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## Raising awareness may increase the likelihood of hematopoietic stem cell donation: a nationwide survey using Artificial Intelligence.

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*Original Article*

**Raising awareness may increase the likelihood of hematopoietic stem cell donation: a nationwide survey using Artificial Intelligence.**

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**FIGURE** 3

**TABLES** 3

**ABSTRACT**

**Background:** In Italy, the demand for allogeneic transplantation exceeds the number of compatible donors in the Italian Bone Marrow Donor Registry (IBMDR). This study aimed to explore the knowledge, beliefs, opinions, values, and feelings of the Italian population regarding stem cell donation.

**Methods:** An online survey was shared via social media. Respondents were retrospectively identified as registered on the IBMDR (donor group) or never registered (non-donor group). Statistical analyses confirmed the relationship between knowledge level and willingness to donate. Six machine learning classifiers were trained using questionnaire responses to predict the probability of IBMDR registration.

**Results:** A total of 1518 respondents participated. Characteristics identified in the non-donor group were a lower level of knowledge regarding donation needs (51.7% vs 24.4%,  $p < 0.001$ ) and negative feelings such as fear ( $Z = -2.2642$ ,  $p = 0.02$ ), confusion ( $Z = 4.4821$ ,  $p < 0.001$ ), and uncertainty ( $Z = 3.3425$ ,  $p < 0.001$ ). Higher knowledge predicted a greater likelihood of IBMDR enrollment. Machine learning analysis showed an AUC ranging from 0.65 to 0.81, depending on the classifier.

**Conclusions:** The results underscore the need to improve strategies to raise awareness and knowledge of stem cell

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11 donation among the Italian population.

12  
13 **KEYWORDS**

14 Hematopoietic stem cell transplantation, stem cell donation, cord blood donation, knowledge, beliefs, awareness,  
15 artificial intelligence.

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17 **STATEMENTS AND DECLARATION**

18  
19 The authors declare that they have no known competing financial interests or personal relationships that could  
20 have appeared to influence the work reported in this paper.

21  
22 **INTRODUCTION**

23  
24 Hematopoietic stem cell transplantation (HSCT) is an effective therapeutic approach that has saved the lives of an  
25 increasing number of patients worldwide. While primarily used for the treatment of both adult and pediatric  
26 patients affected by hematology malignancies such as leukemias, lymphomas, and myelomas, this procedure is  
27 also suitable for patients affected by inborn errors, autoimmune diseases, and solid tumors [1–3]. Autologous  
28 transplantation uses the patient's own stem cells (SCs), while allogeneic HSCT uses SCs from a donor that may  
29 be a family member (related) or unrelated. SCs are collected from the peripheral blood, bone marrow, or cord  
30 blood and infused to the recipient after high-dose chemo-radiotherapy-based conditioning regimen. A high level  
31 of matching donor–recipient human leucocyte antigen (HLA) is essential to improve outcomes and to avoid  
32 immuno-mediated complications such as graft versus host disease (GvHD) [4]. The great variety of the HLA  
33 systems among humans decreases the likelihood of finding compatible donors for HSCT patients. The genetic  
34 variability within a population as well as between different populations must therefore be considered in unrelated  
35 HSCT donor search algorithms [5].

36 In 2021, over 47,000 patients received HSCT in Europe, of whom fewer than 20,000 were allogeneic recipients.  
37 A continuously increasing trend in the use of both unrelated and haploidentical SC sources has been observed over  
38 the last decade, with Italy being one of the leading European countries in terms of the number of transplants  
39 performed and of outcomes [6]. Here, the practice of allogeneic HSCT has steadily increased over time, stabilizing  
40 at above 1900 transplants per year over the last 5 years. Just over a half of these were performed using cells  
41 provided by unrelated donors [7].

42 These advances in the field of transplantation have inevitably led to an increasing need to involve a growing  
43 number of potential donors for allogeneic transplantation [2]. The Italian Bone Marrow Donor Registry (IBMDR)  
44 was established in 1989, with its activities institutionally recognized by Italian Law No. 52 in March 2001. Its  
45 mission is to search for compatible, unrelated, volunteer donors for patients needing HSCT who lack an ideal  
46 donor (HLA identical sibling), wherever they are around the world.

47 The IBMDR is part of a worldwide bone marrow (BM), SC, and cord blood (CB) donor registry network that  
48 coordinates all processes related to donor search and selection, donation and collection, and transport up to the  
49 patient's bed [8].

50 Joining IBMDR is a compassionate choice that can truly save a life. Individuals must be between 18 and 35 years  
51 of age, weigh more than 50 kilograms, and have good health to be considered for IBMDR enrollment [9]. However,  
52 despite the broad range of eligible donors, these must have very well-defined characteristics [10], resulting in the  
53 fact that the probability of finding full HLA compatibility among family donors (siblings) amounts to 25%,  
54 whereas the probability of HLA compatibility with an unrelated donor is only 1 out of 100,000 [9]. This scenario  
55 suggests that, although many people may volunteer as potential donors, only a small percentage will actually  
56 become donors. Therefore, it is of primary importance to encourage the enrollment of as many individuals as  
57 possible in the IBMDR, thereby maximizing the chances of finding a compatible donor.

58 As is well known, the COVID-19 pandemic introduced significant changes both in people's daily life and in  
59 healthcare systems, thus impacting both the HSCT process and the registration of new donors [11]. A small  
60 reduction in transplant activities was reported in Europe [12] along with an increased demand for donors, reflecting

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11 the challenges introduced by the international restrictions during the pandemic [13].  
12 The decision to become a donor seems to be influenced by various factors, including age, sex, education,  
13 occupation, ethnicity, and religion [14–18]. In addition to these factors, individuals' level of understanding of  
14 HSCT and donation emerges as a complex and contradictory theme, where awareness of the implications of  
15 donation and accurate knowledge of the HSCT process, including its component functions and methods becomes  
16 a crucial aspect to dispel stereotypes and promote donation. The shortage of donors could also be attributable to  
17 misconceptions, such as the belief that donation may be a risky or painful procedure, when in real life, peripheral  
18 blood stem cell (PBSC) and umbilical CB sources currently represent 80% of donations and require simple,  
19 minimally invasive, safe procedures [19].  
20 In this context, our study aimed to thoroughly assess the experience, information, opinions, values, and beliefs of  
21 the Italian population regarding SC donation in order to identify specific areas that require targeted interventions  
22 so as to increase voluntary SC donation.

## 22 **METHODS**

### 23 **Study design**

24  
25 A nationwide online questionnaire survey directed to the general population of Italy over the age of 16 was  
26 conducted on behalf of the Gruppo Italiano Trapianto di Midollo Osseo (GITMO) from July 2022 to July 2023.  
27 The questionnaire was developed by a panel of experts that included members of the GITMO, the Italian Bone  
28 Marrow Donor Registry (IBMDR), the National Transplant Center (Centro Nazionale Trapianti – CNT), the  
29 National Blood Center (Centro Nazionale Sangue – CNS), and the University of Bari. The survey was prepared  
30 on the Google Forms<sup>®</sup> platform, and the link to access the survey was shared through the GITMO network contacts,  
31 the Italian Leukemia Association (Associazione Italiana Leucemie – AIL) contacts, and on social media platforms  
32 such as Twitter (now X<sup>®</sup>) and Facebook<sup>®</sup>. A snowballing procedure was adopted to recruit participants by  
33 including a cover letter asking the individual to involve family members and friends as well as to share the link on  
34 their social media accounts.

### 35 **The Questionnaire**

36 The data collection tool was created to investigate respondents' knowledge, beliefs, feelings, opinions, values, and  
37 information needs regarding SC donation. The experts consulted the available literature during the development  
38 of the questionnaire; the final version was tested for clarity and readability on 20 participants, then was divided  
39 into 9 sections composed by closed ended questions accepting single or multiple responses. The sections were: 1)  
40 Sociodemographic information (8 items); 2) General knowledge of donation process (10 items); 3) Knowledge of  
41 SCs' role and function (18 items); 4) Knowledge of SC collection methods (5 items); 5) Respondents' beliefs (5  
42 items); 6) Respondents' feelings (22 items); 7) Opinions and values (8 items); 8) Information/education needs (4  
43 items); 9) Reasons to enroll in the IBMDR or not (2 items).

### 44 **Ethical approval**

45 A cover letter presenting the aims of the study and containing information on ethical management was included at  
46 the beginning of the questionnaire, which was completely anonymous. Both the consent to participate and data  
47 utilization were considered as acquired after questionnaire completion and submission. The study was approved  
48 by the Ethics Committee of the University of Bologna (Protocol No. 0026388 dated 02 February 2023). The  
49 questionnaire's structure adhered to the guidelines set forth by the Italian Data Protection Authority (DPA).

