Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

There are several limitations inherent to the analysis by Anagnostou and colleagues. First, the time-to-event endpoints must be considered in the context of the total therapy provided. For some of the studies, this included planned stem-cell transplantation for patients achieving complete remission. For other studies, stem-cell transplantation while in remission was generally reserved for patients following a concerning clinical course, such as early loss of CAR T-cell engraftment or emergence of minimal residual disease. Particularly given the potentially shorter persistence of CD28 co-stimulated CAR T-cell products compared with CAR T-cell products containing 4-1BB,[8] understanding the role of stem-cell transplantation in achieving durable complete remission will be important,[9] especially as data with longer-term follow-up emerge.

Differences in the design of studies included in the analysis might have diminished the ability to detect differences across CAR T-cell products. In particular, different cytokine release syndrome grading systems were used across studies of 4-1BB or CD28 co-stimulatory products, with greater use of the University of Pennsylvania (Penn) grading scale for studies of products with 4-1BB co-stimulatory domains (appendix). The ability to show an association between co-stimulatory domain of the product and risk of severe cytokine release syndrome is limited by the different grading scales used. The recent consensus cytokine release syndrome grading criteria developed by the American Society for Transplantation and Cellular Therapy will be important to overcome this limitation in future analyses.[10]

Other important differences between studies in the analysis include the timing of the baseline disease assessment—ranging from assessments at study enrolment (sometimes months before CAR T-cell infusion) to immediately before CAR T-cell infusion. This might have reduced the ability to detect an association between disease burden and outcome, if one exists. Real-world data from registries such as the Center for International Blood and Marrow Transplant Research, with consistent data-capture instruments across products, might begin to answer some of these remaining questions.

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See **Online** for appendix

Science over stigma: the need for evidence-based blood donation policies for men who have sex with men in the USA

The ongoing COVID-19 pandemic has decimated the US blood product supply, with more than 46 000 community-based blood drives cancelled as of September, 2020, resulting in the loss of more than 1 million donations.[1] The paucity of blood donations has coincided with increased demand for convalescent plasma as an investigational treatment for seriously ill patients with COVID-19. Through expanded-access compassionate-use programmes and clinical trials (eg, NCT04338360), more than 80 000 US patients with COVID-19 have received convalescent plasma, which now has emergency use authorisation. If proven effective in ongoing trials, plasma or plasma-derived antibody products will remain important therapeutic


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options for patients in the USA and internationally. In July, 2020, the Red Cross announced an emergency shortage of convalescent plasma and began offering serological COVID-19 testing to attract more donors. Additionally, resumption of elective surgical procedures in many US hospitals is expected to precipitate a more than 30% spike in demand for blood products.[2]

With these compounding pressures on the blood product supply, attention has turned to blood donation policies. In 1985, during the early HIV/AIDS epidemic in the USA, blood donation by men who have sex with men (MSM) was banned. At that time, although HIV transmission was poorly characterised, the risk of parenteral acquisition was recognised, with more than 12 000 documented cases of transfusion-associated HIV.[3] Because assays at the time could not reliably diagnose HIV infection or detect virus in blood products, donor restrictions were one of few available approaches to limit transmission. Accordingly, the US Food and Drug Administration (FDA) and Centers for Disease Control and Prevention prohibited blood donation by members of groups with high HIV prevalence, including MSM, people from Haiti or sub-Saharan Africa, and people who inject drugs. These practices effectively reduced transfusion-related HIV transmission, with rates dropping to approximately one in 500 000.[4]

In the intervening period since 1985, both testing modalities and our understanding of HIV transmission have advanced substantially, but rules surrounding MSM blood donation have not kept pace. In 2015 in the USA, the lifetime ban for this population was modified to a 1-year deferral policy—ie, MSM who reported abstinence for at least 12 months would become eligible to donate blood. This abstinence requirement was abbreviated to 3 months in April, 2020. Similar abstinence periods are required for people who inject drugs, individuals who have exchanged sex for money, and people with specific types of tattoos or piercings. Although the reduction to 3 months is an important change, it remains a de facto ban for many MSM, including those with few objective risks for HIV acquisition. Moreover, these restrictions are rooted in antiquated and prejudicial logic, reinforce harmful stigma, and limit the availability of potentially life-saving treatments, and thus merit further reconsideration.

