Improving outcomes for hospital patients with critical bleeding requiring massive transfusion: the Australian and New Zealand Massive Transfusion Registry study methodology

J. C. Oldroyd1*, K. M. Venardos1, N. J. Aoki1, A. J. Zatta1, Z. K. McQuilten1,2, L. E. Phillips1, N. Andrianopoulos1, D. J. Cooper2,5, P. A. Cameron3,5, J. P. Isbister4 and E. M. Wood1

Abstract

Background: The Australian and New Zealand (ANZ) Massive Transfusion (MT) Registry (MTR) has been established to improve the quality of care of patients with critical bleeding (CB) requiring MT (≥ 5 units red blood cells (RBC) over 4 h). The MTR is providing data to: (1) improve the evidence base for transfusion practice by systematically collecting data on transfusion practice and clinical outcomes; (2) monitor variations in practice and provide an opportunity for benchmarking, and feedback on practice/blood product use; (3) inform blood supply planning, inventory management and development of future clinical trials; and (4) measure and enhance translation of evidence into policy and patient blood management guidelines. The MTR commenced in 2011. At each participating site, all eligible patients aged ≥18 years with CB from any clinical context receiving MT are included using a waived consent model. Patient information and clinical coding, transfusion history, and laboratory test results are extracted for each patient’s hospital admission at the episode level.

Results: Thirty-two hospitals have enrolled and 3566 MT patients have been identified across Australia and New Zealand between 2011 and 2015. The majority of CB contexts are surgical, followed by trauma and gastrointestinal haemorrhage. Validation studies have verified that the definition of MT used in the registry correctly identifies 94 % of CB events, and that the median time of transfusion for the majority of fresh products is the ‘product event issue time’ from the hospital blood bank plus 20 min. Data linkage between the MTR and mortality databases in Australia and New Zealand will allow comparisons of risk-adjusted mortality estimates across different bleeding contexts, and between countries. Data extracts will be examined to determine if there are differences in patient outcomes according to transfusion practice. The ratios of blood components (e.g. FFP:RBC) used in different types of critical bleeding will also be investigated.

Conclusions: The MTR is generating data with the potential to have an impact on management and policy decision-making in CB and MT and provide benchmarking and monitoring tools for immediate application.

Keywords: Critical bleeding, Massive transfusion, Registry
Advances in critical care and surgical techniques have resulted in more patients with critical bleeding (CB) who require large volume blood transfusion support [5]. These “massive transfusions” (MT) have variously been defined as 10 or more units of red blood cells (RBC) transfused in 24 h or the “transfusion of half of one blood volume in 4 h, or more than one blood volume in 24 h” (adult blood volume is approximately 70 ml/kg) [6]. MT are important because the risks of transfusion are amplified when larger volumes of products are administered [7–9]. The consequences of variations in MT practice on patient outcomes are unknown. Reported mortality rates for patients requiring MT are between 25 and 48% [10–14]. Massive transfusion also poses logistical challenges for blood services/laboratories/hospitals as CB requiring MT is often unpredictable. These challenges relate to the need to have blood available—including Group O RhD negative RBCs and other blood components such as fresh frozen plasma (FFP), cryoprecipitate and platelets.

The evidence base for transfusion practice is incomplete, particularly in patients with CB. In 2011, Australia’s National Blood Authority (NBA) published patient blood management (PBM) Guidelines for CB [6] which summarised the available evidence and made recommendations for practice where the body of evidence was sufficient. Where there was insufficient evidence, “practice points” were developed though a consensus-based process to guide clinical practice. The PBM Guidelines identified major evidence gaps including: (1) the role of RBC transfusion; (2) dose, timing and ratio of component therapies; (3) effect of non-transfusion interventions; and (4) impact of blood component therapies on patient outcomes as particularly important [6]. Although high quality randomised controlled trials have recently been published [15–17], practices such as the routine administration of a 1:1 ratio of RBC to FFP [10, 11, 18–21] and greater use of recombinant activated factor VII (rFVIIa) are originally derived from the trauma setting without randomised controlled trial evidence. They have subsequently been extrapolated to non-trauma settings despite important differences in the pathophysiology of CB events in other settings, especially obstetrics [22]. Currently, there is no process for the systematic evaluation of compliance with the PBM Guidelines. In addition, there are major challenges associated with supplying blood products across Australia and New Zealand given their geographies, and a dearth of information available on clinical outcomes associated with blood transfusion.