### 50 **Statistical analysis**

51 The data were collected in an electronic database (Microsoft Excel<sup>®</sup> 2016). Respondents were clustered into 2  
52 groups: the “Donor Group” (DG), representing those who were currently/formerly enrolled in the IBMDR, and  
53 the “Non-Donor Group” (NDG), representing those who had never enrolled in the IBMDR. Descriptive statistical  
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11 calculations were performed on the entire sample, with mean and standard deviation (SD) for continuous variables  
12 and frequencies and percentages for categorical variables.  
13 To identify differences between the 2 groups, the Mann-Whitney U-test was employed. Artificial Intelligence (AI)  
14 stands out for its ability to extract complex features from data, and AI models are particularly suited to large-scale  
15 predictions. However, this characteristic might make AI predictions difficult to interpret and control. In this study,  
16 AI was used to understand whether the questionnaire results could be predictive of enrollment in the donor registry,  
17 while inferential statistics were made through traditional methods to have mechanistic understanding of the  
18 phenomena. For open-ended questions, generative Artificial intelligence (ChatGPT version 3) was used to  
19 cluster similar responses and provide a summary of the results. To confirm the positive correlation between  
20 knowledge and willingness to donate, the probability of enrolling in the IBMDR was predicted using machine  
21 learning (ML). The questionnaire responses were used as features to train various classifiers. Statistical  
22 significance was set at a threshold of  $p < 0.05$ . All statistical computations were performed using MATLAB  
23 software, version R2023b.

### 23 Machine Learning

24 To confirm that greater knowledge increases the willingness to donate, a supervised ML approach was employed  
25 to predict the probability of becoming an SC donor using the significant factors identified through statistical  
26 analysis. This approach aimed to determine how the participant's knowledge of implantation impacts the  
27 willingness to donate. These factors, along with respondents' knowledge, information, opinions, beliefs, and values  
28 regarding SC donation, were utilized as features to train various ML classifiers. Six distinct classifiers – Naive  
29 Bayes (NBs), Support Vector Machine (SVM), Decision Trees (DTs), Error-correcting output codes (Ecoc),  
30 Discriminant Analysis using Ensemble (DAE), and Artificial Neural Network (ANN) – were applied to identify  
31 the most suitable model for the predictive task. The features were normalized to a range of 0–1 using min–max  
32 normalization on the training dataset. The same normalization parameters were subsequently applied to the test  
33 set. The training procedure employed the 5-fold cross-validation approach. To evaluate the classifier's performance  
34 and ascertain the optimal threshold for predictions, the receiver operating characteristic (ROC) curve was  
35 employed. Based on the optimal operating point of the ROC curve, a binary classifier was derived. The area under  
36 the ROC curve (AUC) and accuracy were utilized as performance metrics. Computational analysis was conducted  
37 using MATLAB software, version R2023b.

## 37 RESULTS

### 38 Sample characteristics.

39 The survey collected 1518 complete responses: 1141 (75.2%) from NDG and 377 (24.8%) from DG. The  
40 sociodemographic characteristics of the two groups are presented in Table 1. Most of the respondents in both  
41 groups were female (75.0% and 76.1%, in NDG and DG, respectively), although the average age was higher in  
42 NDG (38.15 vs 36.02,  $p = 0.01$ ), and over half of the sample in both groups was not married (51.3% in NDG; 56.8%  
43 in DG). In the DG, respondents lived predominantly in northern Italy (56.8%), while in the NDG, most lived in  
44 the South and Islands (51.7%), with a significant difference in distribution between the groups ( $p < 0.001$ ).  
45 Regarding education level, most respondents had a university degree (54.2% in NDG; 57.3% in DG) and were  
46 employed mainly in the public sector (32.3% in NDG; 25.2% in DG) or in the private sector (23.5% in NDG;  
47 34.0% in DG). Of note, healthcare professionals accounted for 49.2% and for 49.3% of NDG and DG, respectively.  
48 In response to the question about religion, the majority in both groups answered that they were Christian (72.3%  
49 in NDG; 64.2% in DG), followed by atheists (24.1% in NDG; 28.9% in DG), with a significant difference in  
50 distribution ( $p = 0.02$ ), as reported in Table 1.

51 **Table 1.** Respondents' sociodemographic characteristics  
52 Please put Table 1 here.

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11 Due to the size of the table, questionnaire items, response frequencies and percentages, and comparisons among  
12 groups are represented in Tables 2 and 3.

### 13 **General knowledge of donation process**

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15 Compared with DG, NDG respondents knew less about the health problems that generate the need for compatible  
16 donors in Italy (75.6% in DG vs 48.3% in NDG,  $p<0.0001$ ); NDG also knew significantly less frequently about  
17 the existence of the IBMDR (85.2% vs 96.0%,  $p<0.0001$ ) and about the activities of volunteer associations  
18 promoting donation (90.2% vs 51.7%,  $p<0.0001$ ). NDG respondents also knew less about CB donation (87.8% vs  
19 83.4%,  $p=0.03$ ) and about the activities of CB banks (67.1% vs 57.4%,  $p<0.0001$ ). Interestingly, 36.5% of NDG  
20 respondents were found to be more willing to donate if they could choose the recipient. Table 1 shows other  
21 significant differences between the groups.

22 As reported by the DG, the main reasons leading to IBMDR enrollment were the desire to do something for others  
23 (82.2%), the awareness raised by volunteer associations (38.5%), the awareness raised by hospital facilities such  
24 as transfusion services (26.8%), having a relative/friend with cancer (19.9%), and other reasons detailed in figure  
25 1. Figure 2 illustrates the main reasons for not enrolling in IBMDR as reported by NDG; major findings include  
26 the lack of knowledge (36.0%) and low level of concern about the problem (36.0%).

### 26 **Fig. 1** Reasons for enrolling in the IBMDR

27 Please put figure 1 here.

### 28 **Fig. 2** Reasons for not enrolling in the IBMDR

29 Please put figure 2 here.

### 30 **Knowledge of stem cell role and function**

31  
32 DG demonstrated greater knowledge than did NDG of SC characteristics such as duplication and self-renewal  
33 (79.3% vs. 66.3%,  $p<0.0001$ ) and differentiation and maturation activities (72.7% vs. 59.6%,  $p<0.0001$ ). This  
34 trend was confirmed responding to more specific questions on SC functions, including red cells (75.3% vs 62.5%  
35 of correct answers,  $p<0.001$ ), white cells (79.4% vs 59.6%,  $p<0.001$ ) and platelet production (71.1% vs 60.0%;  
36  $p<0.001$ ). DG had greater knowledge of where the SCs can be harvested for or not, thus SC can be collected from  
37 the BM for 93.1% of respondents in DG versus 84.5% in NDG ( $p<0.001$ ). Excluding that on UCB donation  
38 ( $p=0.06$ ), significant differences with the same direction were found for all questions of this section. Look at table  
39 2 for more details.

### 40 **Knowledge of stem cell collection methods**

41  
42 NDG had limited familiarity with collection sources compared to DG. For instance, NDG demonstrated less  
43 knowledge of SC harvesting methods such as BM explant through repeated punctures of the iliac crests (67.7%  
44 vs. 86.5%,  $p<0.0001$ ), stem cell harvesting through apheresis (62.1% vs. 83.8%,  $p<0.0001$ ), and collection from  
45 the umbilical cord vessels (61.3% vs. 70.5%,  $p=0.004$ ). Other differences between the groups are presented in  
46 Table 2, items 4.0–4.5.

### 47 **Table 2** Respondents' knowledge of stem cell donation.

48 Please put Table 2 here

### 49 **Respondents' beliefs about stem cell donation**

50  
51 Awareness of the safety of SC collection methods (PBSC collection, BM harvesting, and CB collection) was  
52 greater among DG than among NDG; 92.3% of DG and 85.5% of NDG ( $p<0.0001$ ) believed that CB collection is  
53 a safe procedure for both the mother and the baby, and 89.1% of DG and 77.2% of NDG ( $p<0.0001$ ) believed that  
54 the PBSC collection procedure was safe. Both groups had a little more fear of BM harvesting as a procedure (Table  
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3. Items 4.0–4.5).

**Respondents’ feelings about stem cell donation**

The emotional levels experienced when thinking about donation were explored by asking all respondents to rate their feelings using a 4-point Likert scale (not at all, a little, moderately, a lot) when considering a set of 22 human emotions applicable to the donation setting. The results revealed differences between the 2 groups: DG experienced less fear ( $p=0.02$ ), hesitation ( $p<0.001$ ), feeling of fragility ( $p=0.01$ ), uncertainty ( $p<0.001$ ), vulnerability ( $p=0.04$ ), refusal ( $p<0.001$ ), and perplexity ( $p<0.001$ ) and greater exaltation ( $p<0.001$ ), curiosity ( $p=0.007$ ), enthusiasm ( $p<0.001$ ), and sense of solidarity ( $p<0.001$ ). Table 3 reports a complete list of the results.

