Improving the availability of unrelated stem cell donors: Evidence from a major donor registry*

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February 17, 2022

Abstract

The unavailability of potential stem cell donors poses a critical challenge for donor registries worldwide. This study investigates the impact of initiatives of a stem cell donor registry to enhance donors' availability for confirmatory typing. Initiatives ask donors to provide a sample for genetic analysis and/or information on their temporal unavailability. We analyzed 91,479 confirmatory typing requests from DKMS Germany, a large stem cell donor registry, exploiting a quasi-random initiative assignment based on observable characteristics. We find that, first, invitation to the initiatives increases donors' availability. Intention-to-treat estimates yield effects ranging from 2.5 to 3.2 percentage points, and local average treatment effects estimates range from 3.8 to 8.2 percentage points (baseline: 77.1%). Second, the difference in availability between participants and non-participants is over 10 percentage points. The initiatives yield a direct positive effect on donor availability and a selection effect through which participation signals a higher commitment.

Keywords: Unrelated stem cell donation, donor availability, registry initiatives, sorting, intention-to-treat, local average treatment effects
JEL Codes: I12, I18

1 Introduction

For many patients suffering from leukemia or other blood diseases who lack a related donor, a 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, consequentially, reducing the chances of survival for many patients.

Stem cell donation is a multi-stage process. First, individuals willing to donate stem cells sign up to

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a registry. Then, potential donors wait for a matching patient, which might take several years, if ever.[1] Once a matching patient is found, a request for confirmatory typing (CT; sometimes called verification typing) 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; Heger et al., 2020). The CT stage is thus *the* crucial milestone in the process of actually becoming a stem cell donor.[2] Unfortunately, stem cell donor registries around the world are faced with considerable donor attrition at the CT stage. This attrition leads to delays in donor search and increases in the time to transplant 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 ultimately are not available for transplantation (Anthias et al., 2020). For example, in the case of DKMS Germany, a major stem cell donor registry and the organization that provided the data for this study, the average attrition rate of potential donors from a CT request was 23% in 2018 (the final year of observation).[3] Thus, it is important for stem cell donor registry managers to understand whether, and how their recruitment and retention practices ultimately affect the availability of donors who are a match for a patient to follow through with the stem cell donation process.

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 CT request. The multi-stage 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, on the other hand, make a non-binding commitment to potentially donate somewhere in the (near or even distant) future. Hence, the donation process is characterized by uncertainty about whether or not an actual donation opportunity will materialize and, if so, when. This setup makes self-commitment problems more likely.

We analyze a set of initiatives implemented by DKMS Germany, a leading stem cell donor registry with more than 10 million registered donors (Schmidt et al., 2020), that attempt to address this challenge and/or may have an impact on donors' self-commitment. The initiatives are directed to individuals who have signed up to the donor registry, but who have not (yet) been requested for CT. Participation in the initiatives involves some costly action for the potential donor. Specifically, the registry asks donors to send in own biological material or schedule a blood draw for genetic retyping ("prospective" initiatives to obtain a higher resolution human leukocyte antigen (HLA) profile), and/or to report periods of unavailability in advance ("status update" initiatives). Low- and intermediate resolution HLA typing and donor unavailability at the CT stage are among the main reasons for registries' inability to provide suitable donors for patients. Retyping initiatives are helpful, because they allow the registry to obtain

[1] The average lifetime donation probability for donors who register with DKMS Germany at age 18 amounts to around 4%, while this number can be much higher for potential donors with unique biological characteristics.

