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SHORT COMMUNICATION

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A forecasting model to estimate the drop in blood supplies during the SARS-CoV-2 pandemic in Italy

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Abstract

Objectives: To estimate the number of actually Severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) infected blood donors applying a statistical forecasting model.

Background: Following the outbreak of the SARS-CoV-2 epidemic, a drop in blood donation has been observed. It is crucial to determine the actual number of potential SARS-CoV-2-positive donors to define the measures and ensure adequate blood supply.

Methods: The cumulative incidence of SARS-CoV-2 positivity, calculated on the general population, was applied to the donor population by estimating the number of positive subjects. The calculation model was validated by the linear interpolation method. The number of blood units actually discarded based on post-donation information was also taken into account.

Results: Three months after the outbreak, 5322 donors were estimated to be positive for SARS-CoV-2 and were therefore potentially excluded from donation. A total of units of blood components were discarded following post donation information. The estimated number of donors deceased (180) and the number of clinically recovered individuals in the same period was also considered.

Conclusion: This forecasting model can be used to obtain information on blood donors' involvement during future SARS-CoV-2 outbreaks, especially in case of changes concerning epidemiology, incidence by age bracket and geographical distribution and also for new outbreaks of emerging viruses.

KEYWORDS
blood donations, safety, SARS-CoV-2, self-sufficiency

1 | INTRODUCTION

After the first warnings of Severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) infection cases in Wuhan, Hubei Province in China, the epidemic spread very rapidly worldwide, with a steep rise in new cases and deaths from Coronavirus disease 2019 (COVID-19). On 30 January 2020, the World Health Organization (WHO) declared the epidemic a Public Health Emergency of International Concern, and on the 11th March the WHO made the assessment that COVID-19 could be characterised as a pandemic.[1,2]

The spread of the new disease had an initial impact on blood and blood component donations, causing a significant reduction in donations in China and in the other countries affected by the epidemic. The reason for this reduction was probably related to logistics

(transfer becoming more difficult as a consequence of lockdown measures adopted) and, above all, to blood donors' fear of contracting the infection in blood donation centres.[3-6]

In Italy, after an initial drop in donations in the first 10 days of March 2020, the pace stepped up because of among other things, the introductions of new national measures aimed at reassuring blood donors and guaranteeing adequate organisational conditions.[7]

Based on the unlikely transmission of SARS-CoV-2 through labile blood components,[8] the Italian National Blood Centre (Centro Nazionale Sangue, CNS), acting as national competent authority issued clear guidelines for blood collection centres (social distancing, temperature control etc.) and put in place a telephone triage service for recruiting donors, including specific questions about any risk behaviours or the appearance of symptoms compatible with SARS-CoV-2 infection, and suggested recruitment only by appointment.

Therefore, during the first phase, the pandemic had a very strong impact on the national health system's ability to respond, particularly with regard to intensive care and resuscitation units. However, overall, the level of self-sufficiency in blood and blood components was not overly affected because, at the same time, hospitals greatly reduced their non-urgent medical and surgical activities.[7]

With the gradual exit from the state of emergency and the lifting of lockdown restrictions, hospitals will restart their routine activities, and the demand for blood components will return to pre-pandemic levels.

In order to evaluate the level of pressure the Italian transfusion system is experiencing during the pandemic and considering the possibility of even more severe future outbreaks with possible different epidemiological pictures, the CNS has adopted a calculation model to estimate the number of donors potentially excluded from donations because they are positive to SARS-CoV-2 and the consequent drop in the number of available blood units.

The forecast function of the calculation model was based on the data relating to the trend of the SARS-CoV-2 pandemic in the general population provided by the national health institutions in the period under examination.

To assess the overall number of units that have failed in transfusion stocks, the number of blood component units actually discarded as a precaution in the same period, following clinical information provided by donors after the donation (post-donation information, PDI), was added to this estimate.

