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Effects of the COVID-19 pandemic on supply and use of blood for transfusion

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The COVID-19 pandemic has major implications for blood transfusion. There are uncertain patterns of demand, and transfusion institutions need to plan for reductions in donations and loss of crucial staff because of sickness and public health restrictions. We systematically searched for relevant studies addressing the transfusion chain—from donor, through collection and processing, to patients—to provide a synthesis of the published literature and guidance during times of potential or actual shortage. A reduction in donor numbers has largely been matched by reductions in demand for transfusion. Contingency planning includes prioritisation policies for patients in the event of predicted shortage. A range of strategies maintain ongoing equitable access to blood for transfusion during the pandemic, in addition to providing new therapies such as convalescent plasma. Sharing experience and developing expert consensus on the basis of evolving publications will help transfusion services and hospitals in countries at different stages in the pandemic.

Background

The ongoing COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is creating major disruption globally at all levels of health-care provision. In the UK, around a third of hospitalised patients with COVID-19 are estimated to die.[1] Transfusion professionals are responding to uncertain patterns of demand for blood components, to reductions in the numbers of donations, and to loss of crucial staff because of sickness. A key activity for transfusion institutions during this period, whether hospital-based or separate blood transfusion services, is the monitoring of supply and demand so that sufficient blood stocks are maintained to support ongoing critical needs, for example, major trauma.

The objective of this Review is to provide a synthesis of the evolving published literature on COVID-19 and to provide expert opinion relevant to transfusion practice in times of potential or real shortage, addressing the entire transfusion chain from donor to patient. The search strategy that underpinned this Review has been regularly updated to incorporate new, relevant information. The focus is on providing practical guidance to support transfusion specialists worldwide at different stages in the pandemic, including as health services reopen for all activities. Further updates of searching will ensure that any new information is highlighted for readers.

Method

A systematic approach was taken to search and identify all published literature relevant to COVID-19. Searches were done using a comprehensive search strategy (appendix p 1). These searches were not limited by language or study type and were run daily by an information specialist. The following databases were searched: WHO COVID-19 global research database,[2] PubMed, and Vox Sanguinis International Society for Blood Transfusion Science Series. In addition, a search was done for relevant general articles on blood and shortage, blood and contingency planning, and blood and major incident planning (appendix pp 1–2).

All identified references were screened by one person using predefined eligibility criteria (appendix pp 2–3). Each eligible reference was tagged with clinical key words, ranging in themed areas from donor to recipient. Any type of study or review was considered relevant. Outputs of searches were reviewed and incorporated by groups of clinicians into five key section themes defined at the onset of the project and described in the following sections of this Review. A table of registered, randomised controlled trials was created by weekly searches of ongoing trial registries, ClinicalTrials.gov, and the COVID-19 subset of the WHO International Clinical Trials Registry Platform database.[3]

Results

From March 23 to April 30, 2020, systematic searches identified over 9000 citations. During April, 2020, 7715 citations were screened for eligibility and 414 were included in the final citation list. Figure 1 shows the steady increase in citations during April and the proportion of citations relevant to the topic of transfusion chain from donor to recipient. The search narrative for emergency planning retrieved 1255 references after duplicates and irrelevant references were removed, from which 121 citations were included. A few ongoing systematic reviews were also identified.[4]

Theme 1: features of SARS-CoV-2 infection that affect patients' needs for transfusion

Characteristics of SARS-CoV-2 infection have been described by multiple reports.[5,6] Understanding these features informs the approaches required to address potential mismatches between blood supply (theme 2) and demand, including the activities of patient blood management implementation (theme 4). Anaemia is uncommon on admission. In patients admitted to

