

Donation and Transplantation of Hematopoietic Stem Cells in Poland – 18 years Perspective

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Abstract

Since 2006, the year when National Transplants Registry has been created, numbers of Polish potential unrelated hematopoietic stem cells donors presented in World Marrow Donor Association database via Search & Match Tool have increased by over 200 times, reaching over two million in 2022 [1]. In the same timespan numbers of allogeneic hematopoietic stem cells (HSC) transplantations performed in Poland increased from 310 to 798 per year, while HSC donations from unrelated donors grew from 13 to 1601 per year. Numbers of international stem cells donations from donors of Polish origin stand out from the global average ratio, which stands at 54 to 46 in favour of donations for domestic recipients, while in Poland 81% of unrelated HSC collection in 2022 were performed for foreign patients. Here, we aim to illustrate the 18 years of evolution in the field of hematopoietic stem cell donation and transplantation using data collected over the years in the Polish national transplant and donor registries.

Keywords: Hematopoietic Stem Cells; Allogeneic Transplants; Polish Stem Cells Donors; Central Bone Marrow Donors; HSC Transplantations

Numbers of potential HSC donors available in the country highly influence not only numbers of collections, but also numbers of allogeneic hematopoietic stem cells (HSC) transplantations performed for domestic patients. Figure 1 presents development of Polish potential HSC donors pool presented in World Marrow Donor Association since 2006 to 2023 [2], 86,7% of them have been recruited by DKMS-Poland Foundation which started to operate in Poland in 2009. In addition to the DKMS Foundation, there are 15 regional donor centers operating in Poland, primarily associated with blood donation centers or medical entities. The largest among them contributes 2.78% to the overall pool of registered donors in the Central Registry. Polish donors share in global World Marrow Donor Association registry stands for 5% in 2023, what places Poland in the fifth position in the world and in the third place in Europe [1] (after Germany and United Kingdom) in terms of the number of available potential national donors (Figure 2). Comparing to other countries Poland has a high registration rate per million residents (58000) fourth in world, after Cyprus, Israel and Germany – what can signify that donation potential is not yet fully utilized.

Not only numbers of donors were growing, also the level and range of HLA typing of potential donors has been improving over the years reaching the international “gold standard.” In 2022 almost 83% of registered donors were typed at least at HLA-A, B, C, DR, DQ, DP loci on high- or intermediate-resolution level, mostly by way of next generation genomic sequencing techniques [3]. Over time, the age structure of the registry changes in an unfavourable manner. In 2023, 78% of registered donors were over 30 years old, and 60% of potential donors are women. It is problematic because as donors age, the risk of medical disqualification increases and women have always higher risk of additional immunization. Furthermore, a clear positive correlation between the younger age of donors and HSC transplantation outcomes has been observed. Together, all of this will always create the need to recruit new donors.

According to current legal regulations in Poland [4] the entity responsible for administering of the Central Bone Marrow Donor Registry (CBMDR) is Polish Trans-

plant Coordinating Center Poltransplant (national competent authority in donation and transplantation), which cares about personal data safety, prevents data loss or destruction and performs statistical analysis of the database at least once a year, sharing the results with Ministry of Health and National Transplant Council. CBMDR gathers all potential bone marrow donors available in the country, recruited by 15 donor’s centers, including DKMS-Poland. Central Registry enables national search units searching the whole pool of bone marrow donors in place and facilitates electronic requests for extended and verification/confirmatory typings, as well as registers all donations from Polish donors for national and international patients. And those numbers increased very significantly since 2006, as it is presented in Figure 3B. In 2022, there were 10,013 international donations of hematopoietic stem cells performed worldwide, of which 7% were collections from Polish donors.

The anonymized data of Polish donors are updated on regular basis at the World Marrow Donor Association Search & Match Service, ensuring their visibility and accessibility to Polish and international search units and registries, resulting in stable growth of activations of Polish donors for transplant procedures, which counted for almost 10 000 in 2022. The total number of HSC donations from Polish donors increased one hundredfold since 2006. Figure 3B illustrates this growth, taking into account the origin of the HSC recipients. Number of donations for national patients increased from 10 in 2006 to 323 in 2022, whereas the number of international donation jumped from 2 to 1292 during the same time span. Moreover, number of national donations oscillates between 200 and 300 over last 8 years while international collections continue to show a rising trend.

