REDUCING REGISTRY MEMBERS' ATTRITION WHEN INVITED TO DONATE

Evidence from a Large Stem Cell Registry

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ABSTRACT

Attrition of stem cell donors at the confirmatory typing (CT) stage nontrivially reduces the supply of life-saving stem cell transplants. Using data from DKMS Germany, a major stem cell donor registry, we study a set of initiatives that collected donors' genetic information or periods of temporary unavailability meant to enhance operating efficiency and registry members' ultimate availability to donate. We analyzed 91,670 CT requests to registry members for whom a matching patient was found. We find that initiatives are robustly associated with lower attrition through both sorting and behavioral channels. Our preferred estimates indicate that the initiatives are associated with between 4.0 and 8.5 percentage point lower attrition, corresponding to 17.5–37.1 percent reduced unavailability to donate. Moreover, the decision of donors to engage in an initiative is predictive of their propensity for attrition at the CT stage. We discuss implications for stem cell registries in terms of operational efficiency, notably their ability to use participation in the initiatives as a signal of higher eventual availability to donate, as well as costs and benefits.

KEYWORDS: stem cell donation, donor availability, registry initiatives, sorting
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I. Introduction

For many patients suffering from leukemia or other blood diseases who lack a related donor, hematopoietic stem cell transplantation (HSCT) from a matching unrelated donor offers the best treatment and chance of survival. HSCTs have extended the lifespan of hundreds of thousands of patients worldwide and enhanced their quality of life (e.g., Gratwohl et al. 2015). However, the unavailability of potential stem cell donors who are in a position to make an actual donation to a patient is a critical challenge hampering the stem cell donation process and, consequently, reducing the chances of survival for many patients.[1]

Stem cell donation is a multistage process. First, individuals willing to donate stem cells join a registry. Then, potential donors wait for a matching patient, which might take several years, if ever. If a matching patient is found, a request for confirmatory typing (CT) by a transplant center (typically via a central registry) is made to the potential donor (e.g., Bergstrom et al. 2009; Lacetera et al. 2014; Dasgupta 2018). The CT stage is thus *the* crucial milestone in the process of actually becoming a stem cell donor.[2] Unfortunately, stem cell donor registries worldwide face considerable donor attrition at the CT stage. This attrition leads to delays in donor search and increases the time until transplants are received for many patients, which can negatively affect survival rates (Lown et al. 2014). Moreover, attrition at CT causes inefficiencies in resource allocation because of the costs of recruiting and handling donors who are ultimately not available for transplantation (Anthias et al., 2020). For example, in the case of DKMS Germany, a leading stem cell donor registry with more than 7 million registered donors and the organization that provided the data for this study, the average attrition rate of potential donors at the confirmatory typing stage was 23 percent in 2018 (the final year of observation in our study).[3]

In this paper, we focus on the challenge of stem cell donor registries to maintain the motivation and commitment of already registered potential donors until they ultimately receive a request for CT. The multistage process of stem cell collection is a unique setting that differs from other medical donations, such as those of blood or plasma, where, typically, the commitment to donate is immediately followed by the actual donation. Stem cell donors, instead, make a nonbinding commitment to potentially donate some time in the (near or

1 The terms "attrition" and "unavailability" are used interchangeably throughout the paper. We also use the terms "potential donor" and "registry member" interchangeably when referring to individuals who are members of the registry, but who have not donated stem cells, yet.

2 The CT is a mandatory and decisive point for the potential donor to decide whether to actually follow through with a donation. At the CT stage, information is collected and tests are performed to confirm whether the donor is genetically suitable and medically eligible for HSCT and still willing to undergo a stem cell collection procedure.

3 Attrition in Germany is lower compared with other countries. For example, in the UK, the attrition rate was 38 percent in 2011 (Lown et al. 2014); more recently, attrition was estimated at 35 percent among Europeans and 56 percent among non-Europeans (Anthias et al. 2020). The attrition rate in Germany is also lower compared with the US, with estimates of 36 percent (Gragert et al. 2014), 40 percent (Switzer et al., 2013), 47 percent (Lown et al. 2014), and most recently 50 percent (Sivasankaran et al. 2018). This emphasizes the large medical and economic benefits of improving the availability of stem cell donors and makes it a pressing issue for donor registries.

distant) future. Hence, the donation process is characterized by uncertainty about whether an actual donation opportunity will materialize and, if so, when. Given this long time span in the donation process, it is possible that some registry members' initial commitment to donate may diminish over time, resulting in some registry members becoming less likely to donate if they eventually receive a request for CT.

We analyze three initiatives implemented by DKMS Germany that attempt to address this challenge and that may have an impact on the motivation and commitment of potential donors in Germany. The initiatives are directed at individuals who are already registry members, but who have not yet been requested for CT. The initiatives require costly action(s) if registry members decide to participate in them. Specifically, in "retyping" initiatives, registry members are asked to provide a genetic retyping through either a cheek swab (which they can do themselves at home) or a blood sample, whereas in "status update" initiatives, registry members are asked to provide information on future dates of known unavailability. Importantly, more time from diagnosis to transplant may adversely affect patient outcomes. Reasons for not being able to proceed to stem cell donation though a matching donor is registered include, notably, low and intermediate resolution or incomplete human leukocyte antigen (HLA) typing (Sauter et al. 2016) and, more importantly, donor attrition at the CT stage (Lown and Shaw 2013). Hence, the purpose of the initiatives is to address these challenges mainly in two ways. First, implementing retyping initiatives offers a remedy by enabling registries to enhance their operational efficiency, updating their databases with more precise information about potential donors as technological advances emerge that allow for more precise typing. Second, updating a registry member's periods of unavailability can also improve the registry's operating efficiency by allowing the registry to optimize the timing of requests it will make for CT.

In addition to improving the operating efficiency of the registry, these initiatives may have beneficial effects through at least two channels: sorting and behavioral. First, voluntary participation in an initiative may signal (through the effort of providing a new tissue sample or additional information) a donor's higher level of commitment. If this occurs, then initiative participation helps identify (i.e., sort) registry members who are more likely to be readily available when called upon to donate. Second, being invited to an initiative might cause potential donors to become more motivated. This may occur for several reasons. For instance, registry members might appreciate the registry's increased efforts to improve efficiency (Heger et al. 2020). Also, registry members who are eventually invited for CT might want to be consistent with both their past decision to join the registry and their decision to participate in initiatives (Heger and Slonim 2022). This view is supported by evidence from Redelmeier et al.'s (2001) randomized comparison trial on the stated willingness to be a kidney donor among nurses in Canada. The treatment group consisted of nurses who were randomly assigned to first test to determine a donor match (versus nurses who were told they were a match right at the beginning). A majority of nurses in the treatment group were willing to be tested for compatibility and, importantly for our setup, after being found to be compatible, showed a higher willingness to donate a kidney.

Despite the potential importance of such initiatives, empirical evidence on how they are related to donor availability at the CT stage is scarce. We address this gap by analyzing 91,670 CT requests issued to DKMS registry members in Germany for the time period 2013 to 2018.

Our data include a rich set of individual and registry-related variables, including those used by DKMS to determine whether potential donors are invited to participate in the initiatives.

In our analysis, we estimate three main econometric specifications. In each specification, our dependent variable is whether registry members were available or unavailable to follow through with CT. Our first specification, an "intention-to-treat" approach, estimates the direct association between receiving a letter from each of the initiatives and CT availability, independent of whether a potential donor participated in the initiative to which he or she was invited. The second analysis examines the "self-sorting" channel, by estimating the predictive effect of the donors' *participation decision* in each of the initiatives. The third specification assesses whether actual participation in the initiative influenced the behavior of registry members (e.g., whether it changed their motivation to follow through with CT) by estimating a local average treatment effect.

The manner in which DKMS selected donors to participate in the three initiatives has several advantages for our empirical analyses. First, the selection of registry members was based on observable, predetermined registry member characteristics, such as biological (e.g., age and sex) and genetic factors (e.g., ABO blood group and genotype frequency). Thus, registry members cannot influence their probability of receiving an invitation letter to an initiative. Second, and most importantly, not all registry members meeting the selection criteria for an invitation to participate in each initiative were invited to participate, primarily owing to cost and technical considerations. Thus, we have a large comparison group of registry members who were not invited to any initiative who have substantial overlap in terms of observable characteristics (including those used to determine assignment to the initiatives).

We find that the CT availability of donors invited to a retyping initiative or an initiative that involved both retyping and status updates were, on average, and after controlling for registry members' observable characteristics, 2.9 percentage points (pp) higher than those who received no invitation (significant at the 1 percent level). Since baseline attrition at the CT stage is 22.9 percent, this corresponds to a 12.7 percent (2.9/22.9) reduction in attrition. However, simply asking for status updates without retyping did not yield significant associations. When we estimate the predictive effects of participation, we find that participants in all of the initiatives were 10.7–14.6 pp more likely to follow through with CT than nonparticipants. The local average treatment effect estimates indicate that the retyping initiative and the retyping plus status update initiative are associated with a 4.9 pp and 8.5 pp higher CT availability, respectively (both statistically significant at the 1 percent level); the status update initiative alone increased availability by 4.0 pp, but this estimated coefficient was not statistically significant. Thus, the initiatives reduced attrition by between 17.5 percent (4.0/22.9) and 37.1 percent (8.5/22.9) for participants. The results remain consistent across various robustness tests. This includes the application of the methodology developed by Oster (2019), which offers a systematic approach to assess the influence of unobservable heterogeneity on the estimated coefficients. Specifically, under the assumption of proportional observed and unobserved selection, we report evidence that selection of unobserved variables would need to be between 1.4 and 2.9 times larger than selection on observable heterogeneity for our results to be invalidated.