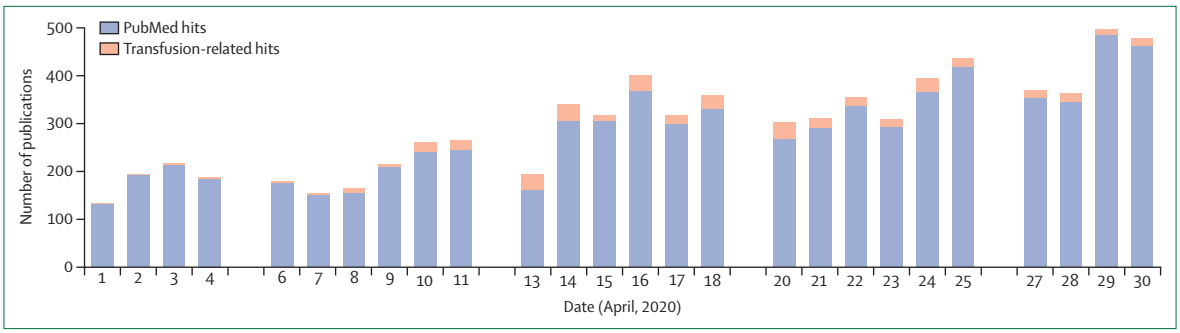

Figure 1: **The total number of COVID-19-related citations and the proportion of those relevant to transfusion**

intensive care, severe anaemia or platelet counts below 100×10^9 cells per L during the first 3 days are also uncommon.[7] The severity of thrombocytopenia, when it does occur, appears to be a marker for poor outcomes.[8–10] These publications support observations that many patients with COVID-19 do not require transfusion.[11,12] For example, data from Italy showed that 39% of patients required transfusion (median duration of hospitalisation of 15 days) for a main indication of anaemia (non-bleeding), with very few patients requiring platelets or plasma.[13] In this study, direct antiglobulin test reactivity was common and anti-red blood cell antibodies were detected in 52 (46%) of 113 patients.[13] Higher transfusion requirements are expected in patients who have extracorporeal membrane oxygenation than in those who do not, but this outcome is relevant to only a small number of patients.[14]

A distinct pattern of coagulation disturbance, including raised D-dimer concentration, has been identified as a poor prognostic marker.[15] Many patients with COVID-19 have elevated fibrinogen, normal platelet counts, and often normal prothrombin time and activated partial thromboplastin time.[16] Viscoelastic testing suggests that hypercoagulability changes are not consistent with a pattern of acute disseminated intravascular coagulation.[17] Between late January and April, 2020, reports described a 25–31% incidence of thrombotic complications in patients admitted to intensive care units with COVID-19.[18,19] A study[18] in France described 64 (43%) clinically relevant thrombotic complications from 150 patients, but only four (3%) patients presented with bleeding complications.[20] Thrombotic changes have also been described post-mortem.[21]

Plasma and cryoprecipitate transfusion to manage isolated abnormalities of coagulation in patients with no evidence of bleeding is not indicated for patients with COVID-19.[22,23] Given the risk of exacerbating any pro-thrombotic tendency, tranexamic acid is not indicated for patients with no bleeding.[24] To date, bleeding complications that could increase transfusion requirements have not been frequently reported in patients with COVID-19, although this observation might require review should escalated schedules for heparin anticoagulation be applied.[25]

In the absence of specific transfusion trial data on patients with COVID-19, it is appropriate to follow general recommendations on restrictive thresholds for red blood cells and platelets.[26,27] Patients with COVID-19 might be elderly with comorbidities, such as cardiac disease. However, no data are available to inform whether patients with SARS-CoV-2 infection, with substantial respiratory symptoms and oxygen dependency, might benefit from red blood cell transfusion to maintain a haemoglobin concentration above 70 g/L. In addition, few data are available on the outcomes of women who develop COVID-19 during pregnancy, and some features might overlap with pre-eclampsia.[28–30] Studies suggest that patients with blood group O have a lower risk of developing COVID-19.[31,32]

Theme 2: what donor and donation factors need to be considered to maintain an adequate supply of blood during the COVID-19 pandemic?