[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 to the UK, with 38% attrition rate in 2011 (Lown et al., 2014) and more recently 35% estimated among Europeans and 56% among non-Europeans (Anthias et al., 2020). Attrition rate in Germany is also lower compared to the US, with estimates of 36% (Gragert et al., 2014), 40% (Switzer et al., 2013), 47% (Lown et al., 2014), and most recently 50% estimated using a machine learning algorithm (Sivasankaran et al., 2018). This emphasizes the large medical and economic benefits from improving the availability of stem cell donors and makes it a pressing issue for donor registries.

more accurate genetic information about potential donors. With status updates, the registry acquires important information about potential donors' (un)availability, which can be used to optimize donor prioritization. These initiatives can potentially have additional beneficial effects through at least two channels. First, voluntary participation in an initiative may signal a donor's level of commitment; if that is the case, participation might allow the registry to identify a select group of donors who are more likely to be readily available when called upon to make an actual donation. Second, being invited to an initiative might cause potential donors to become more committed or motivated, which may in turn have a positive effect on availability to make an actual donation. However, if the initiatives are perceived as burdensome by registered donors, they could potentially reduce motivation or commitment. Therefore, whether the initiatives have an overall positive or negative effect on availability at CT is an empirical question.

Understanding the impact of these initiatives can help answer important questions relevant for both stem cell donor registries and scholars interested in donation behavior. Despite the potential importance of such initiatives, empirical evidence on how they influence donor availability at the CT stage is scarce. We address this gap in the literature by empirically analyzing 91,479 CT requests issued to potential donors registered with DKMS Germany for the time period 2013 to 2018. The data include a rich set of donor- and registry-related variables that determine being invited to participate in the initiatives. We investigate whether the initiatives have an effect on donor availability at CT (direct effect) as well as whether donors who chose to actively participate in the initiatives are more likely to be available at CT (selection effect). Invitation to the initiatives was based entirely on observable, pre-determined (i.e., exogenous) characteristics of potential donors such as biological traits (e.g., age and sex) and genetic characteristics. This implies that invitees could not influence their probability of receiving an invitation letter to an initiative. Importantly, for cost reasons, not all potential candidates for receiving invitations by letter were invited, providing a large comparison group with substantial overlap in terms of observables. This means selection variables do not perfectly predict invitation, providing unsystematic variation in the invitations.

We perform the following empirical analyses. First, we evaluate the impact of retyping and status update initiatives on potential donors' CT availability. This analysis is unconditional on donor participation in these initiatives; in particular, we implement an intention-to-treat approach (ITT). Second, we analyze the predictive power of participation in the initiatives for CT availability, by exploiting information on the participation or non-participation of registered donors in these initiatives. Third, we estimate a local average treatment effect (LATE) using the invitation as an instrument for participation, to test whether there is an impact of initiatives on CT availability for the participants, net of observable selection effects.

We find that the CT availability of donors invited to a retyping initiative or to an initiative that involved both retyping and status update were 3.2 and 2.5 percentage points (pp), respectively, higher than of those who received no invitation (both significant at the one percent level). Since baseline attrition at the CT stage is 22.9%, this corresponds to a 14.0% (3.2/22.9) and 10.9% (2.5/22.9) reduction in attrition. However, simply asking for status updates without retyping did not yield significant effects.

We also estimate predictive effects of participation, and find that participants in all of the initiatives are 13-15pp more likely to follow through with CT than non-participants. The LATE estimates indicate that the retyping initiative and the retyping plus status update initiative led to 4.3pp and 8.2pp higher CT availability, respectively (both statistically significant at the one percent level); the status update initiative alone increased availability by 3.8pp, but this estimated effect was not statistically significant. Thus, the initiatives reduce attrition by between 16.6% (3.8/22.9) and 35.8% (8.2/22.9) for participants. Also, comparing the LATE to the selection effects for participants, our findings imply that between 40% and 60% of the availability increase of participants is due to the initiatives' causal impact, with the remaining portion being a selection effect. The results are robust to several robustness checks; in particular, using the methodology of Oster (2019), we conclude that our findings would still hold under reasonable assumptions about unobserved selection.

