Estimation of the number of blood donors during the COVID-19 incubation period across China and analysis of prevention and control measures for blood transfusion transmission

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BACKGROUND: The aim of this study was to estimate the number of blood donors during the COVID-19 incubation period across China.

STUDY DESIGN AND METHODS: In this study, we developed a predictive model to estimate the number of blood donors during the COVID-19 incubation period among 34 provincial regions in China. Our main assumption was that blood donors of all ages in different regions have a stable blood donation intention and the same infection risk.

RESULTS: First, we estimated the number of blood donors during the COVID-19 incubation period in Wuhan city, Hubei Province, and China, from December 31, 2019 to March 17, 2020. Second, we compared the number of blood donors during the COVID-19 incubation period in all provinces across China. In addition, we found that if all RBCs, plasma, and cryoprecipitation were stored in isolation until the 14th day, the potential risk of SARS-CoV-2 transmission through blood transfusion was reduced by at least 65.77% after the blood donor safely passed the COVID-19 incubation period. Moreover, if the detection of SARS-CoV-2 RNA was carried out on all platelets, the potential risk would be reduced by 77.48%.

CONCLUSIONS: Although the risk is low, with the rapid spread of the COVID-19 and the appearance of alarmingly high infectivity and a high fatality rate, appropriate measures should be taken by health departments to ensure the safety of clinical blood.

The new coronavirus is an enveloped single-stranded positive-sense RNA virus and the seventh member of the family of coronaviruses that can infect humans. It was discovered in December 2019 due to a case of coronavirus disease 2019 (COVID-19) in Wuhan, Hubei Province, and named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Virus Classification (ICTV) on February 10, 2020.[1,2] The virus electron micrographs of SARS-CoV-2 particles, which belong to the genus Betacoronavirus, showed a generally spherical shape with some polymorphism. The diameter varied from approximately 60 to 140 nm.[3] Its genetic characteristics are significantly different from those of SARS-CoV and MERS-CoV. A genome-wide sequence alignment showed that SARS-CoV-2 has more than 88% homology with bat SARS-like coronavirus (Bat-SL-CVZC45). For SARS-CoV-2, the average incubation period is 5.2 days (the 95% CI is 4.1-7.0), and the 95th percentile of the incubation period

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distribution is 12.5 days.[4] As of March 18, 2020, the virus has rapidly spread to 34 provincial regions and 337 city-level cities in China, causing 81151 patients to be infected and 3242 patients to die.[5] Moreover, the virus quickly spread to 159 countries around the world.[6]

SARS-CoV-2 is transmitted mainly through respiratory droplets and close contact. Although the possibility of SARS-CoV-2 transmission through blood and blood products remains unclear, SARS-CoV-2 positivity in blood during the incubation period is still an important potential threat to the safety of blood.[7,8] Previous studies showed that SARS-CoV, which belongs to the same viral genus as SARS-CoV-2, can be detected in the blood of infected patients. The patterns of viremia differ among different SARS patients, and some patients have more protracted viremia than others.[9-12] Early reports have identified SARS-CoV-2 RNA in the blood of 15% of patients studied in a small Chinese series in the Report of Impact of 2019 Novel Coronavirus and Blood Safety released by the AABB on January 31, 2020.[13] According to a report by Korean Red Cross, six patients with COVID-19 had donated blood in the 2 weeks prior to diagnosis, and the blood had been transfused to nine patients in multiple locations of South Korea.[14] Although there is no evidence for the presence of infectious virus or RNA in asymptomatic individuals during the incubation period, it is not clear whether SARS-CoV-2 is transmitted through blood transfusion, and at least in theory, the possibility of such transmission exists.

To scientifically and effectively estimate the number of blood donors during the COVID-19 incubation period across China, based on the situation of voluntary blood donation in Guangzhou in 2016[15] and the *Epidemic Situation Reports Of Health Commissions* at all levels in China, we have successfully developed a predictive model to estimate the number of potentially infectious donations. In addition, we have proposed a new strategy to reduce the potential risk of transmission of SARS-CoV-2 through blood transfusion.