In addition to self-sorting into the initiatives, there is one more stage of potential selection, which comes at the later stage when registry members are called upon for CT. To examine

how much of the direct (intention-to-treat) association can be attributed to sorting into CT requests and how much can be explained by the motivation of potential donors changing, we use inverse probability weighting (Wooldridge 2010). Specifically, we apply inverse probability weights based on the participation status in a particular initiative, age, and gender. Using these weights in our analyses makes the sample of first CT requests representative of the entire donor registry in terms of these variables. Comparing the unweighted with weighted analyses informs whether our main estimates are driven by sorting.[4] We find that the estimated association between the retyping plus status update initiative and availability at CT is predominantly driven by sorting, and that the retyping initiative is potentially also driven by increased motivation. Hence, this exercise helps us identify the broad mechanisms by which initiatives are associated with aggregate CT availability.

Our study contributes to several streams of literature (e.g., Roth et al. 2004; Craig et al. 2017). First, we examine a new context on medical donations. Importantly, in the context of stem cell donation, the point in time of stating the initial willingness to give differs from the time of donation. In contrast, in the case of whole blood (and plasma), the donation takes place immediately after the registration and a health check (e.g., Wildman and Hollingsworth 2009; Stutzer et al. 2011; Lacetera et al. 2012; Slonim et al. 2014; Goette and Stutzer 2020). For stem cell donations, it is not uncommon that several years elapse between registration and a first CT request. Compared with organ donation, where the majority of transplants are from deceased donors, stem cell donations are from living donors (Grieco et al. 2018).[5] Finally, compared with blood donation, donating stem cells is a thin market (i.e., a one-to-one market), which makes donation decisions pivotal (Slonim et al. 2014). Also, donating stem cells via peripheral blood stem cell collection or extraction from the iliac crest is generally safe (Schmidt et al. 2017), but nevertheless carries more risks and discomfort than blood donation (but less risk than a kidney donation).

In the context of designing volunteer markets, the blood-donation literature has shown that creating a registry for blood donors has substantial benefits (Heger et al. 2020). However, with stem cell donations, the much longer and more uncertain time horizon makes it difficult for registries to maintain donor commitment and, ultimately, to guarantee their CT availability. The analysis of initiatives commonly conducted by stem cell donor registries during the potentially long interim stage between registration and donation is a novel contribution to the literature and yields practical insights for the management of donor registries. Based on reported periods of future unavailability of participating donors, for example, the registry can block its members from receiving a request for CT for their unavailable

4 The weighted analyses remove the direct impact of initiatives on the composition of donors at the CT request stage from the estimates. Hence, the difference between the weighted and unweighted analyses is the "sorting effect" of the initiatives.

5 For example, from January to June 2021, 21,061 organ transplants were performed in the United States, 17,821 of which came from deceased donors, and 3,240 of which came from living donors (https://optn.transplant.hrsa.gov/data/, accessed August 5, 2021). Of the 47,499 unrelated stem cell transplants performed in the US between 2019 and 2023, 4 percent were from cord blood, the rest being from peripheral blood after stem cell mobilization or bone marrow (https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplant-activity-report, accessed September 3, 2025).

time, and hence reduce the time search coordinators at transplant centers spend trying to contact them. This would render the donation process more efficient. Beyond medical donations, our findings offer insights potentially applicable to other contexts where altruistic individuals sign up to a registry expressing the intention to make a contribution should the need arise; examples include volunteer teaching (Coffman et al. 2017) and other volunteer work in general (Exley and Petrie 2018).

Second, we contribute to the medical and health literature that assesses motivations of stem cell donors for attrition at the CT stage. While the number of potential donors enrolled in registries like DKMS has increased steadily (see, for instance, Bergstrom et al. 2009; Schmidt et al. 2020a), it has been widely documented that a significant number of donors across many countries withdraw their consent for donation after registration.

Several papers assess factors that relate to attrition at the CT stage. Correlates of attrition are ethnic background (Switzer et al. 2004; Myaskovsky et al. 2004; Onitilo et al. 2004; Lown et al. 2014), which can be due to religious and medical objections to donation, less trust that stem cells would be allocated equitably, and a greater likelihood of having been discouraged from donating (e.g., Onitilo et al. 2004; Switzer et al. 2013). Other correlates include time in the registry (Switzer et al. 1999; Monaghan et al. 2021), whether registration was "patient-centered" (meaning that the search for donors is targeted to a specific patient in need of a transplant) (Switzer et al. 2004), age (Switzer et al. 2013), sex (Lown et al. 2014; Fingrut et al. 2018), and communication of being the only known donor match to the patient (Switzer et al. 2018). Anthias et al. (2020) find that a donor's mental and physical health, as well as interaction with the registry, correlate with CT availability. Also, Switzer et al. (2004) find that intrinsic motivation to donate, realistic expectations about donation, and more contact with the registry are associated with being available. Ambivalence about donation in the form of having doubts and worries about stem cell donations, feeling unsure about donating, or wishing someone else would donate instead are strong drivers of attrition (Switzer et al. 2013). Other papers assess motivations for registering with a stem cell donor registry (Switzer et al. 2003; Aurelio et al. 2011; Mclaren et al. 2012; Bart et al. 2014) and find that these motivations also affect CT availability. As a result, intrinsic registration motives predict much higher donation availability than extrinsic motives (e.g., social pressure or incentives) (La Casta et al. 2019).

The remainder of the paper is organized as follows. Section II provides further background on the process from enrolling to becoming a stem cell donor and on the retyping and status update initiatives. In Section III, we describe our data set and present initial descriptive analyses. Section IV presents our estimation results, discusses potential mechanisms, and describes implications in terms of costs and benefits for the registry. Finally, Section V discusses limitations, and concludes.

II. Background

A. THE STEM CELL DONATION PROCESS

Typically, stem cell donations take two forms. They are either autologous donations, which means that stem cells are extracted from the patient before a cancer treatment and

retransplanted after the treatment, or allogeneic, where stem cells are collected from another person (related or unrelated). In the United States, for example, about 40 percent of stem cell transplants between 2015 and 2019 were allogeneic.[6] We collaborated with DKMS, a stem cell donor registry that provides unrelated-donor data for stem cell donor searches for patients in need of an unrelated allogeneic transplant. DKMS is one of the world's largest registries,[7] with more than 11 million registered donors in seven countries: Chile, Germany, India, Poland, South Africa, the United Kingdom, and the United States. More than 65 percent of registered DKMS donors belong to the German branch. Since its foundation in 1991, DKMS has facilitated over 95,000 stem cell collections, and its share of all unrelated stem cell donations worldwide amounts to about 40 percent (Schmidt et al. 2020a). Our data set comprises donors registered with DKMS living in Germany.

Figure 1 illustrates the multistage process, from registering with a stem cell donor registry to actually becoming a stem cell donor. First, potential donors join the registry by providing oral mucosa cells via cheek swabs or small blood samples, which are then typed for HLA by a genotyping service provider (Schöfl et al. 2017). The donors' typing results are then listed on a computerized registry ($t = 0$). Potential occasions to register include public community drives, which might evolve around a specific patient requiring a donation (patient-centered); company drives; donor drives targeted at specific populations such as students, visitors of sports events, police, or military staff (special projects); or online registration.[8]

Once someone has joined the registry, the registry members then need to wait until they are matched with a patient (i.e., between $t = 0$ and $t = 1$), which could be anywhere from days to years or never. The quality of a match between a potential donor and a patient is mainly determined by the fit in their genetic information (HLA type).[9] Besides the HLA type, age and genetic parameters such as the ABO blood group and markers such as the cytomegalovirus (CMV) antibody status[10] are secondary criteria for selecting a suitable donor. DKMS has been recruiting potential donors for about 30 years. During this period, the medically desirable and technically and financially feasible methods of typing potential donors have evolved considerably because of the emergence of next-generation sequencing-based HLA typing (Schmidt et al. 2020a). It therefore continues to be essential to invest in the quality of potential donors' genetic information (high-resolution typing) in the database by retyping donors with low-resolution profiles (sometime after the initial registration at $t = 0$) using up-to-date laboratory methods.

6 See https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics.

7 For an overview, see https://statistics.wmda.info.

8 For example, DKMS figures from 2018 indicate that 139,146 potential stem cell donors were recruited at 427 public drives, of which 109 drives were patient-centered. The average recruitment number at patient-centered drives was 948, while at drives without focus on a specific patient the average number was 109. A total of 115,388 potential donors were recruited at 1,117 special drives, with an average recruitment number of 103. However, more than half of actual members come from online registration.

9 The six most relevant genes are HLA-A, HLA-B, HLA-C, HLA-DRB1, HLA-DQB1, and HLA-DPB1 (Dehn et al. 2019).

10 The donor's CMV antibody status is an important transplantation-relevant parameter. For transplant patients with a weakened immune system, a CMV infection can have life-threatening consequences.