Clinical quality registries are one of the most effective means of monitoring and encouraging uptake of healthcare guidelines [23]. They lead to improved quality of care by providing clinicians with credible risk-adjusted outcome data, enabling them to benchmark their outcomes against local and international data [24–26]. Given the incomplete evidence base in CB, the need for data on practice/blood product use in Australia and New Zealand and the current lack of monitoring of variations in practice, we established the Massive Transfusion Registry (MTR) to improve the quality of care of patients with CB requiring MT.

Methods
Study aims
The MTR was established to: (1) improve the evidence base for transfusion practice by systematically collecting data on MT practice and clinical outcomes; (2) monitor variations in practice and provide an opportunity for benchmarking, feedback on practice/blood product use, quality and safety in hospital practice and accreditation; (3) inform blood supply planning, inventory management and development of future clinical trials; and (4) measure and enhance translation of evidence into policy and PBM Guidelines.

Health care systems in Australia and New Zealand
Health care systems in Australia and New Zealand consist of public and private providers, including hospitals, primary health care, clinicians, nurses, other health professionals, and government and non-government organisations [27, 28]. They deliver many services for the prevention and treatment of diseases. In both countries, government funds public sector health services and private health service providers are owned and operated by the private sector.

Overview of Australia and New Zealand blood bank networks
The blood bank networks in Australia and New Zealand consist of several interconnected organisations involved in the supply and management of blood and blood products. National blood services providing allogeneic components and fractionated plasma products are operated by the Australian Red Cross Blood Service or New Zealand blood service, funded by national governments. There are national regulators (e.g. Therapeutic Goods Administration in Australia and Medsafe in New Zealand) and national blood services operate hospital blood banks for storage, cross-matching and issue of blood.
Governance
A steering committee oversees the conduct, development and outputs from the registry. The steering committee includes practising clinicians (haematologists, intensivists, emergency physicians, obstetricians, anaesthetists), a statistician and representatives from blood sector partner organisations. Terms of reference for the MTR steering committee, a data access and publications policy and a communications plan are in place. Access to aggregate data is provided to steering committee members. Each party agrees to treat the data in accordance with their obligations under their applicable national legislation for intellectual property and privacy. External interested parties, including local investigators at participating sites and government agencies, submit formal data requests to the steering committee for approval prior to being granted data access.

Ethics, consent and permissions
Ethical approval to establish the MTR was granted by Monash University Human Research Ethics Committee. In addition, ethical approval to collect identifiable patient level data has been obtained from all 32 participating hospital sites. It was not practical to obtain individual patient consent to participate because the cases are unpredictable, many are emergencies, and there is a high early mortality in CB/MT. Therefore, a waived consent model was chosen. The MTR qualifies for the conditions for waived consent as outlined in the NHMRC National Statement on Ethical Conduct in Human Research on the basis that: (1) involvement in the registry carries no more than low risk to participants (2) the benefits from the registry justify any risks of harm associated with not seeking consent (3) it is impracticable to obtain consent (4) there is no known or likely reason for thinking that participants would not have consented if they had been asked, and (5) there is sufficient protection of their privacy and an adequate plan to protect the confidentiality of data. Consent waiver was also suitable on the basis that: (1) Australian Commission on Safety and Quality in Health Care guidelines suggest that complete data must be collected from the entire eligible population in order to minimise selection bias [29], (2) obtaining written consent is impractical for many registries [30], and (3) consent waiver improves case-capture [26].

The MTR collects unique patient identifiers (medical record number, full name, date of birth and gender) which are used for the sole purpose of data linkage.