METHODS

Data sources

We estimated the number of blood donors during the COVID-19 incubation period in 34 provincial regions of China since the outbreak of SARS-CoV-2. Based on the literature reports of Guangzhou Blood Center, the blood donation situation of whole blood and apheresis platelets, the age composition of blood donors and the blood donation ratio in Guangzhou in 2016 were extracted.[15] The age range and infection ratio of 313 patients infected with SARS-CoV-2 in Guangzhou were extracted from the epidemic situation report of Guangzhou Municipal Health Commission.[16]

Predictive model

The legal age for blood donation in China is 18-60 years.[17] In this study, we divided this age range into four age groups (n) for analysis: 18-30, 31-40, 41-50, and 51-60 years. We divided the patients infected with SARS-CoV-2 in Guangzhou into nine age groups: 0-10, 11-17, 18-30, 31-40, 41-50, 51-60, 61-70, 71-80, and ≥80 years. Considering the legal age for blood donation in China, only patients aged 18 to 60 years are potential blood donors.

Based on the analysis of the age structure of blood donors and SARS-CoV-2-infected patients during the incubation period in Guangzhou, we established a predictive model to estimate the number of blood donors during the COVID-19 incubation period in the T area. The formula is as follows:

$$P(T) = \sum_{i=1}^{n} Ni(T) \times Ci$$

T is for a particular province or city. $Ni\ (T)$ is the number of blood donors during the COVID-19 incubation period at age i in the T province or city, and the calculation method of Ni is $Ni = t \times A \times Bi \times R$. t is the number of people infected with SARS-CoV-2 in the T province or city; A is the proportion of blood donation in Guangzhou in 2016; Bi is the proportion of blood donors of different ages in Guangzhou in 2016; and R is the incubation period coefficient, calculated by $R = M/365$, where $M = 5.2$ (mean incubation period).[4] Ci is the proportion of the SARS-CoV-2-infected population in the i age group. In this formula, all donations given during the incubation period are assumed to be infectious, despite the 15% rate of RNA found in the blood.

Assumptions

We assumed that the proportion of infected people in different age groups in various regions is the same as that in Guangzhou, the proportion of blood donation in various regions is the same as that in Guangzhou in 2016, and the proportion of blood donation in different age groups in various regions is similar to that in Guangzhou in 2016. We also assumed that blood donors during the COVID-19 incubation period in various regions still have the same willingness to donate blood as usual under the prerequisite of not knowing their infection status. Therefore, as of March 17, 2020, we estimated the number of blood donors during the COVID-19 incubation period in 34 provincial regions of China.

Analysis of intervention measures

By changing some variables, we analyzed the influence of SARS-CoV-2 on blood safety under different conditions. 1) All RBCs, plasma, and cryoprecipitation were stored and quarantined until the 14th day and then distributed after the confirmation of no SARS-CoV-2 infection of the

donor. The effective storage times of RBCs, plasma, and cryoprecipitation are all ≥35 days,[18-20] which does not seriously affect the overall balance of blood supply and demand. 2) The detection of SARS-CoV-2 RNA was carried out on whole blood (or its separated blood components) and apheresis platelets through RT-qPCR. Early research reports found that SARS-CoV-2 RNA could be detected in the blood of 15% of infected people.[13]

Statistical analysis

In this study, R2018a (MathWorks® Inc., Beijing, China) was used to analyze the data.

RESULTS

Baseline blood and SARS-CoV-2 infection data

The proportion of blood donation in different age groups in Guangzhou in 2016 is shown in Fig. 1A. The proportion of the youngest blood donation group (18-30) was 59.94%, followed by the 31-40 group (24.18%) and 41-50 group (13.20%), and the age group 51 and above had the smallest proportion of blood donation (2.68%). In sharp contrast to the proportion of blood donation, among the above mentioned age groups, the 18-30 age group had the lowest infection rate, at only 13.74%, while the infection rates for the 31-40, 41-50 and 51-60 age groups were 16.93%, 18.21%, and 18.53%, respectively (as shown in Fig. 1B).