**Opinions and values**

This section of the questionnaire used a 5-point Likert scale for each question, with the extremes being “Extremely Disagree” and “Strongly Agree”. No difference between the groups was found regarding their agreement that SC should be used in clinical trials and research ( $p=0.14$ ). The groups had similar opinions on the need to have more information on donation facilities ( $p=0.08$ ) and on the usefulness of receiving information on transplant outcome after donation ( $p=0.32$ ). Interestingly, the whole sample agreed that CB should be collected by default (81.4% of DG and 79.0% of NDG,  $p=0.37$ ). A high variability in opinions was found regarding whether the identities of the donor and recipient should be shared, with no differences between groups ( $p=0.79$ ). Significant differences in the distribution of answers between the groups were seen. A high percent of respondents in both groups agreed that HSCT is a lifesaving treatment (92.6% of DG and 91.9% of NDG,  $p<0.001$ ), and that SC donation should be considered by everyone who is eligible (92.3% in DG and 88.3% in NDG,  $p<0.001$ ). According to 55.7% of DG and 45.2% of NDG ( $p=0.04$ ), IBMDR enrollment should be mandatory for everyone who is eligible.

**Information and education needs**

This section of the questionnaire investigated the willingness of participants to receive more information. In NDG, 66% of the sample did not consider themselves informed enough about donation, compared 33.1% of DG ( $p<0.001$ ). Interestingly, both groups reported they were interested in receiving further information and education (82.2% and 86.4% of DG and NDG, respectively), with significantly more in NDG ( $p=0.04$ ). However, even with high percentages in both groups (82.2% of DG and 75.5% of NDG), NDG appeared to be less interested in participating in awareness initiatives on SC donation.

**Table 3.** Beliefs, feelings, values, and education needs  
Please put Table 3 here

**Probability of becoming an SC Donor**

A complex network of reasons and attitudes influencing the decision to enroll in the IBMDR emerged; key findings were the lack of information and feelings such as fear and lack of trust in the donation process. In contrast, respondents enrolled in IBMDR expressed their deep willingness to contribute to the wellbeing of others, with various factors supporting their choice. However, more and better knowledge appeared to be positively associated with the decision of whether to donate. The questionnaire findings were then used for ML of 6 classifiers to predict the probability of enrolling in the IBMDR; the result obtained was an average accuracy (AUC) of 76.7% ( $\pm 5.4$ ). Figure 3 illustrates the ROC curves generated by each classifier.

**Fig. 3** ROC curves describing performance of each classifier.  
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**DISCUSSION**

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To our knowledge, this is the first study to thoroughly assess the knowledge, information, feelings, opinions, values, and beliefs of the Italian population regarding SC donation. To identify specific areas requiring targeted interventions to increase donation, the sample of 1518 individuals was divided into 2 groups retrospectively: NDG (participants never enrolled in the IBMDR) and DG (participants currently or formerly enrolled in the IBMDR at the time of data collection).

In line with previous published papers [20–22], 24.8% of the sample was made up of individuals who were enrolled in the IBMDR. However, considering that online survey adherence might be affected by personal attitudes and experience and that a significant portion of the population might be not aware of online surveys, this percentage may be overestimated, which emphasizes the need for additional efforts to increase awareness of SC donation among the general population. A detailed response analysis revealed, especially among NDG respondents, a lack of knowledge and a limited awareness of SC donation, for example, no knowledge of the activity of volunteer associations throughout the country. The most important knowledge gaps that emerged concerned more specific topics and technical information, such as the different SC sources and collection methods as well as on their role and functions. We are aware that this information may not be included in what institutional awareness campaigns normally provide; however, in light of our findings, it is worth reflecting on whether awareness campaigns should provide more detailed information on the SC donation process and procedures to help potential donors take this decision.

Of particular interest were the feelings expressed by the NDG when thinking about donation; they showed significantly higher levels of fear, uncertainty, perplexity, vulnerability, and refusal. Some of these feelings have already been recognized to negatively impact donation intention [23].

The results of the "Beliefs" section are comforting in terms of their prevalence in both groups, although they were significantly worse in NDG. This suggests that the lower levels of information, knowledge, and awareness in our sample were associated with a higher inclination to formulate incorrect beliefs. Some negative beliefs were generated by misunderstandings and by a lack of knowledge. For example, many people in Italy confuse "midollo osseo" (bone marrow) with "midollo spinale" (spinal cord) due to the assonance of the respective terms in Italian and the greater familiarity with the consequence of spinal cord lesions than with those caused by bone marrow issues. The fear of possible negative health consequences such as paralysis or other neurological disorders may also be due to issues at the local level. Instead, NDG's high level of fear of developing a blood disorder could be due to incorrect information and/or misinterpretation of the risk factors of disease development [24]. Respondents in DG experienced higher levels of emotions such as solidarity, enthusiasm, curiosity, and exaltation at the thought of possibly donating, even though they had not yet had this experience. This finding suggests that the decision to enroll in the IBMDR may lead to positive life experiences.

The majority of respondents identified "lack of information" and "concerns about their health" as the main reasons for deciding not to become a donor [23]. These results align with the findings of other studies [20,25]. It is interesting to note that the fear of pain could negatively influence the attitude of subjects towards SC donation, as reported by other authors [21,25]. However, considering the general lack of knowledge on SC collection methods, potential donors may be not aware on their characteristics: e.g.: that certain procedures, such as umbilical CB donation is harmless and painless, while and PBSC collection requires, are painless minimally painful procedures such as vascular access positioning and subcutaneous administration of growing factors. Indeed, CB and PBSC collection are well-established, safe nonsurgical procedures to collect blood-forming cells for bone marrow transplants [9]. Furthermore, although both BM and PBSC collection are recognized as safe procedures [26], the need to harvest BM surgically and to administer mobilization drugs before PBSC donation may be important procedure-related factors that cause an individual to be reluctant about becoming a donor and thus about enrolling in the registry [24,27].

Furthermore, it is noteworthy that almost all respondents claimed they agreed or strongly agreed with the importance of HSCT as a lifesaving therapy, suggesting that awareness of the effectiveness of donation as a means of treatment may be a powerful motivational driver. This indicates that developing campaigns that increase awareness that SC donation is crucial to saving lives and that thus leverage solidarity may be opportune. Of note were the respondents of the 2 groups who stated that they would be more inclined to donate if they had the opportunity to know who the recipient was. The desire importance of knowing the health status of the recipient also emerged as a motivational factor in both groups. This preference revealed a deeper and more specific

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11 emotional involvement than the general motivation that leads to donation. These is particular groups could therefore be a key targets for educational campaigns that emphasize the possibility of having a direct role in the lifesaving treatment of hematology patients without having information about the recipient. The protection of both patient and donor privacy is strictly regulated by laws as a mandatory conditions to warrant the principles of anonymity, voluntariness and gratuity. The equity and the transparency of the entire donation process as well as of the National registry activities are based on these issues. Thus, our findings highlighted that these topics did not well understood by the participants, and specific educational campaigns should be organized with the aim of improving their understanding among potential donors and becoming the theme of privacy protection a considerable stimulus to donation instead an obstacle.

~~The importance of knowing the health status of the recipient also emerged as a motivational factor in both groups. Although the law does not allow a donor to know who the recipient is, the limited information that a donation center can provide may be a compromise between regulation compliance and satisfying a donor's desire for emotional connection. This suggests that transparency regarding the process and its positive impact on the lives of those involved could be a considerable stimulus to encourage donation.~~

The ML results suggest that a higher level of knowledge and information about SC donation is associated with a greater likelihood of enrolling in the IBMDR. This implies that a deeper understanding of the processes involved in donation and of the benefits to recipients as well as assurances to donors all play a key role in encouraging donation. These results underscore the importance of promoting educational interventions to shape opinions and decisions regarding donation. In light of this, as healthcare professionals play a fundamental role in promoting awareness about donation, involving them in raising public awareness and increasing participation in education campaigns may be crucial [3,25,28]. The literature also highlights that including lectures on the topic in university curricula may be associated with an increased willingness among college students to donate [29,30]. Indeed, it has been observed that integrating specific content in degree programs provides students with the opportunity to learn more about the issues related to donation, thereby raising their awareness and promoting positive attitudes towards this form of medical solidarity.

Despite the study's efforts to use a widely accessible communication channel to engage a representative sample of the population and to thus obtain generalizable results, it is important to carefully consider the intrinsic limitations of the study, including the limited size of the sample. The snowballing procedure of the online questionnaire survey was performed starting by the networks of a hematology-related society (GITMO), this might led to an unavoidable selection bias. The high participation to the survey of healthcare professionals can confirm this limit. In addition, Additionally, there is the possibility that respondents' answers were influenced by social perception rather than expressing their sincere opinions. This may have led to truthful answers but not necessarily resulting in action. Another limitation to consider is the nature of the questions posed; result distortion may have occurred as respondents may have exaggerated or downplayed their experiences related to the examined theme. Furthermore, the data presented comes from a specific socio-cultural context (Italy), and different results might appear if similar analyses were conducted in other countries. Additionally, our findings could produce different changes in donor recruitment strategies between countries. Finally, this survey was designed by focusing on the Italian donor shortage and what the participants knew, felt and thought on SC donation. The authors assessed carefully the potential informative and educational value of the research tool before its diffusion. Some fundamental themes of the donation process such as donation-associated adverse events and the donor's privacy protection had approached with caution to avoid misunderstanding that could worsen the situation, also taking into account that these topics are strictly regulated by National and International laws and guidelines.