The increasing pool of donors accessible through CBMDR enhances the likelihood of locating a donor within Polish resources, minimizing, but not eliminating the necessity to turn to international registries. Figure 4 shows changes in proportion of Polish patients without any potentially matched low resolution donor in Poland from 2006 to 2023. Percent of patients with poor prognostics is decreasing but not reaching zero. There is always 14% of searches which have to be broadcasted internationally.

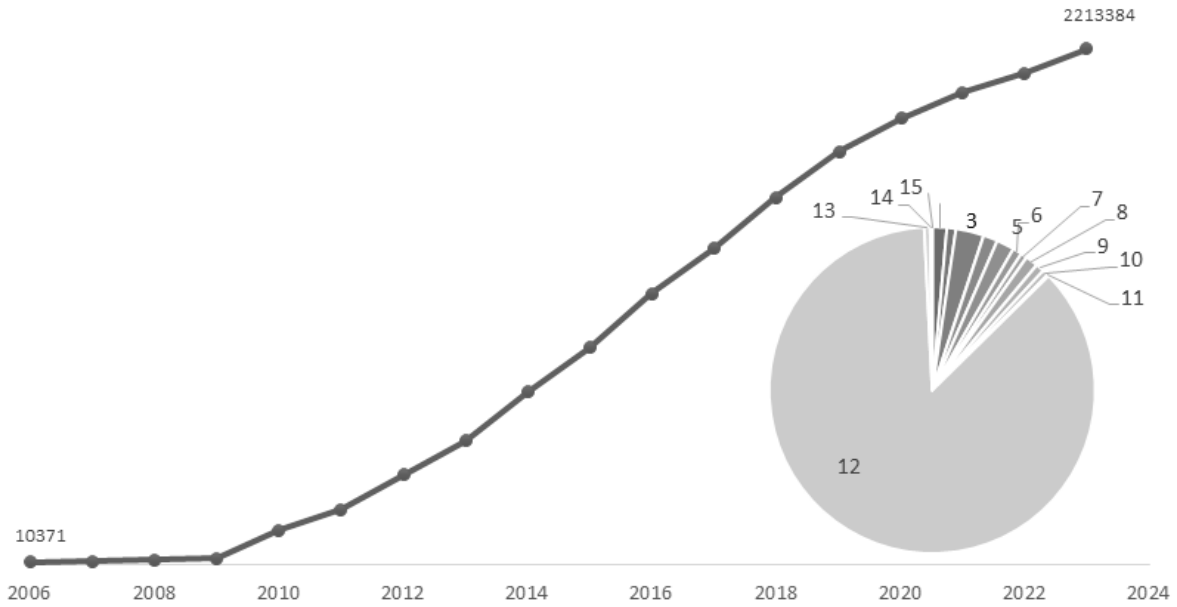


Figure 1: Numbers of potential unrelated donors registered in the Central Bone Marrow Donors and Cord Blood Registry “Poltransplant” (1. the Regional Blood Transfusion Center in Katowice, 2. the Regional Blood Transfusion Center in Lublin, 3. the Regional Blood Transfusion Center in Poznan, 4. the Regional Blood Transfusion Center in Kielce, 5. the Regional Blood Transfusion Center in Bialystok, 6. the Institute of Hematology and Blood Transfusion in Warsaw, 7. the Military Institute of Medicine in Warsaw, 8. the MEDIGEN Warsaw, 9. the University Clinical Center in Gdansk, 10. the Lower Silesian Oncology Center in Wroclaw, 11. the Ursula Jaworska Foundation in Warsaw, 12. the DKMS Poland Foundation in Warsaw, 13. the Central Clinical Hospital in Lodz, 14. the Central Clinical Hospital in Warsaw).

