

Mass casualty events: blood transfusion emergency preparedness across the continuum of care

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Transfusion support is a key enabler to the response to mass casualty events (MCEs). Transfusion demand and capability planning should be an integrated part of the medical planning process for emergency system preparedness. Historical reviews have recently supported demand planning for MCEs and mass gatherings; however, computer modeling offers greater insights for resource management. The challenge remains balancing demand and supply especially the demand for universal components such as group O red blood cells. The current prehospital and hospital capability has benefited from investment in the management of massive hemorrhage. The management of massive hemorrhage should address both hemorrhage control and hemostatic support. Labile blood components cannot be stockpiled and a large surge in demand is a challenge for transfusion providers. The use of blood components may need to be triaged and demand managed. Two contrasting models of transfusion planning for MCEs are described. Both illustrate an integrated approach to preparedness where blood transfusion services work closely with health care providers and the donor community. Preparedness includes appropriate stock management and resupply from other centers. However, the introduction of alternative transfusion products, transfusion triage, and the greater use of an emergency donor panel to provide whole blood may permit greater resilience.

Mass casualty events (MCEs) in medical terms are “single or simultaneous event(s) where the normal major incident response of one or several health organisations must be augmented by extraordinary measures in order to maintain an efficient, suitable and sustainable response.”¹ Most are marked by a relatively sudden and dramatic event that causes a surge in numbers of patients. MCEs are an important health care issue. Despite a plateau in the rate of all types of disasters recorded worldwide in the past 8 years, there has been a continued increase in man-made disasters and MCEs. The mortality from terrorist incidents alone has more than doubled since 2007.^{2,3} Planned mass gatherings such as sporting and religious events also provide the potential for MCEs. Massive casualty events have the potential to generate many trauma

ABBREVIATIONS: DCR = damage control resuscitation; EDP(s) = emergency donor panel(s); MCE(s) = mass casualty event(s); MHP(s) = major hemorrhage protocol(s); NHSBT = NHS Blood and Transplant; RDCR = remote damage control resuscitation.

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The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the institutions.

Received for publication September 30, 2015; revision received December 14, 2015; and accepted December 15, 2015.
doi:10.1111/trf.13488

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TRANSFUSION 2016;56;S208–S216

victims; therefore, health care services must be prepared across the continuum of care.

The medical response to the multisite terrorist attacks in Paris in November 2015 was elegantly described by Hirsch and colleagues.⁴ The medical response was described as the civil application of war medicine and included prehospital and hospital-based damage control resuscitation (DCR). DCR assumes hemorrhage control, restricted use of crystalloid, and access to blood. MCE and disaster planning has traditionally relied on stockpiles of virtually indestructible crystalloid with a shelf life measured in decades. Disaster planning reliant on perishable blood and blood components is clearly more problematic. A cross-sectional approach to transfusion planning that is nested within wider health care emergency management is required.

The delivery of transfusion support in the context of these incidents has received increasing interest. The appropriate management of severe hemorrhage offers a window of opportunity for improving MCE outcomes.⁵⁻¹³ This opportunity has developed primarily through our further understanding of the role blood and, more specifically, coagulation therapy, plays in DCR.¹⁴⁻¹⁷ Driving the focus on optimal transfusion support in DCR is the increasing use of major hemorrhage protocols (MHPs) to ensure early delivery of red blood cells (RBCs) and hemostatic components.^{18,19} In addition, there has been a wider acceptance of the restricted use of prehospital non-blood-based fluids, in favor of waiting until MHPs can be provided within hospitals.²⁰⁻²³ The early provision of blood has driven an international movement toward the delivery of these products in the prehospital environment in an effort to further improve trauma outcomes.²⁴⁻²⁶ The practice of prehospital blood transfusion combined with additional hemostatic adjuncts such as tourniquets and tranexamic acid form part of the new overall paradigm of remote DCR (RDCR).^{27,28}

Providing DCR and RDCR in the setting of an MCE is still relatively untested. The prospect of delivering blood components in the volumes now expected in major hemorrhage already presents a recognized challenge to MCE planners. Previous studies have illustrated the effect of applying modern-day MHPs during previously reported MCEs, showing a possible three to four times increase in the demand for hemostatic components in certain events.¹³ The addition of delivering this in the prehospital setting further complicates the issue and is an aspect of transfusion service preparedness for MCEs that has not been previously discussed. The objective of this short article is to review the variation in the landscape of transfusion response to MCEs internationally, through the comparison of two northern European countries with similar systems of government-funded health care deliverance.