When considering the broader issues for blood supply planning during the pandemic, a key consideration for transfusion services is maintaining the balance between supply and demand.[33–35] Donor attendance might fall, as it did by 10–30% in the state of Washington, USA,[36] and by 30% at Canadian Blood Services (Goldman M, unpublished). However, in the early stages of the pandemic this trend was compensated by a reduction in demand for blood because of a decrease in elective surgery and medical treatment.[11,12,33–36] Blood providers have planned to maintain or increase the inventory of fresh components, which are sustained with public appeals to donate and by ensuring that blood donation is regarded as a permitted activity during lockdown. Blood collection staff might be concerned about exposure to donors, become sick, or self-isolate through family exposure. These factors could lead to substantial reductions in staff availability to collect and process blood. Overall, many reports show that sufficiency of supply has been maintained to date, but in some areas shortages have been observed.[37]

Donor screening and testing strategies, the management of postdonation information for donors diagnosed with COVID-19, and changes in other transfusion practices are

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See **Online** for appendix

	Considerations	Possible actions
Donor recruitment[34,46-48]	Donors tend to respond well to public appeals in situations of perceived exceptional need (eg, September 11 attacks and mass shooting events); a large influx of donors is to be expected, at least initially; donors are more tolerant to longer waiting times; platelet donations require close attention because of their short shelf life; some donors might be prevented from donating because of stay-at-home orders (eg, older, reliable donors)	Encourage appointments but discourage walk-ins; track donor characteristics (first-time donor *vs* repeat donor, as well as age, sex, etc); reinforce platelet aphaeresis donation programmes; consider increasing reliance on whole blood-derived platelets; more forcefully target first-time and reactivated donors for future donations
Donor eligibility[40,49-53]	Some donor-selection criteria could be relaxed without any meaningful effect on donor or product safety (for examples, see possible actions column); this approach can only be justified if supply cannot meet demand and changes need to be planned in advance because of their complexity (eg, regulatory aspects, IT system changes, and training of personnel); consideration should be given on the acceptability of reinstating pre-pandemic criteria after the pandemic is over (easier to explain to donors for some measures [eg, Haemoglobin concentrations] than others, such as reinstating permanent deferrals for variant Creutzfeldt–Jakob disease); some procedures can also be interrupted to increase compliance with public health recommendations, including social distancing; the COVID-19 situation might exacerbate criticisms over deferral policies for men who have sex with men, although shortening the deferral period will likely yield few additional donors	Discussions could be held with regulatory authorities regarding mechanisms for urgent implementation and expedited reviews; some procedures and criteria regarding donor safety could be considered for relaxation (eg, salty snacks on blood drives before and during donation, heart rate and blood pressure measurements, interdonation intervals, haemoglobin thresholds, and age restrictions); some procedures and criteria regarding recipient safety could be considered for relaxation (eg, deferral period for travel in a malaria-risk area; deferral period for tattoos, piercings, and needle-stick injuries; deferrals for men who have sex with men; and deferrals for variant Creutzfeldt-Jakob disease risk)
Blood drive planning[36]	Decreasing and increasing demand; suitability of donation sites; public health recommendations and governmental communications regarding confinement; public appeals for donation; staff availability	Adjust the number and size of upcoming blood drives; review physical distancing requirements when choosing locations for mobile blood drives; consider expanding collections on fixed sites; work with public health advisors and government communicators to emphasise the importance of blood donation as a reason for travel; work with health authorities to coordinate public appeals for donation, if and when appropriate
Inventory management[54]	Demand is hard to predict and might vary in different phases of the pandemic	Keep close contact with hospital customers, including regular updates of inventory; track system-wide inventory closely; monitor activities requiring increased blood use (eg, elective surgery and transplantation)
Protection of staff and donors[36,47,55-58]	Use of personal protective equipment for donors, staff, and volunteers; practice physical distancing; monitor COVID-19 illness among staff and donors; message donors before arrival on the blood drive regarding wellness; prescreening for COVID-19 signs and symptoms	Align practices with public health recommendations; review availability of personal protective equipment; implement a communication plan for occupational risk; disseminate guidelines for COVID-19 signs and symptoms among personnel, donors, and volunteers (quarantine and testing, etc); consider screening donors, personnel, and volunteers for symptoms and elevated temperature before entering facilities and donation sites
Availability of personnel[36,40,59,60]	Effect of COVID-19 on staff: illness, quarantine, and fear of disease	Prepare contingency plans for staff replacement (eg, reassignment and training of other non-essential staff); communicate clear supportive policies for sick leave; encourage staff to self-report illness or concerns; offer and strengthen psychological support for personnel
Plasma for fractionation[61,62]	The effect on supply of plasma for fractionation is uncertain, including the supply of immunoglobulins; blood providers might temporarily decrease their source plasma donation programmes to shift their capacity to whole blood donations	Efforts should be made to maintain or increase source plasma donations in the context of the pandemic; reconsider the need for certain procedures and criteria in donor screening, such as the annual physical exam; blood providers could take advantage of the influx of new and repeated donors to increase collections of source plasma collections
Product safety[38-45,63]	To date, there is no evidence of SARS-CoV-2 transmission by transfusion; some infected people appear to have detectable RNA in their blood, even when they do not have severe symptoms; RNA has been found in a few blood donors, but the concentrations are low, and the results might represent false positives; RNA in blood does not necessarily represent infectious viral particles; the South Korean lookback study[39] found no evidence of transmission	Do additional studies to establish the presence of virus in blood donors; do lookbacks and tracebacks when appropriate; reinforce postdonation information protocols; evaluate the availability and appropriateness of blood screening tests for donors; communicate risk assessments to relevant stakeholders; eligibility criteria should be applied to reduce the risk of collecting blood from infected donors; deferral periods should be applied for confirmed or suspected cases, for travel in countries or regions at high risk, and for exposure to confirmed cases (also important for safety of staff and other donors)

SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

Table 1: **Donor and donation factors to consider for maintaining an adequate supply of blood during the COVID-19 pandemic**

based on theoretical or confirmed risks of transmission. Because SARS-CoV-2 is a new virus, its potential for transfusion transmission, including by an asymptomatic viraemic donor, is uncertain.[38] From experience, including with other coronaviruses, the risk is currently considered low.[39,40] Although SARS-CoV-2 RNA can be found in the bloodstream of infected individuals,[41–44] this might not equate to infectious viraemia. In one study, blood transfused from donors who were subsequently diagnosed with COVID-19 did not transmit SARS-CoV-2;[39] however, data relating to SARS-CoV-2 are scarce and the number of blood donors with presymptomatic or asymptomatic COVID-19 when donating are not defined. To minimise risk of virus transmission, countries are developing guidance on the selection of donors, with precautionary deferral periods following infection and symptom

reporting following donation. Haemovigilance systems should be in place to monitor any potential cases of transfusion transmission (WHO interim guidance, 2020).[45]

Table 1 provides additional information on the capacity to maintain and adjust access to blood donors and specific types of donations in the context of the COVID-19 pandemic. Actions to counteract the effects of the pandemic on blood availability might include changing practices that are applied to protect donors and recipients, including eligibility criteria. The risks incurred by relaxing some of these practices should be proportional to the benefit of sufficiency. Any changes need to be discussed with relevant stakeholders (regulatory bodies, and donor and patient representatives).

Theme 3: modifications to production, specification, and storage of blood components to help prevent blood shortage

Changes to processing and storage of blood components might contribute to maintaining the blood supply during a pandemic. Modification of donor and component testing criteria, including any additional safety measures for groups such as neonates, might have to be addressed. A more complete consideration of the different options should be based on factors such as the likely magnitude of gain, the perceived effect on clinical risk, the regulatory requirements, and the extent of complexity and ability to deliver change in the system. Changes that require substantial resources to implement might not be feasible during a pandemic, and therefore simplicity and forward planning is key. The panel describes modifications that could be considered, risk assessed, and discussed with stakeholders. These options should continue to be reviewed to account for the potential increase in demand for blood as non-COVID-19-related hospital activities are resumed (theme 4).

A first step is to review measures to minimise wastage. This strategy might support the temporary extension of component shelf life. Storage age for red blood cells and platelets is typically defined at a national level and varies across countries, with a red blood cell shelf life of 35–49 days for most. A shelf life extension for red blood cells should be considered early on, as once shortages occur the components will be used before reaching the maximum storage time. Randomised trials do not provide evidence of considerable adverse effects with longer storage for red blood cell transfusion.[64,65] Individual blood providers could review the flexibility of manufacturing processes to allow the extension of whole blood holding times, provided there is internal validation on component quality.