Study population
Patients (≥18 years) at participating hospitals are included if they receive ≥5 units RBC within any 4-h period of hospital admission [31]. This definition was chosen after verification that it optimised case-capture [31]. This was necessary because no standard definition of MT exists in the international literature and use of some definitions may lead to bias. For example, defining MT as 10 or more units of RBCs in 24 h (10/24 h) may exclude trauma patients who die within the first 24 h (‘survivorship bias’) whereas patients who do not require blood early on, but have a high cumulative transfusion requirement over a longer period, may be disproportionately represented (‘catch-up’ bias). These may be overcome by the use of time-dependent MT definitions (e.g. ≥5 units RBC in 4 h and ≥6 units RBC in 6 h), which focus on acuity of MT requirements during the resuscitation period (in the first 2–6 h following injury). We performed a validation study to examine the completeness of capture of CB events using three different definitions of MT (5U RBC in 4 h; 6U RBC in 6 h; 10U RBC in 24 h) [31]. The most inclusive definition with minimal bias was the 5U RBC in 4 h, which captured 94 % of all CB events and all types of CB events, including obstetric haemorrhage. The least inclusive definition was the 10U RBC in 24 h with less than 50 % of patients identified. Consequently, the registry uses 5U RBC in 4 h to define MT.

Given the difficulty of measuring bleeding reliably and identifying when CB occurs across many different clinical contexts and hospital sites, eligible patients are identified using a computer-generated algorithm to query hospital blood bank databases to ensure a centralised and systematic approach. Each hospital created its own queries based on the information system specific to the hospital. Hospital participation was contingent on hospitals having the data informatics capability to run these scripts and manage large volumes of transfusion data. Common informatics problems encountered were the inability to develop or run a script to identify MT patients, inability to conform to the data extraction template, and informatics systems which required manual extraction of laboratory data.

Data items
MTR data items are extracted for each patient for each hospital admission. A hospital admission represents a patient’s entire hospital stay and is demarcated by an admission date (the date they were admitted to hospital) and a separation date (the date they were discharged from hospital or the date of their death). Some patients will also have episodes of care (EOC), which are phases of treatment received by a patient within their hospital admission. An EOC ends when the principal clinical intent changes or when a patient formally separates from the hospital. There can be more than one EOC within one admission.
The MTR uses existing, electronically stored clinical data from hospital information systems. MTR data are captured within three packages (see Fig. 1, Table 1): (1) Patient demographic and outcome data in conjunction with diagnosis and procedure clinical coding from the hospital information services (HIS) or patient administration system; (2) full transfusion history for a patient’s hospital admission including information on all fresh blood products, fractionated plasma products, and adjunctive therapies. Both Australia and NZ have nationally standardised products for processes like leucodepletion (100%). Red cells are all whole blood-derived in both countries. Platelets are both whole blood or apheresis-derived, but they are a standardised product in terms of manufacturing specifications. Only products transfused (not issued then returned unused), are stored within the registry; and (3) Laboratory results for the patient’s hospital admission, both pre- and post-MT, from Laboratory Information Systems (LIS). Unique patient identifiers, required for verification and linkage, are collected in each package.

**Derived variables**
Derived variables are generated within the registry using raw data. They are generated automatically for speed, accuracy and efficiency. They include the Charlson Comorbidity Index (CCI) to estimate disease burden [32, 33]; counts of ICD10 diagnosis codes; unique bleeding contexts within an EOC; counts of each transfusion product, laboratory tests for each EOC and survival status on discharge and 24 h post-MT.

**Data management**
Requests for data extraction are made retrospectively on a quarterly basis from data custodians at participating sites. Retrospective recruitment ensures availability of all data items at the time of extraction, especially clinical coding data. All data extracts from sites are transferred via password protected secure file transfer protocol. Subsequent data processing involves source file verification for file completeness, formatting and layout (Fig. 2). Site-specific conversion modules have been created and are used to import the data packages. The conversion modules mean that hospitals need to extract data in the same way each quarter. Data are imported into the database into ‘staging’ and ‘target’ tables which are accessible via remote server. These table views provide opportunities to check for discrepancies and inconsistencies within hospital datasets and whether data from all three packages (HIS, transfusion history and LIS) have been successfully linked. Staging table checks include checks to ensure that specific rules to clean data have been applied; that there has been correct linkage; that mapping of various codes from reference or look-up tables built within the database has occurred; and that consistent terminology and descriptions of variables for all sites have been assigned. Target table checks include the application of unique constraints to remove any duplicates and generate
a number of derived variables using the raw cleaned data contained within the various tables. Target checks also show whether the database has assigned unique internal patient identification numbers associated with unique episode IDs, which are in turn associated with unique HIS, transfusion history and LIS results. Verification
queries in the target server are also run to check for orphan data. Following these quality assurance checks the data is deployed to the ‘production’ table from which data cuts are taken for all reporting and analyses.

