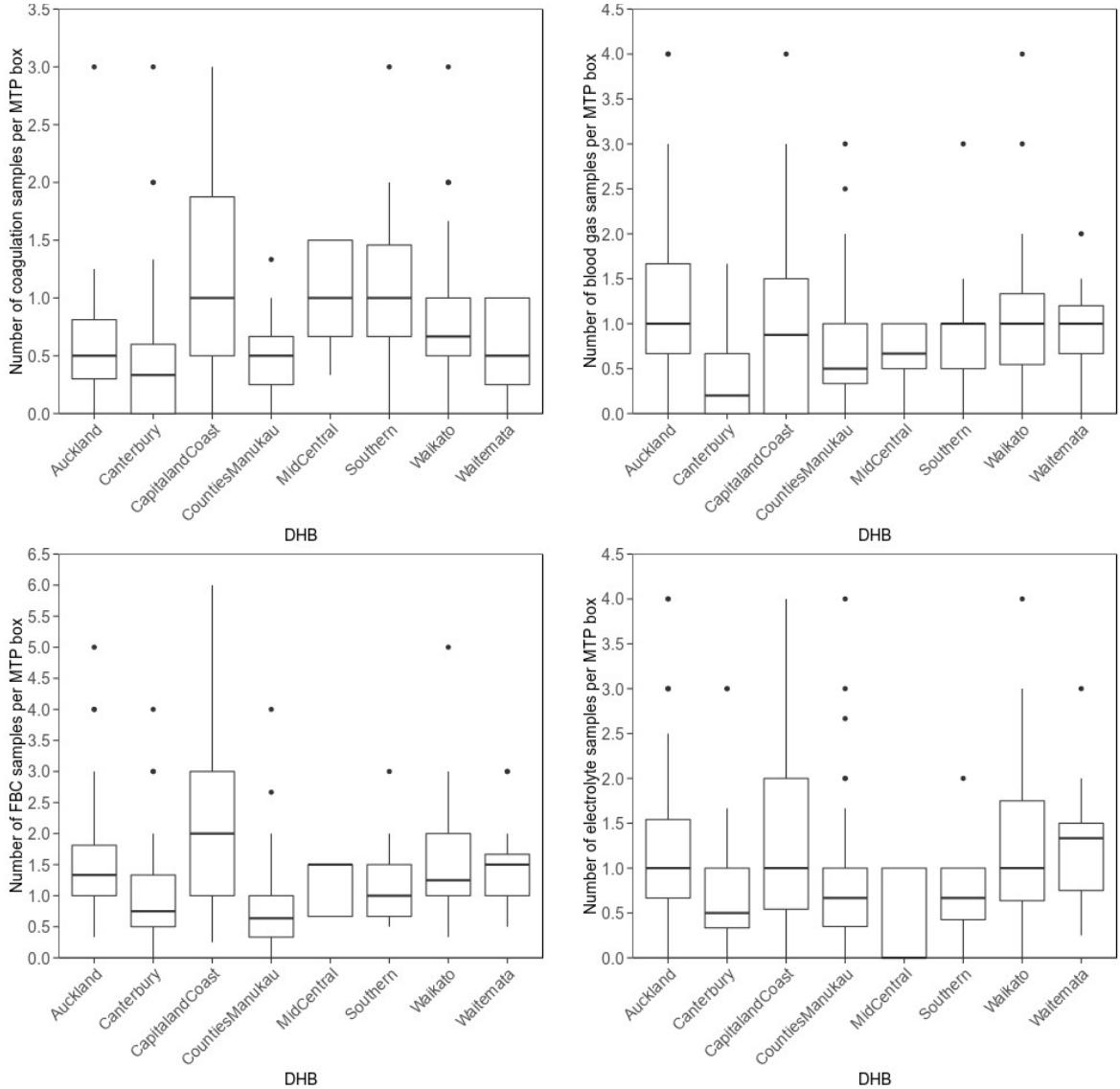
Figures 9 (a-b): *Hb and platelet results following each of the first four boxes of the MTP*



Figures 9 (c-h): *INR, aPTT, fibrinogen, pH, ionised calcium, potassium results for each of the first four boxes of the MTP*

The median INR/PR rose, peaking after box 3 with a median of 1.25 (note: some laboratories report INR while others report Prothrombin Ratio). APTT was well-maintained though it did appear to rise slowly. The median APTT after box 4 was 41 seconds. Fibrinogen showed most variation initially, but generally showing values in excess of 1g/L in 93% of measurements. pH was the most consistently abnormal of the laboratory results audited, albeit stably so, with a median of 7.26 overall and medians per box all between 7.23 and 7.28. Ionised calcium was audited as citrate in blood components is known to lower this. Although there appears to be a trend towards falling ionised calcium over the number of boxes used, the correlation was poor (R^2=0.05). Potassium appeared to show a rise over time but there was a poor correlation in this regard (figure 5).