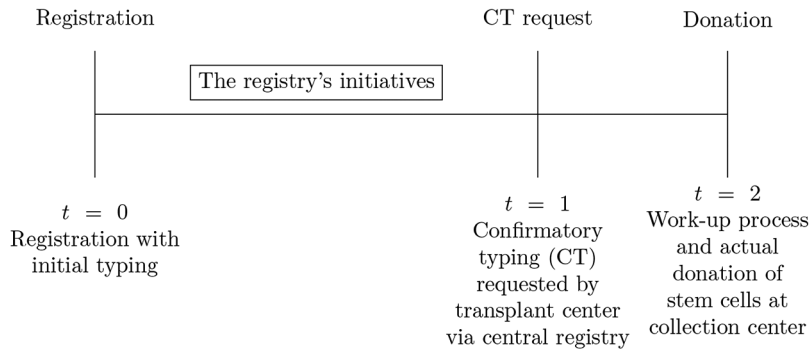

FIGURE 1. Overview of key events for potential stem cell donors

Second, whenever a potential donor turns out to be a suitable match for a patient, the transplant center responsible for the patient's treatment requests that the potential donor undergo CT ($t = 1$). The objective is to confirm that this person is suitable, still committed, and medically eligible for a stem cell collection. During the CT stage, potential donors participate in a phone consultation and a questionnaire-based medical clearing. Fresh blood samples are requested to confirm the donor–recipient HLA match, and to test for infectious disease markers, including the CMV antibody status. The CT stage is thus *the* critical milestone in the process of becoming a stem cell donor. Finally, if a suitable donor for HSCT is identified during the CT stage, the "work-up" process, which includes the scheduling of the donation date, a medical examination at the collection center, and the organization of travel and accommodation, begins. Subsequently, the actual donation process may be initiated ($t = 2$).

The process from registration to actual donation carries several uncertainties for the stem cell donor registries that might hinder the efficient search for a potential donor. First, it is uncertain whether a potential donor, who is potentially a good genetic match, is (still) readily available in case of a request for CT. Typical reasons for unavailability include pregnancy and long-term stays abroad. Second, the quality of the initial typing might be insufficiently precise, leaving it uncertain whether the initially determined HLA type is confirmed by high-resolution typing methods. This problem occurs predominantly with donors whose original HLA typing dates back many years. In donors typed in recent years, unconfirmed results are very rare (Baier et al. 2019). Finally, it is uncertain whether potential donors are still committed to donating stem cells once they are asked for CT, in particular if there is a long time span between registration and CT stage. The initiatives implemented by DKMS and outlined in the next section are meant to address these issues.

B. THE REGISTRY'S INITIATIVES

B.1. ASSIGNMENT OF REGISTRY MEMBERS TO INITIATIVES. Over the years, DKMS Germany has launched a set of initiatives aimed at mitigating the aforementioned problems of low-resolution typing, missing information about periods of donor unavailability, and lacking

donor commitment at the CT stage. As depicted in Figure 1, after signing up with the stem cell donor registry, but before the call for CT, a group of potential donors is asked to participate in an initiative via a written invitation letter. In general, registry members who are more likely requested for CT[11] are asked to participate in the initiatives.

During our observation period, DKMS selected potential donors for initiatives based on biological and genetic characteristics, including age, gender, and genotype frequency. Importantly for our analysis, because of cost and technical considerations, DKMS invites only a subset of registry members who meet the criteria for each initiative, and it does so quasi-randomly. Specifically, the selection is based on practical factors, such as the date when the laboratory reports the typing result from the initial registration to the IT database. As the registration of members does not follow any particular order, a draw of registry members based on this specific date can thus be seen as akin to a random draw. The fact that only a subset of registry members are invited to the initiatives ensures a large overlap in the supports of all observable characteristics between the baseline (no initiative) group and the registry members invited to the initiatives. Combined, the assignment features of DKMS's initiatives allow us to estimate robust comparisons of registry members invited to an initiative and those not invited to any initiative with regards to their subsequent behavior when asked for CT.

B.2. DESCRIPTION OF THE INITIATIVES. Next, we provide details about the initiatives we study. During our observation period, we studied three initiatives: Retyping (years 2013–18), Status update (2015–18), and Status update–blood (2013–17). Below, we describe the initiatives as well as DKMS's motivation for introducing them. Table A.1 in the Appendix provides additional details.

First, the RETYPING initiative asks registry members for retyping (either via cheek swab or a blood draw) and to complete a short health questionnaire. Typically, donors with incomplete (low-resolution) HLA profiles are asked to participate. Further criteria for registry members to be invited to the initiative RETYPING are age, sex, HLA genotype frequency, BMI, and missing CMV antibody status. Updating the typing profile of a prospective donor can ultimately accelerate the donor search process, as the search coordinator has more detailed information on the donor's suitability. In fact, incompletely typed donors may remain unidentified in donor searches, even if they are full matches for the patient (Sauter et al. 2016). Potential donors invited to this initiative were reminded only once to send the sample in and were not excluded from the registry if they did not participate.

The second initiative, STATUS UPDATE, began in 2015 as high-resolution typing upon donor recruitment became more commonplace. In the invitation letter, this initiative

11 For the group of donors with the most common HLA genotypes, 18- to 20-year-old male donors with known CMV antibody status show, for instance, a 12.5 times higher donation probability as compared with female donors of the same genotype frequency, age, and known CMV antibody status (Sauter et al. 2022). For example, younger donors are also preferentially asked to donate, as they are associated with improved survival in transplant recipients (Kollman et al. 2001, 2016). As another example, women are less likely to be asked to donate because of potentially being pregnant or nursing a baby (Lown et al. 2014). Finally, transplant centers are more likely to invite registry members with known CMV antibody status since a CMV infection can negatively influence the outcome of a transplantation (Kollman et al. 2001).

informs registry members that, based on certain biological and genetic characteristics, they are more likely to be matched to a patient needing a stem cell donation. Additionally, the letter explains that in order to minimize delays if they are matched, registry members are asked to complete a short health questionnaire and to report any future unavailability that lasts longer than three weeks (e.g., due to a planned stay abroad or pregnancy). By collecting information on reported periods of future unavailability of participating donors, the registry is able to block these donors for the corresponding time period, ensuring they are not requested by a search coordinator during these times.

The third initiative, STATUS UPDATE–BLOOD, was similar to STATUS UPDATE (notification of temporary unavailability), but it required high-resolution retyping through a *blood draw*. The reason was that a considerable number of donors had incomplete typing profiles at the time of their registration. Finally, STATUS UPDATE–BLOOD, unlike the other initiatives, framed the invitation to registry members to be part of a "team of quickly available donors," which could have potentially added another motivation to follow through.

It could be the case that donors received invitations to multiple initiatives. In these cases, we assign potential donors to their first initiative, as donors who move on after the first initiative to conduct CT will no longer be eligible for subsequent initiatives in our data.[12] In all regressions, we also control for incidences of multiple initiatives.

III. Methods

A. DATA AND VARIABLES

The initial data set contains the universe of 104,116 observations from *first* CT requests and associated individual-level information for potential donors, who registered with DKMS Group and reside in Germany, for the time period from November 1, 2013, to October 31, 2018. From the initial data set, we excluded observations with CT cancellations on the patient side, prior to the registry member making a decision on the CT request (5,931 observations), since it cannot be determined whether these donors would have followed through with the CT request. We also excluded observations where the latest retyping request before the CT request originated from a transplant center in the context of a search for a specific patient (6,990 observations). Some individuals had both a confirmatory typing cancellation from the patient and a patient-related retyping request; hence, 12,446 observations were removed from the analysis. This leaves us with 91,670 individual-level observations for analysis. The sample collected contains only first CT requests per potential donor, since availability here is of primary interest to stem cell donor registries. If a potential donor does not take part in the first CT, the likelihood that they will be available for further CT requests is lower (in our data, it amounts to an average of 47 percent).

The outcome of interest is potential donors' completion of the CT request. This is a binary variable called "availability": Potential donors are regarded as available (coded 1) if

12 We thank the editor, Mireille Jacobson, for pointing this out. Rather than assigning potential donors to their first initiative, donors could be assigned to the initiative closest in time to the CT request as the decisive initiative. All results remain qualitatively unchanged.

they could be contacted and successfully completed the CT process, or as unavailable (coded 0) if they did not complete the CT process. More specifically, available donors declared they were willing to donate, provided the requested blood samples, filled out the health questionnaire, and were medically eligible. Reasons for unavailability include no longer being interested in donating, medical ineligibility due to illness, or temporary unavailability (e.g., being overseas or having an important reason limiting the time available to donate). Quite noteworthy, DKMS is able to track persons who have changed their address and did not inform DKMS about this, through the municipality where the person was last registered.[13] As a result, there are only 779 cases in our sample where potential donors could not be contacted.

As mentioned above, donors might receive invitations to multiple initiatives. In this case, we assign potential donors to their first initiative. In all regressions, we also include a dummy variable (called "multiple invitations") as a control. We ignore all CT requests where the most recent initiative was explicitly part of a donor search for a specific patient initiated by a transplant center, since noncompliers with this initiative are excluded from receiving a further CT request, which introduces a significant sample-selection bias.[14]

Table A.2 in the Appendix provides an overview of the covariates, which can be categorized into registry-related and potential donor–related characteristics. All summary statistics refer to nonmissing covariate values from the regression sample.[15] The former category comprises the type of registration and the sample collection method. The type of registration includes the categories: public drive centered\not centered around a specific patient, company drive, special projects (such as donor drives at a school, university, sports event, and among police, firefighters, and armed forces), and online registration. Sample collection was performed either by blood draw or by cheek swab. We also account for seasonality by controlling for the month of the CT request.

Potential donor–related variables include the prospective donors' sex, age at CT request, self-reported ancestry,[16] the federal state of residence, the population size at their place of residence, the potential donors' body mass index (BMI), and the date of registration (which we sort into the following categories: registration before 2007, from 2007 to 2010, from 2011 to 2014, and from 2015 to 2018). Most of the potential donors' characteristics

13 In Germany, there is mandatory registration of addresses to the local municipality, so one can track where people have moved to within Germany.