Our study contributes to several streams of literature. First, we contribute to the economics literature on medical donations. Unlike other medical donations such as blood and organs (e.g., Roth et al., 2004; Craig et al., 2017), the stem cell donation process varies significantly in several aspects. First, the point in time of stating the willingness to give is different from the point in time of the decision to actually donate. In case of whole blood (and plasma), for example, 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). Second, for stem cell donations, it is not uncommon that several years lie between registration and a first CT request. Compared to organ donation, where most transplants are from cadavers, stem cell donations are from living donors (Grieco et al., 2018).[4] Finally, donating stem cells is typically a high-stakes decision with life-saving implications for the recipient. 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 larger risks and discomfort than blood 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) find in a field experiment with blood donors that when there are shortages in volunteer markets for blood donation, creating a registry can increase responsiveness by 66%. However, with stem cell donation, the much longer and uncertain time horizon makes it difficult for registries to maintain donors' commitment and, ultimately, to guarantee their CT availability and donation. The initiatives we analyze in this paper attempt to address this problem, and take place during the potentially long interim stage after registration, but before an actual donation opportunity arises.

Findings on the effects of initiatives commonly conducted by stem cell donor registries, such as those we analyze in this paper, yield practical insights for the management of donor registries. In particular, we find that the association between CT availability and registered donors' participation in an initiative

[4]For example, from January to June 2021, 21,061 organ transplants were performed in the United States of America, 17,821 of which came from deceased donors, and 3,240 of which came from living donors: (https://optn.transplant.hrsa.gov/data/, accessed on August 5, 2021). Of the 24,522 unrelated stem cell transplants performed 2014-2018 in the US, 14% were from cord blood, the rest being from peripheral blood after stem cell mobilization or from bone marrow. Data retrieved on August 5, 2021, from https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplant-initiative-report.

is positive and larger in magnitude than the negative association of non-participants. Donors' decision to participate in an initiative, which requires a status update, yields practical information to the registry which would otherwise not be available. Based on reported periods of future unavailability of participating donors, for example, the registry is able to block the donor for the corresponding time period and this donor will not be requested by search coordinators of transplant centers. This would obviously render the donation process more efficient. As a consequence, donor registries should be given the possibility to make such information available to search coordinators. By uncovering these empirical relations, our paper makes a novel contribution to the literature and is of direct relevance to donor registries. Besides blood donation, our findings may also offer insights 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 the DKMS has increased steadily (see, for instance, Bergstrom et al., 2009; Schmidt et al., 2020), 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 the 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 (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 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 is associated with being available. Ambivalence about donation in the form of doubt and uncertainty, or wishing someone else would donate instead, is a strong driver of attrition across all ethnic groups (Switzer et al., 2013). Other papers assess the donors' 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).

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 HLA typing (Sauter et al., 2016) and, more importantly, donor attrition at the CT stage (Lown and Shaw, 2013). Thus, it is interesting whether the retyping initiatives, which should increase the possibility of finding a matching donor, are related to the attrition at the CT stage. We are one of the first to empirically assess the impact of initiatives requiring a status update, which are aimed at identifying a select group of donors to report unavailability in advance, so

they can be removed from searches during this time.

The remainder of the paper is organized as follows. Section 2 provides further background on the process from enrolling to becoming a stem cell donor and on the retyping and status update initiatives. In Section 3, we describe our data set and present initial descriptive analyses. Section 4 presents our estimation results. Finally, section 5 describes implications of our findings, discusses limitations, and concludes.

2 Background

2.1 The process from registering with a stem cell donor registry to donating

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 re-transplanted after the treatment, or allogeneic, where stem cells are collected from another person (related or unrelated). To put this into perspective, in the United States, for example, about 40% of stem cell transplants between 2015 and 2019 were allogeneic.[5] We consider the stem cell donor registry DKMS Germany, 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[6] with more than eleven million registered donors in seven countries: Chile, Germany, India, Poland, South Africa, United Kingdom, and the United States (more than 65% of registered donors are registered in Germany). Since its foundation in 1991, DKMS has facilitated over 95,000 stem cell collections, and its share of all unrelated stem cell donations worldwide actually amounts to about 40% (Schmidt et al., 2020).