Finally, to evaluate the impact of the epidemic event on the donor population, the number of positive donors who, after resolution of symptoms or discontinuation of therapies, are theoretically readmitted to donation and the number of donors definitively excluded due to death from complications from COVID-19 were also estimated.

2 | MATERIALS AND METHODS

The duration considered for the study ranges from 18 February 2020 (epidemic start date in Italy) to 28 May 2020 (3 months). The estimates presented in this paper are based on national epidemiological data, more specifically:

1. the COVID-19 integrated surveillance data relating to the number of positive subjects and the number of deceased subjects in the general population, published online by the Italian National Institute of Health (Istituto Superiore di Sanità, ISS). Here are reported all the cases of SARS-CoV-2-positive subjects divided by 10-year age brackets (between 0 and over 90) and by gender.[9,10]
2. The number of clinically recovered patients available on the Ministry of Health website.[11]
3. The number of PDIs reported by the competent regional authorities to the CNS.

The estimated number of donors who were potentially infected with SARS-CoV-2 was obtained first by calculating the probability that an infected subject in the general population belonging to the 18–69 age bracket, that is, those that include the blood donor population, may have tested positive for SARS-CoV-2.

The cumulative incidence of SARS-CoV-2 positivity, calculated on the general population for each 10-year age bracket, was then applied to the donor population age bracket (18–69). Therefore, the probability values per year of age, taken from the incidence classes of the general population, were recomposed to constitute the age brackets used for donors.

Finally, to estimate the number of positive cases expected in the donor population per each age bracket, the estimated probability for each donor age bracket was multiplied by the number of donors detected for the year 2019 on the information system of the Italian transfusion services.

Considering the 3 month period of observation, the estimated number of positive donors was considered equivalent to the number of donations.

To validate the calculation made, an additional statistical method based on linear interpolation was applied using the R Stats Package programme (version 4.0.0).

The number of blood component units effectively not transfused due to PDI was calculated on the basis of the real number of post-donation reports notified by the Regional Blood Centers to the CNS in the first 3 months of the epidemiological emergency. Donors were made aware of the importance of promptly informing the Transfusion service of reference if they noticed any symptoms compatible with the SARS-CoV-2 infection, if they had been diagnosed with SARS-CoV-2 infection in the 14 days following donation or if they had been in close contact with a person prior to the donation who was only subsequently diagnosed with SARS-CoV-2 infection.

In the first two cases, the Transfusion services discarded the donated blood components as an extreme precautionary measure.

The number of clinically recovered donors was calculated using general population data provided by the Ministry of Health.[11] Distribution by age bracket is not available for these individuals, so the total percentage figure on the number of infected individuals was therefore considered. The number of potentially deceased donors was also

estimated by applying the same calculation method used for estimating positive donors and on the basis of weekly reports published by the ISS and available online.[10]

3 | RESULTS

As shown in Table 1, the ISS reports, on which this study was conducted, showed 230 778 positive cases in the general population, 27% of them asymptomatic, and 31 851 deaths distributed by gender and by 10-year age brackets. The number of clinically recovered patients on 28 May 2020, was 147 101 (64% of the total).

3.1 | Estimate of SARS-CoV-2-positive donors

The data, obtained from the analysis on the general population, made it possible to estimate 5322 (95% CI: 5187–5460) cases of SARS-CoV-2 expected in the donor population, 3 months after outbreak, against 650 000 active donors in the same quarter of 2019.[7]

The calculation of the cumulative incidence of SARS-CoV-2 on the general population, on 26 May 2020, highlighted a greater distribution of positivity in over 69 years of age, that is, those not eligible to donate blood (Figure 1A).

The age brackets that include the blood donor population (18–69), highlighted with the pattern filling in Figure 1A, show positivity values that gradually decrease in the younger age brackets.

The cumulative incidence value, calculated for each 10-year age bracket of the general population, was then redistributed to the age brackets of the donor population (Figure 1B).

Against the 230 778 positives detected overall in the Italian population, in the 3 months following the outbreak of the epidemic, 134 058, or slightly more than half, belonged to the age brackets of the population that include blood donors and were equally distributed between males and females (64 404 males, 69 654 females).