Base-case predictions and regional variations

Since the SARS-CoV-2 outbreak began on December 31, 2019, the number of confirmed COVID-19 cases was obtained from the epidemic situation report of Wuhan city (the city with the most severe SARS-CoV-2 infection outbreak), Hubei Province (the province with the most severe SARS-CoV-2 infection outbreak), and China (as shown in Fig. 2A and Table S1, available as supporting information in the online version of this paper). Through the above mentioned functional relationship model, the number of blood donors infected by SARS-CoV-2 in the incubation period was estimated in Wuhan city, Hubei Province, and the whole country at different times. As of March 17, 2020, the number of infected blood donors during the COVID-19 incubation period was 2.51, 3.40, and 4.05 in Wuhan city, Hubei Province, and the whole country (Fig. 2B), respectively, which may lead to infection of up to 10.02, 13.59, and 16.21 people with SARS-CoV-2 (a whole blood donation can be divided into four blood products, such as red blood cells, cryoprecipitates, whole blood-derived platelets and frozen plasma). The number of blood donors during the COVID-19 incubation period in Wuhan city and Hubei Province accounts for 61.82% and 83.82% of the whole country, respectively, which is directly proportional to the number of confirmed COVID-19 cases in the city or the province.

In addition, we estimated directly the number of potentially infectious blood donors during the COVID-19 incubation period in 34 provincial regions through the functional model mentioned above (Fig. 2C and Table S1, available as supporting information in the online version of this paper). The results showed that in addition to Hubei Province (3.40), provinces with the largest number of blood donors during the SARS-CoV-2 infection incubation period (>0.04) were Guangdong, Henan, Zhejiang, Hunan, Anhui, and Jiangxi, with the number of 0.07, 0.06, 0.06, 0.05, 0.05, and 0.05, respectively. Again, numbers of blood donors during the COVID-19 incubation period were 0.04, 0.03, 0.03, 0.03, 0.02, and 0.02 in the provinces of, Shandong, Jiangsu, Chongqing, Sichuan, Heilongjiang, and Beijing, respectively. The number in provinces of Shanghai, Hebei, Fujian, Guangxi, and Shaanxi varied between 0.01 and 0.02. The numbers in other provinces were all <0.01. This finding suggests that it is necessary to strengthen safety monitoring of blood components in Hubei Province, especially in Wuhan city, to prevent possible SARS-CoV-2 blood transmission.

Analysis of intervention measures

When all RBCs, plasma, and cryoprecipitation were quarantined until the 14th day[4,13] and distributed to clinical patients after confirming no SARS-CoV-2 infection in the blood donors. At least 65.77% of the whole blood and its separated components were excluded from SARS-CoV-2 infection (Fig. 3A). If all donations were to be tested for SARS-CoV-2 RNA, up to 15% of donors in the incubation phase

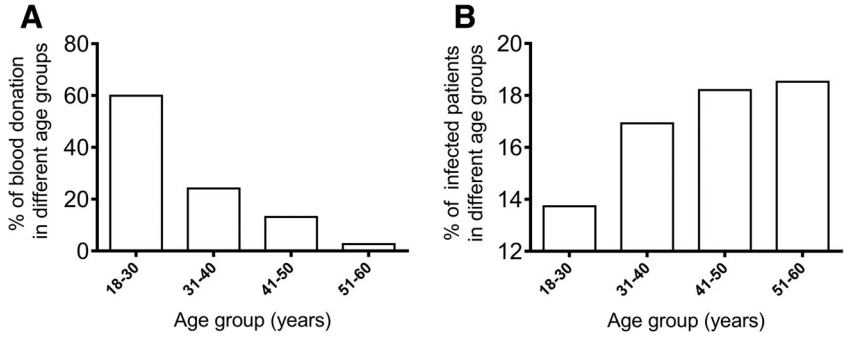

Fig. 1. The percentages of blood donation in Guangzhou in 2016 (A) and infected patients (B) across different age groups in Guangzhou in 2019.