Figure 1 illustrates the multi-stage 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 buccal swabs or small blood samples, which are then typed for human leukocyte antigens (HLA) by a genotyping service provider (Schöfl et al., 2017). 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.[7]

The quality of a match between a potential donor and a patient is mainly determined by the fit in their genetic information (HLA type).[8] Besides the HLA type, age and genetic parameters such as the ABO blood group and markers as the cytomegalovirus (CMV) antibody status[9] are secondary criteria to

[5] See `https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics`.

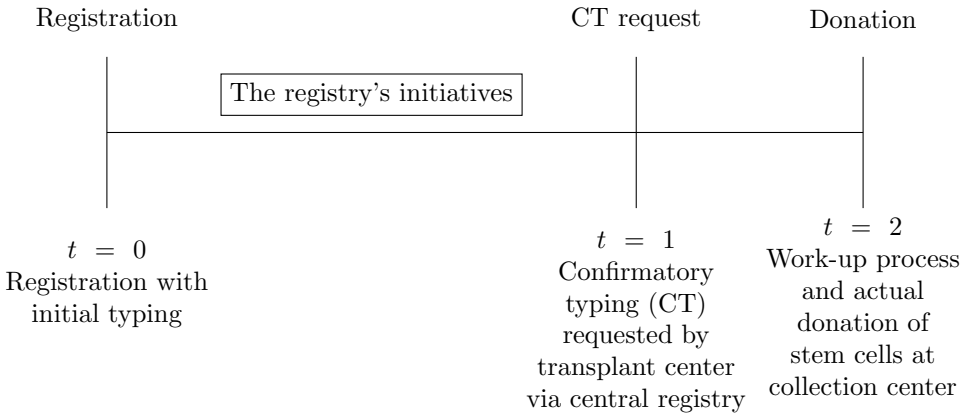
[6] See https://statistics.wmda.info for an overview.

[7] 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. 115,388 potential donors were recruited at 1,117 special drives with an average recruitment number of 103. However, more than half of actual donor recruits come from online registration.

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

[9] 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 registered stem cell donors



select 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 prospective donors have evolved considerably (Schmidt et al., 2020). It therefore continues to be essential to invest in the quality of prospective donors' genetic information (high-resolution typing) in the database by retyping donors with low-resolution profiles (some time after the initial registration at $t = 0$) using up-to-date laboratory methods.

Second, whenever a prospective donor turns out to be a suitable match for a patient based on HLA types and other characteristics, the transplant center responsible for the patient's treatment requests that the donor undergoes a CT ($t = 1$). The objective is to confirm that a donor is suitable, still committed, and medically eligible for a stem cell collection. During the CT stage, prospective donors participate in a phone consultation and a questionnaire-based medical clearing. Fresh blood samples are requested from the donor 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* important 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 prospective donor. First, it is uncertain whether a prospective donor, who is potentially a good genetic match, is (still) readily available in case of a CT request. 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 prospective donors are still committed to donate stem cells once they are asked for a 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.

2.2 The registry's initiatives

Over the years, DKMS Germany has launched several initiatives aimed at mitigating the above-mentioned problems of low-resolution typing, missing information about periods of donor unavailability, and lacking donor commitment at the CT stage. A group of potential donors is asked to participate in an initiative some time after signing up with the stem cell donor registry, but before the call for a CT.[10] Table 1 outlines the initiatives.