As suggested in figure 8, supporting laboratory investigations were well managed during the MTP with most key parameters being monitored between MTP boxes (figures 10 a-d).



Figures 10 (a-d): *Number of samples sent between boxes for full blood count, coagulation profile, blood gases and electrolytes per DHB*

Viscoelastography (TEG or ROTEM) was used in 26% of MTPs (table 12). One DHB's auditor (Waitemata) not accessing viscoelastography results and one DHB (Southern) did not have an instrument at that time. Amongst the DHBs that did, there was a preference for theatre cases (38%) as well as delivery suite, ICU and ED cases (28%, 15%, 14%).

	no of MTPS	% MTPs with VE	average tests/MTP
Auckland	76	13%	3.9
Canterbury	57	47%	1.0
Capital & Coast	53	6%	3.3
Counties Manukau	84	33%	2.4
MidCentral	6	33%	1.0
Southern	14	0%	-
Waikato	45	49%	1.7
Waitemata	18	0%	-
Overall	353	26%	2.0

Table 12a: *Viscoelastography testing by DHB*

	No. components transfused		
Component	VE tested	VE not tested	p
Red cells	5.3	8.5	0.001
FFP	3.7	6.8	<0.001
Platelets	0.4	1.0	0.003
Cryoprecipitate	1.5	3.0	0.001

Table 12b: *Components issued per MTP, comparing patients tested with or without viscoelastography (VE)*

There was a clear association between the use of viscoelastography and the number of different component types transfused (see table12b). However, there was no significant difference for viscoelastography for survival, whether immediately after MTP, at 24 hours or at 30 days.

Despite the urgency surrounding massive transfusions, vital sign observations were generally performed to a high level, with the exception of temperature (table 13). It is likely that observations would have happened regardless of transfusion as part of the monitoring of the patients' haemorrhage. This may explain why the temperature and respiratory rate observations are lower than other parameters. Interestingly there was no overall difference in respiratory rate observations in theatre cases (presumably ventilated) compared with other locations (p=0.34). Canterbury's lower rates of observations are noteworthy as is MidCentral's lack of BP measurements (likely artefact). Like many aspects of the audit, this may be a reflection of documentation. It should be noted here that oxygen saturation is not part of transfusion observations, with changes being a late phenomenon in a transfusion reaction.

DHB	Resp rate	Temp	BP	Pulse	O_2 sats	n
Auckland	89%	79%	95%	96%	88%	76
Canterbury	30%	18%	51%	56%	37%	57
Capital & Coast	81%	55%	64%	94%	81%	53
Counties Manukau	95%	81%	98%	96%	90%	84
MidCentral	83%	67%	0%	83%	83%	6
Southern	50%	64%	100%	100%	93%	14
Waikato	71%	91%	91%	98%	93%	45
Waitemata	94%	61%	94%	94%	94%	18
Overall	76%	66%	82%	90%	80%	353

Table 13: *Transfusion observations*

Documentation of the MTP itself, as well as retaining records of all components transfused for traceability, varied by DHB with some excellent performances by some DHBs (table 14).