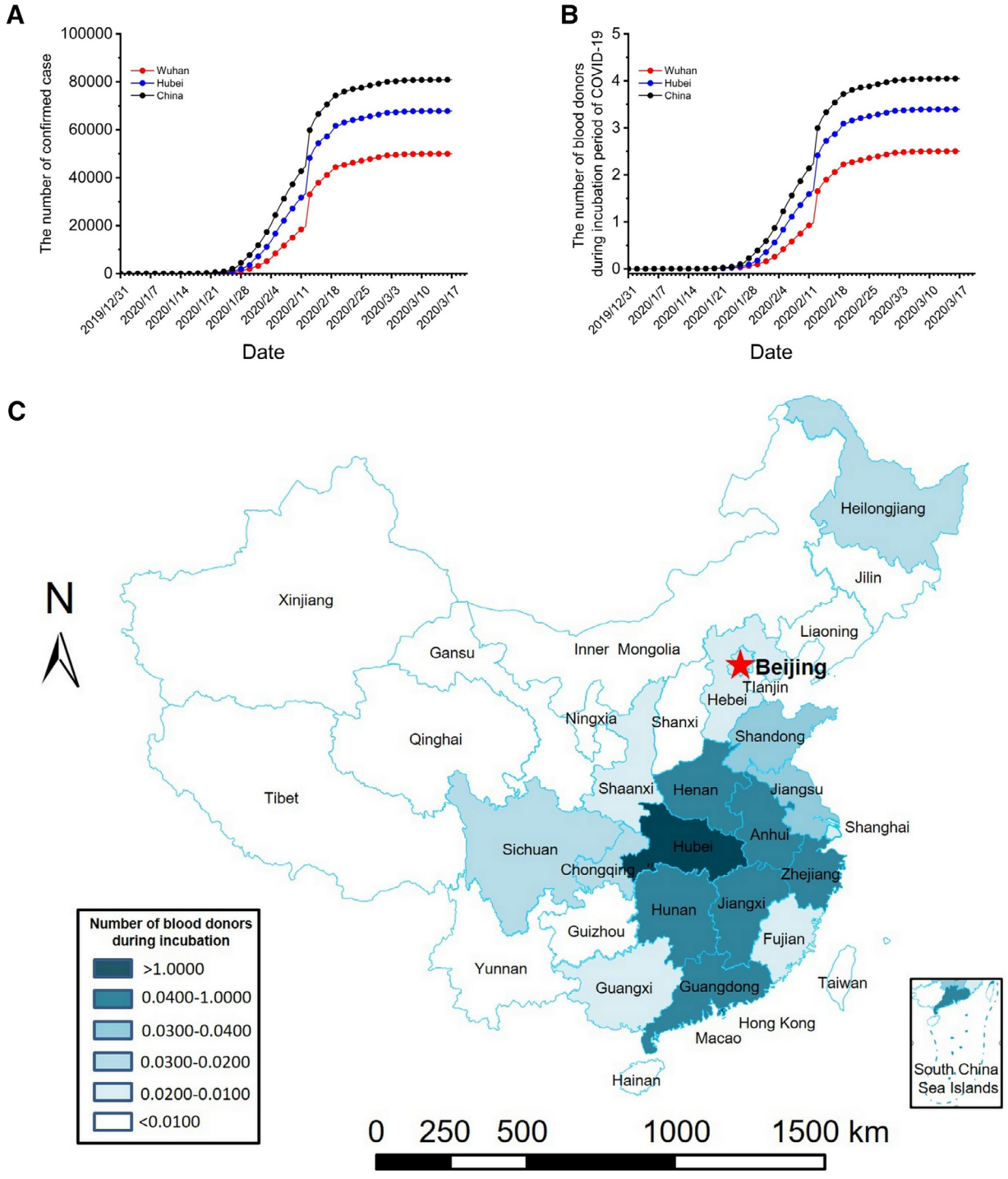

Fig. 2. Predicted number of blood donors during the COVID-19 infection incubation period. (A) The number of confirmed COVID-19 cases in Wuhan, Hubei, and the whole country. (B) The number of blood donors during the COVID-19 infection incubation period in Wuhan, Hubei, and the whole country. (C) Predicted number of blood donors during the COVID-19 infection incubation period in 34 provincial regions of China. [Color figure can be viewed at wileyonlinelibrary.com]