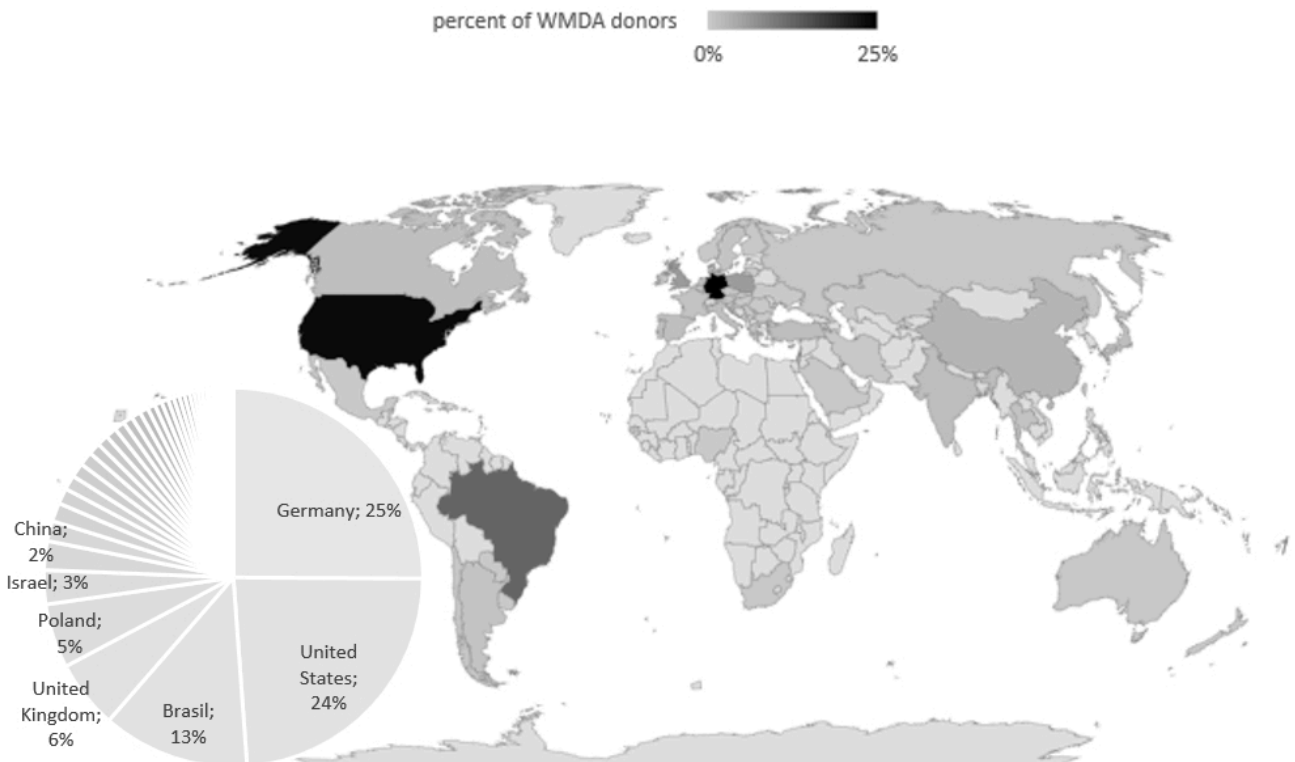


Figure 2: World Marrow Donor Association database and shares of specific countries in the worldwide hematopoietic stem cells donors pool. WMDA Search & Match Tool collect data from 57 different countries, but their shares are not equal.