## CONCLUSIONS

The study findings provide a clear indication of the crucial role that increased knowledge plays in shaping attitudes toward SC donation.

The identified lack of awareness, especially among NDG participants, underscores the imperative need to implement targeted initiatives to enhance health education and to raise public awareness about SC donation, confirmed by the correlation between a deeper understanding of the donation process and a greater inclination to

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enroll in the IBMDR.

Information campaigns should be directed both to non-donors, emphasizing donation procedures and methods, and to current donors to reinforce their knowledge and awareness of the importance of their participation; this strategy can help overcome psychological barriers and concerns associated with donation. In this context, the active involvement of healthcare professionals and the incorporation of specific content into academic curricula could play a significant role in increasing willingness to donate. Implementation of these and other initiatives should be encouraged to reach a broader audience and to foster a culture of awareness about SC donation, from the early stages of higher education on.

Overall, the conclusions underscore the need for a strategic commitment at the social, educational, and informational levels to address existing gaps in the understanding of SC donation. Only through an integrated and multidimensional approach will it be possible to increase awareness, promote active participation, and cultivate a culture of solidarity toward SC donation in Italy.

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### **Conflicts of interest/Competing interests**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### **Ethics approval**

The study was approved by the Ethics Committee of the University of Bologna (Protocol No. 0026388 dated 02/02/2023).

### **Consent to participate**

Information on ethical management was put at the beginning of the online questionnaire. The survey was completely anonymous, and both the consent to participate and data utilization were considered as acquired after questionnaire completion and submission.

### **Consent for publication**

Not Applicable

### **Availability of data and material**

The data that support the findings of this study are available from the last author (Stefano Botti, email stefano.botti@ausl.re.it) upon reasonable request.

### **Code availability**

Not Applicable

### **Authors' contributions**

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11 Investigation: Chiara Ianne; Visualization: Luana Conte; Validation: Luana Conte, Roberto Lupo; Writing -  
12 original draft preparation: Luana Conte, Massimo Martino; Writing - review and editing: Stefano Botti, Simonetta  
13 Pupella; Funding acquisition: N/A; Resources: Luana Conte, Elsa Vitale; Supervision: Giorgio De Nunzio, Donato  
14 Cascio, Fabio Ciceri.

#### 15 **Authors' Agreement**

16 We confirm that the submitted version of the manuscript has been read and approved by all named authors and  
17 that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that  
18 the order of authors listed in the manuscript has been approved by all of us.

#### 20 **REFERENCES**

- 22 1. Hatzimichael E, Tuthill M. Hematopoietic stem cell transplantation. *Stem Cells Cloning* [Internet]. 2010;3:105–  
23 17. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24198516>
- 24 2. Janowiak-Majeranowska A, Lebedziński F, Majeranowski A. Bone marrow donation in Poland: 2021 update,  
25 and the impact of the coronavirus disease 2019 pandemic on haematopoietic stem cell transplantation. *Clin Ethics*  
26 [Internet]. 2022;17:22–31. Available from: <http://journals.sagepub.com/doi/10.1177/14777509211036643>
- 27 3. Toraldo DM, Toraldo S, Conte L. The Clinical Use of Stem Cell Research in Chronic Obstructive Pulmonary  
28 Disease: A Critical Analysis of Current Policies. *J Clin Med Res* [Internet]. 2018;10:671–8. Available from:  
29 <http://www.ncbi.nlm.nih.gov/pubmed/30116436>
- 30 4. Jo T, Arai Y, Kondo T, Mizuno S, Hirabayashi S, Inamoto Y, et al. Advantages of peripheral blood stem cells  
31 from unrelated donors versus bone marrow transplants in outcomes of adult acute myeloid leukemia patients.  
32 *Cytotherapy* [Internet]. 2022;24:1013–25. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/35729020>
- 33 5. Tiercy J-M, Claas F. Impact of HLA Diversity on Donor Selection in Organ and Stem Cell Transplantation.  
34 *Hum Hered* [Internet]. 2013;76:178–86. Available from: <https://karger.com/HHE/article/doi/10.1159/000358798>
- 35 6. Eurostat. Stem cell transplantation in the EU [Internet]. 2020 [cited 2023 Nov 23]. Available from:  
36 <https://ec.europa.eu/eurostat/web/products-eurostat-news/-/edn-20201010-1>
- 37 7. GITMO. Transplant activity [Internet]. 2021 [cited 2023 Nov 23]. Available from:  
38 [https://www.gitmo.it/storage/gitmo/article/pdf/65/743-Transplant activity 2019 e 2020.pdf](https://www.gitmo.it/storage/gitmo/article/pdf/65/743-Transplant%20activity%202019%20e%202020.pdf)
- 39 8. Ente Ospedaliero Ospedali Galliera. Registro Italiano Donatori di Midollo Osseo [Internet]. 2022 [cited 2024  
40 Jan 12]. Available from: [https://www.ibmdr.galliera.it/ibmdr/info/informazioni-per-i-donatori/la-donazione-di-](https://www.ibmdr.galliera.it/ibmdr/info/informazioni-per-i-donatori/la-donazione-di-cellule-staminali-emopoietiche)  
41 [cellule-staminali-emopoietiche](https://www.ibmdr.galliera.it/ibmdr/info/informazioni-per-i-donatori/la-donazione-di-cellule-staminali-emopoietiche)
- 42 9. Italian Ministry of Health. Cellule Staminali Emopoietiche [Internet]. 2018 [cited 2024 Jan 11]. Available  
43 from: [https://www.salute.gov.it/portale/p5\\_1\\_2.jsp?id=210&lingua=italiano#:~:text=Come avviene la](https://www.salute.gov.it/portale/p5_1_2.jsp?id=210&lingua=italiano#:~:text=Come%20avviene%20la%20donazione%3F,e%20dura%20circa%20un%20ora)  
44 [donazione%3F,e dura circa un'ora](https://www.salute.gov.it/portale/p5_1_2.jsp?id=210&lingua=italiano#:~:text=Come%20avviene%20la%20donazione%3F,e%20dura%20circa%20un%20ora)
- 45 10. El-Kadiry AE-H, Rafei M, Shammaa R. Cell Therapy: Types, Regulation, and Clinical Benefits. *Front Med*  
46 [Internet]. 2021;8:756029. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/34881261>
- 47 11. Russo D, Polverelli N, Malagola M, Farina M, Leoni A, Bernardi S, et al. Changes in Stem Cell Transplant  
48 activity and procedures during SARS-CoV2 pandemic in Italy: an Italian Bone Marrow Transplant Group  
49 (GITMO) nationwide analysis (TransCOVID-19 Survey). *Bone Marrow Transplant* [Internet]. 2021;56:2272–5.  
50 Available from: <https://www.nature.com/articles/s41409-021-01287-w>
- 51 12. Passweg JR, Baldomero H, Chabannon C, Corbacioglu S, de la Cámara R, Dolstra H, et al. Impact of the  
52 SARS-CoV-2 pandemic on hematopoietic cell transplantation and cellular therapies in Europe 2020: a report from  
53 the EBMT activity survey. *Bone Marrow Transplant* [Internet]. 2022;57:742–52. Available from:  
54 <https://www.nature.com/articles/s41409-022-01604-x>
- 55 13. Bordat J, Maury S, Leclerc M. Allogeneic hematopoietic stem cell transplantation in the COVID-19 era. *Front*  
56 *Immunol* [Internet]. 2023;14. Available from:  
57 <https://www.frontiersin.org/articles/10.3389/fimmu.2023.1100468/full>
- 58 14. Perlow JH. Patients' knowledge of umbilical cord blood banking. *J Reprod Med* [Internet]. 2006;51:642–8.  
59 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/16967635>
- 60 15. Karagiorgou LZ, Pantazopoulou M-NP, Mainas NC, Beloukas AI, Kriebardis AG. Knowledge about umbilical