DHB	MTP documented	Units traceable
Auckland	99%	96%
Canterbury	65%	98%
Capital & Coast	57%	91%
Counties Manukau	61%	99%
MidCentral	17%	100%
Southern	93%	100%
Waikato	67%	76%
Waitemata	83%	94%
Overall	58%	98%

Table 14: *Documentation of MTP and traceability of components following MTP by DHB*

DHB	Blood Bank	Consultant	Registrar	RMO	Midwife	RN	Other	Unknown	Overall
Auckland	1%	41%	30%	0%	0%	13%	14%	0%	76
Canterbury	0%	44%	35%	11%	0%	5%	5%	0%	57
Capital & Coast	8%	26%	25%	0%	6%	15%	11%	9%	53
Counties Manukau	0%	62%	31%	2%	0%	2%	1%	1%	84
MidCentral	0%	0%	17%	0%	0%	0%	83%	0%	6
Southern	0%	14%	7%	0%	7%	43%	29%	0%	14
Waikato	0%	36%	36%	0%	0%	9%	20%	0%	45
Waitemata	33%	50%	11%	0%	0%	0%	6%	0%	18
Overall	3%	42%	29%	2%	1%	9%	11%	2%	353

Table 15: *Type of staff member announcing the cessation of the MTP to Blood Bank*

Prompt notification of cessation of the MTP is important to the Blood Bank to minimise component wastage as well as to free up staffing resources to assist with transfusions in other areas of the hospital. The pattern of who took responsibility for this (table 15) is similar to that seen on activation (table 5). Of concern is Waitemata's high level of Blood Bank cessation of the MTP.

In the audit, it was not possible to identify when bleeding stopped or when cessation could have been called. As a surrogate, table 16 shows the length of time taken to cease the MTP after the last box was issued. This could only be calculated for those activations that used up to a maximum of 4 boxes only due to audit tool limitations.

DHB	Average (minutes)	Std Deviation (minutes)	Median (minutes)
Auckland	46	56	21
Canterbury	62	148	55
Capital & Coast	52	85	20
Counties Manukau	12	85	15
MidCentral	22	23	20
Southern	39	35	35
Waikato	37	54	20
Waitemata	46	28	51
Grand Total	39	89	22

Table 16: *Time from last box issued to cessation (where cessation called, and where no more than four boxes issued)*

Massive transfusion often forms part of a continuum of transfusion and this is reflected in table 17 and 18, showing the proportion of patients who had received blood components prior to MTP activation and continued to receive blood components after the MTP has ceased.

DHB	red cells	FFP	Platelets	Cryoprecipitate	Whole blood	O neg	n
Auckland	24%	13%	8%	11%	7%	11%	76
Canterbury	7%	4%	2%	2%	0%	2%	57
Capital & Coast	43%	9%	8%	4%	15%	6%	53
Counties Manukau	45%	13%	7%	5%	1%	0%	84
MidCentral	0%	0%	0%	0%	0%	17%	6
Southern	29%	21%	14%	7%	0%	7%	14
Waikato	47%	20%	13%	4%	7%	13%	45
Waitemata	61%	28%	11%	17%	0%	0%	18
Overall	34%	13%	8%	6%	5%	6%	353

Table 17: *Proportion of patients receiving transfusions in the 24 hours prior to MTP activation*

DHB	n	red cells	FFP	platelets	cryoprecipitate
Auckland	76	29%	12%	13%	9%
Canterbury	57	14%	11%	2%	4%
Capital and Coast	53	26%	21%	21%	25%
Counties Manukau	84	24%	12%	14%	7%
MidCentral	6	17%	17%	0%	0%
Southern	14	50%	50%	43%	43%
Waikato	45	31%	18%	22%	13%
Waitemata	18	44%	17%	11%	17%
Overall	353	27%	16%	15%	12%

Table 18: *Proportion of patients receiving transfusions in the 24 hours following MTP activation*

On average, nineteen components were transfused per patient with six units returned and three units discarded. Tables 19 a-c below show the proportion of components wasted. Despite a significant emphasis in recent literature on the role of plasma and fibrinogen in the role of haemostasis, FFP and cryoprecipitate were the components with the highest rate of return and wastage. In at least one site, Southern, Box 2 is prepared concurrently with Box 1. However, only 56% of MTPs proceed beyond Box 1, giving rise to a significant opportunity for wastage.