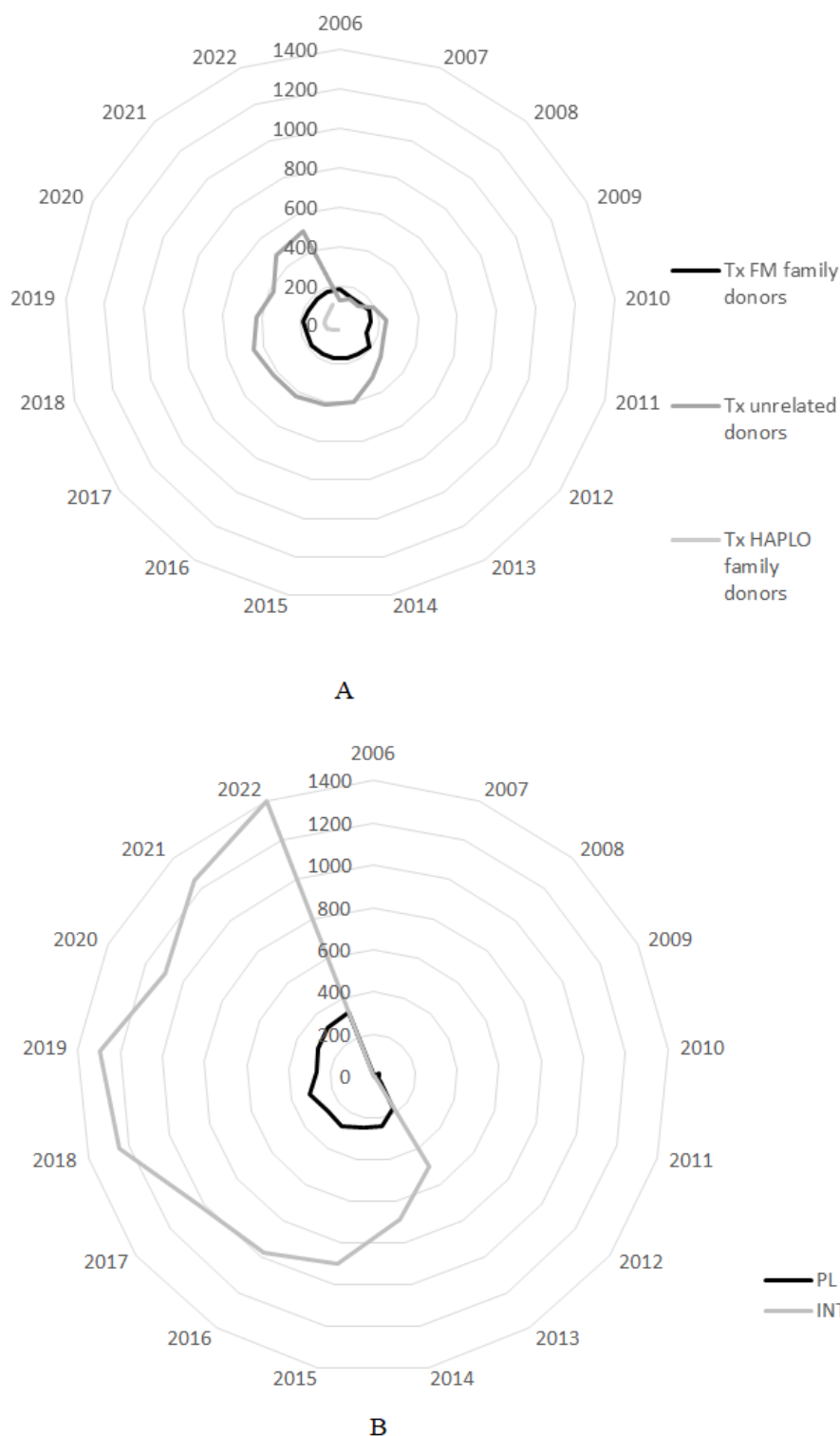


Figure 3: Number of allogeneic transplantation performed in Poland in years 2006-2022 (A) and number of unrelated HSC donations from Polish donors performed for international (INT) and national (PL) patients (B) presented in the same scale.

Although in 2006, just 15% of Polish HSC recipients received transplant from Polish donors, by 2018 the proportion reached 66% and during last four years oscillates between 60-65% (Figure 5). This is a significant qualitative change that improves the situation for Polish transplant patients, primarily due to the availability of local donors,

streamlining the activation procedures, organizing the collection and transport of materials, and reducing associated costs, what proves that CBMDR is an example of proper strategy on registry development. Observed trends impact patients outcomes and resource allocation as well as health-care availability for leukemic patients in Poland. Figure 6 al-