**Quality assurance**

Quality assurance measures are applied to data item selection, requests for data items, data coding and data entry (Fig. 2). Data items selected are standardised across sites and are provided in most cases by personnel trained in data management such as business analysts, HIS staff or information technology managers. Requests for data items are standardised in project protocols. The data importing process includes extensive source file checks, the application of business rules and verification of successful linkage. As data move through the registry to the production database, further checks are applied to verify that data are moving correctly, linked successfully, derived variables are correct and internal identification numbers are generated.

---

**Fig. 2** Flowchart of data extraction into the MTR
**Hospital Data Reports to participating sites are generated bi-annually.** They allow benchmarking of practice with comparable health services. Here, de-identified individual site data are presented and compared with national and overall MTR data. Data reports are also customised for individual sites by clinical bleeding contexts to facilitate meaningful comparison and to identify local targets for audit or clinical investigation.

External communication consists of a MTR Newsletter (for progress reports/updates, upcoming events and publications of interest), the Transfusion Outcomes Research Collaborative (TORC)/MTR website (for project details), a TORC Biennial Report (overview of study achievements), Annual Investigator meetings (strategic planning and networking), MTR special interest group meetings (for the investigation of specific clinical questions) and data reports to partner organisations (project updates to funders).

**Pilot data**

The MTR builds on the Haemostasis Registry (2005–2010) which collected data on the off-label use of rFVIIa in CB from 96 hospitals and included approximately 3500 patients in Australia and New Zealand [34]. A pilot MTR study was undertaken to test the feasibility of collecting MT data at six hospitals and verified that much of the information required to analyse CB/MT events is already collected for other purposes. The pilot MTR developed mechanisms to identify MT patients at sites, extract relevant data from each source, securely transfer data to Monash University, link data from each source, and implement a coding framework to co-ordinate the large volume of data supplied. Validation studies were undertaken to test assumptions and methodologies and verify the data [31, 35].

**Research arising from the MTR**

**Validation study**

A study limitation is that MTR transfusion time is the product issue time from the hospital blood bank, which will not always be the same as the exact time the patient was administered the product. Therefore, a validation study was conducted to examine whether hospital ‘time of issue’ of blood products from the blood bank is a reliable estimate of the ‘time of transfusion’ [35]. Good concordance was found with the median transfusion time for the majority of fresh products being ‘product event issue time’ from the blood bank plus 20 min (>30 min for FFP), which reflected the expected time to transport, check and prepare the transfusion. For the purpose of a registry, these results support the use of hospital blood bank computer records as an appropriate source of blood product information for linking with other data sources.

**Data linkages**

Data linkage between the MTR and the National Death Index (NDI) in Australia and the New Zealand Ministry of Health mortality data is performed annually to assess 30- and 90-day mortality. Collaborative linkage projects with other clinical registries available through the Department of Epidemiology and Preventive Medicine, Monash University are being explored to provide context specific information and additional outcomes. Data linkage with other clinical registries will allow case–control comparisons of in hospital mortality, hospital and ICU LOS and ventilation times with matched patients who did not receive MT.

Another opportunity that exists is linkage with Blood Net, Australia’s national online inventory management system. This would allow an exploration of questions relating to blood utilisation at the time of MT (including the number of group O, RhD negative RBC). Such a linkage would also allow an examination of blood utilisation for MT as a proportion of overall inventory according to institution type, geographical location and type of CB/MT events, and against PBM guidelines.

**Supplementary data collection**

Specifically designed sub-studies requiring supplementary data collection are underway. Transfusion nurses or transfusion quality/safety officers or other trained staff at participating sites collect the supplementary data.

**Economic analyses**

Health economic data will be collected in order to estimate costs to the health system of CB/MT, as well as modelling economic impacts of variation in practice and outcome, and estimates of cost savings and patient benefits that could be realised by improved practice. This will enable the conduct of cost-effectiveness analyses to determine values of different practices and/or therapies, such as the availability of pre-thawed FFP, use of tranexamic acid (TXA, an antifibrinolytic agent) and variations in inventory holdings.