DHB	Whole blood issued	%returned	%wasted*	Red cells issued	%returned	%wasted*
Auckland	85	18%	5%	689	34%	1%
Canterbury	26	4%	0%	479	21%	10%
Capital and Coast	28	7%	0%	323	28%	11%
Counties Manukau	0	-	-	688	39%	7%
MidCentral	0	-	-	66	30%	5%
Southern	0	-	-	99	26%	17%
Waikato	7	0%	0%	456	19%	17%
Waitemata	0	-	-	108	35%	6%
Overall	146	12%	3%	2908	30%	8%

DHB	FFP issued	%returned	%wasted*	Platelets issued	%returned	%wasted*
Auckland	563	51%	4%	90	28%	10%
Canterbury	363	20%	12%	33	15%	3%
Capital and Coast	347	31%	23%	37	16%	8%
Counties Manukau	630	38%	30%	52	25%	12%
MidCentral	41	24%	24%	0	-	-
Southern	69	29%	29%	4	0%	0%
Waikato	378	32%	28%	34	15%	12%
Waitemata	75	39%	21%	7	29%	14%
Overall	2466	36%	19%	257	22%	9%

DHB	Cryo issued	%returned	%wasted*	n
Auckland	258	33%	7%	76
Canterbury	143	31%	26%	57
Capital and Coast	140	36%	34%	53
Counties Manukau	248	38%	40%	84
MidCentral	9	0%	0%	6
Southern	26	31%	23%	14
Waikato	174	36%	36%	45
Waitemata	20	30%	30%	18
Overall	1018	34%	27%	353

Table 19 (a-c): *Wastage of components following MTP activation by DHB*
(%wasted is the proportion of units returned to blood bank that were unsuitable to return to stock)*

Wastage of donations is a significant concern to the New Zealand Blood Service, the donors and the clinicians using the components. There is also a financial cost incurred in the production and testing of these components. Table 20 shows the cost, using prices from the 2018/19 financial year, of wastage arising from MTPs. Patients who did not survive the MTP were excluded from this analysis. Significant variation between DHBs is evident.

DHB	Cost per MTP	Total cost	Wastage per MTP	Total wastage	% Wastage per MTP
Auckland	$4,928	$374,561	$300	$22,766	6%
Canterbury	$5,201	$296,454	$726	$41,386	14%
Capital & Coast	$4,705	$249,381	$966	$51,210	21%
Counties Manukau	$5,016	$421,319	$1,235	$103,740	25%
MidCentral	$4,690	$28,141	$530	$3,181	11%
Southern	$4,065	$56,911	$877	$12,284	22%
Waikato	$7,180	$323,097	$1,707	$76,797	24%
Waitemata	$2,838	$51,075	$493	$8,868	17%
Overall	$5,102	$1,800,939	$907	$320,232	18%

Table 20: *MTP cost and wastage per DHB using 2018/19 prices, excluding MTPs where the patient died during the MTP*

Ultimately, the aim of a massive transfusion is to keep the patient alive. Survival was 89%, 86%, 76% at cessation of the MTP, 24 hours and 30 days respectively (figure 11). Survivors to the end of the MTP and to 24 hours had a statistically better minimum pH compared with non-survivors (7.0 vs 7.2, p< 0.01) but there was no statistical difference in minimum fibrinogen and platelet count. There was no statistical difference in survival across the eight DHBs (p=0.22, 0.31 and 0.70 respectively).

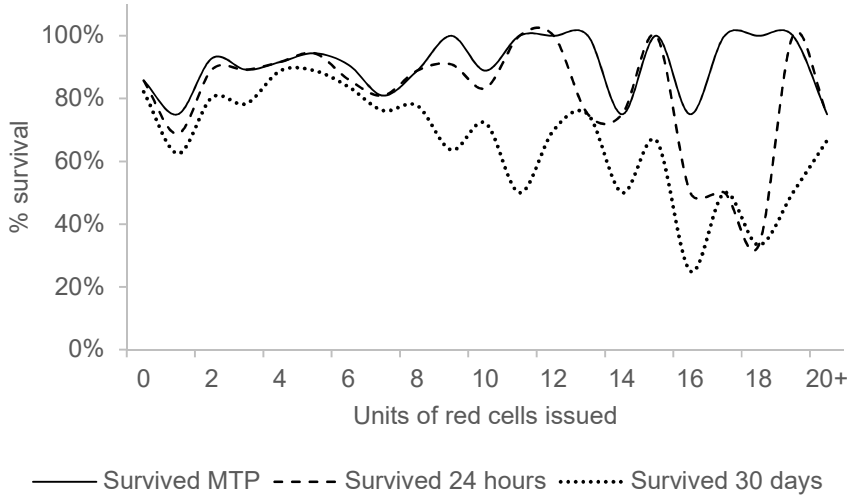


Figure 11: *Survival following MTP activation*

DISCUSSION

This audit, of an entire year at the eight largest DHBs in the country has shown some interesting patterns. Although there is a single national approach to massive transfusion protocols, significant variation was noticed across the eight DHBs taking part in the audit.