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11 cord blood banking among Greek citizens. *Blood Transfus* [Internet]. 2014;12 Suppl 1:s353-60. Available from:  
12 <http://www.ncbi.nlm.nih.gov/pubmed/24120604>  
13 16. Matijević R, Erjavec K. Knowledge and attitudes among pregnant women and maternity staff about umbilical  
14 cord blood banking. *Transfus Med* [Internet]. 2016;26:462–6. Available from:  
15 <http://www.ncbi.nlm.nih.gov/pubmed/27714885>  
16 17. Jordens CFC, Kerridge IH, Stewart CL, O'Brien TA, Samuel G, Porter M, et al. Knowledge, beliefs, and  
17 decisions of pregnant Australian women concerning donation and storage of umbilical cord blood: a population-  
18 based survey. *Birth* [Internet]. 2014;41:360–6. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/24988997>  
19 18. Aurelio MT, Aniasi A, Haworth SE, Colombo MB, Dimonopoli T, Mocellin MC, et al. Analysis of the  
20 motivation for hematopoietic stem cell donation. *Transplant Proc* [Internet]. 2011;43:981–4. Available from:  
21 <http://www.ncbi.nlm.nih.gov/pubmed/21620031>  
22 19. Rennert W, Cormier K, Sprott S. The Donor – Recipient Weight Ratio is a Reliable Marker for Cell Yield in  
23 Hematopoietic Stem Cell Donations. *OBM Transplant* [Internet]. 2021;5:1–1. Available from:  
24 <http://www.lidsen.com/journals/transplantation/transplantation-05-04-156>  
25 20. Sikora A, Wiorkowski K, Szara P, Drabko K. Knowledge and attitude of Lublin universities students' toward  
26 the opportunity of becoming unrelated bone marrow donor. *Folia Med Cracov* [Internet]. 2014;54:27–33.  
27 Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25648307>  
28 21. Narayanan P, Wolanskyj A, Ehlers SL, Litzow MR, Patnaik MS, Hogan WJ, et al. Medical Students'  
29 Knowledge, Familiarity, and Attitudes towards Hematopoietic Stem Cell Donation. *Biol Blood Marrow Transplant*  
30 [Internet]. 2016;22:1710–6. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1083879116301495>  
31 22. Zaini R, Al-Thagafi A. Medical Students' knowledge, attitude towards hematopoietic stem cell transplantation  
32 and donation behaviour at Taif university. *Heal Educ Care* [Internet]. 2020;5. Available from:  
33 [https://www.oatext.com/medical-students-knowledge-attitude-towards-hematopoietic-stem-cell-transplantation-](https://www.oatext.com/medical-students-knowledge-attitude-towards-hematopoietic-stem-cell-transplantation-and-donation-behaviour-at-taif-university.php#gsc.tab=0)  
34 [and-donation-behaviour-at-taif-university.php#gsc.tab=0](https://www.oatext.com/medical-students-knowledge-attitude-towards-hematopoietic-stem-cell-transplantation-and-donation-behaviour-at-taif-university.php#gsc.tab=0)  
35 23. AlSubaie RS, Alhamaid YA, Alali RS, Alaha MA, Aldalbahi AA, Ibrahim Ali S. Factors Influencing  
36 Individuals' Decision-Making Regarding Hematopoietic Stem Cell Donation: A Cross-Sectional Study in Saudi  
37 Arabia. *Cureus* [Internet]. 2023; Available from: [https://www.cureus.com/articles/186813-factors-influencing-](https://www.cureus.com/articles/186813-factors-influencing-individuals-decision-making-regarding-hematopoietic-stem-cell-donation-a-cross-sectional-study-in-saudi-arabia)  
38 [individuals-decision-making-regarding-hematopoietic-stem-cell-donation-a-cross-sectional-study-in-saudi-arabia](https://www.cureus.com/articles/186813-factors-influencing-individuals-decision-making-regarding-hematopoietic-stem-cell-donation-a-cross-sectional-study-in-saudi-arabia)  
39 24. Switzer G, Goycoolea J, Dew M, Graeff E, Hegland J. Donating stimulated peripheral blood stem cells vs bone  
40 marrow: do donors experience the procedures differently? *Bone Marrow Transplant* [Internet]. 2001;27:917–23.  
41 Available from: <https://www.nature.com/articles/1703011>  
42 25. Cavicchi I, Regano D. L'attitudine alla donazione di cellule staminali ematopoietiche da sangue periferico:  
43 uno studio cross sectional sugli studenti di infermieristica. *Nurs Sci*. 2023;60:e46–54.  
44 26. Bosi A, Bartolozzi B. Safety of bone marrow stem cell donation: a review. *Transplant Proc* [Internet].  
45 2010;42:2192–4. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/20692441>  
46 27. Bredeson C, Leger C, Couban S, Simpson D, Huebsch L, Walker I, et al. An evaluation of the donor experience  
47 in the canadian multicenter randomized trial of bone marrow versus peripheral blood allografting. *Biol Blood*  
48 *Marrow Transplant* [Internet]. 2004;10:405–14. Available from:  
49 <https://linkinghub.elsevier.com/retrieve/pii/S1083879104000874>  
50 28. McGlade D, Pierscionek B. Can education alter attitudes, behaviour and knowledge about organ donation? A  
51 pretest-post-test study. *BMJ Open* [Internet]. 2013;3:e003961. Available from:  
52 <http://www.ncbi.nlm.nih.gov/pubmed/24381257>  
53 29. Ruta F, Delli Poggi A, Ferrara P, Lusignani M. Analisi degli atteggiamenti, delle conoscenze e della  
54 disponibilità a donare gli organi degli studenti di Infermieristica. *Prof Inferm*. 2020;72:247–52.  
55 30. Hazzazi AA, Ageeli MH, Alfaqih AM, Zakri AK, Elmakki EE. Knowledge and attitude towards hematopoietic  
56 stem cell transplantation among medical students at Jazan University, Saudi Arabia. *Saudi Med J* [Internet].  
57 2019;40:1045–51. Available from: <https://smj.org.sa/lookup/doi/10.15537/smj.2019.10.24294>  
58  
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**Table 1.** Respondents' sociodemographic characteristics.

Sociodemographic characteristics	NDG (n=1141) N (%)	DG (n=377) N (%)	Z value	P value
<b>Age (y)</b>				
Mean ( $\pm$ SD)	38.15 ( $\pm$ 13.53)	36.02 ( $\pm$ 12.61)	2.5305	<b>0.01</b>
Range	16-79	18-89		
<b>Sex</b>				
Female	855 (75.0)	287 (76.1)	0.4650	0.64
Male	286 (25.0)	90 (23.9)		
<b>Geographic Area</b>				
North	376 (33.0)	214 (56.8)	4.4256	<b>&lt;0.001</b>
Center	175 (15.3)	40 (10.6)		
South/Islands	590 (51.7)	123 (32.6)		
<b>Marital status</b>				
Married	475 (41.7)	143 (37.9)		
Not married	585 (51.3)	214 (56.8)	-0.7715	0.44
Divorced	72 (6.3)	20 (5.3)		
Widowed	9 (0.7)	0 (0.0)		
<b>Education level</b>				
Advanced degree	169 (14.8)	57 (15.1)		
University degree	449 (39.4)	159 (42.2)		
High school diploma	445 (39.0)	138 (36.6)	0.8257	0.40
Middle school	70 (6.2)	21 (5.6)		
Elementary school	7 (0.6)	2 (0.5)		
None	1 (0.0)	0 (0.0)		
<b>Employment status</b>				
Public employee	369 (32.3)	95 (25.2)		
Private employee	269 (23.5)	128 (34.0)		
Housewife	48 (4.2)	9 (2.4)		
Student	252 (22.1)	78 (20.7)	1.4069	0.15
Retired	52 (4.6)	11 (2.9)		
Self-employed	107 (9.5)	42 (11.1)		
Unemployed	44 (3.8)	14 (3.7)		
<b>Healthcare professional</b>				
No	580 (50.8)	191 (50.7)	-0.0570	0.95
Yes	561 (49.2)	186 (49.3)		
<b>Religion</b>				
Christianity/Judaism	824 (72.3)	242 (64.2)		
Buddhism	8 (0.7)	8 (2.2)		
Asian religions*	2 (0.2)	2 (0.5)		
Islam	5 (0.4)	2 (0.5)	2.3038	<b>0.02</b>
Agnosticism	20 (1.7)	10 (2.7)		
Atheism	275 (24.1)	109 (28.9)		
Prefer not to answer	1 (0.1)	2 (0.5)		
Other	6 (0.5)	2 (0.5)		

**Legend:** NDG = Non-Donor Group; DG = Donor Group.

Significant differences are reported in bold.

\*Asian religions = Chinese religions (Traditional Chinese, Confucianism, Taoism, etc.), Indian religions (Hinduism, Sikhism, Jainism, etc.), Shintoism, Caodaism.