**Future directions**

Further recruitment of regional and rural sites will allow comparisons of clinical practices in non-urban settings where blood supply and administration practices may differ from metropolitan settings. A preliminary comparison suggests there are differences in Australian MT patients by hospital type (assigned using Australian hospital peer groups) [36] (Table 2). Securing ongoing
funding is required for the long-term sustainability of the registry.

**Strengths and limitations**

The MTR has developed a critical mass of clinicians, laboratory scientists and other health professionals regularly discussing issues around MT, including at annual investigator meetings and seminars. The MTR is an efficient and effective use of resources because it is using existing, electronically stored hospital data. It is bi-national and has representation across Australia and New Zealand from metropolitan and regional sites, including the private sector. The datasets received from sites are consistent and remove the need for an individual interpretation of patient data or selection of patients. The MTR uses an internationally recognised coding system for disease classification (ICD10 diagnosis coding) and for mapping and assigning bleeding contexts. A further strength is that the MTR offers the possibility of linkage with other registries and databases.

Although the registry has broad participation it is not yet nationally representative of Australia or New Zealand. Currently 15 Australian and 5 New Zealand sites (n = 20; 63 %) of the possible 32 sites with ethical approval are contributing data (Table 3). The three participating private hospitals were opportunistically recruited. Greater representation from the private sector is needed. One of the main limitations of the MTR is that only data existing

---

**Table 2 Characteristics of Australian MT patients (n = 2451), by type of Australian peer group hospital contributing data to the MTR (n = 15) [36]**

| Principal referral hospitals | Women’s hospitals | Private acute group B hospitals | Public acute group A hospitals | Public acute group C hospitals |
|-----------------------------|-------------------|---------------------------------|-------------------------------|-------------------------------|
| n = 9ᵃ | n = 1ᵃ | n = 3ᵃ | n = 1ᵃ | n = 1ᵃ |
| No. of MT cases (≥5 units in 4 h); n (%) | 15 (0.6) | 46 (1.9) | 206 (8.4) | 26 (1.1) |
| No. of MT cases (≥10 units in 24 h); n (%) | 8 (53.3) | 9 (19.6) | 83 (40.3) | 6 (23.1) |
| Gender (male); n (%) | 1378 (63.9) | 0 (0) | 19 (41.3) | 134 (65.0) | 16 (61.5) |
| Median age (years); [IQR] | 63 [48–74] | 40 [38–57] | 68 [50–78] | 69 [54–77] | 73 [62–84] |
| Median hospital length of stay (days); [IQR] | 18 [9–35] | 9 [6–10] | 15 [8–22] | 12 [7–28] | 6 [5–10] |
| Admitted to ICU; n (%) | 1730 (80.2) | 0 (0) | 43 (93.4) | 143 (69.4) | 24 (92.3) |
| Median ICU length of stay (hrs.); [IQR] | 75 [17–197] | 0 (0) | 75 [38–143] | 48 [0–120] | 85 [15–150] |
| Median ventilation time (hrs.); [IQR] | 0 [0–52] | 0 (0) | 0 (0) | 19 [0–134] | 0 [0–5] |
| Survival to hospital discharge; n (%) | 1706 (79.0) | 15 (100) | 38 (82.6) | 160 (77.7) | 24 (92.3) |
| Median RBC units in 24 h post-MT onset; [IQR] | 8 [6–12] | 9 [6–11] | 6 [6–8] | 8 [6–11] | 6 [6–9] |
| Median FFP units in 24 h post-MT onset; [IQR] | 5 [2–10] | 4 [4–7] | 2 [0–4] | 4 [2–7] | 1 [0–2] |
| Median Cryo units in 24 h post-MT onset; [IQR] | 2 [0–10] | 0 [0–6] | 0 [0–6] | 0 [0–8] | 0 [0–0] |
| Median Plts units in 24 h post-MT onset; [IQR] | 1 [0–2] | 1 [0–1] | 0 [0–1] | 0 [0–1] | 0 [0–0] |
| Median RBC:FFP ratio in 24 h post-MT onset; [IQR] | 1.5 [1.1–2.0] | 1.5 [1.5–2.0] | 2 [1.5–3.5] | 1.8 [1.5–2.8] | 4 [3–6] |