14 Also, for participation variables, we have 32 cases from RETYPING, where the participation decision was unclear, and these are recoded into the comparison group.

15 We have 46 (59) missing observations for the registration method (region) and 3,393 missing observations of ancestry (since this was not mandatory information), and otherwise full covariate information for all CT requests. These missing values have been included in all analyses using an extra dummy for each variable (for ethnicity, a 0–1 dummy), or a separate category for the type of registration.

16 We categorize this variable in German and non-German, as there is a large number of minority backgrounds in the sample. Overall, there were 143 reported different nationalities, of which the 10 most common were German (87.6 percent), Turkish (4.7 percent), Polish (0.9 percent), Russian (0.9 percent), Italian (0.8 percent), Greek (0.3 percent), Kazakh (0.3 percent), Romanian (0.2 percent), Austrian (0.2 percent), and French (0.2 percent).

are mandatory information, which is collected at the recruitment stage, such as sex, address, weight and height, and date of birth.[17] All base control variables, except the potential donors' age at CT and month of CT request, have already been determined prior to DKMS sending out invitation letters or the decision of the potential donor to react to these invitations.

B. DESCRIPTIVE STATISTICS

Table 1 provides an overview of the registry members' availability, first by the initiative they had been invited to (panel A) and second conditional on whether registry members participate in an initiative (panel B). Out of 91,670 registry members with CT requests in our sample, 5,180 were invited to the initiative RETYPING, while 11,140 potential donors were invited to STATUS UPDATE–BLOOD, and 2,113 to STATUS UPDATE. That implies that around 80 percent of all registry members who received a request for CT were not invited to any of the initiatives (73,237 out of 91,670).

We observe the highest CT availability (82.5 percent) among registry members who had been invited to the initiative STATUS UPDATE–BLOOD. For initiatives STATUS UPDATE and RETYPING, CT availability is slightly lower with 80.8 percent and 79.8 percent, respectively. Among the registry members who did not receive an invitation, 77.1 percent were available for CT.

As participation in any of these initiatives was voluntary, it is instructive to analyze differences in participation levels between the initiatives. The participation rate for RETYPING is 60.3 percent (3,103 participants, 2,045 nonparticipants). For the initiatives STATUS UPDATE and STATUS UPDATE–BLOOD, we observe participation rates of 30.8 percent and 33.3 percent, respectively.

We are also able to compare the participation rates in the initiatives within our sample among potential donors without a request for CT. Analyzing data for members from the registry unconditional on having a request for CT, we observe a 48 percent participation rate in the RETYPING initiative. For STATUS UPDATE–BLOOD, the participation rate was 24.4 percent, and for STATUS UPDATE it was 25 percent. The fact that participation rates in the initiatives are higher in the CT request sample suggests that the initiatives may lead to a positive selection of donors who are invited to CT. To address this issue, in our analyses below we will correct our estimated intention-to-treat coefficients by taking participation rates unconditional on CT requests into account.

Table 1 shows that CT availability varies with the potential donors' participation in the initiatives. As a general pattern across all initiatives, we observe that initiative participants show a considerably higher availability for CT that nonparticipants. For the initiative RETYPING, the difference in availability is greatest with 14.9 pp. The availability difference is 11.3 pp and 12.0 pp between participants and nonparticipants for the initiatives STATUS UPDATE and STATUS UPDATE–BLOOD, respectively. Put differently, considering the *un*availability of potential donors, participation in an initiative yields substantial decreases in the potential donors' CT unavailability. For example, for the initiative RETYPING, the unavailability

17 Potential donor BMI ranges from 13 to 40, and is 24 at the median. The potential donors' age upon CT request ranges from 17 to 60 years, with an average of 30 (median 28). The country of origin is self-reported (as additional information on a consent form) and was available for 96.3 percent of the studied donors.

TABLE 1. CT availability by initiative and participation

	Obs. (1)	Average CT availability (%) (2)
A. Initiatives		
RETYPING	5,180	79.8
STATUS UPDATE	2,113	80.8
STATUS UPDATE–BLOOD	11,140	82.5
No invitation to initiative (baseline)	73,237	77.1
B. Initiatives and participation		
RETYPING; Participation	3,103	85.7
RETYPING; No participation	2,045	70.8
STATUS UPDATE; Participation	651	88.6
STATUS UPDATE; No participation	1,462	77.3
STATUS UPDATE–BLOOD; Participation	3,714	90.5
STATUS UPDATE–BLOOD; No participation	7,426	78.5

Note: This table describes availability rates across initiatives for $N = 91,670$ first confirmatory typing (CT) requests from November 1, 2013, to October 31, 2018, at DKMS Germany. Column 1 shows the number of observations by initiative invitation category, and column 2 shows the average CT availability. For 32 invitations to the RETYPING initiative, it is unclear whether the potential donor participated, which marks the difference between the sum of RETYPING; PARTICIPATION and RETYPING; NO PARTICIPATION.

is more than 50 percent smaller for participants in the initiative (14.3 percent not available) compared with nonparticipants (29.2 percent not available). These descriptive results are suggestive of a potential "sorting effect" of the initiatives and also highlight differences between the initiatives with respect to their participation "cost" for the registry members. Specifically, registered donors who agree to participate in a high-cost initiative (including the time to complete a cheek swab, blood draw, and questionnaire) could be signaling a relatively high level of commitment to go forward with the process should they be asked to donate.[18]

C. EMPIRICAL STRATEGY

C.1. INTENTION-TO-TREAT REGRESSION SPECIFICATION. We apply linear probability models (LPM) to investigate the association between the various initiatives and the potential donors' availability at CT.[19] The unit of observation is at the person level. Our first goal is to measure the overall effectiveness of these initiatives to increase CT availability,

18 Table A.3 in the Appendix reports the number of observations and univariate differences in availability rates across registry-related and individual characteristics.

19 In Table B.3 in the Online Appendix, we estimate logistic models instead of LPMs. All results remain qualitatively unchanged.

unconditional on actual participation of donors in these initiatives, and controlling for registry-related and potential donor–related characteristics.

The dependent variable, AVAILABLE_i, measures the availability for CT upon the first request, which equals 1 if a registry member is available, and 0 otherwise. Hence, we estimate the following regression specification:

$$\begin{aligned}\text{AVAILABLE}_i = \beta_0 + \beta_1 \text{RETYPING}_i + \beta_2 \text{STATUS UPDATE-BLOOD}_i \\ + \beta_3 \text{STATUS UPDATE}_i + \delta \boldsymbol{X}_i + u_i\end{aligned} \quad (1).$$

Here, the independent variables are indicators equal to 1 if the registry member was invited to a specific initiative and 0 otherwise. The reference group consists of registry members who were not invited to any of the initiatives. In each regression specification, we include a rich set of individual- and registry-related control variables, as described in Table A.2 in the Appendix. We report robust standard errors in all specifications.

Regarding the issue of selection, one concern is that the characteristics of registry members who were invited to the initiatives and those who were not invited might not be perfectly balanced, and some of these characteristics could be associated with the outcome variable of interest, availability at CT. This creates identification concerns. However, although DKMS does not randomly assign registry members to initiatives, the selection criteria are known and consist of observable biological and genetic characteristics (see Section B.1). Table 2 reports results from tests of whether there are significant differences in

TABLE 2. Balance checks

Variable	Baseline	RETYPING	STATUS UPDATE	STATUS UPDATE–BLOOD
Age	30.7067[a]	−0.5405[a]	−3.3475[a]	−1.8576[a]
	(0.0365)	(0.1208)	(0.1581)	(0.0723)
Female	0.3950[a]	−0.0485[a]	−0.1082[a]	−0.0766[a]
	(0.0018)	(0.0069)	(0.0100)	(0.0048)
Genotype frequency	3.0147[a]	−0.1548[a]	−.7998[a]	−0.5649[a]
	(0.0038)	(0.0150)	(0.0197)	(0.0092)
BMI	24.3548[a]	−0.0887[c]	−0.0301	0.0819[a]
	(0.0122)	(0.0467)	(0.0684)	(0.0310)
E-mail address known	0.9016[a]	0.0567[a]	0.0851[a]	0.0773[a]
	(0.0011)	(0.0030)	(0.0027)	(0.0018)

Note: $N = 91,670$. This table reports differences in main selection criteria between our initiatives and the baseline group. In each row, we regress one of the selection criteria on dummies for the three initiatives (linear models). The constant shows the baseline group mean, whereas the reported coefficients show the differences between our initiatives and the baseline group (with the *p*-value in parentheses). Variables for age and BMI are continuous. All other variables are categorical (female and e-mail address known are dummy variables, lower values for genotype frequency correspond to more frequent genotype frequency ranks). [a]represents a significance level of 1%. [c]represents a significance level of 10%. Constant not shown.

potential donor–related selection criteria between the three initiatives and the baseline group. In each row, we regress one of the selection criteria on dummies for the three initiatives. The constant shows the baseline group mean, whereas the reported coefficients show the differences between the initiatives and the baseline group (with the *p*-value in parentheses). As expected, potential donors in our initiatives tend to be younger, are less likely to be female, show more frequent genotype ranks, and are more likely to share their e-mail address upon registration. As described in Section B, only a subset of donors with the requisite characteristics were invited to the initiatives, which ensures a large overlap in the supports of all observable characteristics between the baseline (no-initiative) group and the registry members invited to the initiatives (see Table A.4 in the Appendix). Yet, the differences in Table 2 are often sizable and statistically significant. However, as we have information on observable selection criteria in our data, we control for these variables in all our empirical analyses. Moreover, we conduct additional robustness checks described below that demonstrate that selection is not the primary mechanism for our results. Thus, though our estimates should not be interpreted as causal effects, they represent robust empirical associations.