The first aim was to determine how often the initial 'first response' units were used. This was put into the MTP to allow resuscitation to commence but without committing to thawing plasma while giving the attending clinicians more time to make an initial assessment of patient. This allows for immediate transfusion of patients with bleeding that can be rapidly controlled while avoiding the

necessity for activating the MTP with consequent waste of thawed plasma products. This has subsequently been confirmed as reducing MTP activation rate[8]. In this audit, the 'first response' units were used between 42% and 96% of MTPs depending on the DHB but this did not correlate with per DHB wastage figures.

Excluding 'first response' units with its separate issues, the number of boxes used corresponded with the right hand side of a bell curve or normal distribution. In this audit, 43% of MTPs that used Box 1 stopped there, compared with 57% that proceeded beyond Box 1. This is the expected outcome and consistent with previous observations by NZBS blood banks (unpublished). Although sometimes frustrating for people involved in providing the single box, who may question why the MTP was activated, it should be apparent that this is the expected outcome and that even five units of red cells ('first response' + Box 1), if transfused in an emergency, is still significant resuscitation.

Interestingly, despite essentially the same protocol being used across all audited sites, the number of units of fresh frozen plasma transfused per unit of red cells ranged from 0.66 to 1.03. This level of variation has been seen elsewhere and the commentary is that a ratio of at least 0.5 FFP unit per red cell (or 1 FFP to 2 red cells) is what has been shown to reduce mortality[7,9], although other authors are not even convinced of the evidence for fixed ratios at all[10]. Platelet transfusions ranged from 0 to 0.12 per red cell unit transfused, or 0 to 0.5 whole-blood derived equivalents (also called single unit recovered platelets) of the type typically quoted in American literature. These ratios are lower than the typically encouraged 1:1:1 based on Borgman's seminal paper from the Iraq war[1]. The large PROPPR trial suggests that there is no difference between a ratio of 1:1:1 (plasma: platelets: red cells) compared with 1:1:2[11]. This is also noted in a recent review[10]. Our ratios overall, with platelets quoted in whole-blood derived equivalents, were 0.8 : 0.4 : 1 or 1.6 : 0.7 : 2, somewhere between 1:1:2 and 1:1:1. Although in theory the ratio is a little light on platelets, the measured platelet counts suggest the patients are well supported using the current ratio.

It could be expected that, if the components are being issued according to a fixed protocol, and some DHBs are transfusing to different ratios, that this would correlate with the level of returns or wastage. However, no relationship between return rates and FFP: red cell ratios was apparent.

Return rates showed variation by DHB as well as by component. This is a known phenomenon where ratios vary over the time of any individual MTP[9] so the final components left will be determined in part by the point at which cessation occurs. The two components with the highest return rates were FFP and cryoprecipitate. On the face of it, this is surprising as current thinking places much emphasis on clot formation and fibrinogen replacement. It is possible that the delay in providing thawed frozen components means that by the time the components are ready, they are no longer required, whereas the ready-to-use components from the Box, red cells and platelets, have already been transfused. One DHB, Auckland uses a rolling stock of thawed FFP for immediate issue to address this delay. However, moving to such an approach requires careful assessment of FFP use vs wastage and will not be appropriate for all DHBs.

Wastage is a significant concern around MTP activation. Overall, the audit encompassed the transfusion of 4,624 components, or a little over 13 components per patient. Inevitably some wastage of components occurs but the variation between DHBs was significant, even after excluding MTPs where the patient did not survive the MTP. One factor in the wastage is the ability to reuse a component. This will depend on whether the component was appropriately stored while outside the blood bank or if it was returned within 30 minutes. Of the components accepted back into stock, the size of the hospital then determines if the component can be reused. For red cells and platelets, the accounting system does not attribute components to a patient where the components were accepted back into stock and then expire. However, once FFP and cryoprecipitate have been thawed, the component is allocated to the initial patient until such time as it is issued to another patient, irrespective of acceptance back into stock from the initial patient. This means that in a large blood bank such as Auckland, the chances are much higher that the plasma component will be reissued than in a smaller blood bank, such as Dunedin. This goes some way to explain Auckland DHB's lower wastage cost per MTP than other DHBs'. However, there is a wide

range of wastage per MTP for similar sized blood banks (Waikato, Wellington and Christchurch). Lastly, the extended shelf-life of FFP in those DHBs using Thawed Plasma further reduces the FFP wastage. All participating DHBs except Waitemata are using Thawed Plasma. Further investigation into this, as well as the return rates and component ratios, is suggested.