**Table 2.** Respondents' knowledge of stem cell donation.

N°	Questions	Items	NDG (n=1141) N (%)	DG (n=377) N (%)	Z-score	p value
<b>1.0</b>	<b>General Knowledge of donation process</b>					
1.1	Have you ever had a close family member or friend who needed to undergo a HSCT?	No Yes	940 (82.4) 201 (17.6)	270 (71.6) 107 (28.4)	-4.5048	<0.001
1.2	Are you aware of the existence of an Italian registry of bone marrow donors?	No Yes	169 (14.8) 972 (85.2)	15 (4.0) 362 (96.0)	-5.5854	<0.001
1.3	Are you aware that there are various donor centers throughout Italy where it is possible to register as a SC donor?	No Yes	364 (31.9) 777 (68.1)	28 (7.4) 349 (92.6)	-9.4104	<0.001
1.4	Are you aware that nonfamilial donations are anonymous, voluntary, and unremunerated?	No Yes	257 (22.5) 884 (77.5)	13 (3.4) 364 (96.6)	-8.3945	<0.001
1.5	Are you aware that donation can occur through BM or PBSC collection following mobilization with hematopoietic growth factor?	No Yes	403 (35.3) 737 (64.7)	27 (7.2) 352 (92.8)	-10.7294	<0.001
1.6	Are you aware that in Italy, over 2000 patients every year need to undergo MUD HSCT as the only life-saving therapy available?	No Yes	590 (51.7) 551 (48.3)	92 (24.4) 285 (75.6)	-9.2377	<0.001
1.7	Are you aware that all mothers can donate their UCB after childbirth?	No Yes	190 (16.6) 951 (83.4)	46 (12.2) 331 (87.8)	-2.0668	0.03
1.8	Are you aware that in Italy, CB units donated for HSCT purposes are stored in public CB banks?	No Yes	516 (45.2) 625 (54.8)	124 (32.9) 253 (67.1)	-4.2025	<0.001
1.9	Would you be more willing to donate HSC if you could choose the recipient?	No Yes	725 (63.5) 416 (36.5)	311 (82.5) 66 (17.5)	6.8512	<0.001
1.10	Do you know if there are volunteer associations aimed to raise awareness about SC donation?	No Yes	551 (48.3) 590 (51.7)	37 (9.8) 340 (90.2)	-13.2914	<0.001
<b>2.0</b>	<b>Knowledge of stem cells' role and function</b>					
2.1	HSC are capable of duplicating and self-renewing.	No Yes I don't know	46 (4.0) 756 (66.3) 339 (29.7)	13 (3.5) 299 (79.3) 65 (17.2)	-4.6161	<0.001
2.2	Are HSC specialized?	No Yes I don't know	388 (34.0) 302 (26.5) 451 (39.5)	179 (47.5) 97 (25.7) 101 (26.8)	3.2270	0.001
2.3	HSC can give rise to various types of cells through processes of differentiation and maturation.	No Yes I don't know	31 (2.7) 680 (59.6) 430 (37.7)	12 (3.2) 274 (72.7) 91 (24.1)	-4.3331	<0.001
2.4	What do HSC do? a – produce energy	No Yes I don't know	432 (37.9) 129 (11.3) 580 (50.8)	197 (52.2) 43 (11.4) 137 (36.4)	4.0839	<0.001
2.5	b - produce serum (the liquid part of the blood)	No Yes I don't know	301 (26.4) 306 (26.8) 534 (46.8)	131 (34.7) 119 (31.6) 127 (33.7)	0.8204	0.41
2.6	c - produce red blood cells	No Yes I don't know	36 (3.1) 713 (62.5) 392 (34.4)	13 (3.5) 284 (75.3) 80 (21.2)	-4.3362	<0.001
2.7	d - produce platelets	No Yes I don't know	48 (4.2) 685 (60.0) 408 (35.8)	18 (4.8) 268 (71.1) 91 (24.1)	-3.5664	<0.001

2.8	e - produce proteins	No Yes I don't know	325 (28.5) 243 (21.3) 573 (50.2)	134 (35.5) 87 (23.1) 156 (41.4)	1.3531	0.17
2.9	f - produce white blood cells	No Yes I don't know	49 (4.3) 680 (59.6) 412 (36.1)	11 (2.9) 288 (76.4) 78 (20.7)	-5.7649	<0.001
2.10	From where can HSC be harvested in large quantities? a - sperm/eggs	No Yes I don't know	660 (57.8) 32 (2.8) 449 (39.4)	292 (77.5) 10 (2.6) 75 (19.9)	6.6049	<0.001
2.11	b - human embryos	No Yes I don't know	370 (32.4) 293 (25.7) 478 (41.9)	211 (56.0) 66 (17.5) 100 (26.5)	7.1701	<0.001
2.12	c - bone marrow	No Yes I don't know	35 (3.1) 964 (84.5) 142 (12.4)	10 (2.6) 351 (93.1) 16 (4.3)	-4.1536	<0.001
2.13	d - spinal cord	No Yes I don't know	394 (34.5) 434 (38.1) 313 (27.4)	225 (59.7) 89 (23.6) 63 (16.7)	7.7945	<0.001
2.14	e - blood	No Yes I don't know	100 (8.8) 777 (68.1) 264 (23.1)	45 (11.9) 293 (77.7) 39 (10.4)	-2.8271	0.004
2.15	f - urine	No Yes I don't know	763 (66.9) 8 (0.7) 370 (32.4)	327 (86.7) 2 (0.6) 48 (12.7)	7.3896	<0.001
2.16	g - saliva	No Yes I don't know	738 (64.7) 17 (1.5) 386 (33.8)	311 (82.5) 10 (2.6) 56 (14.9)	6.2179	<0.001
2.17	h - vertebral column	No Yes I don't know	522 (45.7) 221 (19.4) 398 (34.9)	259 (68.7) 50 (13.3) 68 (18.0)	6.9837	<0.001
2.18	i - umbilical cord	No Yes I don't know	17 (1.5) 979 (85.8) 145 (12.7)	16 (4.3) 339 (89.9) 22 (5.8)	-1.8214	0.06
<b>3.0</b>	<b>Knowledge of stem cell collection methods</b>					
3.1	The collection of hematopoietic stem cells can occur: a - by harvesting BM through repeated punctures of the iliac crests (pelvic bones)	No Yes I don't know	65 (5.7) 773 (67.7) 303 (26.6)	20 (5.3) 326 (86.5) 31 (8.2)	-6.6384	<0.001
3.2	b - from peripheral blood through an apheresis machine (such as in platelet donation)	No Yes I don't know	72 (6.3) 709 (62.1) 360 (31.6)	28 (7.4) 316 (83.8) 33 (8.8)	-7.0589	<0.001
3.3	c - by puncturing the blood vessels (veins) of the umbilical cord after the baby's birth	No Yes I don't know	63 (5.5) 699 (61.3) 379 (33.2)	25 (6.7) 266 (70.5) 86 (22.8)	-2.8805	0.004
3.4	To collect HSC from peripheral blood, does the donor need to take a medication that stimulates the cells to increase in number and exit the bone marrow?	No Yes I don't know	231 (20.3) 361 (31.6) 549 (48.1)	59 (15.6) 255 (67.7) 63 (16.7)	-10.0076	<0.001
3.5	Does the collection of SC from BM require the administration of anesthesia (spinal or general)?	No Yes I don't know	223 (19.5) 497 (43.6) 421 (36.9)	66 (17.5) 256 (67.9) 55 (14.6)	-6.5942	<0.001

**Legend:** NDG = Non-Donor Group; DG = Donor Group; HSCT = Hematopoietic Stem Cell Transplantation; SC = Stem Cell; BM = Bone Marrow; PBSC = Peripheral Blood Stem Cell; MUD = Matched Unrelated Donor; UCB = Umbilical Cord Blood; CB = Cord Blood; HSC = Hematopoietic Stem Cell.  
**Significant differences are reported in bold.**

**Table 3.** Beliefs, feelings, values, and education needs.

N°	Questions	Items	NDG (n=1141) N (%)	DG (n=377) N (%)	Z-score	p value
<b>4.0</b>	<b>Respondents' beliefs about stem cell donation</b>					
4.1	UCB collection causes pain for the mother and/or the baby.	No Yes I don't know	985 (86.3) 19 (1.7) 137 (12.0)	350 (92.9) 5 (1.3) 22 (5.8)	3.3294	<0.001
4.2	UCB collection poses risks for the mother and/or the baby.	No Yes I don't know	976 (85.5) 20 (1.8) 145 (12.7)	348 (92.3) 5 (1.3) 24 (6.4)	3.3793	<0.001
4.3	PBSC collection poses risks of developing blood diseases.	No Yes I don't know	881 (77.2) 38 (3.3) 222 (19.5)	336 (89.1) 10 (2.7) 31 (8.2)	4.9090	<0.001
4.4	BM explant carries the risk of paralysis.	No Yes I don't know	789 (69.2) 63 (5.5) 289 (25.3)	319 (84.6) 17 (4.5) 41 (10.9)	5.6122	<0.001
4.5	BM explant results in visible scars.	No Yes I don't know	792 (69.4) 48 (4.2) 301 (26.4)	302 (80.1) 23 (6.1) 52 (13.8)	3.5976	<0.001
<b>5.0</b>	<b>Respondents' feelings about stem cell donation</b>					
5.1	Acceptance	Not at all A little Moderately A lot	182 (15.9) 279 (24.5) 414 (36.3) 266 (23.3)	80 (21.2) 43 (11.4) 102 (27.1) 152 (40.3)	0.8145	0.41
5.2	Fear	Not at all A little Moderately A lot	396 (34.7) 499 (43.7) 188 (16.5) 58 (5.1)	199 (52.8) 157 (41.6) 19 (5.1) 2 (0.5)	-2.2642	0.02
5.3	Anxiety	Not at all A little Moderately A lot	393 (34.4) 508 (44.5) 179 (15.7) 61 (5.4)	205 (54.4) 147 (39.0) 22 (5.8) 3 (0.8)	-1.0824	0.28
5.4	Solidarity	Not at all A little Moderately A lot	19 (1.7) 78 (6.8) 458 (40.2) 586 (51.3)	4 (1.1) 16 (4.2) 97 (25.7) 260 (69.0)	-3.7582	<0.001
5.5	Indifference	Not at all A little Moderately A lot	1023 (89.6) 84 (7.4) 27 (2.4) 7 (0.6)	355 (94.2) 17 (4.5) 4 (1.1) 1 (0.2)	0.7181	0.47
5.6	Enthusiasm	Not at all A little Moderately A lot	135 (11.8) 343 (30.1) 442 (38.7) 221 (19.4)	13 (3.4) 49 (13.0) 142 (37.7) 173 (45.9)	4.4260	<0.001