C.2. INITIATIVE PARTICIPATION SPECIFICATION. We also observe whether registry members who have been asked to participate in any of these initiatives accept the invitation and participate or whether they decline or do not respond to the invitation.[20] This motivates a second analysis, where we estimate differences in complying to CT requests for participants ("yes") and nonparticipants ("no") in the initiatives. We estimate the following regression specification:

$$\begin{aligned} \text{AVAILABLE}_i = {} & \beta_0 + \beta_4 \text{RETYPING, YES}_i + \beta_5 \text{RETYPING, NO}_i \\ & + \beta_6 \text{STATUS UPDATE-BLOOD, YES}_i \\ & + \beta_7 \text{STATUS UPDATE-BLOOD, NO}_i \\ & + \beta_8 \text{STATUS UPDATE, YES}_i + \beta_9 \text{STATUS UPDATE, NO}_i \\ & + \delta \mathbf{X}_i + u_i \end{aligned} \tag{2}$$

The analysis intentionally includes a selection effect, as a potential donor chooses whether to participate. This is particularly important from the perspective of a manager running a stem cell donor registry, since one aim of these initiatives is to identify pools of readily available donors with a high level of commitment, and also to collect additional medical information (e.g., high-resolution HLA typing profile, CMV status, or blood group). From a practical perspective, the analysis may indicate whether these initiatives can effectively sort for more available donors on factors that are otherwise unobserved, as well as collecting more information about these donors that is match-relevant. If potential donors who participate not only are better typed by the registry, but also show higher motivation to follow through, this can, ceteris paribus, provide grounds for prioritization of a participating donor over one who did not participate in these initiatives, given that this information is available to the search coordinator.

20 One mechanical reason for the nonresponses is that individuals cannot be contacted by DKMS (e.g., after someone has moved away). This can be considered very unlikely, as DKMS Germany has access to resident data through the local residents' registration offices.

C.3. LOCAL AVERAGE TREATMENT EFFECTS. In the next specification, we assess the impact of invitations to the initiatives on the subgroup that actually participated, by estimating a local average treatment effect parameter (Imbens and Angrist 1994; Abadie and Cattaneo 2018). Here, the endogenous variable of interest takes the value 1 if a person participated in the relevant initiative and 0 otherwise, and it is defined for each of the three initiatives where there is an endogenous participation decision. The endogenous variables are each instrumented by a dummy for being invited to the initiative. The second stage is

$$\begin{aligned}\text{AVAILABLE}_i = \beta_0 + \beta_1 \text{RETYPING, YES}_i + \beta_2 \text{STATUS UPDATE-BLOOD, YES}_i \\ + \beta_3 \text{STATUS UPDATE, YES}_i + \delta \mathbf{X}_i + u_i\end{aligned} \tag{3},$$

and the first stage is a system of three equations, one for each initiative:

$$\begin{aligned}\text{RETYPING, YES}_i &= \gamma_0 + \gamma_1 \text{RETYPING}_i + \gamma \boldsymbol{X}_i + r_i \\ \text{STATUS UPDATE, YES}_i &= \rho_0 + \rho_1 \text{STATUS UPDATE}_i + \rho \boldsymbol{X}_i + r_i \\ \text{STATUS UPDATE-BLOOD, YES}_i &= \tau_0 + \tau_1 \text{STATUS UPDATE-BLOOD}_i + \tau \boldsymbol{X}_i + r_i\end{aligned} \tag{4},$$

which we estimate with robust standard errors.

IV. Results

A. MAIN RESULTS

Table 3 reports intention-to-treat regression results from linear probability models using availability at first CT request as the dependent variable. The first two columns show intention-to-treat estimates excluding (model 1) and including (model 2) our main set of controls. These regression results are unconditional on the potential donors' participation status in DKMS initiatives. Focusing on the regression including our base controls in model 2, the RETYPING initiative is associated with a 2.86 pp greater predicted probability of being available at CT for donors invited to this initiative, compared with receiving no invitation (significant at the 1 percent level).

Focusing next on the status update initiatives, being requested to participate in the initiative STATUS UPDATE–BLOOD is associated with an average increase in predicted CT availability of 2.91 pp, compared with receiving no request (significant at the 1 percent level). Considering that participation in the initiative is 33.3 percent, this result is sizable. We also find that the coefficients on STATUS UPDATE–BLOOD and RETYPING are not statistically different from each other ($p = 0.9491$, Wald test). Being invited to the STATUS UPDATE initiative is associated with a 1.31 pp increase, but this is not statistically significant. STATUS UPDATE–BLOOD has a 1.6 pp larger association with availability than STATUS UPDATE ($p = 0.083$, Wald test). STATUS UPDATE is not different from the initiative RETYPING ($p = 0.1489$, Wald test). In sum, this corresponds to a reduction in unavailability of 5.7–12.7 percent (based on the baseline unavailability of 22.9 percent (calculated as 100 percent minus the outcome mean of the reference group of 77.1 percent).

Model 3 of Table 3 shows the predicted CT availability of potential donors by participation status in DKMS initiatives. Participation is defined as the active, voluntary choice by

TABLE 3. Relationship between initiatives and potential donors' CT availability

Dependent variable:	CT availability			
Method:	LPM	LPM	LPM	2SLS
Model:	(1)	(2)	(3)	(4)
RETYPING	0.0267[a]	0.0286[a]		
	(0.0058)	(0.0060)		
STATUS UPDATE	0.0369[a]	0.0131		
	(0.0087)	(0.0091)		
STATUS UPDATE–BLOOD	0.0545[a]	0.0291[a]		
	(0.0039)	(0.0043)		
RETYPING, NO			−0.0565[a]	
			(0.0100)	
RETYPING, YES			0.0892[a]	0.0491[a]
			(0.0068)	(0.0103)
STATUS UPDATE, NO			−0.0218[c]	
			(0.0113)	
STATUS UPDATE, YES			0.0869[a]	0.0398
			(0.0130)	(0.0293)
STATUS UPDATE–BLOOD, NO			−0.0073	
			(0.0054)	
STATUS UPDATE–BLOOD, YES			0.1002[a]	0.0853[a]
			(0.0053)	(0.0125)
Controls	No	Yes	Yes	Yes
Observations	91,670	91,670	91,670	91,670
R^2	0.0021	0.0419	0.0456	0.0447
Outcome mean (no invitation)		0.7709		
Wald tests (*p*-values)				
Retyping = Status update		0.1489		
Retyping = Status update–blood		0.9491		
Status update = Status update–blood		0.0830		
Retyping, yes = Retyping, no			0.0000	
Status update–blood, yes = Status update–blood, no			0.0000	
Status update, yes = Status update, no			0.0000	
Retyping, yes = Status update, yes			0.8735	0.7614
Retyping, yes = Status update–blood, yes			0.1907	0.0200
Status update, yes = Status update–blood, yes			0.3400	0.1495

TABLE 3. *Continued*

Dependent variable:	CT availability			
Method:	LPM	LPM	LPM	2SLS
Model:	(1)	(2)	(3)	(4)
Retyping, no = Status update, no			0.0208	
Retyping, no = Status update–blood, no			0.0000	
Status update, no = Status update–blood, no			0.2407	

Note: This table shows an intention-to-treat linear probability model (LPM) (models 1 and 2), linear probability model by participation status (model 3), and local average treatment effect using two-stage least squares (2SLS) (model 4), using a potential donor's availability for first confirmatory typing (CT) request as the dependent variable. The control variables comprise registration method, mode of sample collection, sex, ancestry, population size of municipality of residence, body mass index (squared), age categories, year of registration, federal state of residence, information letter dummy, multiple invitation dummy, and month of request. We include dummies (or separate categories) for missing continuous (categorical) covariates. Base category in all specifications: no invitation. Robust standard errors are reported in parentheses. [a]represents a significance level of 1%. [c]represents a significance level of 10%. Constant not shown.

a registry member to take part in an initiative, after having received an invitation letter, under the condition that she is medically eligible. We observe that, if donors actively decided to participate in an initiative, their availability in a future CT request is significantly higher than for donors who do not receive any invitation (base group). Second, if donors did not agree to participate in an initiative, their future availability is significantly lower than that of the base group. This applies to all of the initiatives we study, and all coefficient tests of the differences between participants and nonparticipants within an initiative are significant at the 1 percent level.

In detail, donors' participation in STATUS UPDATE–BLOOD is associated with a 10.0 pp higher predicted CT availability (significant at the 1 percent level), while STATUS UPDATE participation is associated with a 8.7 pp higher availability rate, compared with the average registry member who does not receive any invitation. Furthermore, donors participating in the initiative RETYPING show a 8.9 pp higher CT availability. Testing the equality of these coefficients, we find that the coefficients are not significantly different from each other. Hence, compared with the reference group, participation in all three initiatives is positively associated with CT availability.