The results show a higher probability of positivity in the male population, especially for those in the older age brackets. On the contrary, females belonging to the older age brackets have a probability level of positivity very close to that of subjects aged between 26 and 45 years. For both genders, however, more generally, the estimated probability is lower in the younger age brackets. The linear interpolation method applied to the same data provided overlapping results.

Overall, of these 5322 estimated positive donors, the estimated number of males was 3545 compared to 1777 females. On the whole, the distribution of expected cases shows a greater concentration of positivity in the northern regions (Lombardy, Emilia-Romagna, Piedmont and Veneto) and a decreasing gradient towards central-southern Italy (Figure 2A).

The distribution of expected cases by gender and age brackets highlights very similar values between males and females for the 18–25 age bracket and with an increase in the male/female ratio in subsequent age brackets (Figure 2B).

3.2 | Post donation information

In the 3-month period considered, a total of 982 donors informed the Transfusion Service of the appearance of symptoms compatible with the SARS-CoV-2 infection in the 14 days following donation.

In particular, 96 donors reported a confirmed diagnosis of SARS-CoV-2 infection, 669 donors reported the sudden onset of at least one of the symptoms compatible with SARS-CoV-2 infection (fever, cough or respiratory distress), and 217 donors reported close contact with a person in the 2 days preceding donation who was subsequently diagnosed with SARS-CoV-2 infection.

TABLE 1 General data and results of the study

	General population (*N*)			Blood donor population (*N*)					
				Real data			Estimated cases		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
SARS-CoV-2-positive subjects	-	-	230 778[a]	-	-	-	-	-	-
SARS-CoV-2-positive subjects belonging to age brackets of blood donors	64 404	69 654	134 058	-	-	-	3545	1777	5322
SARS-CoV-2-positive dead subjects	-	-	31 851[a]	-	-	-	-	-	180
Recovered subjects	-	-	147 101[b]	-	-	-	-	-	3652
Blood units discarded on PDI data 2020						765[c]			
Blood donations in the quarter						650 000[c]			
Total blood unit missed									6087[d]

Note: General data obtained from the reports of Italian National Institute of Health, Ministry of Health and Italian National Blood Centre from February to May 2020 and results generated from application of the forecasting model.
Abbreviations: *N*, number; PDI, post-donation information.
[a]Data from Italian National Institute.
[b]Data from Ministry of Health.
[c]Data from Italian National Blood Centre.
[d]Obtained from 5322 + 765.