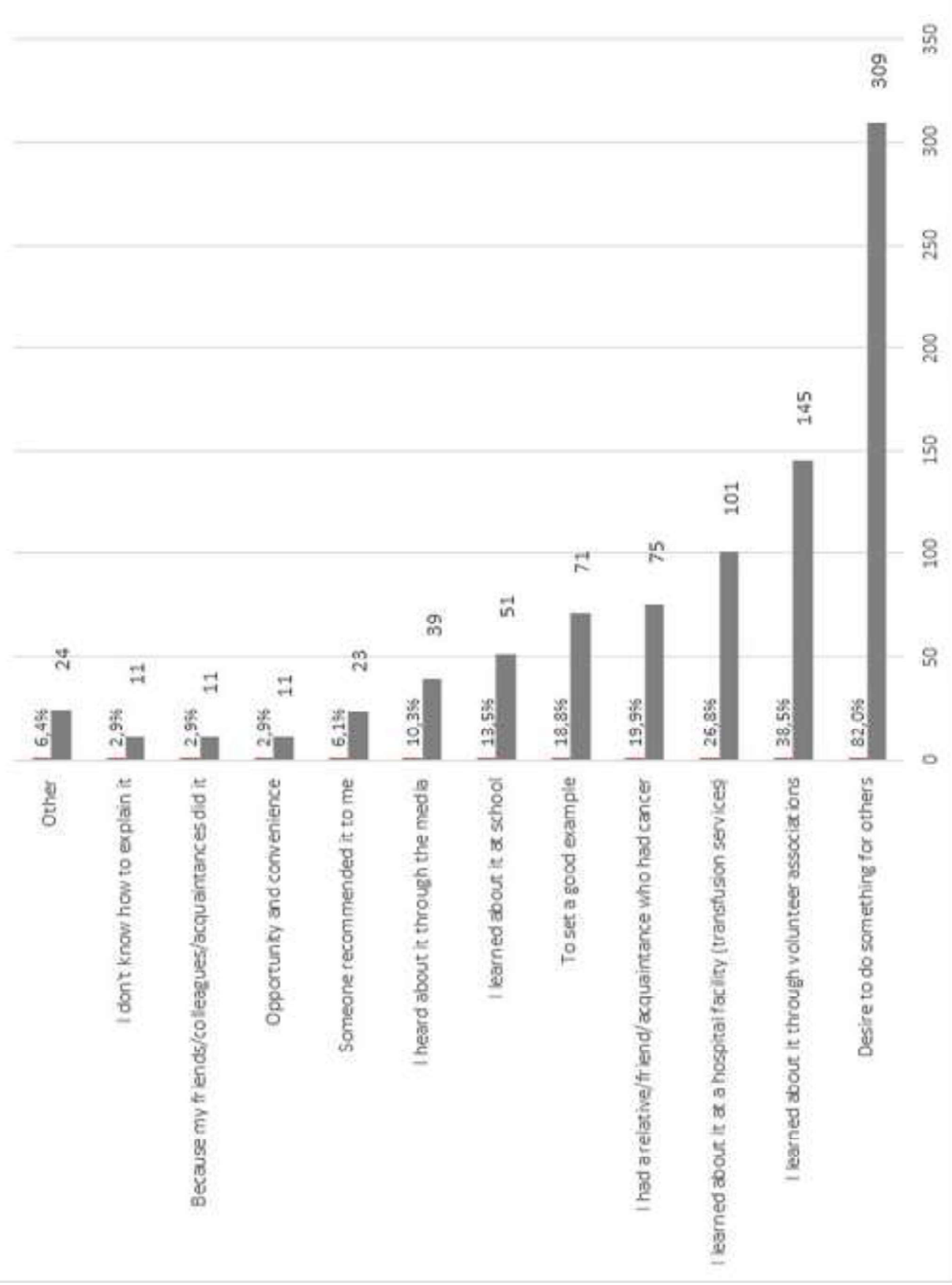
5.7	Gratification	Not at all A little Moderately A lot	63 (5.5) 218 (19.1) 501 (43.9) 359 (31.5)	14 (3.7) 32 (8.5) 132 (35.0) 199 (52.8)	0.1577	0.87
5.8	Grief	Not at all A little Moderately A lot	1023 (89.7) 84 (7.4) 29 (2.5) 5 (0.4)	342 (90.7) 27 (7.2) 5 (1.3) 3 (0.8)	-0.3432	0.73
5.9	Empathy	Not at all A little Moderately A lot	86 (7.5) 185 (16.2) 473 (41.5) 397 (34.8)	16 (4.2) 30 (8.0) 126 (33.4) 205 (54.4)	0.2260	0.82
5.10	Satisfaction	Not at all A little Moderately A lot	51 (4.5) 210 (18.4) 488 (42.8) 392 (34.3)	8 (2.1) 40 (10.6) 123 (32.6) 206 (54.7)	-0.6572	0.51
5.11	Dignity	Not at all A little Moderately A lot	68 (6.0) 227 (19.9) 479 (42.0) 367 (32.1)	18 (4.8) 51 (13.5) 123 (32.6) 185 (49.1)	-0.7476	0.45
5.12	Hesitation	Not at all A little Moderately A lot	436 (38.2) 526 (46.1) 136 (11.9) 43 (3.8)	261 (69.2) 98 (26.0) 13 (3.5) 5 (1.3)	3.5263	<0.001
5.13	Apprehension	Not at all A little Moderately A lot	393 (34.4) 532 (46.6) 160 (14.1) 56 (4.9)	196 (52.0) 160 (42.4) 19 (5.1) 2 (0.5)	-1.1302	0.25
5.14	Terror	Not at all A little Moderately A lot	729 (63.9) 292 (25.6) 94 (8.2) 26 (2.3)	309 (82.0) 56 (14.8) 11 (2.9) 1 (0.3)	1.4963	0.13
5.15	Fragility	Not at all A little Moderately A lot	586 (51.4) 428 (37.5) 105 (9.2) 22 (1.9)	252 (66.8) 98 (26.0) 24 (6.4) 3 (0.8)	2.5598	0.01
5.16	Concern	Not at all A little Moderately A lot	367 (32.2) 570 (50.0) 160 (14.0) 44 (3.8)	189 (50.1) 163 (43.2) 23 (6.1) 2 (0.5)	0.0161	0.98
5.17	Uncertainty	Not at all A little Moderately A lot	518 (45.4) 469 (41.1) 119 (10.4) 35 (3.1)	276 (73.2) 86 (22.8) 14 (3.8) 1 (0.2)	3.3425	<0.001
5.18	Vulnerability	Not at all A little Moderately A lot	589 (51.6) 404 (35.5) 118 (10.3) 30 (2.6)	269 (71.4) 87 (23.1) 17 (4.5) 4 (1.1)	1.9607	0.04