First, the initiative PROSPECTIVE, which was conducted between 2013 and 2018, requests retyping of potential donors usually via buccal swab or blood draw through a physician. The initiative also involves a short health questionnaire. Typically, donors with low resolution HLA profiles are asked to participate. Further criteria for potential donors to be invited to the initiative PROSPECTIVE are age, sex, HLA genotype frequency, BMI, and missing CMV antibody status. A request for retyping can be issued directly by the registry (the focus of our paper) or a transplant center (Schmidt et al., 2011). Updating the typing profile of a donor can ultimately accelerate the donor search process, as the search coordinator has more detailed information on the donor's suitability. Besides, it increases the chance that the donor will be requested in future donor searches. 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.

Second, since high-resolution typing upon recruitment became more commonplace, DKMS introduced an initiative in 2015, which we label STATUS UPDATE. This initiative emphasizes in the invitation letter that the potential donor has, based on certain biological parameters, a higher likelihood of actually being matched to a patient in need of a stem cell donation. The motivation for this initiative was to minimize delays at the future CT stage by asking donors to complete a short health questionnaire and to report any future unavailability that lasts longer than three weeks, for example, due to a longer stay abroad or a pregnancy. Based on reported periods of future unavailability of participating donors, the registry is able to block the donor for the corresponding time period and the donor cannot be requested by a search coordinator, which should increase CT availability. Furthermore, as the commitment to report future unavailability dates requires a particularly high donor motivation, the initiative was also intended to create a pool of high-availability donors.

Third, similarly to STATUS UPDATE, the initiative STATUS UPDATE-BLOOD aims to identify a subgroup of potential donors who have, by virtue of their common HLA genotype, age, sex, or other parameters a higher probability of actually being asked to donate at the CT stage. Again, the motivation was to minimize delays at the CT stage by bringing forward specific parts of the CT. Since a considerable number of donors were typed at an intermediate or a low resolution during their registration, this initiative included, in addition to a health questionnaire, high-resolution retyping through blood draw (which is different as compared to STATUS UPDATE). Another key aim of this initiative is again an increase in CT availability, as donors were also requested to inform DKMS in cases of temporal future unavailability. In

[10] DKMS selects these donors mainly based on exogenous, biological factors. These factors are predetermined prior to the invitations and the donors are highly unlikely to be aware of these in advance to the invitation.

Table 1: Overview on the registry's initiatives

	Initiatives		
	Prospective	**Status update**	**Status update−Blood**
A. Initiative properties			
Years run (within our sample period)	2013-2018	2015 - 2018	2013 - 2017
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.
Invitation letter	Focus on technological advancement in retyping (e.g., CMV antibody status, additional locus)	They are asked since they have higher chance of being matched	They are asked since they higher chance of match; 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
Re-typing required	Yes	No	Yes
Sample	New/Frozen	No	New

Notes. 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 only consider potential donors with a CT request.

contrast to STATUS UPDATE, the invitation letter to the initiative STATUS UPDATE-BLOOD also contains an explicit team framing, as DKMS asks invitees in the invitation letter to become part of a "team of quickly available donors". Invitees were also told that participants in the initiative are more genetically likely to be requested to donate stem cells, compared to non-participants. Between 2015 and 2017, the initiatives STATUS UPDATE and STATUS UPDATE-BLOOD were run simultaneously, and from 2018 onwards the STATUS UPDATE-BLOOD initiative was discontinued.

The invitation to each of the initiatives is done on a rolling basis, where blocks of prospective donors are created for each genotype frequency rank. For each rank, a pre-specified number of donors is selected who simultaneously meet additional selection criteria.

3 Methods

3.1 Data and variables

The initial DKMS data set contains the universe of 104,116 observations from *first* CT requests, and associated donor information, from 1 November 2013 to 31 October 2018. From the initial data set, we excluded observations with CT cancellations from the patient side prior to the registered donor 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 (7,198 observations). Some individuals had both a CT cancellation from the patient side and a patient-related retyping request, hence 12,637 observations were removed from the analysis. This leaves us finally with 91,479 observations for analysis.

The sample collected only contains first CT requests, 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%).

