Impact of COVID-19 pandemic on global unrelated stem cell donations in 2020—Report from World Marrow Donor Association

TO THE EDITOR:
The ongoing COVID-19 pandemic has an unprecedented impact on national health care systems including hematopoietic stem cell transplantation (HSCT). Early in the pandemic this prompted the Worldwide Network for Blood and Marrow Transplantation [1] and The European Society for Blood and Marrow Transplantation [2] to publish guidelines regarding the care of patients in need of an HSCT. As World Marrow Donor Association (WMDA) promotes global collaboration for the benefit of stem cell donors and transplant patients, we were interested in examining the impact of the COVID-19 pandemic on unrelated hematopoietic stem cell (HSC) donation numbers. WMDA activities include yearly recording the number and details of unrelated HSC donations performed globally and compiling into a Global Trends Report (GTR). We used the 2020 WMDA GTR to examine trends in unrelated HSC donations during the COVID-19 pandemic globally, per continent and per country/region by comparing it with the 2019 WMDA GTR [3].

Number and details of HSC donations are collected through an online questionnaire and database developed for WMDA, which organisations can access through a secure website using their own account. Quality control measures include validity cross checks within the online questionnaire system and cross checks between years manually by WMDA staff. One-hundred-three (103) donor registries (DRs) and cord blood banks (CBBs) from 61 countries participated in the 2020 GTR, compared to 106 DRs and CBBs from 59 countries in the 2019 GTR. In 2019, 5 organisations reported having no activity and 3 did not respond. In 2020, 8 organisations reported having no activity (2 new organisations) and 8 did not respond. In addition in 2020, 2 organisation merged into 1 and 1 split into 2 reporting organisation. For 104 collections, lower donor availability, slight changes in donor selection could include disrupted courier utilisation due to travel restrictions, lower donor availability, slight changes in donor selection, prioritisation of patients with acute diseases. The noticeable decrease in BM collections and intercontinental/cross-border shipments can be explained by logistically complex processes, and increased risk to the donor of being exposed to COVID-19 during an operative procedure. These observations are in line with published data in the early stages of the pandemic [6, 7]. Use of CBUs as a stem cell source was expected to increase given that the

HSC donations from unrelated donors (PBSC and BM) decreased by 3.5% \( (n = -707) \) from 20,330 in 2019 to 19,623 in 2020, compared to an average annual growth rate of +3.9% from 2015 to 2019. The slowest development in that period was in 2015 with a growth rate of +0.5%. A negative development has not been observed before. The 3.5% decrease is composed of a 29.0% \( (n = -1139) \) decrease for BM and a 2.6% \( (n = +428) \) increase for PBSC, resulting in a drop in the BM share of unrelated HSC donations from 19.3% in 2019 to 14.2% in 2020. The percentage of national use of HSC products (PBSC and BM) \( (\text{i.e. products which did not cross a national border}) \) increased from 51.2 to 53.5%. The share of HSC donations requiring intercontinental transport decreased from 24.6% in 2019 to 21.9% in 2020. The number of cord blood unit (CBU) shipments globally decreased by 3.5% \( (n = -101) \) from 2851 to 2750.

When considering the continent on which the patient was transplanted (Table 1), the change rate of use of donated HSC products (BM and PBSC) ranged from −28.0% \( (n = -155) \) in South America to +18.2% \( (n = +6) \) in Africa in 2020 vs. 2019. In absolute numbers, the largest decrease of HSC donations (BM and PBSC) occurred for patients in Asia \( (n = -478; -9.1\%) \) followed by Europe \( (n = -205; -2.4\%) \), and the largest increase occurred in North America \( (n = +88; +1.7\%) \) followed by Oceania \( (n = +19; +4.8\%) \).

Regarding country/region of transplant (Table 1), in absolute numbers, the largest decrease in HSC donations (BM and PBSC) occurred in Turkey with \( n = -147 \ (-14.5\%) \), and Japan following with \( n = -128 \ (-10.5\%) \) (although Japan saw an increase of CBU use of \( n = +106 \ (+7.5\%) \)). In absolute figures, the greatest increase occurred in Italy \( (n = +67; +8.1\%) \) and the Netherlands \( (n = +66; +17.2\%) \). The two countries for which most HSC products were collected showed no major changes: USA: +0.6% \( (n = +30) \) (although a decrease for CBU of 21.0% \( (n = -149) \) was observed) and Germany: −2.4% \( (n = -61) \).

We did not find any significant correlation between number of COVID-19 cases or COVID-19-related deaths per 1 million inhabitants with HSC donation numbers in 2020 (Spearman’s \( \rho = 0.098 \) \( (p = 0.446) \) for cases and \( \rho = 0.130 \) \( (p = 0.311) \) for deaths).