5.19	Refusal	Not at all A little Moderately A lot	930 (81.5) 164 (14.4) 40 (3.5) 7 (0.6)	354 (93.9) 17 (4.5) 6 (1.6) 0 (0.0)	3.3950	<0.001
5.20	Curiosity	Not at all A little Moderately A lot	226 (19.8) 396 (34.7) 386 (33.8) 133 (11.7)	84 (22.3) 93 (24.7) 135 (35.8) 65 (17.2)	2.6662	0.007
5.21	Exaltation	Not at all A little Moderately A lot	515 (45.1) 325 (28.5) 231 (20.2) 70 (6.2)	138 (36.6) 79 (21.0) 88 (23.3) 72 (19.1)	4.5051	<0.001
5.22	Perplexity	Not at all A little Moderately A lot	622 (54.5) 407 (35.7) 94 (8.2) 18 (1.6)	302 (80.1) 62 (16.4) 12 (3.2) 1 (0.3)	4.4821	<0.001
<b>6.0</b>	<b>Opinions and values</b>					
6.1	I am in favor of the use of HSCs for research or clinical trials	Strongly Disagree Disagree Undecided Agree Strongly Agree	50 (4.4) 1 (0.1) 52 (4.6) 502 (44.0) 478 (41.9)	20 (5.3) 12 (3.2) 14 (3.7) 140 (37.1) 191 (50.7)	-1.4554	0.14
6.2	HSCT is a life-saving therapy	Strongly Disagree Disagree Undecided Agree Strongly Agree	38 (3.3) 34 (3.0) 20 (1.8) 401 (35.1) 648 (56.8)	14 (3.7) 12 (3.2) 2 (0.5) 67 (17.8) 282 (74.8)	-5.2654	<0.001
6.3	The donation of HSCs is a choice that everyone should consider	Strongly Disagree Disagree Undecided Agree Strongly Agree	42 (3.7) 1 (0.1) 45 (3.9) 402 (35.2) 606 (53.1)	15 (4.0) 9 (2.4) 5 (1.3) 70 (18.6) 278 (73.7)	-3.9862	<0.001
6.4	CB donation should be done by default	Strongly Disagree Disagree Undecided Agree Strongly Agree	45 (3.9) 107 (9.4) 88 (7.7) 355 (31.1) 546 (47.9)	19 (5.0) 26 (6.9) 29 (7.7) 94 (25.2) 212 (56.2)	-0.8844	0.37
6.5	Enrollment in the donor registry should be mandatory for everyone, except for contraindicated cases	Strongly Disagree Disagree Undecided Agree Strongly Agree	162 (14.2) 309 (27.1) 154 (13.5) 290 (25.4) 226 (19.8)	34 (9.0) 79 (21.0) 54 (14.3) 89 (23.6) 121 (32.1)	2.0022	0.04
6.6	The general population should have access to more information about HSCs donation	Strongly Disagree Disagree Undecided Agree Strongly Agree	45 (4.0) 38 (3.3) 44 (3.9) 282 (24.7) 732 (64.1)	18 (4.8) 6 (1.6) 8 (2.1) 63 (16.7) 282 (74.8)	-1.7255	0.08
6.7	If I were to donate my HSCs, I would like to know who receives them	Strongly Disagree Disagree	253 (22.2) 182 (16.0)	93 (24.7) 63 (16.7)	-0.2591	0.79

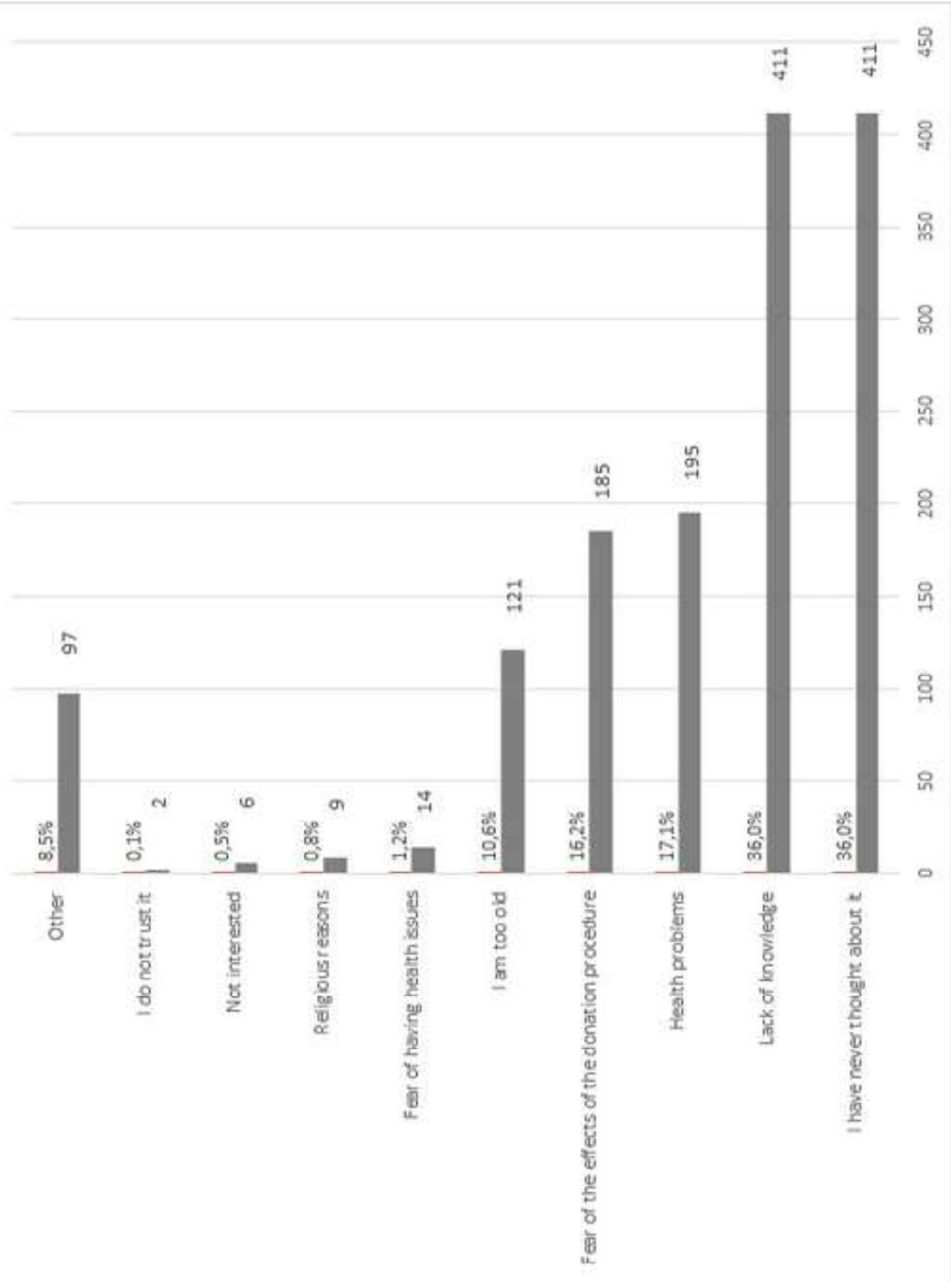
			Undecided Agree Strongly Agree	304 (26.6) 251 (22.0) 151 (13.2)	94 (24.9) 78 (20.7) 49 (13.0)		
6.8	If I were to donate my HSCs, I would like to know the recipient's condition		Strongly Disagree Disagree Undecided Agree Strongly Agree	116 (10.2) 103 (9.0) 124 (10.9) 424 (37.1) 374 (32.8)	40 (10.6) 23 (6.1) 36 (9.6) 106 (28.1) 172 (45.6)	-0.9840	0.32
<b>7.0</b>	<b>Information and education needs</b>						
7.1	How well-informed do you consider yourself regarding HSC donation?		Not at all Somewhat Enough A lot	279 (24.5) 474 (41.5) 320 (28.0) 68 (6.0)	22 (5.8) 103 (27.3) 180 (47.8) 72 (19.1)	8.0066	<0.001
7.2	Would you like to receive more information about HSC donation?		No Yes	155 (13.6) 986 (86.4)	67 (17.8) 310 (82.2)	1.9941	0.04
7.3	If awareness events on HSC donation were organized in your area, would you be interested in attending?		No Yes I don't know	43 (3.8) 861 (75.5) 237 (20.7)	15 (4.0) 310 (82.2) 52 (13.8)	-2.5771	0.01
7.4	Would you agree the Institutional providing of information material on HSC donation to every newly young adult?		No Yes	17 (1.5) 1124 (98.5)	6 (1.6) 371 (98.4)	0.1396	0.88

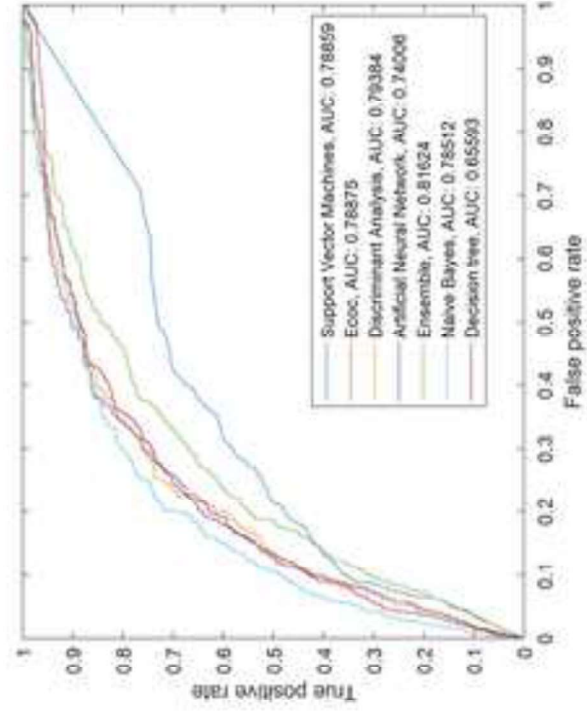
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Reasons for IBMDR enrollment (n. 377)



Reasons for not enrolling in IBMDR (n. 1141)





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2) Manuscript title:

**Raising awareness may increase the likelihood of hematopoietic stem cell donation: a nationwide survey using Artificial Intelligence.**

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5) Reasons for the changes in authorship:

The authorship change was made to include Prof. Donato Cascio, who was inadvertently omitted in the original submission due to an oversight. This adjustment ensures proper recognition of his contributions to the work.

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