The outcome we are interested in is prospective donors' completion of the CT request. This is a binary variable called "availability": Prospective donors are regarded as available (coded 1) if 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 are, for instance, no longer being interested in donating, medical ineligibility due to illness, or temporary unavailability (e.g. being overseas or having an important reason limiting time available to donate). Importantly, DKMS is able to track persons who have changed address and not informed DKMS about this through the local municipality the person was last registered at.[11] As a result, there are only 779 cases in our sample where potential donors could not be contacted.

In case donors received invitations to multiple initiatives, we consider the initiative closest to the

[11] In Germany, there is mandatory registration of address to the local municipality, so one can track where people have moved to within Germany.

CT request as the decisive initiative that can affect the CT availability for reasons of salience.[12] In these cases, we 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 non-compliers with this initiative are excluded from receiving a further CT request, which introduces a large sample-selection bias.[13]

Table 2: Description of control variables included in our regression analyses

Variable	Description
A. Registry-related characteristics	
Registration method	Categorical variable indicating whether prospective donor 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, fire fighters, and armed forces), or online via the DKMS website.
Mode of sample collection	Categorical variable measured at time of prospective donor's registration for collection through blood draw or buccal swab.
Month of CT request	Categorical variable for month of CT request.
B. Donor-related characteristics	
Sex	Dummy variable for female (zero for male).
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 prospective donors' 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 prospective donors' state of residence: <50,000, 50,000 to 99,999, 100,000 to 199,000, 200,000 to 499,999, and $\geq$ 500,000.
BMI	Continuous variable comprising prospective donors' body mass index (BMI).
Date of registration	Categorical variable for time when registration took place: before 2007, from 2007 to 2010, 2011 to 2014, and 2015 to 2018.
Information letter	Dummy indicating whether prospective donors received an information letter that their frozen sample was used for retyping.
Previous initiative	Dummy indicating that prospective donor had been previously invited to another initiative.

[12] For example, if a donor is only invited to STATUS UPDATE, which is a dummy variable, they receive a 1. A person is also coded as 1 for STATUS UPDATE if he or she had earlier been invited to the PROSPECTIVE initiative, but later received a STATUS UPDATE invitation.

[13] Also, for participation variables, we have 34 cases from PROSPECTIVE, where the participation decision was unclear, and these are re-coded into the comparison group.

Table 2 provides an overview of the rich set of covariates, which can be categorized into registry-related and donor-related characteristics. All summary statistics refer to non-missing covariate values from the regression sample.[14] 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, fire fighters, and armed forces), and online registration. Sample collection was performed either by blood draw or by buccal swab. We also account for seasonality by controlling for the month of the CT request.

Donor-related variables include prospective donors' sex, age at CT request, self-reported ancestry,[15] the federal state of residence, the population size at their place of residence, prospective 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 are mandatory information, which is collected at the recruitment stage, such as sex, address, weight and height, and the date of birth.[16]

3.2 Descriptive statistics

Table 3 provides an overview on donors' availability by initiative they had been invited to (Panel A) and conditional on whether prospective donors participate in an initiative (Panel B). Out of 91,479 potential donors with CT requests in our sample, 5,193 were invited to the initiative Prospective closest to the CT request, while 10,905 potential donors were invited to Status update-Blood, and 2,144 to Status update closest to the CT request. That implies that around 80% of all donors who received a CT request were not invited to any of the initiatives (73,237 out of 91,479).

We observe the highest CT availability (82.4%) among potential donors who had been invited to the initiative Status update-Blood. For initiatives Status update and Prospective, CT availability is slightly lower with 80.7% and 79.5%, respectively. Among the donors who did not receive an invitation, 77.1% were available for a 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 Prospective is 58.6% (3,021 participants, 2,138 non-participants). For the initiatives Status update and Status update-Blood, we observe participation rates of 31.3% and 34.7%, respectively.

We are also able to compare the participation rates in the initiatives within our sample among potential donors without a CT request. Analyzing data for potential donors from the registry unconditional on having a CT request, we observe 48% participation rate in the Prospective initiative. For Status

[14] We have 47 missing observations for the registration method and 3,431 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.