Transfusion service delivery for MCEs in the United Kingdom

The United Kingdom has a population of approximately 64.5 million with a land mass of just under 250,000 km².²⁹ Less than 20% of this area consists of mountains, moorlands, or similar terrain, which would present a challenge to an emergency service MCE response and the distribution of emergency blood products.³⁰ Approximately 85% of the nation's transfusion needs are provided by the English Blood Service, NHS Blood and Transplant (NHSBT). NHSBT undertook a review of its MCE transfusion response plans in preparation for the 2012 London Olympic Games³¹ and is currently reviewing the implications of the Paris MCE.

NHSBT applies a policy of maintaining blood stocks at levels appropriate for the current risk level utilizing planned donor drives in preparation for periods of potential or expected surge in demand such as winter supply shortages. Currently, whole blood is not utilized in the United Kingdom. Transfusion support is based on components. This system aims to rapidly deliver the principal blood components: RBCs, fresh-frozen plasma (FFP), platelets (PLTs), and cryoprecipitate.³¹ After an MCE there is no reliance on emergency donation for the immediate provision of blood products to casualties; instead, the response to such incidents is based on optimizing supply from existing stock and the forward planning of replacement donation.

During the lead-up to a period of expected heightened demand, NHSBT calibrates stock levels through a process of both bottom-up and top-down planning. Bottom-up plans are based on establishing a range of potential scenarios and therefore casualty load to which both a transfusion per casualty requirement and a hospital demand factor are applied to give an overall stock demand for an event. This is performed for all four of the major components. In addition, top-down plans, similar to business continuity planning for day-to-day needs, rely on the recent evidence from previous MCE transfusion responses to ensure the quantities applied in the bottom-up stage are appropriate and justified.³¹ International blood demand prediction tools in trauma have focused predominantly on early individual casualty physiology and laboratory results to predict a "dichotomous outcome" of whether or not a massive transfusion will be required.³²⁻³⁵ However, UK plans assume wider use of all blood components.

Prediction and planning tools for transfusion service and hospital deliverance are now going further with the use of computer modeling techniques. Simulation models have been developed to improve our understanding of blood provision following MCEs, as well as test potential strategies for managing instances of overwhelming demand in future events.³⁶ The standard blood stock

levels held at individual hospitals and within networks are determined based on the average daily blood use and can be increased when required. This is controlled and managed centrally through a hub-and-spoke approach that informs rapid resupply after an MCE. The overall component availability can also be manipulated through alterations to the central manufacturing processes. For example, increased plasma and PLT production can be generated from whole blood.³¹

The aim of in-hospital management of MCEs in the United Kingdom is to provide as close to the gold standard level of care as possible within the resource constraints generated by the surge casualty demands. Major trauma centers form the focus of the response for the most severely injured casualties providing DCR through MHPs with the aim of minimizing further blood loss, restoring circulating volume and preventing or treating trauma-induced coagulopathy.^{18,37} The current approach to pre-hospital care delivery in the United Kingdom in terms of transfusion support focuses primarily on prevention of further blood loss and the development of trauma-induced coagulopathy through hemostatic adjuncts and restrictive transfusion protocols. Hemostasis is led through compression of active bleeding, the use of tourniquets, and application of pelvic binders where appropriate. Topical hemostatic agents such as factor concentrators, mucoadhesives, and procoagulant dressings are not widely used within the civilian setting.

Current practice advocates the use of tranexamic acid within 3 hours of injury combined with restrictive use of nonhematologic fluids to maintain a central pulse. Other pharmaceutical adjuncts such as recombinant activated factor (FVII), while showing some benefit in reducing RBC requirements after trauma, are not in routine use within the UK system. However, it has been employed for major hemorrhage at certain UK hospitals after previous MCEs.³⁸⁻⁴⁰ The use of prehospital blood is a relatively new concept in the United Kingdom. The London Air Ambulance was the first to begin carrying RBCs out into the field in 2012. Since then, a number of regional and national air ambulance services in the United Kingdom have introduced a range of capabilities including lyophilized plasma and tranexamic acid.