Most blood providers assign a shelf life of 5 days to platelets, or 7 days if they are either tested for bacteria or undergo pathogen inactivation treatment. Depending on the exact method of production and satisfactory validation data, platelet storage might be extended to 8 days with a considered assessment of the risks (eg, bacterial contamination and platelet viability). For relevant countries, consideration could also be given to stopping bacterial testing, with a possible concomitant reduction in shelf life, or testing platelets earlier in shelf life to release platelets to stock sooner. However, the latter will only alleviate short-term supply issues and might be less beneficial than in times of prolonged shortages. Cold storage of platelets at 2–6°C could also be considered, as this method might allow a shelf life of 7–14 days without the need for agitation.[72] Stocks of frozen platelets, if available and expanded, might provide a haemostatic effect, in part because of the content of platelet microparticles.[85]

To increase platelet supply for prophylactic transfusions, one option could be to reduce the dose of platelets by

***Panel*: Strategies to modify production, specification, and storage of blood components to help prevent blood shortage**

Red blood cells

Extend shelf life if validated and within regulations

Review manufacturing process.[64,65]

Platelets

Extend shelf life from 5 days to 7 days with appropriate bacterial testing or pathogen inactivation

Recovery and survival of platelets, as well as count increments following transfusion, decline with increasing storage duration.[66,67] Bacterial risk depends on the timing of sampling, sample volume, and the length of culture; delayed culture methods with 7 day storage have been shown to be effective.[68] Depending on screening methodology, a further test at day 4 or at the end of storage might be required.

Extend shelf life to 8 days after review of internal laboratory data to guide feasibility

Review internal laboratory data to guide feasibility, and review data on bacterial risk. There is scant clinical data beyond day 7. At day 8, the recovery of fresh platelets manufactured from buffy-coats is nearly 70% and platelet survival is 45%.[69,70] Improved recovery and survival of platelets with prolonged storage has been observed with some types of additive solution.[69,70]

Reduce dose for prophylactic transfusion (split products)

Some countries already issue split products for neonatal transfusion. Consider half doses, or methods to produce two-thirds to three-quarter doses, such as pooling fewer so-called buffy coats or splitting aphaeresis collections into more doses.[71]

Consider use of cold-stored platelets with 7–14-day shelf life for patients with bleeding only

Studies in healthy volunteers suggest that the survival of platelets from whole blood or platelet concentrates refrigerated for 10–15 days might maintain acceptable viability. Laboratory data suggest that platelets remain functional for 14–21 days without the need for agitation.[72,73–76]

Consider frozen platelets for bleeding patients only[77,78]

Plasma

Remove requirements to freeze plasma

Consider use of liquid (never frozen) plasma if freezer capacity or staff to freeze plasma are in short supply.[79]

Whole Blood

Use of whole blood

Consider if staff to manufacture components are in short supply or for massive transfusion.[80–84]

	Considerations	Possible actions
Red blood cell usage	Red blood cell shortages	Review the threshold of red blood cell transfusions for patients who are stable and low risk (eg, adults and children with mild symptomatic but not life-threatening anaemia)[86-88]
Platelet usage	Platelet shortages for prophylactic transfusion	Use of platelets as prophylaxis should be restricted in patients with hypoproliferative thrombocytopenia without clinical bleeding, including autologous transplantation[89]
Major bleeding	Blood shortages for patients with bleeding	Review local policies that are usually based on the use of blood components defined by ratio-driven therapy, preferably 1:1:1 for red blood cells, plasma, and platelets, or 1:1 for red blood cells and plasma if platelets are not available. If red blood cells are in short supply, consider giving plasma first or blood components at ratios of 1:2:1 (red blood cells, plasma, and platelets);[90,91] if platelets are scarce, consider cold-stored or frozen platelets, or whole blood;[80,92,93] consider prothrombin complex concentrate and fibrinogen concentrates if frozen plasma or cryoprecipitate is in short supply for patients with bleeding;[92] if type AB plasma is unavailable, consider use of type A plasma for massive transfusion[93]
Alternatives for transfusion	Emphasising use of alternatives to transfusion at times of blood shortages	Ensure that alternative measures to increase haemoglobin are offered where appropriate (eg, parenteral iron and erythropoietin);[94] tranexamic acid should be offered to patients with severe hypoproliferative thrombocytopenia or outpatients with chronic thrombocytopenia; desmopressin should also be considered for patients with uraemia or inherited platelet disorders who are at risk of bleeding, although few data exist for other patient populations[95,96]