[15] 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 ten most common were German (87.8%), Turkish (4.7%), Polish (0.9%), Russian (0.9%), Italian (0.7%), Greek (0.3%), Kazakh (0.3%), Romanian (0.2%), Austrian (0.2%), and French (0.1%).

[16] Potential donor BMI ranges from 13 to 40, and is 24 at median. Potential donors' age upon CT request ranges from 17 to 60 years with an average of 30 (median 28). Country of origin is self-reported (as additional information on a consent form) and was available for 94.8% of the studied donors.

Table 3: CT (un)availability by initiative and participation

	(1) Obs.	(2) Average CT availability (%)
A. Initiatives		
PROSPECTIVE	5,193	79.5
STATUS UPDATE	2,144	80.7
STATUS UPDATE-BLOOD	10,905	82.4
No invitation to initiative (baseline)	73,237	77.1
B. Initiatives and participation		
PROSPECTIVE; Participation	3,021	85.8
PROSPECTIVE; No participation	2,138	70.6
STATUS UPDATE; Participation	671	88.2
STATUS UPDATE; No participation	1,473	77.3
STATUS UPDATE-BLOOD; Participation	3,783	90.4
STATUS UPDATE-BLOOD; No particip.	7,122	78.2

Notes. This table describes availability rates across initiatives for N=91,479 first CT requests from 1 Nov 2013 to 31 Oct 2018 at DKMS Germany. Column 1 shows the number of observations by initiative invitation category, column (2) the average CT availability. For 34 invitations to the PROSPECTIVE initiative, it is unclear whether the prospective donor participated.

UPDATE-BLOOD, the participation rate was 24.4%, and for STATUS UPDATE is was 25%. Since participation rates in the initiatives are higher in the CT request sample, the initiatives themselves may lead to a positive selection of donors that are invited to CT. To address this issue, we later correct our estimated intention-to-treat effects by taking participation rates unconditional on CT requests into account.

Table 3 shows that CT availability varies with the prospective donors' participation in the initiatives. As a general pattern across all initiatives, we observe that participants of the initiatives show a considerably higher availability for CT that non-participants. For the initiative PROSPECTIVE, the difference in availability is greatest with 15.2pp. The availability difference is 10.9pp and 12.2pp between participants and non-participants 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 potential donors' CT unavailability. For example, for the initiative PROSPECTIVE the unavailability is more than 50% smaller for participants in the initiative (14.2% not available) compared to non-participants (29.4% not available). These descriptive results already indicate the potential sorting effect of the initiatives, and also some differences between the initiatives with respect to their implied burden to the participants (i.e., registered donors who agree to participate in a high-burden initiative are signaling a relatively high level of commitment to go forward with the process should they be asked to donate).[17]

[17] Table A.1 also reports the number of observations and univariate differences in availability rates across registry-related and donor-related characteristics.

3.3 Empirical strategy

3.3.1 Intention-to-treat regression specification

We apply a logistic regression approach to investigate the impact of the different initiatives on the potential donors' availability at CT. The unit of observation is at the CT request level. Our goal is to measure the overall effectiveness of these initiatives to increase CT availability, unconditional on actual participation of donors in these initiatives, and controlling for registry-related and donor-related characteristics.

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

$$\text{P}(\text{AVAILABLE}_i|\mathbf{x}) = \Lambda(\beta_0 + \beta_1 \text{PROSPECTIVE}_i + \beta_2 \text{STATUS UPDATE-BLOOD}_i + \beta_3 \text{STATUS UPDATE}_i + \delta \mathbf{X}_i), \quad (1)$$

where $\Lambda(x) = exp(x)/(1 + exp(x))$. Here, the independent variables are indicators of the invitation to the different initiatives. For each category, we include one dummy, apart from when the donor is not invited to any of the initiatives, which forms the reference group. In each regression specification, we include a wide range of donor- and registry-related control variables as described in Table 2. We report average marginal effects for all independent variables of interest, and report robust standard errors in all specifications.