lows for the comparison of total allogeneic transplants (A) and allogeneic transplants from unrelated donors (B) performed in specific regions (voivodeships) of Poland in terms of per one million inhabitants in years 2006 and 2022 [5,2]. In 2006 there was only one region in Poland with overall allogeneic HSCT rate above 10 per one million inhabitants and on average only 3 allo HSCTs were performed per year per 1 million of inhabitants in the whole country. In 2002, the average number of allo HSCTs performed per million inhabitants increased to about twenty (what means a fivefold increase), and in four voivodeships, this rate exceeded 30. In 2006, the leading regions in HSCT were Silesia and Lower Silesia; they still maintain their positions but are now followed by the rest of the voivodeships, particularly in northern and central Poland. The observed increase is striking not only in absolute numbers but also in terms of enhancing the accessibility of the HSCT procedure for residents across all regions of the country. The development and growth of transplantation centers in Poland have certainly been influenced by financial resources acquired through collections of HSC for both Polish and foreign recipients. All Polish transplantation centers actively performing transplants from unrelated donors have approval from the Minister of Health for both collection and transplantation, and they demonstrate activity in both fields. It proves that the development of national bone marrow donors registries is crucial for HSC transplantation programs. Polish stem cells donors are also more and more important for international patients. Polish donors, constituting 5% of the

WMDA pool, were the source of cells in 7% of international workups organized in 2022. In that year 1462 HSC products (BM and PBSC) were shipped internationally to 45 different countries on 6 continents, mainly to USA (270), Germany (241) and France (93).

Summarizing, growing numbers of potential unrelated HSC donors in national pool obviously increases the chances of finding a matched donor within the country, facilitates the donor matching and collection procedures, and reduces costs associated with obtaining transplant material, but on the other hand this growth drives the number of donations, what subsequently positively influences the experience and incomes of local collection centers, which frequently are organized together with transplant facilities.

However, it doesn't mean that the Polish Registry doesn't require any improvements or initiatives. The popularity of Polish donors over the last several years has been attributed to their young age, availability, and high-resolution typing. However, these factors can change over time. Therefore, the Registry and Donor Centers need to focus on optimizing their recruitment strategy for new donors and retaining the available pool of potential donors. This may involve targeting young, male donors and ethnic minorities, whose numbers have increased since the outbreak of the war in Ukraine, and maintaining updated records by regularly engaging with recruited donors. Additionally, older records should be re-typed using newer NGS methods, which were not available in 2006. All of these activities require a significant financial investment.

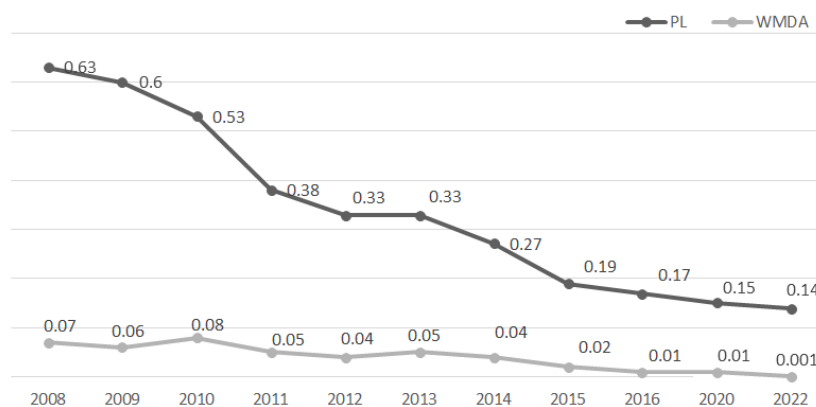


Figure 4: Proportions of potential recipients without any potentially fully matched donor ABCDRDQ at low resolution level in WMDA (grey) and in Poland (black) over the years.