Transfusion service delivery for MCEs in the Kingdom of Norway

The Kingdom of Norway's population is less than 1/10th of the United Kingdom at just over five million people; however, this populace is spread over an area 1.4 times larger than the United Kingdom at nearly 350,000 km². In addition and in contrast to the United Kingdom, half of this land is mountainous terrain or moorland with difficult access, numerous transportation barriers, and seasonal challenges, especially with prolonged winter

periods.⁴¹ Blood and products from blood banks located and run by local and regional hospitals meet the transfusion needs. The hospital blood bank will maintain blood-stock levels to match ordinary hospital activity usage for 10 to 14 days for RBCs, approximately 30 days for plasma, and 4 days for PLTs. Only larger hospitals make PLT concentrates.

In one of the four health regions in Norway the hospital blood banks have plans to meet minor surges of blood and blood products. At times of larger crisis these may be extended to any affected regional hospital, although on an ad hoc basis. Single hospitals have their own contingency plans, but none are scaled to cope with MCEs. There is no control or coordination of the transfusion needs at a national level and no government body evaluating national blood stock levels related to current risk levels or expected potential surges. In the aftermath of the most severe civilian MCE in Norway on July 22, 2011,⁴² improved contingency plans have been made to improve obvious shortcomings in nearly all areas except transfusion. In this incident, blood product needs were largely met, and any need for a change in national civilian transfusion strategies was therefore deemed unwarranted. There is presently no national policy in place on how to meet transfusion needs after an MCE in Norway.

Trauma teams are located at regional hospitals and will rely on a balanced transfusion policy of RBCs, FFP, and PLTs provided by the hospital blood bank as one "trauma package" containing a balanced quantity of the three components. No regional hospital provides whole blood as a part of its DCR program. Most regional air ambulance services now fly with lyophilized plasma, but only a few with RBCs and, as of December 2015, one with PLT-sparing, leukoreduced whole blood. As in the United Kingdom, there is no reliance on donation following an MCE for the rapid provision of blood components to casualties; indeed the regional blood bank involved in the July 22, 2011, terrorist incident managed successfully to stem the flow of nonregistered donors at an early time.¹¹

However, one regional blood bank (Bergen) is in the process of implementing contingency plans that will involve prescreened group O low-titer emergency donors. The donors will be recruited from three locations, at a local naval base, among the regional hospital employees, and from city suburbs, and called to donate whole blood to be fully tested and utilized as soon as possible. These plans are coordinated with the Norwegian Armed Forces Medical Services contingency plans for blood product needs in emergencies. Donated blood is to be leukoreduced with PLT-sparing filters, tested, and dispensed as whole blood for immediate use or cold storage. The plan is based on a projected initial demand of 50 units of whole blood to meet the demand of five immediate massive transfusion cases; however, the scheme is easily upscalable.

Literature review

We have briefly described the organization and planned response to MCEs by transfusion providers in two countries. One blood bank in Norway is redeveloping the use of whole blood as a part of its resilience plan. It is a novel approach for Europe and stimulates debate. Many countries have faced MCEs but the literature concerning transfusion support is limited. Blood demand in MCEs has been comprehensively reviewed by Glasgow and colleagues.¹³ The publications and reports of transfusion service deliverance for MCEs in North America and Israel are particularly valuable. These nations have significant experience with a wide range of MCEs and face their own environmental and logistical challenges in mounting an effective response.¹³ Hess and Thomas⁴³ and Schmidt⁴⁴ both highlighted the issues associated with the US experiences of emergency donation in the immediate aftermath of such events during their reviews of blood and disaster. Colleagues in Israel have also described their substantial experience with delivering transfusion support in MCEs, both providing detailed plans of their transfusion response and offering planning estimates for future MCE blood needs.⁵

Dann and coworkers⁵ stated in a review of the response to nine individual terrorist MCEs in Israel that the established protocol is to prepare three RBC units for each patient “likely to require blood.” In comparison, Shinar and coworkers⁴⁵ reviewed 1645 terrorist attacks, again in Israel, from 2000 to 2005, involving 7497 casualties. These authors, from the Magen David Adom (MDA), the national supplier of blood products to Israel, reported a mean number of units supplied per MCE casualty of 1.3 U of RBCs and 0.9 U of other components. Using the total number of casualties as a denominator, that is, “per casualty,” is a much broader descriptor for planners than the units per individual casualty expected to require blood. However, the volume of casualties actually requiring blood is relatively small compared to the overall injury burden from an event.^{13,43,44}