The decline in number of unrelated HSC donations in 2020 suggests an impact of the COVID-19 pandemic. Reasons could include disrupted courier utilisation due to travel restrictions, lower donor availability, slight changes in donor selection (related and haplo-identical donors vs. unrelated donors) and prioritisation of patients with acute diseases. The noticeable decrease in BM collections and intercontinental/cross-border shipments can be explained by logistically complex processes, and increased risk to the donor of being exposed to COVID-19 during an operative procedure. These observations are in line with published data in the early stages of the pandemic [6, 7]. Use of CBUs as a stem cell source was expected to increase given that the...
Table 1. HSC donations per patient continent and country/region.

| Patient continent, country/ region | 2019 BM/PBSC  | 2020 BM/PBSC  | Δn (%) BM/PBSC  | 2019 CBUs  | 2020 CBUs  | Δn (%) CBUs  | COVID-19 cases/ 1 M inhab | COVID-19 rel deaths/ 1 M inhab |
|------------------------------------|--------------|--------------|----------------|------------|------------|--------------|---------------------------|-------------------------------|
| Africa                             | 33           | 39           | +6 (+18.2%)     | 0          | 0          | 0            |                           |                               |
| Asia                               | 5256         | 4778         | −478 (−9.1%)    | 1637       | 1662       | +25 (+1.5%)  |                           |                               |
| Europe                             | 8718         | 8513         | −205 (−2.4%)    | 332        | 374        | +42 (+12.7%) |                           |                               |
| North America                      | 5288         | 5376         | +88 (+1.7%)     | 765        | 627        | −138 (−18.0%)|                           |                               |
| Oceania                            | 395          | 414          | +19 (+4.8%)     | 39         | 27         | −12 (−30.8%) |                           |                               |
| South America                      | 554          | 399          | −155 (−28.0%)   | 78         | 60         | −18 (−23.1%) |                           |                               |
| Total                              | 20,330       | 19,623       | −707 (−3.5%)    | 2851       | 2750       | −101 (−3.5%) |                           |                               |

Top 10 increased

| Country                  | 2019 BM/PBSC  | 2020 BM/PBSC  | Δn (%) BM/PBSC  | 2019 CBUs  | 2020 CBUs  | Δn (%) CBUs  | COVID-19 cases/ 1 M inhab | COVID-19 rel deaths/ 1 M inhab |
|--------------------------|--------------|--------------|----------------|------------|------------|--------------|---------------------------|-------------------------------|
| Italy                    | 827          | 894          | +67 (+8.1%)     | 24         | 20         | −4 (−16.7%)  | 34,851                     | 1227                          |
| Netherlands              | 383          | 449          | +66 (+17.2%)    | 72         | 69         | −3 (−4.2%)   | 47,178                     | 673                           |
| Canada                   | 509          | 557          | +48 (+9.4%)     | 45         | 57         | +12 (+26.7%) | 15,564                     | 418                           |
| Iran                     | 136          | 175          | +39 (+28.7%)    | 20         | 0          | −20 (−100%)  | 14,586                     | 657                           |
| USA                      | 4773         | 4,803        | +30 (+0.6%)     | 710        | 561        | −149 (−21.0%)| 60,943                     | 1063                          |
| Australia                | 339          | 365          | +26 (+7.7%)     | 37         | 24         | −13 (−35.1%) | 1,115                      | 36                            |
| Taiwan                   | 210          | 235          | +25 (+11.9%)    | 19         | 11         | −8 (−42.1%)  | 34                         | 0                             |
| Spain                    | 446          | 459          | +13 (+2.9%)     | 17         | 22         | +5 (−29.4%)  | 41,242                     | 1087                          |
| Finland                  | 89           | 100          | +11 (+12.4%)    | 1          | 0          | −1 (−100%)   | 6517                       | 101                           |
| Portugal                 | 62           | 72           | +10 (+16.1%)    | 1          | 0          | −1 (−100%)   | 40,570                     | 677                           |

Top 10 decreased

| Country                  | 2019 BM/PBSC  | 2020 BM/PBSC  | Δn (%) BM/PBSC  | 2019 CBUs  | 2020 CBUs  | Δn (%) CBUs  | COVID-19 cases/ 1 M inhab | COVID-19 rel deaths/ 1 M inhab |
|--------------------------|--------------|--------------|----------------|------------|------------|--------------|---------------------------|-------------------------------|
| Turkey                   | 1013         | 866          | −147 (−14.5%)   | 4          | 0          | −4 (−100%)   | 26,188                     | 248                           |
| Japan                    | 1222         | 1094         | −128 (−10.5%)   | 1416       | 1522       | +106 (+7.5%) | 1864                       | 28                            |
| China                    | 1571         | 1469         | −102 (−6.5%)    | UNK        | UNK        | NA*          | 66                         | 3                             |
| Brazil                   | 366          | 265          | −101 (−27.6%)   | 16         | 8          | −8 (−50%)    | 36,112                     | 917                           |
| Russia                   | 165          | 73           | −92 (−55.8%)    | 0          | 0          | 0            | 21,430                     | 386                           |
| UK                       | 1078         | 989          | −89 (−8.3%)     | 101        | 140        | +39 (−38.6%) | 36,771                     | 1084                          |
| India                    | 197          | 111          | −86 (−43.7%)    | 0          | 0          | 0            | 7454                       | 108                           |
| Germany                  | 2540         | 2479         | −61 (−2.4%)     | 6          | 2          | −4 (−66.7%)  | 20,850                     | 403                           |
| Argentina                | 129          | 96           | −33 (−25.6%)    | 1          | 1          | 0            | 35,966                     | 957                           |
| South Korea              | 569          | 539          | −30 (−5.3%)     | UNK        | UNK        | NA*          | 1205                       | 18                            |