Turning to nonparticipants, we find a sizable and statistically significant negative correlation with CT availability for two out of three initiatives. The largest negative estimated coefficient can be found for nonparticipation in the RETYPING initiative, with a 5.7 pp lower average availability. For status update initiatives, the predicted availability of nonparticipating donors is between less than 1 pp (STATUS UPDATE–BLOOD, NO) and 2.2 pp (STATUS UPDATE, NO) lower than the reference group, with the coefficient of STATUS UPDATE–BLOOD, NO being not significant. The difference between RETYPING, NO and STATUS UPDATE–BLOOD, NO is significant ($p = 0.0000$), as is the difference between RETYPING,

NO and STATUS UPDATE, NO ($p = 0.0208$). However, the difference between STATUS UPDATE–BLOOD, NO and STATUS UPDATE, NO is not significant ($p = 0.2407$). Overall, these results show that participants in the registry's initiatives are more likely to be available than nonparticipants.

Model 4 of Table 3 shows the estimated local average treatment effect for each initiative. STATUS UPDATE–BLOOD has the highest association with CT availability with an 8.5 pp magnitude, followed by RETYPING with an estimated coefficient of 4.9 pp. However, the coefficient for STATUS UPDATE is not significantly different from zero, which might be partly explained by the smaller number of observations for this initiative. Based on the outcome mean of the reference group, our results correspond to a reduction in unavailability of 17.5–37.1 percent, depending on the initiative. Further, they are largely in line with the intention-to-treat estimates. However, they show a larger impact of the initiatives.

These results suggest that the initiatives do not just sort donors on availability, but are associated with their participation decision. The magnitude of the local average treatment effect associated with STATUS UPDATE–BLOOD is about 85 percent the size of the associated coefficient in the *by participation* specification, suggesting that 15 percent of the coefficient from the *by participation* specification is due to a self-selection of potential donors into the initiative. Similar computations can be made for the RETYPING initiative, where 45 percent of the "yes" coefficient in the *by participation* specification is due to self-selection.

B. ROBUSTNESS AND MECHANISMS

In the Online Appendix, Section B.1, we replicate our main intention-to-treat results using a linear regression adjustment model to estimate the average treatment effects on the treated (ATET) individuals, where "treated" denotes all individuals invited to an initiative (not just participants). This analysis estimates how the CT availability of those persons in the registry who were invited to an initiative would have changed, had they not been invited. The ATET regression adjustment estimator thus estimates the predicted potential outcomes fitted separately for the group of treated individuals, conditional on their covariates, with the estimated potential outcome differences for each covariate value being weighted by the probability of having the particular value of the covariate (Abadie and Cattaneo 2018). This approach ensures that, with regard to the individuals who receive the "treatment," the control group is valid for statistical comparison, since our treated group is a subset of the comparison group in terms of covariates by virtue of the selection criteria for each initiative. The results are qualitatively robust to this test, and the estimated coefficients are slightly larger in magnitude than those from our main LPM estimates in Table 3.

Further, results including additional control variables in Table B.5 in the Online Appendix, specifically the knowledge of potential donors' e-mail addresses at CT, year fixed effects, and the HLA genotype rank, show robustly positive correlations of the RETYPING and STATUS UPDATE–BLOOD initiatives. These controls are not included in the main specification we presented above, as they are measured later than baseline; also, they could potentially be outcomes of the independent variables of interest. Nevertheless, they account for substantial variation in the outcome variable.

Next, we use the methodology of Oster (2019) to assess the potential role of unobserved confounding factors in explaining our estimated coefficients. Specifically, we estimate

Oster's δ, that is, the degree of proportional selection generated by unobservable confounders, relative to observables, that would be needed for our results to be fully explained by omitted variable bias (hence, that would nullify our estimated coefficients). Estimates of δ for our preferred specifications range between 1.4 and 2.9. These estimates were generated assuming that the maximum R^2 is 1.3 times the R^2 from our regressions with controls. Because selection on unobservables would need to be substantially larger than the selection on our observed controls for our estimated coefficients to be nullified, we conclude that the positive relationship between our initiatives and CT availability is unlikely to be entirely the result of unobserved selection (see Online Appendix, Section B.2, for more details). It is important to reemphasize that in our regression analyses, we include controls for all of the selection criteria used by DKMS to make invitations to the initiatives.

The analysis presented in Table 3 aims to account for potential selection into initiatives based on observed criteria that make registered donors eligible to be in the initiative. These results therefore account for sorting at the stage of selection into the initiatives. However, there is one more stage of potential selection, which comes at the later stage of selecting registry members into CT requests. Hence, in a further robustness check in Table 4, we test whether the initiatives are associated with CT availability through sorting registry members into *CT requests* on observable characteristics, or whether the initiatives correlate with the CT availability of a *randomly drawn member* of the registry population. Note that, among DKMS's total registry population, some members have received a request for CT and some have not. However, as we are interested in the drivers of CT availability, we use only the subsample of registry members who have received at least one CT request from 2013 to 2018, and not the overall registry population. Thus, any analysis of initiatives and CT availability, which does not account for the selection into the sample of first CT requests, could be due to the initiatives being associated with a different selection of registered donors upon invitation to CT.

For this exercise, we re-weight the sample to be representative of the overall population of DKMS registry members in Germany based on age, gender, and their participation status in the initiatives. Importantly, this relies on persons who have not (yet) received a request for CT. If we observe a correlation between initiatives and outcomes after re-weighting the sample to be representative of potential donors in the whole registry, this would indicate that the invitation letters explain CT availability on top of sorting on the observables used for weighting. If the correlation reduces after re-weighting, then the coefficient is potentially driven by sorting via the initiatives based on the observable characteristics used to weight the sample.

Our weighting analysis relies on data from approximately 19 million donor-years, where a donor-year is the observation of a potential donor in a specific year on the registry. These donor-year weights represent the average probability of being asked to donate from the entire German DKMS registry over the sample period 2013 to 2018 and, hence, capture the overall composition of the registry in our sample period. In detail, the weights are constructed as follows. First, by gender, age bracket, and initiative participation status (i.e., whether someone participated in a specific initiative [yes or no], and also a separate category for the control group that has no invitation), we calculate the average number of donors in the registry for the entire year in each year of observation, and again take the average of this

TABLE 4. Initiatives and potential donors' CT availability: Inverse probability weight analysis

Dependent variable:	CT availability	
Method:	LPM	LPM
Model:	(1)	(2)
RETYPING	0.0376[a]	0.0299[b]
	(0.0103)	(0.0122)
STATUS UPDATE	0.0454[a]	0.0134
	(0.0158)	(0.0168)
STATUS UPDATE–BLOOD	0.0524[a]	0.0043
	(0.0078)	(0.0080)
Controls	No	Yes
Observations	89,748	89,748
R^2	0.0011	0.0466
Wald tests (p-values)		
Retyping = Status update		0.4325
Retyping = Status update–blood		0.0754
Status update = Status update–blood		0.6250

Note: This table shows results from an intention-to-treat linear probability model (LPM), using a potential donor's availability for first confirmatory typing (CT) request as the dependent variable. The estimations use inverse probability weights to make the sample representative of the total donor registry in terms of the participation decision in the initiatives, age, and gender. The control variables comprise registration method, mode of sample collection, sex, ancestry, population size of municipality of residence, body mass index (squared), age categories, year of registration, federal state of residence, information letter dummy, multiple invitation dummy, and month of request. We include dummies (or separate categories) for missing continuous (categorical) covariates. Base category in all specifications: no invitation. Robust standard errors are reported in parentheses. [a]represents a significance level of 1%. [b]represents a significance level of 5%. Constant not shown.

over the sample period. In each cell (age bracket, gender, participation status), we also calculate the average number of *CT requests* per year over the sample period. The average number of CT requests per cell in the sample period divided by the average number of donor-years per cell in the sample period gives us the probability of being selected into the sample. We use the inverse of this probability to weight observations in a set of analyses below.

In Table 4, we first replicate the main results of our intention-to-treat analyses and find that, while the RETYPING initiative has a positive correlation with aggregate CT availability, both STATUS UPDATE and STATUS UPDATE–BLOOD are not significantly correlated with availability. Further, the coefficient of the STATUS UPDATE–BLOOD initiative is quite precisely zero, which makes it likely that the point estimate from our main results of STATUS

UPDATE–BLOOD is primarily due to the initiative's impact of sorting donors on observable characteristics that are correlated with availability. The RETYPING initiative, on the other hand, still positively correlates with availability after taking gender and age composition of CT requests into account, which indicates that it may impact availability through some other channel on top of any sorting.

C. IMPLICATIONS FOR THE STEM CELL REGISTRY

Results from the previous section confirm that the initiatives by DKMS are indeed robustly associated with higher CT availability rates. A natural question is whether it is more cost-effective to recruit additional potential donors to the registry (at the current level of availability) or to provide the initiatives with more resources to increase potential donors' availability. In the following, we offer a simple thought experiment that compares the marginal costs for an additional successfully processed confirmatory typing request in case of (1) recruiting a new member to the registry and (2) inviting an already registered potential donor to one of DKMS's initiatives described above.

We first consider the case of someone who has been recruited to the registry. The allocated full costs per recruited registry member, upon initial registration, are €40.[21] This amount comprises the following: laboratory typing costs (60 percent), marketing and communication costs (17 percent), personnel costs (12 percent), and infrastructure and other administrative costs (11 percent).[22] Considering infrastructure and other administrative costs to be sunk, marginal costs per recruited member upon initial registration amount to €35.6 (€40 · 0.89).

Defining p as the likelihood of an average registry member, who has not been invited to any initiative, to be invited for confirmatory typing, it costs €X $(35.6/p)$ for each person who will be asked to follow through. Recall from Table 1 that the average CT availability rate for a potential donor, who has not been invited to any initiative, amounts to 77.1 percent. Hence, the marginal costs for a successful follow-through from recruiting a new registry member are €$35.6/(p \cdot 0.771)$ or €$46.2/p$.