Most recently, another group from Israel reported the use of just over 3 units of RBCs “per casualty admitted to hospital,” therefore negating the issues of accounting for all casualties with very minor injuries who may be dealt with at the scene or in minor injury units. The 3 RBC units per admission figure is supported by a separate report from a combat hospital in Iraq,⁴⁶ which describes their response to three separate civilian MCEs. The most recent report also stands out in its detailed discussion of component use and attainment of modern-day transfusion ratio deliverance after MCEs affecting civilian communities.⁹ Blood use is greatest in casualties involved in terrorist MCEs with injury severity scores greater than 15 (ISS > 15). Blood use in the most severely injured was 7 to 8 units of RBCs supported by components. UK military and civilian experience suggested even greater requirements for the most severely injured by improvised explo-

sive devices, with median requirements of 16 (9-25) units of RBCs and proportionate amounts of components.^{40,47}

The proportion of injured requiring blood varies enormously and is dependent on the event, hemorrhage control, and availability of blood. After the London bombings, only 23 patients received blood during the first 24 hours out of an estimated 700 injured.⁴⁰ The planning for the Olympics assumed a similarly small proportion. The Paris attacks in 2015 with shootings at four sites and three explosions have highlighted the requirement to support many more severely injured. However, there was good blood component availability during the crisis, demonstrating that large volumes of components can be rapidly mobilized if already stocked.

DISCUSSION

MCEs continue to challenge health care emergency preparedness. The definition of MCEs implies that critical sufficiency and supply of resources will be constrained. MCEs involving improvised explosive devices are characterized by massive bleeding. The widespread adoption of lessons learned on the battlefield has led to a more aggressive approach to hemorrhage control. However, the same paradigm has also led to the introduction of cautious fluid resuscitation and the early use of blood components in resuscitation. Such an expectation challenges health care planners and developed blood transfusion services especially when a large surge of patients is involved. Effective prehospital care and emergency system preparedness across the continuum of care has the potential to reduce morbidity and mortality as well as reduce the demand for blood.

Transfusion planning has not traditionally been a part of MCE planning; however, we suggest that integration is essential for both blood demand and supply management. The two European examples presented illustrate two complimentary approaches currently being used to prepare for MCEs. Both countries have recently responded to terrorist bombings. The UK example is a national example based on component therapy with access to redistributed stock. The Norwegian example (Bergen) is that of a relatively geographically isolated community using a whole blood program to supplement existing stocks of blood components. The two transfusion services' support to MCE is summarized in Table 1.

Continuity of care

The UK has dealt with a number of civilian disasters but it was the response to the July 7, 2005, London bombings that led to the first transfusion service review.⁴⁰ The review highlighted a number of issues that have been incorporated into subsequent planning. These include the provision of a large volume of universal components. The

TABLE 1. Comparison summary of MCE transfusion preparedness

| Transfusion preparedness | England | Norway |
|--|--|--|
| MCE response planning | | |
| Historical experience of MCEs | Periodic | Limited |
| Integrated military and civilian responses | No | Yes* |
| Blood stock management and redeployment | Coordinated at national level | Regional |
| Donor management systems | National call center | Local call-up |
| In hospital | | |
| Whole blood available to civilian community | No | Regional initiative. Use of leukoreduced PLT spared whole blood.* |
| Principal blood components held within standard inventories | RBCs, FFP, PLTs, and cryoprecipitate | RBCs, FFP, and PLTs |
| Emergency blood donation program | National blood service | Local pool of emergency volunteer donors* |
| Routine use of tranexamic acid | Yes (within 3 hr) | Yes |
| Routine use of recombinant activated FVII for massive hemorrhage | No† | No |
| Prehospital | | |
| Tranexamic acid | Increasing use | Yes |
| Tourniquets | Yes | Yes |
| Routine access to hemostatic dressings | No | No |
| Prehospital transfusion | RBCs with limited availability of lyophilized plasma | Lyophilized plasma with limited availability of RBCs and leukoreduced PLT-spared whole blood |

* Recent initiative or currently in development.
† Reports of occasional use in response to MCEs.

demand was three times greater than the actual amount of RBCs used during the first 24 hours. This ratio of over-ordering has previously been described.^{5,7} The proportion of group O RBCs ordered during July 7, 2005, was 80% whereas the proportion of group O in the UK population is 45%. In addition, there was a demand for hemostatic components including FFP, PLTs, and cryoprecipitate. Despite overordering, there was very little reported wastage due to the amendment of hospital blood bank standing orders and the subsequent use of blood. The subsequent use of blood is due to the ongoing care required for the severely injured. Early revision surgery leads to demand for both theater time and blood. The care of the severely injured may continue for many years and transfusion support should be mindful of the continuity of care. The other reason for continued blood use is the return to planned health care activity.