HSC donations shipped within and to that continent/country/region; *The 2020 numbers for CBU in China were incomplete; −The 2019 numbers for CBU in South Korea were incomplete.
NA Not available, UNK unknown.
BM/PBSC bone marrow/peripheral blood stem cell.
CBUs cord blood units.

In 2019 86 BM/PBSC and in 2020 104 BM/PBSC were shipped to unknown continent/country/region and therefore are only included in the total number.
product is already available for shipping. However, on a global scale our data does not show increased use of CBU suggesting that clinical decision making about using CBU as a stem cell source did not change during the pandemic.

The success of handling this COVID-19 pandemic as a DR or CBB depended on many factors including: quality and size of the pre-pandemic unrelated donor repository/ CBU inventory; having a solid network of collection and transplant centers in place with the ability to move patients and donors to hospitals in less affected regions; shifting towards donations from national donors; fast and adequate response to international transport challenges; cooperation with national/international authorities and collaboration with international colleagues.

Self-reporting is a clear limitation of this data, however the difference in total number of HSC donations reported due to slight differences in participation between the GTR data of 2019 and 2020 was relatively small (BM = 4, PBSC = 8, CBU = 32), and therefore we do not believe explains the trends we observe in HSC donations during the first year of the pandemic.

We were unable to demonstrate a correlation between country/region-specific severity of the pandemic and HSC donation numbers. We suspect this is due to data quality and variability of reported number of COVID-19 cases and COVID-19-related deaths. Furthermore, the amplitude and nature of each wave had a different impact in different countries depending on regional factors, population size, type of travel restrictions and, later in the pandemic, vaccination rates. COVID-19 related changes in HSC donations are dynamic with stronger effects in the beginning of the pandemic and gradual adaptation later on. Unfortunately, we do not gather monthly data in the WMDA GTR and therefore could not specify pandemic waves.

The decrease in unrelated HSCT actually performed could be larger than our figures on HSC donations suggest, because at times during the pandemic a clear majority of all products were cryopreserved. This practice was relatively rare before the pandemic and it is reported by some DRs that a certain amount of these cryopreserved products are not transfused [6, 8, 9].

The emergence of new COVID-19 variants causing potential new waves and the drop in donor recruitment and CBU banking during 2020 (data not shown) could affect the donation rate in the coming years. However, from anecdotal reports by several DRs and CBBs we learned that levels of HSC donation returned to normal or increased in 2021. Therefore, the outlook for HSC donation and transplantation is positive, especially since organisations are now better equipped to deal with any COVID-19 related disturbance to their operations.

In conclusion, despite logistic and other challenges posed by the pandemic, global exchanges of HSC products continued and only decreased slightly. This is an extraordinary achievement by DRs, CBBs, collection/transplant centers, couriers and all willing unrelated donors, and is a testament to the importance of international collaborations facilitated through WMDA.

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DATA AVAILABILITY

The data that support the findings of this study are not openly available. The data was shared with WMDA by donor registries and cord blood banks under a Data Use Agreement (DUA). However, the data are available from the authors (MMJ and LF) upon reasonable request and with permission of donor registries and cord blood banks.

A summary of the data can be found on the WMDA website: https://wmda.info/wp-content/uploads/2021/05/GTR-2020-Summary-slides.pdf

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AUTHOR CONTRIBUTIONS

MMJ was responsible for collecting data and writing the WMDA GTR 2020 report; extracting, analysing and interpreting the data; writing the paper; creating reference
list; creating table. AHS, SNB and SJF were responsible for the idea for this paper; contributed to interpretation and analyses of the data, writing the paper and provided feedback. JF, NS, HE, DF, FO, DO, KLY, SAM, SM, MA, JV, MMF, GSC, TJ, SMD, PG, RM and CH were responsible for submitting their data for the WMDA GTR 2020 and 2019 and provided feedback. BES, SJF and LF provided feedback. All authors participated in review and approval of the final version of the paper.

COMPETING INTERESTS
The authors declare no competing interests.

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