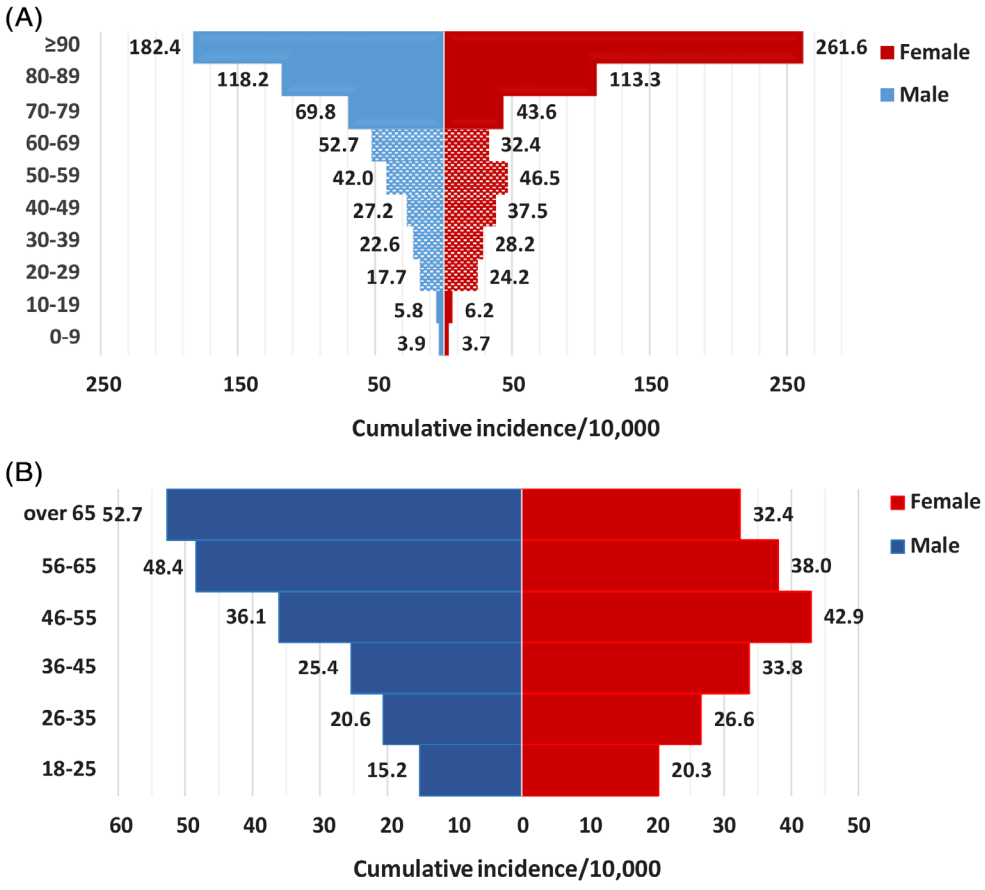

FIGURE 1 SARS-CoV-2 cumulative incidence in the general and blood donor population in Italy. (A) Distribution of the SARS-CoV-2 cumulative incidence in the general population in Italy. The age brackets that include the blood donor population (18–69) are highlighted with the pattern filling. (B) Redistribution in the blood donor population of the cumulative incidence values observed in the general population, divided by age brackets [Color figure can be viewed at wileyonlinelibrary.com]