The impact of military practice on civilian care

Military practice has left a legacy across the continuum of care. It has changed trauma care and planning and has stimulated collaborative research. It has also contributed to MCE planning. MCE planning is facilitated by trauma networks with shared policies and massive hemorrhage protocols. A series of guidelines for the management of massive hemorrhage have developed over the past 5 years.^{17,48,49} All have been underpinned by military transfusion practice and enhanced by the developing evidence. Transfusion guidelines now promote hemorrhage control, early use of tranexamic acid, and a foundation of RBCs and FFP in a 1:1 to 3:2 ratio followed by goal-directed therapy.^{23,50} Good organization is essential to

success with the early involvement of senior experienced clinicians, well-rehearsed teams, and trauma registries.^{17,48,51} The concepts of prehospital care, registry reviews, standardized massive transfusion protocols, cross-sector planning principles were successfully integrated into the blood transfusion service for the 2012 London Olympics.³¹

The use of whole blood has traditionally been used by defense medical services and offers considerable logistic advantages in the austere medical environment.^{52,53} The Bergen team has spearheaded the concepts of RDCR with the use of emergency donor panels (EDPs) and the introduction of cold whole blood for military units.⁵⁴ The use of emergency whole blood is not restricted to the military community but may be lifesaving in civilian situations such as the cruise industry.⁵⁵ The Bergen model for transfusion support demonstrates a further example of military practice used in wider support of the civilian community, that is, the use of EDPs for whole blood. EDPs are pretested donors who are prepared to give in emergencies. Donors are required to maintain their currency as donors and are normally screened at the time of donation. It represents the most agile of systems and is an ideal solution for a geographically isolated population with a low prevalence of transfusion transmitted infection. However, it also requires careful preparation and demand planning.

Transfusion triage and demand planning

Transfusion demand planning is primarily designed to meet the normal needs of the population at risk. In addition, consideration must be given to emergency-

TABLE 2. Guidance for blood component use during the 2012 London Olympics

| Priority | RBCs (U) | FFP (U) | PLTs* | Cryoprecipitate (pool of 5 donations) | Category definition |
|----------|----------|---------|-------|--|---|
| P1 | 10 | 6 | 1 | 1-2 | Immediate, requiring immediate intervention |
| P2 | 4 | 0 | 0 | 0 | Urgent, requiring intervention < 6 hr |
| P3 | 0 | 0 | 0 | 0 | Delayed, walking wounded |

* PLT minimum dose of 2.4×10^{11} per adult therapeutic dose (Ref: internal reporting to NHSBT by H. Doughty).

preparedness. Emergency-preparedness must respond to not only the emergency but also ensure the continuity of critical services. The primary role of the blood transfusion services and hospital blood banks is to provide blood components. The wider use of “massive transfusion” protocols has led to an increased initial demand for “universal” components such as group O D– RBCs and AB FFP. Alternative universal components can be substituted. Examples are the use of group A plasma for all and group O D+ RBCs for males and women over 50.⁴⁸ Military experience has demonstrated that hemostatic resuscitation and the introduction of point-of-care testing may increase the demand for PLTs and cryoprecipitate.⁴⁷ Resuscitation teams have become accustomed to large volumes of components for individual patients. Such trends must be factored into local and national demand planning.