Admission type

| Elective n (%) | 649 (30.1) | 6 (40.0) | 44 (95.7) | 50 (24.3) | 5 (19.2) |
| Emergency n (%) | 1252 (58.0) | 3 (20.0) | 2 (4.3) | 156 (75.7) | 18 (69.2) |
| Maternity n (%) | 32 (1.5) | 6 (40.0) | 0 (0) | 0 (0) | 3 (11.5) |
| Unknown n (%) | 225 (10.4) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |

* Numbers are counts of Australian hospitals contributing data to the MTR.
within hospital systems can be extracted. Therefore data collection from the medical record to obtain further information, for example on medication history, adverse events or use of MT protocols, will be required for specific sub-studies.

Conclusions
The MTR is generating data with the potential to have an impact on management and policy decision-making in CB and MT and providing benchmarking and monitoring tools for immediate application.

Abbreviations
MTR: Massive Transfusion Registry; CB: critical bleeding; MT: massive transfusion; ICU: intensive care unit; RBC: red blood cells; FFP: fresh frozen plasma; PBM: patient blood management; NBA: National Blood Authority; NHMRC: National Health and Medical Research Council; MTP: massive transfusion protocol; TXA: tranexamic acid; HIS: hospital information services; LIS: laboratory information services; ICD10: international disease classification 10; ACHI: protocol; TXA: tranexamic acid; HIS: hospital information services; LIS: laboratory information services; CCI: charlson comorbidity index; ACSQHC: Australian Commission on Safety and Quality in Health Care.

Authors’ contributions
JCO led with writing the paper and contributed to data analysis and reporting of results. AJZ, EMW, KMW, JPI, LEP, NA, PAC, and ZKMcQ contributed to study design, registry development, data collection and analysis, and reporting of results. AJZ, DJC, EMW, JPI, LEP, NA, PAC and ZKMcQ contributed to writing the NHMRC Partnership Grant. All authors read and approved the final manuscript.

Author details
1 Transfusion Research Unit, Department of Epidemiology and Preventive Medicine, Monash University, Clayton, VIC 3004, Australia. 2 Centre of Research Excellence for Patient Blood Management in Critical Illness and Trauma, Monash University, Clayton, VIC 3004, Australia. 3 Emergency and Trauma Centre, The Alfred Hospital, Melbourne, VIC 3004, Australia. 4 Department of Haematology, University of Sydney, Royal North Shore Hospital, St Leonards, Sydney, NSW 2065, Australia. 5 Department of Epidemiology and Preventive Medicine, Monash University, Clayton, VIC 3004, Australia.

Acknowledgements
This study is funded by an NHMRC Partnership grant. We acknowledge the support of our blood sector and industry partner organisations. We thank Tania Richter for project support including ethics management. Dr Rasa Ruseckaitė, Senior Research Fellow and Project Manager on the MTR reviewed the manuscript. We also acknowledge the work of the Monash University Centre for Data Management Services, hospital transfusion nurses, scientists, haematologists, information analysts and all other staff who have contributed to the registry.

Competing interests
The authors declare that they have no competing interests.

Availability of data and materials
Data will not be shared in a public repository since the registry uses a waived consent model and therefore, permission to do this has not been obtained from patients.

Funding
The MTR is funded by an NHMRC Partnership Grant and funding from blood sector and industry partner organisations, namely, Australian Red Cross Blood Service, New Zealand Blood Service, CSL Behring, Department of Health and Human Services (Victoria), NBA, St John of God Pathology, NHMRC Centre of Research Excellence in Patient Blood Management in Critical Illness and Trauma and Monash University.

Received: 2 April 2016 Accepted: 27 September 2016

Published online: 06 October 2016

References
1. Australian Red Cross Blood Service. Adverse events. 2016. http://www.transfusion.com.au/adverse_events_overview. Accessed 5 Mar 2016.
2. Galas FR, Almeida JP, Fukushima JT, Osawa EA, Nakamura RE, Silva CM, de Almeida EP, Auler JO, Vincent JL, Hajjar LA. Blood transfusion in cardiac surgery is a risk factor for increased hospital length of stay in adult patients. J Cardiothorac Surg. 2013;8(1):1. doi:10.1186/s13019-013-0278-y.
3. Moore FA, Moore EE, Saaaua A. Blood transfusion. An independent risk factor for post injury multiple organ failure. Arch Surg. 1997;132(6):620–4.
4. Bolton-Maggs PH, Cohen H. Serious hazards of transfusion (SHOT) haemovigilance and progress is improving transfusion safety. Br J Haematol. 2013;163(3):303–14. doi:10.1111/bjh.12547.
5. Dzik WS, Ziman A, Cohen C, Pai M, Lozano M, Kaufman RM, et al. Survival after ultramassive transfusion: a review of 1360 cases. Transfusion. 2015;00:1–6.