Next, we consider the case of a registry member who participates in the STATUS UPDATE–BLOOD initiative. As can be seen from Table 1, the CT availability rate now increases from 77.1 percent to 90.5 percent. Marginal costs in the STATUS UPDATE–BLOOD initiative arise for completion of donor typing, postage, and personnel and sum up to about €24 per potential donor. Defining q as the likelihood of a registry member who is part of the initiative to be invited for CT, the total marginal cost for a participating member to follow through at the CT stage can be characterized as €$24/((0.905 - 0.771) \cdot q)$ or €$179.1/q$.

Comparing the two cases shows that the marginal costs of generating one additional successful donor-CT with the STATUS UPDATE–BLOOD initiative would be lower than the marginal costs of getting an additional follow-through via recruiting someone onto the registry if $(179.1/q) < (46.2/p)$, or $q/p > 3.9$. Donor registry practice typically shows that retyping efforts significantly exceed this ratio. For example, gaining additional information

21 €1 is equivalent to $1.0808 (May 19, 2023; see https://www.ecb.europa.eu/stats/policy_and_exchange_rates/euro_reference_exchange_rates/html/eurofxref-graph-usd.en.html).

22 See https://www.dkms.de/aktiv-werden/geld-spenden.

on a registered donor's CMV antibody status through the STATUS UPDATE–BLOOD retyping initiative strongly affects donation probabilities (see Figure 3 of Schmidt et al. [2020b]). For donors aged between 18 and 25 years, information on CMV antibody status increased donation probabilities for males by a factor of 4.5 (3.6) when the serostatus was positive (negative). The corresponding factors for female donors were 3.7 and 2.9, respectively. These factors represent relative differences in donation probabilities that are highly correlated with the above parameters p and q and hence show that CMV retyping as a part of STATUS UPDATE–BLOOD more than covers the cost of retyping younger (male) donors, who are most preferred. This indicates that such retyping initiatives will be very likely to reduce the marginal cost for each completed stem cell donation, at least for donors below a certain age (older donors are generally less often requested by transplant physicians). Further, more complete HLA typing profiles have been shown to make donors between 2 and 8 times more likely to donate when comparing well-typed donors with those with less comprehensive typing (Müller et al., 2012).

Moreover, it is important to stress that the above calculations only focus on costs, while ignoring potential benefits such as an increased availability and an accelerated donor search process, which is of utmost importance for patients who urgently need a stem cell transplant. The status update initiatives contribute to reducing time to transplant, as registry members can be temporarily excluded from the donor search process because of health reasons or reported periods of unavailability, thus preventing search coordinators from requesting them for CT firsthand and thus losing time. Furthermore, CT processing time itself is also shortened as the registry always possesses up-to-date contact and health status information of potential donors who are in regular contact with the registry via our initiatives. This is relevant also for donor registry efficiency, as often the donor who has gone through the CT process the fastest is ultimately selected.

For registries with lower initial rates of successful follow-through, the STATUS UPDATE–BLOOD initiative might be considered even more cost-effective, since the positive impact on availability might be even higher here (i.e., initiatives would even more significantly exceed the above-mentioned ratio). To conclude, focusing on benefits, the above considerations show that the mentioned initiatives involving retyping (the other initiatives are much less expensive) result in significant additional requests (CT requests and subsequent requests for stem cell collections) and associated revenue for DKMS. In sum, our analyses show that the initiatives reduce the marginal costs while increasing the benefits for the registry to provide stem cell donations when needed.

V. Discussion and Conclusion

We studied a set of initiatives implemented by DKMS Germany, a large stem cell donor registry, meant to improve the registry's operating efficiency and the ultimate availability to continue the donation process by registry members who are a match for a patient in need of a transplant. Our results indicate that the initiatives were beneficial for two reasons. First, our results suggest that the invitation to participate had a direct positive impact on completing the CT request and, hence, a large relative reduction in attrition. Second, we find that, by providing registry members an opportunity to sort themselves into participants

and nonparticipants, the initiatives improved DKMS's ability to identify potential donors who were more likely to follow through at CT when requested. Our results imply that the attrition at CT of participants in the initiatives was between 17.5 percent and 37.1 percent lower than for nonparticipants.

Our findings are likely related to the varying costs that registry members must bear to participate in the initiatives. Specifically, in the STATUS UPDATE initiatives, donors are asked to inform the registry in advance about future periods when they will be unavailable. By reporting their unavailable dates, donors enable DKMS to make CT requests more efficiently. This is because DKMS can avoid inviting potential donors for CT during times they have already indicated they are unavailable. Moreover, the request to report periods of unavailability might also lead to an increase in donor availability because of a psychological effect whereby the act of considering and formally acknowledging their availability might reinforce their commitment to move forward with the donation when requested. That is, it is possible that once donors commit to reporting their unavailability, the perceived cost of being unavailable for CT is perceived as more significant. This could mean that donors feel a greater sense of responsibility or obligation after agreeing to this reporting process, which might influence their decisions regarding availability. Further, in the RETYPING initiative, registry members are requested to submit cheek swabs or to go in to give a blood sample to either improve the resolution of the factors relevant for a transplantation or to include further parameters (e.g., CMV status) that might be helpful in potential future donor searches (see Table A.1). However, these proactive requests from the RETYPING initiative might be perceived as burdensome by the registry members. This perception arises because the immediate benefits of complying with these requests may seem minimal to the individual donor, especially when compared with the upfront effort and time involved in providing new samples for retyping. These perceived costs could be even larger if donors have strong time preferences (Andreoni and Serra-Garcia 2021). As a result, those registry members who opt to participate in the RETYPING initiative are likely those who are willing to accept these costs. This willingness to incur such costs is likely indicative of a deeper commitment to the cause, suggesting a higher likelihood of being available for confirmatory typing (CT) when their participation is requested.

Our findings provide some practical implications for stem cell registries and, more generally, registries of donors of substances of human origin. The benefits of any market mechanism designed to match donors and patients, such as stem cell donor registries, can only unfold if registered potential donors participate when called. Participation in market mechanisms specifically designed to increase tissue and organ transplants remains a substantial issue, sometimes requiring additional mechanisms and incentives to succeed (e.g., Sönmez et al. 2020). Our results indicate that the participation choice of potential donors in an initiative contains information on CT availability. Since participants are more available than nonparticipants, this information from participation decisions can be used to identify committed donors. Thus, given two biologically matched donors for a patient, all other things equal, one would prefer to ask a potential donor participating in an initiative for confirmatory typing, if faced with the constraint of only being able to invite one potential donor at a time. This strategy can potentially lead to a faster transplantation and a reduced risk of the CT not being carried out for a matching donor, which would mean having to go back to

other matches and starting the work-up process over again. From a managerial point of view, when managing a registry organization, it is important to understand whether and how recruitment and retention practices ultimately affect the availability of donors to follow through with the donation process. From a health-policy perspective, our results have implications for the information exchange between donor registries and transplant centers. In particular, to improve the efficiency of the donation process, donor registries should have the possibility of making such information available to transplant search coordinators, which is currently not always feasible.

This study has strengths and limitations. One of the main strengths is our analysis of a large data set, which includes more than 90,000 CT requests along with a rich set of individual characteristics. This data set is particularly valuable because it contains information on initiatives that involved either retyping patients or asking them about their future unavailability. The significance of this large data set is underscored by the fact that the average lifetime probability of receiving a request for CT is about 4 percent for an 18-year-old. Therefore, a large number of invitations were sent out to registered donors beforehand. Additionally, our data set stands out in the context of existing research. While there is substantial research in health economics focusing on blood donation, studies on stem cell donations are relatively scarce. This distinction is crucial because the context of stem cell donation differs significantly from blood donation, particularly in terms of the time frame involved. Our data encompass a potentially long period from the initial registration and various initiatives to the eventual CT request. This extended timeline is a key factor that sets stem cell donation apart and underscores the value of our research in this less-explored area.

A limitation of our study is that the assignment to the initiatives was not randomized. However, there are two important considerations to note in this context. First, despite the lack of randomization, we had access to detailed information about the criteria used for assignment to these initiatives. This allowed us to control for relevant variables in our analysis. Additionally, because of cost and technical constraints, only a subset of registry members who met these criteria were actually invited to participate in the initiatives. This situation provided us with a unique opportunity to draw comparisons between those who were invited and a relevant baseline sample of registry members who were not invited. Second, it is also important to emphasize that obtaining randomized data over such an extended period and for such a large number of CT requests, as we have managed with data from DKMS, is fairly rare. The scale and duration of the data we analyzed are exceptional in this field, and while the lack of randomization is a limitation, the breadth and depth of the data still offer significant insights into the dynamics of stem cell donation and the effectiveness of different initiatives. That said, the lack of randomization also limits our ability to identify the precise mechanism(s) through which the initiatives might have had their impact. For instance, conducting a randomized controlled field experiment would enable us to discern the specific behavioral channels at play. Such an experiment could reveal how different appeals, tailored to various preferences or psychological constructs, might effectively engage registry members who are more inclined to donate. Consider, for example, our findings that suggest that the STATUS UPDATE–BLOOD initiative can serve as a commitment device. It is possible that the effectiveness of this initiative is partly due to the way the invitation letter frames

participation as "joining a team," which could resonate with certain registry members. However, without the clarity that randomization provides, we cannot definitively ascertain this or other similar behavioral pathways.[23]

In sum, our study indicates that the retyping and status update initiatives can meaningfully enhance donor availability at the CT stage and help to sort potential donors before the crucial CT stage is initiated, thus saving costs and time by eliminating the need to invite donors who are less likely to follow through. These initiatives can help optimize the stem cell donation process, increasing the likelihood of requested registry members' availability and reducing delays in the donation process, thereby improving patient outcomes. Our findings provide insights on refining recruitment and status update strategies in two-stage volunteer markets, ensuring a high follow-through rate among registry members. This approach facilitates a quicker, more efficient donor search, which is essential for patients needing a transplant. Our findings also offer insights potentially applicable to other areas of volunteering, where people are called upon to receive training in between initially signing up to be, for example, an emergency first-aid helper, or a volunteer firefighter or rescuer, and the actual call to duty (Coffman et al. 2017; Exley and Petrie 2018). In such settings, asking volunteers to refresh their status as a member, or continually provide updates, can help increase their ultimate commitment toward the cause, or preselect the volunteers based on participation in certain initiatives.