Stock management of labile components such as blood and PLTs is a challenge when there is unpredictable demand. Large stock holding in blood services or blood banks is associated with wastage due to time expiry, whereas insufficient stocks may lead to clinical disaster. It should be assumed that in the unplanned event the demand for blood components may exceed supply. The use of preprepared blood shortage plans provides valuable guidance in the event of RBC and PLT shortages.^{56,57} In addition, transfusion triage can provide guidance for both clinicians and the blood transfusion services. The guidance issued for the Olympics is shown in Table 2. While such schemes are applicable to individual casualties where information may be in abundance, in an MCE scenario such detail is often unavailable, both at the planning stage and early in the course of the event. Historically, it has been repeatedly shown that blood demand is greatest within the first few hours of an event and that expectedly this period correlates with the arrival of the most severely injured casualties.^{58,59} Experimental simulation modeling has recently explored the impact of restricting both the total number of RBCs and emergency group O blood in MCEs.³⁶ Restrictive transfusion protocols appear to increase the overall treatment rates where there are large casualty loads.

Transfusion safety

Demand planning and stock management should consider blood group mix. There will be considerable pressure

on the universal components. Demand management of group O blood may promote the early use of group specific or ABO-compatible blood. However, the greatest risk associated with transfusion especially in the context of MCEs is the use of ABO-incompatible blood and the initial use of group O may be the safest option. Note that the use of group O before blood grouping may lead to “mixed fields” and staff should have guidance as to when to revert to group specific blood. Identification bands should be worn by patients receiving blood. Emergency identification should use gender and be compatible with laboratory information management systems. Attention must also be paid to cold chain management especially during the transport of blood between organizations and departments. Transfusion is a highly regulated area of health care. The European Blood Directive 2002/98/EC sets standards for the collection, testing, processing, storage, and distribution of human blood and blood components.⁶⁰ Requirements of the legislation include the traceability of blood used and hemovigilance. These are potentially challenging within the context of MCEs but must be managed.

Back to whole blood

Most national blood services have developed component programs designed to meet civilian patient requirements. The drivers for transfusion support in the UK are medical patients, in particular, those requiring haematology support.^{61,62} Components permit not only optimal care of individual patient groups but also optimal storage. National component development programs have focused on targeted safety measures such as those designed to reduce the risk of transfusion-related acute lung injury and prion disease rather than MCEs.⁶³ The current management of traumatic hemorrhage requires hemostatic components. Frozen products can be stockpiled but must be thawed to be used which takes time unless prethawed. Component development such as liquid and lyophilized plasma may address some of the logistic constraints and permits treatment in the prehospital space. However, labile products such as RBCs and PLTs cannot be stockpiled. For instance PLTs have a shelf life of 5 to 7 days unless cryopreserved. Another method of delivery of PLTs is whole blood.

Few European civilian blood services provide whole blood either routinely or as part of their emergency response. However, the use of whole blood for hemostatic resuscitation is predicted to become more mainstream as evidenced by its inclusion as a research priority in the NHLBI Transfusion Medicine State of the Science Symposium Summary Statement.⁶⁴ Fresh whole blood not only addresses the concerns about the storage lesion, but also provides a supply of both liquid plasma and a small dose of PLTs with less anticoagulant than component therapy. PLT function is normally related to posttransfusion circulation time and PLTs stored at 1 to 6°C have reduced circulation time. However, whole blood stored cold has the potential to provide some hemostatic effect over a longer period.^{54,65} Whole blood availability may be limited due to other barriers including leukoreduction. However, there is now an FDA-approved PLT-sparing filter.⁶⁶ Well-rehearsed collection, testing, and release can yield a continuous flow of whole blood bags. The use of whole blood is a potentially more agile and responsive approach and should be considered as a part of resilience measures. Indeed, as of December 2015 cold-stored, leukoreduced, PLT-containing whole blood has been offered to the Emergency Department at the Mayo Clinic in Rochester, Minnesota.

CONCLUSIONS

Transfusion support is a key enabler in the health care response to MCEs. Historical reviews have recently supported MCE blood demand planning; however, each new event offers further insights for resource management. The challenge remains balancing demand and supply. The intervention priority to reduce demand is hemorrhage control. However prehospital and hospital care has benefited from early access to transfusion support. A surge in demand for blood components remains a challenge for any blood provider and transfusion may need to be triaged and demand managed. The options for increasing supply include redeployment of existing stock, altered manufacturing, and careful donor management. The introduction of alternative transfusion products and rapid access to pretested emergency donor panels may also offer resilience. In conclusion, transfusion support in MCEs is important and should be an integrated part of health care emergency-preparedness.

ACKNOWLEDGMENT

The authors acknowledge the editorial assistance of Dr Emma Watkins.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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