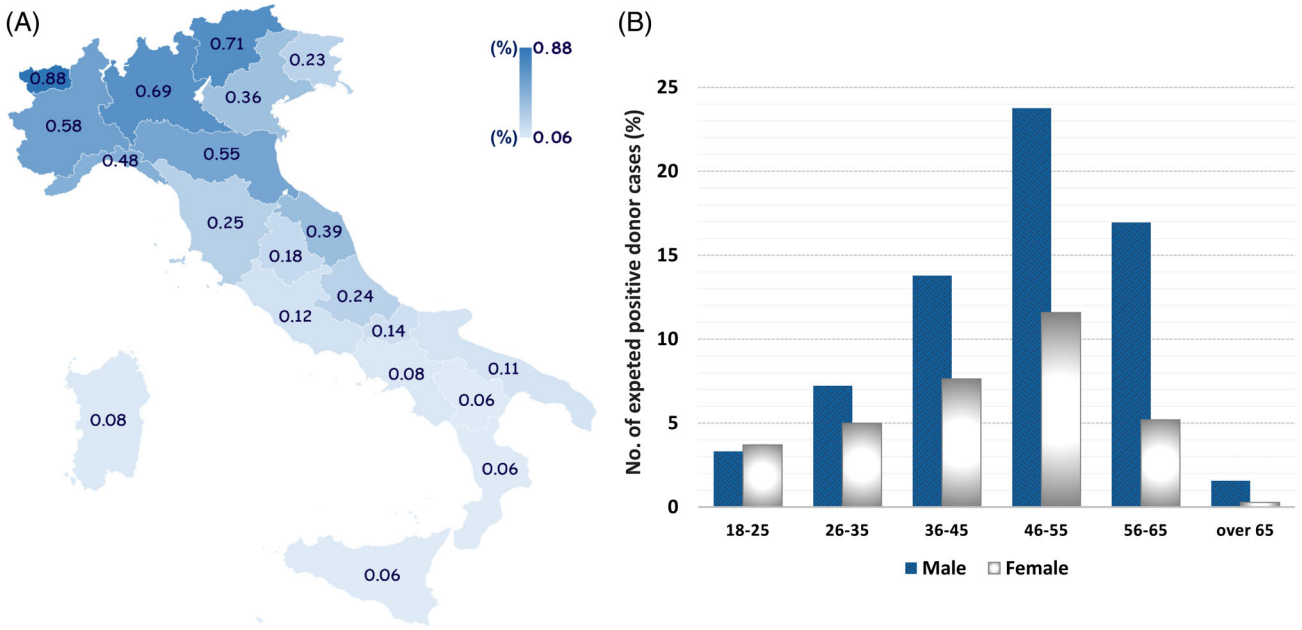

FIGURE 2 Distribution of blood donor cases expected in Italy by north–south gradient and by gender and age brackets. (A) Regional distribution, with north–south colour gradient, of expected SARS-CoV-2 cases in Italian blood donors from February to May 2020. The data are reported as a percentage of the total donor population for each region. (B) Distribution of expected cases of SARS-CoV-2 positivity in the Italian blood donor population divided by gender and age brackets from February to May 2020. The data are reported as a percentage of the total donor population [Color figure can be viewed at wileyonlinelibrary.com]

As the CNS' indication to the Transfusion Services was to eliminate the blood components donated by donors that fall within the first two conditions as a precautionary measure, 765 (96 + 669) units of blood components were discarded.

3.3 | Estimate of SARS-CoV-2 positive donors deaths

The number of donors potentially deceased following SARS-CoV-2 infection was 180. This estimate was arrived at using the same method utilised for the evaluation of infected cases expected in the donor population 3 months after outbreak.

3.4 | Estimate of donors readmitted to donation after recovery

The number of clinically recovered patients in the same period, provided by the Ministry of Health and equal to 147 101, corresponds to 64% of the total infected subjects. Therefore, it is conceivable, that out of 6087 deferred donors, 3652 are theoretically readmitted for donation.

4 | DISCUSSION

The rapid spread of the SARS-CoV-2 pandemic caused a serious overload for healthcare facilities in numerous countries, with the need to increase the reception capacity in hospitals or even to set up new ones in a very short time.

In the first weeks of the spread of the epidemic, the transfusion system also detected a reduction in blood donations, creating the concern of not being able to satisfy all transfusion requests.

This was followed by numerous initiatives aimed at reducing the consumption of blood components, ensuring the safety of donors and premises and preventing access to subjects at risk of SARS-CoV-2 infection.

In Italy, the response of donors to the appeal launched by the authorities was immediate, and the restoration of blood stocks was achieved in a short time.[7]

At the moment, the number of new cases of infection in the national population is on a downward trend, but the proportion of the population susceptible to infection remains very high.[12] There is therefore concern that an epidemic resurgence could also lead to new epidemic peaks in the near future.

By using the institutional surveillance data of the general population and for a defined period of time, the adopted calculation model makes it possible to make a quick estimate of the impact of SARS-CoV-2 infection on blood availability in the country on the basis of the probable distribution of the infection among donors.

The number of blood units discarded following PDI was added to this estimate.

The first parameter used was that of the total number of SARS-CoV-2 positive cases observed in the general population in the 3 months following the outbreak of the epidemic: compared to the 230 778 positives detected, 134 058, slightly more than half, belonged to the age brackets of eligible blood donors. Among the 134 058 eligible blood donors, our forecasting model allowed us to estimate 5322 potentially infected donors, corresponding to an equal number of lost donations.

The second figure considered, equal to 765 units, was that of the blood component units discarded after donation following a PDI reporting symptoms compatible with SARS-CoV-2 infection or a confirmed diagnosis of SARS-CoV-2 infection.