would be excluded (Fig. 3B). Combining Scheme I and Scheme II, in which all RBCs, plasma, and cryoprecipitation were quarantined until the 14th day, the detection of SARS-CoV-2 RNA was carried out on platelets, after confirming that the blood donors were free from SARS-CoV-2 infection, 77.48% of the blood could be excluded from SARS-CoV-2 infection (Fig. 3C). Considering the low blood donation intention during the epidemic period,

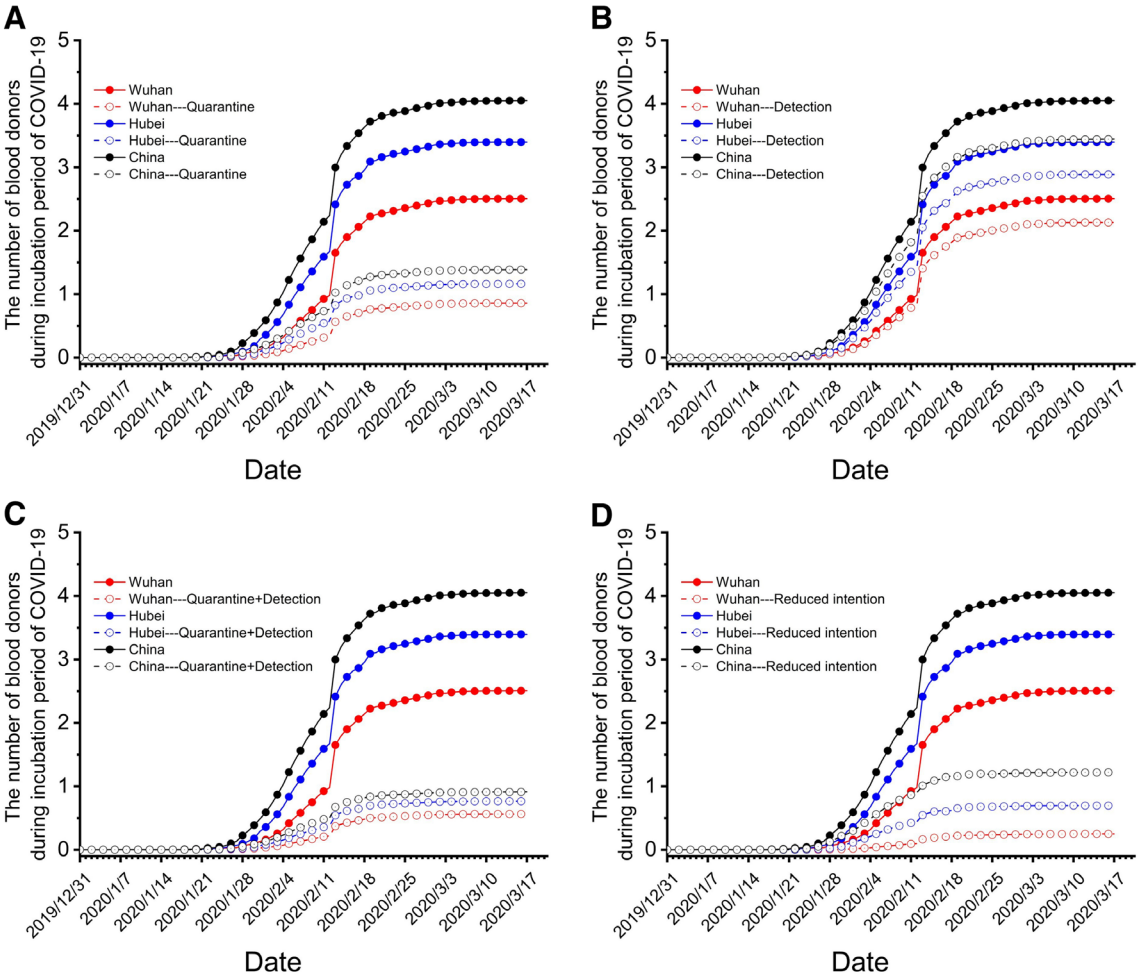

Fig. 3. Predicted the number of blood donors during the COVID-19 incubation period in different ways. (A) All RBCs, plasma, and cryoprecipitation were isolated until the 14th day. (B) All blood components were analyzed to detect SARS-CoV-2 RNA. (C) Scheme I (all RBCs, plasma and cryoprecipitation) + Scheme II (platelets). (D) The blood donation intention was reduced in Wuhan, Hubei Province, and China. [Color figure can be viewed at wileyonlinelibrary.com]

we set the blood donation intention as 10%, 50%, and 80% of the original in Wuhan, Hubei Province (except Wuhan city), and China (except Hubei province), respectively; the possibility of SARS-CoV-2 transmission through blood transfusion would then be reduced by 90.00%, 79.50%, and 69.88% in Wuhan city, Hubei Province, and China, respectively (Fig. 3D).

DISCUSSION

Blood transfusion is an indispensable treatment in modern medicine.[21,22] However, blood transfusion may also lead to the occurrence of related blood transfusion-mediated infectious diseases.[23,24] Although the infectivity of SARS-CoV-2 for blood recipients is not known at present, the transmission of SARS-CoV-2 through blood transfusion is theoretically possible. Considering the strong infectivity and high mortality rate of SARS-CoV-2,[2,3,8] the occurrence of blood transfusion-mediated infectious diseases may result in the potential for harm to recipients and society.

In this study, by establishing a predictive model, the number of potentially infectious blood donors during the COVID-19 incubation period in all provinces of China was estimated and analyzed. Meanwhile, we proposed several strategies to decrease the risk of SARS-CoV-2 transmission through blood transfusion. In addition, we also proposed the following overall strategies, which are very important to ensure blood safety management in China and other countries during the COVID-19 epidemic.

Strategy I. Education