Table 3 Current MTR site recruitment (n = 32)

| Characteristic                     | No. sites n (%) |
|------------------------------------|-----------------|
| Country                            |                 |
| Australia                          | 26 (81)         |
| New Zealand                        | 6 (19)          |
| Australian States                  |                 |
| Australian Capital Territory       | 0               |
| New South Wales                    | 8 (25)          |
| Northern Territory                 | 0               |
| Queensland                         | 3 (9)           |
| South Australia                    | 3 (9)           |
| Tasmania                           | 0               |
| Victoria                           | 7 (22)          |
| Western Australia                  | 5 (16)          |
| Public vs private                  |                 |
| Public                             | 29 (91)         |
| Private                            | 3 (9)           |
| Regional vs Metro                  |                 |
| Regional/Rural                     | 2 (6)           |
| Metropolitan                       | 30 (94)         |
| Current Australian hospital peer groups¹ |               |
| Principal referral hospitals       | 16 (50)         |
| Women's hospitals                  | 3 (9)           |
| Private acute group B hospitals    | 3 (9)           |
| Public acute group A hospitals     | 2 (6)           |
| Combined Wwomen's & Cchildren's hospitals | 1 (3)          |
| Public acute group C hospitals     | 1 (3)           |
| Remoteness area                    |                 |
| Major cities                       | 24 (75)         |
| Inner regional                     | 1 (3)           |
| Outer regional                     | 1 (3)           |