In fact, if on the one hand we can estimate the number of potentially infected donors, and therefore of the units lost, on the other hand, not knowing the recovery times and the clinical evolution of each case of infection, we are unable to define the period necessary for healing. Even assuming, on the basis of data from the Italian National Institute of Health, that 27% of donors (asymptomatic donors) are readmitted to donate in a short time, this is insufficient to estimate the effects on the donor population in quantitative terms. Therefore, to understand the impact of the epidemic on the donor population in quantitative terms, the number of subjects healed in Italy in the same period (equal to 64% of the total number of infected) was considered.

This figure could correspond to the share of clinically recovered patients (tested negative for SARS-CoV-2 RNA in at least two consecutive nasopharyngeal swab specimens collected $\geq$24 h apart) and, therefore, also to the total number of unsuitable donors who currently can be theoretically readmitted for donation 14 days from the resolution of the symptoms or from the suspension of the therapy.

The estimated number of donors who died following SARS-CoV-2 infection is included in the number of estimated positives and corresponds to 3.4% of them. Therefore, for a correct evaluation of the quota of patients who, once cured, could be readmitted for donation, the estimate of deaths should be subtracted from the total number of estimated positives. However, considering that the number of deaths compared to the total number of donors is negligible, this figure is not relevant for the purposes of this study.

The forecast function of the calculation model used is based on individuals in the general population diagnosed with SARS-CoV-2. The projection made, therefore, refers to donors who would not be able to donate because they tested positive for SARS-CoV-2 infection or because they were considered unsuitable on the basis of anamnestic screening or because they were self-excluded.

The positivity data, collected by the ISS and processed in this study, also include a quota of asymptomatic individuals (~27%); however, this is not an exact figure as it does not include any asymptomatic individual not tested for SARS-CoV-2.[13] This category also includes the quota of asymptomatic donors not tested for SARS-CoV-2 who, at least in part, could still be intercepted by the triage or medical selection process that has been put in place in the Italian transfusion system, for example, in the event of close contact with infected individuals.

However, the actual magnitude of asymptomatic subject is currently unknown, and in absence of symptoms or other historical events related to SARS-CoV-2, they will not be deferred from blood donation and could not be included in this forecasting model.

Therefore, in the period under examination, overall, there was an estimated loss of 6087 blood units due to the SARS-CoV-2 infection (5322 unsuitable donors estimated to be positive for SARS-CoV-2 + 765 units discarded following PDI).

It should be noted that, although the number of units discarded following PDI is real and refers to the 3-month period examined, the estimate of donors potentially infected with SARS-CoV-2 was made with respect to the entire blood donor population in 1 year in Italy.

However, even if we want to consider the worst case scenario, in which it can be assumed that the maximum number of blood units (total 6087) could be lost during the quarter considered, without readmitting clinically recovered individuals for donation, the drop in the number of available blood units would correspond to 0.9% of the total donations usually collected in the same period of the year in Italy, which is an average of 650 000 units.

In conclusion, the estimated number of infected donors in the 3-month period examined and considering the worst-case scenario is much lower than the actual reduction in donations in the first week of the epidemic (10%)[7] and was largely compensated in the following weeks after the appeals to donate blood launched by the competent authorities. The readmission to donate of the previously infected donors could be also considered one of the reasons of this response.

This confirms that, to date, the number of donors infected with SARS-CoV-2 is relatively low and the reduction or increase in donations detected during this outbreak, therefore, is not attributable to the SARS-CoV-2 infection in blood donors but rather to motivations related to donors' fear of contracting the virus or organisational aspects of the transfusion network.

This forecasting model can be a useful tool to obtain information on blood donors involvement both during future SARS-CoV-2 outbreaks, especially in case of changes concerning epidemiology, incidence by age bracket and geographical distribution, and also for new outbreaks of emerging viruses.

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CONFLICT OF INTEREST

The authors have no competing interests.

AUTHOR CONTRIBUTIONS

Giancarlo M. Liumbruno, **Claudio Velati** and **Ilaria Pati:** Conceptualised and designed the study; **Claudio Velati**, **Ilaria Pati** and **Carlo Mengoli:** Performed the research work; all authors contributed to drafting of the manuscript.

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