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23 The wording of the invitation letters in STATUS UPDATE–BLOOD and STATUS UPDATE initiatives differed. Letters for the STATUS UPDATE–BLOOD initiative emphasized the recruitment of "quickly available team members," whereas in STATUS UPDATE, the letter is framed more neutrally. The effect of informing donors about their higher likelihood of being asked to donate, without nudging potential donors to participate, is likely to be small. Overall, the results support the intuition that bringing forward part of the costs of the CT request can improve availability by acting as a commitment device.

Appendix

TABLE A.1. Overview of the registry's initiatives

	Initiatives		
	Retyping	Status update	Status update–blood
A. Initiative characteristics			
Years run (within our sample period)	2013–18	2015–18	2013–17
Motivation for initiatives	Typing profile incomplete or low resolution.	Increase in CT availability for the group of participating donors, in particular by allowing them to report periods of unavailability for CT request; bringing forward parts of the CT process.	Increase in CT availability for the group of participating donors, in particular by allowing them to report periods of unavailability for CT request; bringing forward parts of the CT process.
Selection criteria	Selection criteria include age, low- or intermediate-resolution (i.e., incomplete) HLA typing profile, BMI, no medical bans, sex, in DKMS database for a specific time span, e-mail address, missing information on CMV antibody status, genotype frequency rank.	Selection criteria include age, genotype frequency rank, sex (in the beginning of the initiative), maximum number of participants per rank, high-resolution HLA typing profile, e-mail address, BMI, no medical bans. Blood type, rhesus factor, and cytomegalovirus immunity status are known.	Selection criteria are analogous to STATUS UPDATE, but blood type, rhesus factor, and cytomegalovirus immunity status are unknown.

TABLE A.1. *Continued*

	Initiatives		
	Retyping	Status update	Status update–blood
Invitation letter	Focus on technological advancement in retyping (e.g., CMV antibody status, additional HLA locus).	They are asked since they have a higher chance of being matched.	They are asked since they have a higher chance of being matched; letter includes team framing.
Our sample: potential donors with CT request	5,193	2,144	10,905
B. Participation requirement in initiative			
Provide unavailability dates	No	Yes	Yes
Health questions	Yes	Yes	Yes
Retyping required	Yes	No	Yes
Sample	New/Frozen (cheek swab/blood)	No	New (blood)

Note: This table provides an overview of the DKMS initiatives that we study in this paper. Notice that this is a subset of a broader set of initiatives run by DKMS. In this study, we consider only potential donors with a confirmatory typing (CT) request. The use of frozen samples was not eligible for all initiatives as, for instance, laboratory protocols change or old samples can deteriorate in quality.

TABLE A.2. Description of control variables included in our regression analyses

Variable	Description
	A. Registry-related characteristics
Registration method	Categorical variable indicating whether potential donors had registered at public drive centered\not centered around a specific patient, company drive, special project drive (e.g., at schools, universities, sports events, and among police, firefighters, and armed forces), or online via the DKMS website.
Mode of sample collection	Categorical variable measured at time of potential donors' registration for collection through blood draw or cheek swab.
Month of CT request	Categorical variable for month of CT request.
	B. Potential donor–related characteristics
Sex	Dummy variable for females (zero for males).
Age	Categorical variable (eight categories) for donors' age at time of CT request: 17 to 25 years, 26 to 30 years, 31 to 35 years, 36 to 40 years, 41 to 45 years, 46 to 50 years, 51 to 55 years, and 56 to 61 years.
Ancestry	Dummy variable for (self-reported) ancestry being either German or from other countries.
State of residence	Categorical variable for registry members' state of residence during registration: Baden-Württemberg, Bavaria, Berlin, Brandenburg, Bremen, Hamburg, Hesse, Lower Saxony, Mecklenburg-Western Pomerania, North Rhine-Westphalia, Saarland, Saxony, Saxony-Anhalt, Schleswig-Holstein, and Thuringia.
Population size at residence	Categorical variable for population size at the municipality of residence: <50,000, 50,000 to 99,999, 100,000 to 199,000, 200,000 to 499,999, and ≥500,000.
BMI	Continuous variable comprising registry members' body mass index (BMI).
Date of registration	Categorical variable for time when registration took place: before 2007, 2007 to 2010, 2011 to 2014, and 2015 to 2018.
Information letter	Dummy indicating whether registry member received an information letter that their frozen sample was used for retyping. No active participation choice of potential donors required.
Multiple invitations	Dummy indicating that registry member donor had been invited to another initiative.

TABLE A.3. Descriptive statistics of categorical variables

Variable name	Variable value	Number of cases	Rate of CT availability (%)
	A. Registry-related characteristics		
Recruitment method	Non-patient-centered public community drive	21,439	75.7
	Patient-centered public community drive	20,134	77.3
	Company drive	4,430	73.7
	Special projects	14,319	74.7
	Online registration	31,302	82.2
	Missing	46	80.4
Sample collection	Blood draw	34,205	76.3
	Cheek swab	48,197	79.6
	Unknown	9,268	75.8
Month of request	January	7,560	78.0
	February	7,262	78.0
	March	7,865	78.8
	April	7,439	78.1
	May	7,476	77.9
	June	7,934	77.8
	July	8,058	77.7
	August	8,114	78.0
	September	7,517	78.4
	October	8,021	77.6
	November	7,254	77.8
	December	7,170	77.6
	B. Potential donor–related characteristics		
Sex	Female	34,876	73.9
	Male	56,794	80.5
Age categories	17 to 25	34,761	79.7
	26 to 30	20,414	77.7
	31 to 35	12,801	75.9
	36 to 40	8,523	78.0
	41 to 45	6,307	79.3

TABLE A.3. *Continued*

Variable name	Variable value	Number of cases	Rate of CT availability (%)
	46 to 50	5,227	76.8
	51 to 55	2,809	72.2
	56 to 61	828	61.5
Ancestry	German	77,304	80.3
	Non-German	10,973	62.6
	Missing	3,393	75.6
Federal state of residence	Baden-Württemberg	14,372	78.4
	Bavaria	15,119	79.3
	Berlin	3,026	76.2
	Brandenburg	1,427	78.6
	Bremen	770	75.8
	Hamburg	2,060	77.6
	Hesse	6,673	77.2
	Lower Saxony	21,081	77.1
	Mecklenburg-Western Pomerania	1,183	76.1
	North Rhine-Westphalia	10,870	78.9
	Rhineland-Palatinate	4,723	78.3
	Saarland	1,019	77.0
	Saxony	2,966	77.0
	Saxony-Anhalt	960	77.7
	Schleswig-Holstein	3,899	78.2
	Thuringia	1,463	77.8
	Missing	59	72.9
Population of place of residence	<50,000	54,540	78.9
	50,000–99,999	8,812	77.2
	100,000–199,000	6,067	75.9
	200,000–499,000	8,279	76.0
	>500,000	13,972	77.2

TABLE A.3. *Continued*

Variable name	Variable value	Number of cases	Rate of CT availability (%)
Year registered	Until end 2006	8,138	74.0
	2007–10	16,435	74.8
	2011–14	39,191	79.2
	2015–18	27,906	79.3
Information letter	No	83,319	78.4
	Yes	8,351	74.4
Multiple invitations	No	90,198	77.9
	Yes	1,472	81.5

TABLE A.4. Summary statistics of potential donor–related characteristics by initiative

Variable	Mean	SD	Count	Min.	Max.
No invitation to initiative (baseline)					
Age	30.71	9.88	73,237	17	60
Female	0.39	0.49	73,237	0	1
German ancestry	0.87	0.34	70,610	0	1
BMI	24.35	3.29	73,237	13	40
Retyping					
Age	30.17	8.29	5,180	18	57
Female	0.35	0.48	5,180	0	1
German ancestry	0.90	0.30	4,515	0	1
BMI	24.27	3.25	5,180	16	38
Status update					
Age	27.36	7.07	2,113	17	55
Female	0.29	0.45	2,113	0	1
German ancestry	0.87	0.34	2,109	0	1
BMI	24.32	3.10	2,113	17	37

TABLE A.4. *Continued*

Variable	Mean	SD	Count	Min.	Max.
Status update–blood					
Age	28.85	6.59	11,140	18	51
Female	0.32	0.47	11,140	0	1
German ancestry	0.93	0.26	11,043	0	1
BMI	24.44	3.00	11,140	16	40

Note: $N = 91,670$. This table shows summary statistics of donor-related characteristics of first CT requests by initiative.

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