Table 2: **Strategies to prioritise blood use for patients in hospitals in the event of predicted shortage**

splitting existing components. The PLADO trial[71] reported no significant dose effect on the incidence of bleeding in patients with hypoproliferative thrombocytopenia, although more transfusions were given in the low-dose patient group. This option will require validation to ensure that platelet quality is maintained throughout storage, and education within hospitals.

Frozen plasma components have a long shelf life (several years) and therefore the ability to build and maintain stocks is more flexible than for cellular components. Liquid plasma (never frozen), which has a shelf life of 7–40 days, might be useful in the context of reduced freezer capacity, a shortage of staff to freeze plasma, or for the production of convalescent plasma (theme 5).

Whole blood was used for transfusion until the mid-1960s when its use ceased in civilian settings in favour of separated component parts—red blood cells, platelets, and plasma. International interest for the use of whole blood in the treatment of actively bleeding patients has been revived. In the context of the pandemic, whole blood is simple to manufacture and could be used if blood stocks are low or staff are in short supply.

Systems for pathogen inactivation of plasma and platelet (but not red blood cell) components are in routine use in some countries, but not all. These systems result in a 3–6 log reduction in infectivity of models of coronaviruses, such as severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), depending upon the technology used.[38,44] The decision to implement pathogen inactivation needs to take account the risk of not doing so, balanced against the cost and the resource required for implementation. For countries that do not already use pathogen inactivation, its rapid introduction is a large task. The risk of transmission through blood appears to be low, although our understanding will improve as the pandemic evolves. Similar considerations need to be given to pathogen inactivation of convalescent plasma.

Theme 4: prioritisation of blood use for patients in hospitals in the event of predicted shortage

A range of local mitigation strategies are required if blood shortages are anticipated (table 2).[33] These policies might initially be based on national guidance documents for planning in the event of blood shortages.[97] Each hospital should establish appropriate local structures to support responses. This strategy might include an Emergency Blood Management group with representation from clinical users, managers, and the hospital transfusion team. Actions will take into account shortage predictions by blood suppliers, inventory simplification, and changes to component shelf life or dose.

Key areas to address will be the use of blood for a non-urgent situation, such as elective surgery, although these activities might already have been restricted early in the pandemic to release staff and space. A pandemic infection leads not only to the deferral of non-urgent interventions, but also to the shielding of patients who are at increased risk of infection or having severe COVID-19. Patients might be reticent to attend health-care facilities, even for potentially serious symptoms. Increased thresholds for exposing patients to immunosuppressive therapy, such as consolidation chemotherapy and stem cell transplantation, have also been described.[98] These changes in behaviour have resulted in a substantial reduction in demand for all blood components. Planning should address ongoing and unavoidable transfusion needs for selected patients with non-COVID-19-related health issues, such as trauma, emergency surgery, transfusion dependency (eg, for cancer, myelodysplastic syndrome, and thalassaemia),[99,100] and acute sickle chest crises requiring exchange transfusion.[101–103]

In the event of falling blood stocks, stringent implementation for all activities of patient blood management is required, which covers transfusion and preoperative anaemia management,[94,104] tightening local guidelines where possible. Audits of blood transfusion have consistently shown that around 20–30% of blood

component use is outside guidance and hence probably unnecessary, reinforcing the need for patient blood management initiatives.[105,106] At more extreme levels of blood shortage, the release of blood components outside local guidelines should be reviewed by the blood transfusion laboratory with support from clinicians.[107] Guidance for local concessionary release of components outside specifications should be developed if not already in place. Integral to the success of any local initiatives is a strong existing framework of accepted guidelines, agreed with clinicians from relevant departments. An ability to rapidly produce and disseminate authoritative national guidelines enables evidence to be assessed and changes updated consistently; for example, guidelines and evidence summaries from the National Institute for Health and Care Excellence.[108]

Finally, as the pandemic is controlled and the health-care system gradually returns to normal or, more probably, responds to increased rates of non-COVID-19-related activity (eg, delayed cancer treatments or postponed surgery), complications could increase following delays and planning for an increase in need for blood is therefore required.