Current screening practices target both donors and their blood products. Modern HIV testing platforms are highly accurate, with improvements in nucleic acid testing and development of fifth-generation antibody and antigen tests increasing sensitivity to almost 100% (95% CI 96·7–100) and specificity to 99·5% (99·1–99·9).[5] Sensitivity of HIV diagnostic testing is limited during the so-called window period—ie, the time during acute infection before systemic virus replication and antibody induction. Currently, the window period is 10–23 days for antibody and antigen testing and 7–15 days for nucleic acid testing. Although missed diagnoses during the window period could be further complicated by use of pre-exposure prophylaxis, blood product testing remains very sensitive to the presence of HIV regardless of ability to diagnose acute infection. Currently, all blood products are subject to rigorous post-donation screening for HIV (among other pathogens), thereby protecting against transfusion of HIV-containing blood.

Screening protocols for some blood-borne infectious agents without FDA-approved detection assays (eg, malaria) mandate indefinite or prolonged deferrals. For other pathogens (eg, *Trypanosoma cruzi* and *Babesia* spp), advances in testing have led to adjustments to screening policies and reversal of donor restrictions. Still, other infections (eg, hepatitis B virus [HBV], which is more prevalent in some populations and more transmissible via blood products than HIV) have no donor restrictions, relying solely on screening of blood products. Risk of contracting HIV from a blood transfusion is estimated at less than one in 2 million, whereas risk for HBV is more than twice as high.[6] This relative risk is compounded by the fact that, in the USA, 85% of people living with HBV are unaware of their status, compared with only 14% of those with HIV.

Stigma is also relevant to MSM blood donation, and perceived stigma is associated with poor mental and sexual health outcomes reported in the LGBTQ+ community. For example, LGBTQ+ individuals living in states in the USA in which same-sex marriage was banned in the early 2000s showed a decline in mental health, whereas legalisation of same-sex marriage was associated with a reduction in suicide attempts by LGBTQ+ youth.[7] Stigma also functions as a barrier to health care; LGBTQ+ individuals are much more likely to delay or avoid medical care compared with heterosexual people. Banning all recently sexually active MSM from donating blood perpetuates damaging stigma,

categorising their blood as undesirable and contributing to their already pronounced alienation from the health-care system.

Although HIV prevalence is higher in MSM than in other populations, recent behaviour and individual risk (eg, having multiple concurrent sexual partners) ultimately establish the likelihood of undiagnosed or recently acquired HIV infection. Thus, a behaviour-based blood donation policy (ie, banning all individuals who recently engaged in unprotected sex from blood donation regardless of sexual orientation) would be more equitable. Several countries have updated their blood donation regulations to a behaviour-based approach. In Spain and Italy, MSM exclusions were replaced with a screening programme that assesses risk via individual interviews with doctors. No change in the frequency of HIV-positive donations was noted in the years after Spain's policy update, although some reports suggest a recent increase, potentially because of increased test-seeking behaviour.[8] Similarly in Italy, this policy change did not lead to an increase in HIV-positive blood donations, suggesting that allowing MSM to donate did not endanger the blood supply.[9] While the rate of HIV-positive donation among all donors is high in Italy compared with the USA, the main driver of this trend is misunderstanding by donors of the definition of high-risk behaviour, which can be mitigated with a more consistent questionnaire format and comprehensive predonation counselling.[10] In view of the effectiveness of risk-based assessment in European donors from the MSM community, the USA could supplement its current standardised health questionnaire system with one in which either materials or trained health-care workers are used to educate potential donors before donation.

Other countries have similarly amended MSM-specific restrictions on blood donation in the past decade, including Argentina, Bolivia, Chile, Israel, Mexico, Peru, and South Africa. In 2016, France began allowing MSM to donate apheresis plasma under the same policy as other donors (ie, plasma from people with more than one recent sexual partner is quarantined for at least 2 months until the donor can return for HIV retesting). Then, in 2019, the country announced whole blood donation regulations would be aligned for gay and straight donors by 2022. In 2020, both Hungary and Brazil repealed bans on blood donation by MSM, with Brazil's Supreme Court ruling that such restrictions were unconstitutional.

2020 has brought many challenges, including combating the devastating global COVID-19 pandemic and dealing with entrenched systemic racism and injustice. The world's response to COVID-19, although sometimes flawed, has shown that innovation and efficient data-driven responses can greatly improve health conditions. Current social justice movements teach us that we can, and must, change long-standing systems when they are founded in unjust rationale. In this spirit, we argue that we should weigh the risks and benefits of current blood donor restrictions with fresh eyes. No transfusion is entirely risk free, and regulations surrounding blood donation must be crafted with careful consideration of all available evidence, including sensitivity of virus detection assays, effectiveness of screening processes for similar pathogens, negative results of stigmatising policies, and success of implementing behaviour-based policies by many countries. In view of the unprecedented need for blood products and our health-care system's commitment to equitable and evidence-based practices, we argue it is time to discard overly restrictive policies and adopt individual behaviour-based risk assessments.

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