Blood collection establishments should carry out knowledge popularization and education regarding blood donation for blood donors in all severe SARS-CoV-2 infection regions in

a more active manner and strengthen the screening of blood donors.[25-27] As recommended by the AABB and FDA, blood donors who meet or may meet criteria for COVID-19 patients should be self-isolated, and individuals could give blood at a reasonable time after full recovery.[4,13]

Strategy II. Multilevel coordination and quarantine

The blood collection establishments should closely cooperate with public health authorities, hospitals, and all blood donors,[26,28] and establish an information sharing system for SARS-CoV-2 infectious diseases to facilitate blood collection establishments inquiring in a timely manner whether the donor is infected with SARS-CoV-2. All RBCs, plasma, and cryoprecipitation should be quarantined until the 14th day in serious SARS-CoV-2 infection regions.[4]

Strategy III. Detection

The blood should be tested for SARS-CoV-2 nucleic acid using RT-PCR and to ensure that the blood is negative for the virus in serious SARS-CoV-2 infection regions.[29-31]

Strategy IV. External support

For some serious SARS-CoV-2 infection regions, blood in the clinic can be obtained in the short term from regions without SARS-CoV-2 infection or with less infection, after approval by relevant departments.[32]

This part of the research is based on the model of the blood donation population and virus infection population in Guangzhou, which has certain limitations. However, the study provides a unique method to observe some possible potential variables and lays a scientific theoretical foundation for preventing SARS-CoV-2 infection by blood transfusion.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

AUTHOR CONTRIBUTION

Conception and design of the study: MR and ZHY; data analysis: MS, ZHY, and DDC; interpretation of data: all authors; initial draft of the manuscript: MR and YMW; critical revision for important intellectual content: all authors; final approval of the version to be submitted: all authors; and agreement to be accountable for all aspects of this study: all authors.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Table S1. The Estimation Process, Results, and 95% CI of Estimation of the Number of Blood Donors During the COVID-19 Incubation Period Across China.