Theme 5: use of convalescent plasma and immunoglobulins

Interest in the role of immunotherapies and convalescent plasma collected from patients who have recovered from COVID-19 is considerable.[109,110] The rationale for convalescent plasma is that patients who have developed neutralising antibodies against SARS-CoV-2 could lower or eliminate the viral load in patients with COVID-19.[111] Convalescent plasma has been used in clinical studies for treating severe acute respiratory syndrome, including infections with SARS-CoV, MERS-CoV, avian influenza A (H5N1), and for Ebola, with some promising results.[112–116] Case series of patients with COVID-19 have described a clinical benefit after receiving convalescent plasma,[117,118] but randomised trials are required given the potential risks associated with this treatment.[119,120]

Many randomised trials of convalescent plasma have been registered and are ongoing in patients with COVID-19. However, there are differences in protocol design, including the use of convalescent plasma to treat adults or children admitted to the intensive care unit, to treat patients in settings other than intensive care, or even as prophylaxis (for people in close contact with those confirmed to have COVID-19).[121] Convalescent plasma from donors could be collected at different stages of recovery (14–28 days after full recovery or >28 days after full recovery) using different products (aphaeresis plasma, whole blood-derived plasma) with various, or even unknown, anti-SARS-CoV-2 antibody titres within the product. Multiple organisational challenges need to be addressed to support and deliver a convalescent plasma programme, including policies for approving plasma donors and testing of donations. Another treatment option is passive immunisation by collecting plasma to extract hyperimmune immunoglobulins. This option will only become available when large amounts of plasma can be collected.

Discussion

This paper has collated information from multiple sources to provide a synthesis of the published literature to help inform the planning for critical imbalances in the blood supply chain during the COVID-19 pandemic. A key observation and challenge for clinicians is the expanding literature, reflected by the extensive number of citations identified. This issue raises considerable challenges for clinicians in keeping abreast of the published literature to identify studies with the most important effect on patient care. The degree to which specific changes are considered or implemented will depend on a variety of factors that apply locally and nationally. Recommendations have not been provided for each theme, although many of the actions described could be considered as best practice suggestions.

Early planning to review mitigation options is recommended; in particular, stock building and the extension of shelf life when stocks are good. Policy documents should include a hospital-based emergency management plan, ideally based on a national plan, integrated with monitoring across the blood component supply chain and rigorous application of the principles of patient blood management.

Transfusion requirements are low, even in patients who are critically ill with COVID-19. There are no robust data on the numbers of presymptomatic or asymptomatic donors who have subsequently seroconverted, or on the potential infectivity of blood with SARS-CoV-2,[38,122] although the risk of transfusion transmission is likely to be low. Recommendations for transfusion should conform to general messages of restrictive use of blood. In collaboration with public health agencies, blood services are well placed to contribute to epidemiological studies and biobanks evaluating the serology, features, and course of the COVID-19 pandemic.

A limitation to this project was the availability of only one individual to do the initial screening. The writing group considered the quality of much of the published literature to be insufficient. Many of the papers identified from searches were observational, including those describing results of primary research, and were open to all the limitations common to this design. However, formal methodological assessments were not done. As the quality of the publications strengthen, further updates of the search will incorporate more specific recommendations.[123] A large number of ongoing randomised trials were identified, addressing areas of practice relevant to this Review (appendix pp 4–7). This progress is testament to the work of many researchers, although sharing protocols at early stages of

development might be beneficial, exploring opportunities to collaborate, and ensuring consistency in outcome measures.[119]

Contributors
SJS, NS, and JT conceived of the idea for the Review. SJS wrote the first draft. SB and CD searched and screened the published literature. All authors contributed to the writing: theme 1 (SJS, DP, NS, JT), theme 2 (MGe, MGo, TOA), theme 3 (RC, HVN, TOA), theme 4 (EM, SJS, NS, DP), and theme 5 (CS-O).

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We declare no competing interests.

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