¹ Australian sites only (n = 26) [36]
6. National blood authority. Patient blood management guidelines: module 1 critical bleeding massive transfusion. Canberra. 2011:1–104.
7. Dunn LK, Thiele RH, Ma JZ, Sawyer R, Nemergut EC. Duration of red blood cell storage and outcomes following orthotopic liver transplantation. Liver Transpl. 2012;18(4):475–81.
8. Stanworth SJ, Morris TP, Gaarder C, Goslings JC, Maegle M, Cohen M, et al. Reappraising the concept of massive transfusion in trauma. Crit Care. 2010;14(6):30.
9. Turan A, Yang D, Bonilla A, Shiba A, Sessler DI, Saager L, et al. Morbidity and mortality after massive transfusion in patients undergoing non-cardiac surgery. Can J Anaesth. 2013;23:23.
10. Maegle M, Lefering R, Pfaffrath T, Tjardes T, Simanski C, Bouillon B. Red-blood cell to plasma ratios transfused during massive transfusion are associated with mortality in severe multiple injury: a retrospective analysis from the Trauma Registry of the Deutsche Gesellschaft für Unfallchirurgie. Vox Sang. 2008;95(2):112–9.
11. Sinha R, Roxby D, Bersten A. Experience with a massive transfusion protocol in the management of massive haemorrhage. Transfus Med. 2013;23(2):108–13.
12. Rose AH, Kotze A, Doolan D, Norfolk DR, Bellamy MC. Massive transfusion—evaluation of current clinical practice and outcome in two large teaching hospital trusts in Northern England. Vox Sang. 2009;97(3):247–53.
13. Campos A, Muñoz M, Garcia-Encisa JA, Ramirez G. Incidence and mortality of massive transfusion in a university hospital study of the period 2001–2005. Med Clin. 2007;129(10):366–71.
14. Sinha R, Roxby D. Change in transfusion practice in massively bleeding patients. Transfus Apher Sci. 2011;45(2):171–4.
15. Holcomb JB, Tilley BC, Baramuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 versus a 1:1:2 ratio and mortality in patients with severe trauma the PROPR randomized clinical trial. JAMA. 2015;313(5):471–82.
16. Jairath V, Kahn BC, Gray A, et al. Restrictive versus liberal plasma transfusion for acute upper gastrointestinal bleeding (TRIGGER): a pragmatic, open-label, cluster randomised feasibility trial. Lancet. 2015;386(9998):137–44.
17. Villanueva C, Colombo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med. 2013;368(1):11–21.
18. Davenport R, Curry N, Manson J, De’ath H, Coates A, Rourke C, et al. Hemostatic effects of fresh frozen plasma may be maximal at red cell ratios of 1.2. J Trauma. 2011;70(1):90–5.
19. Kautza BC, Cohen MJ, Cuscheri J, Minei JP, Brackenridge SC, Maier RV, et al. Changes in massive transfusion over time: an early shift in the right direction. J Trauma Acute Care Surg. 2012;72(1):106–11.
20. Magnotti LJ, Zarzaar BL, Fischer PE, Williams RF, Myers AL, Bradburn EH, et al. Improved survival after hemostatic resuscitation: does the emperor have no clothes? J Trauma. 2011;70(1):97–102.
21. Mitra B, Cameron PA, Gruen RL. Aggressive fresh frozen plasma (FFP) with massive blood transfusion in the absence of acute traumatic coagulopathy. Injury. 2012;43(1):53–7.
22. Pasquier P, Gayet E, Raccurtboom T, La Rosa J, Tashkandi A, Tesnier E, et al. An observational study of the fresh frozen plasma: red blood cell ratio in postpartum hemorrhage. Anesth Analg. 2013;116(1):153–61.
23. Review McKeon. Strategic review of health and medical research—better health through research summary report. Canberra: For the Department of Health and Ageing; 2013. p. 1–56.
24. Evans SM, Bohensky M, Cameron PA, McNeil J. A survey of Australian clinical registries: can quality of care be measured? Intern Med J. 2011;41(1a):42–8.
25. Evans SM, Scott IA, Johnson NP, Cameron PA, McNeil JJ. Development of clinical-quality registries in Australia: the way forward. Med J Aust. 2011;194(7):360–3.
26. McNeil JJ, Evans SM, Johnson NP, Cameron PA. Clinical-quality registries: their role in quality improvement. Med J Aust. 2010;192(S):244–5.
27. Australian Institute of Health and Welfare. Australia’s Health System. 2016. http://www.aihw.gov.au/australias-health/2014/health-system/. Accessed 1 Sept 2016.
28. New Zealand Ministry of Health. New Zealand Health System. 2016 http://www.health.govt.nz/new-zealand-health-system. Accessed 1 Sept 2016.
29. Australian Commission on Safety and Quality in Health Care. Operating Principles for Australian Clinical Quality Registries. 2010. http://www.safetyandquality.gov.au/wp-content/uploads/2012/03/Operating-Principles-for-Australian-Clinical-Quality-Registries-Brochure-2011.pdf. Accessed 1 Feb 2016.
30. Tu JV, Willison DJ, Silver FL, Fang J, Richards J, Laupacis A, et al. Impracticability of informed consent in the registry of the Canadian stroke network. N Engl J Med. 2004;350:1414–20.
31. Zatta AJ, McQuilten ZK, Mitra B, et al. Elucidating the clinical characteristics of patients captured using different definitions of massive transfusion—evaluation of current clinical practice and outcome in two large teaching hospital trusts in Northern England. Vox Sang. 2014;107(1):660–70.
32. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.
33. Depuy RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992;45(6):63–9.
34. Zatta A, McQuilten Z, Kandane-Rathnayake R, Ibister J, Dunkley S, McNeil J, Cameron P. The Australian and New Zealand Haemostasis Registry: ten years of data on off-licence use of recombinant activated factor VII. Blood Transfus. 2015;13(1):86–99.
35. McQuilten ZK, Schembri N, Polizzotto MN, Akers C, Wills M, Cole-Sinclair J, Cameron PL. The Australian and New Zealand Haemostasis Registry: ten years of data on off-licence use of recombinant activated factor VII. Blood Transfus. 2015;13(1):86–99.
36. Australian Institute of Health and Welfare. Australian hospital peer groups. Health services series no. 66. Cat. no. HSE 170. Canberra: AIHW. 2015. http://www.aihw.gov.au/publication-detail/?id=60129553446. Accessed 1 Sept 2015.