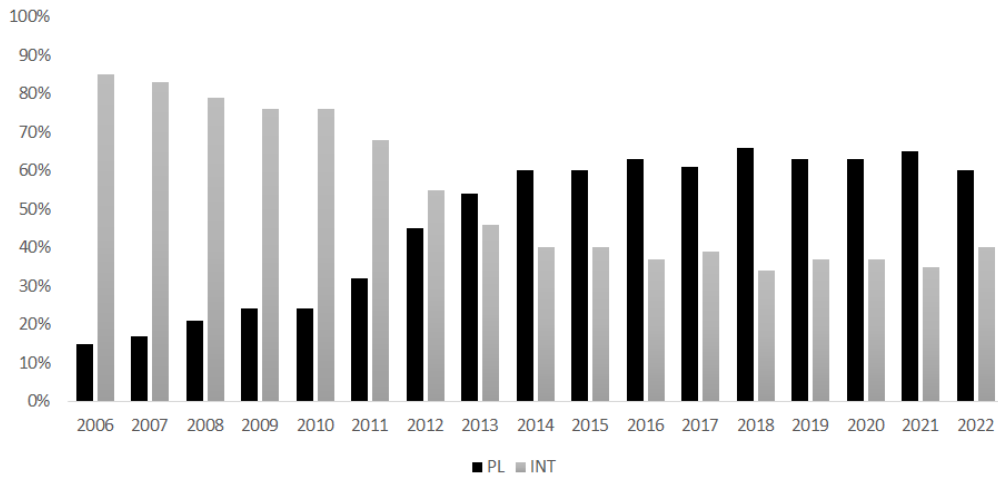


Figure 5: Changes in HSC transplantations performed using material from national (PL) and international donors (INT) in Poland from 2006 to 2022.

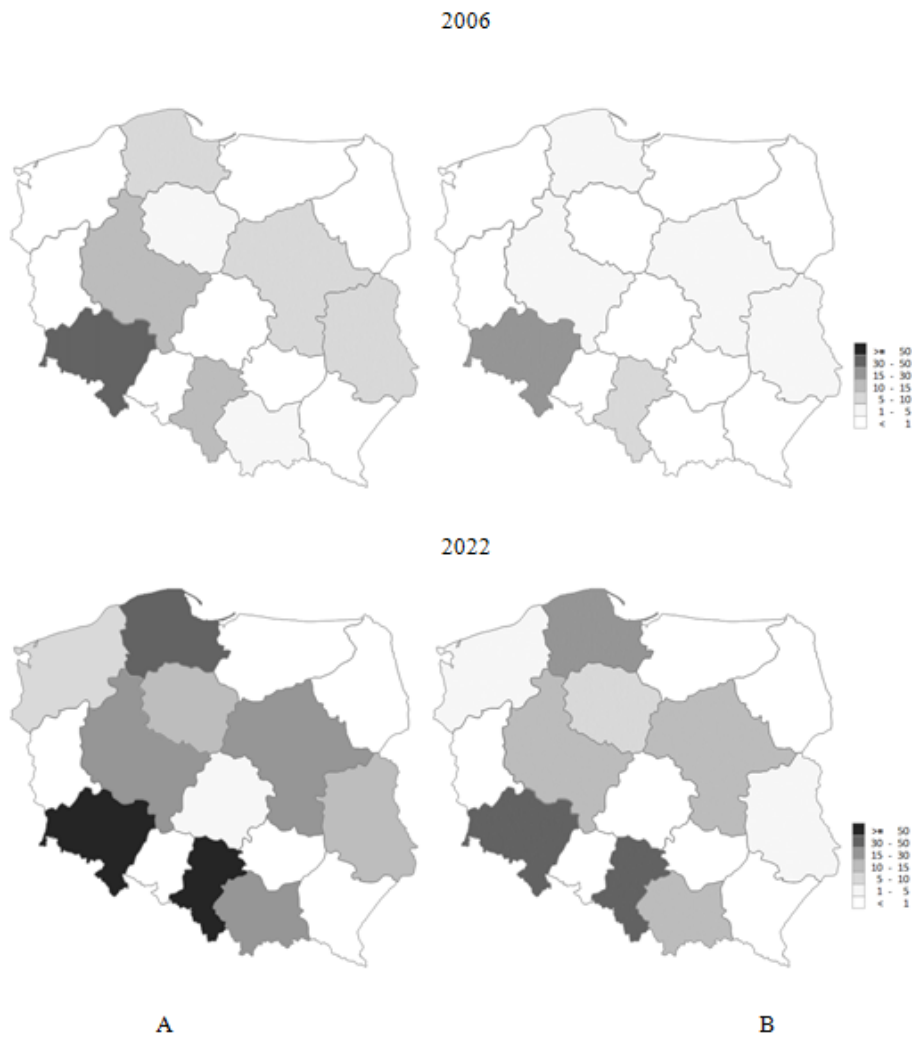


Figure 6: Numbers of total allogeneic transplantations (A) (together from related matched, haploidentical and unrelated donors) and transplantations from unrelated donors only (B) per 1 million inhabitants performed in different Polish regions (voivodeships) in 2006 and 2022.

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