Laboratory testing was generally well performed with a good frequency of testing and range of parameters tested. In general, the laboratory values held up well over the course of the MTPs. This provides reassurance that the component ratios and timings are fit for purpose. Viscoelastography was used in 26% of cases with an average of two samples per tested patient. Although there was no correlation between viscoelastography use and survival, a significant relationship with fewer components transfused in patients tested this way. Caution should be exercised in drawing conclusions from this as other factors, e.g. types of haemorrhage seen in situations where viscoelastography is available, may be playing a role. The size of the role that viscoelastography plays is of interest and is consistent with increasing use in this context internationally[12].

We looked at specific medications used as part of the MTP. Only 46% of patients received tranexamic acid. This is despite a meta-analysis of over 40,000 patients (predominantly CRASH2[13] and WOMAN trials) indicating that immediate treatment improved survival by more than 70% but the survival benefit decreased by 10% for every 15 min of treatment delay until 3 hours, after which there was no benefit[14]. Although the trials are still somewhat controversial, the consensus appears to be that tranexamic acid is of benefit and should be commenced early. Documentation of its administration may be an issue, either as a consequence of lack of documentation or documenting in places not seen by the auditors. This is a concern raised by a number of DHBs.

Factor VIIa was used in only five patients. This is consistent with published studies[15,16] showing little benefit to the use of factor VIIa in haemorrhage other than possibly as a last resort option.

There was little difference between MTPs in Delivery Suites, Emergency Departments, Intensive Care Units and Theatres once the total number of units was accounted for, other than cryoprecipitate. Consistent with concerns that pregnant women's fibrinogen is physiologically higher initially, there is greater emphasis on fibrinogen replacement in obstetrics.

Haemorrhage due to trauma was the commonest indication for calling an MTP but there was a wide spread of specialties making that call, consistent with the experience of others[7]. Surgical bleeding, especially that associated with abdominal aortic aneurysms was the next commonest indication followed by post-partum haemorrhages and gastrointestinal haemorrhage. This emphasises the need for a hospital-wide massive transfusion protocol.

As with all transfusions, there is a need to observe for adverse events as well as document the transfusion. Observations were reasonably well recorded, given the circumstances, but clearly not meeting recommended best practice. Respiratory rate was better recorded than in the previous bedside transfusion practice audit, noting that the latter was in non-emergency transfusions. Other recorded parameters were worse though. This is of some concern as it would impair the ability to diagnose a transfusion reaction, potentially leading to incorrect management.

Traceability of the compatibility labels in the notes was similar to the previous bedside transfusion practice audit, and at 98% overall was good.

Ceasing the MTP is an important step that is often forgotten, leading to unnecessary thawing of frozen components with consequent wastage. There was a wide range of time after the last box was issued before the Blood Bank was notified that the MTP was stopping. For most DHBs there was a correlation between mean time to cessation and overall wastage. Counties Manukau and, to a lesser extent, Waikato DHBs were outliers for this.

Patient outcomes were comparable with other studies[7,17] with 90% of patients surviving to the end of the MTP, 86% to 24 hours and 77% to 30 days.

RECOMMENDATIONS

1. Hospitals should review their systems around MTP activations to ensure
    a. traceability of components
    b. timely notification of cessation of MTPs
    c. transfusion observations are performed, notably respiratory rates, a key component of transfusion Early Warning Systems (EWS)
2. Blood banks and hospitals together should look at ways to reduce wastage, e.g. moving to extended life plasma.
3. Use of tranexamic acid appears low. Hospitals should review whether this is an issue of lack of use or poor documentation.
4. Tranexamic acid should be given early with even short delays reducing the benefit of treatment.
5. Despite the lack of evidence for 1:1:1 component ratios relative to 1:1:2, consideration should be given to whether the MTP is fit for achieving these ratios and whether clinical practice is responding to international guidance on the higher use of FFP in massive transfusion.

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