The identifying assumptions of a causal effect of an invitation into a treatment (i.e., an initiative) would imply that the intention to treat is as good as randomly assigned, conditional on selection criteria $\mathbf{X}$, that are applied to select participants for initiatives. Potentially, characteristics of a prospective donor can be correlated with the outcome variable of interest, availability, and the initiatives, causing an omitted variables bias problem. But in our setting, the selection into initiatives is primarily based on *exogenous*, biological factors that are predetermined prior to the treatment and the donor is unlikely to be aware of these in advance, for example, upon registration or before receiving an invitation letter to an initiative. Hence, potential donors are unable to behaviorally influence the probability to be invited to an initiative, once they are enrolled in the registry, which should mitigate endogeneity concerns.

3.3.2 Initiative participation specification

We also observe whether registered donors 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.[18] This motivates a second analysis, where we estimate differences in complying to CT requests for participants ("yes") and non-participants ("no") in our initiatives. We estimate the following regression specification:

$$\begin{aligned}\text{P}(\text{AVAILABLE}_i|\mathbf{x}) = \Lambda(&\beta_0 + \beta_4 \text{PROSPECTIVE\_YES}_i + \beta_5 \text{PROSPECTIVE\_NO}_i + \beta_6 \text{STATUS UPDATE-BLOOD\_YES}_i \\ &+ \beta_7 \text{STATUS UPDATE-BLOOD\_NO}_i + \beta_8 \text{STATUS UPDATE\_YES}_i + \beta_9 \text{STATUS UPDATE\_NO}_i + \delta \mathbf{X}_i). \quad (2)\end{aligned}$$

[18] One mechanical reason for the non-responses 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.

The analysis intentionally includes a selection effect, as a potential donor chooses whether or not 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 high 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 donors who participate are not only 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 that did not participate in these initiatives, given this information is available to the search coordinator.

3.3.3 Local average treatment effects

In the next specification, we assess the impact of donor invitations on the subgroup that actually participate, net of self-selection into the initiatives, by estimating a local average treatment effect (LATE) (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 exists 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

$$\begin{aligned}\textsc{available}_i = \beta_0 + \beta_1 \textsc{Prospective yes}_i + \beta_2 \textsc{status update-blood yes}_i \\ + \beta_3 \textsc{status update yes}_i + \delta \mathbf{X}_i + u_i, \quad (3)\end{aligned}$$

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

$$\begin{aligned}\textsc{Prospective yes}_i &= \gamma_0 + \gamma_1 \textsc{Prospective}_i + \gamma \mathbf{X}_i + r_i, \\ \textsc{Status update yes}_i &= \rho_0 + \rho_1 \textsc{Status update}_i + \rho \mathbf{X}_i + r_i, \\ \textsc{Status update-blood yes}_i &= \tau_0 + \tau_1 \textsc{Status update-blood}_i + \tau \mathbf{X}_i + r_i,\end{aligned} \quad (4)$$

which we estimate with robust standard errors.

This analysis assumes that conditional on observable characteristics, the initiative assignment is exogenous. We control for all observable criteria for being selected into initiatives. This also assumes that the instrument (i.e., having received an invitation) can only affect CT availability through the endogenous variable (i.e., participating in an initiative). The last assumption likely holds, since participation is otherwise impossible. Also, there is one-sided non-compliance, which means the comparison group never participates, but the group invited to participate does not fully participate.

4 Results

Table 4 reports average marginal effects from intention-to-treat (logit) regressions using donor availability at first CT request as the dependent variable. The first two columns show intention-to-treat effects excluding (Model 1) and including (Model 2) our main set of controls.[19] These regression results are unconditional on potential donors' participation status in DKMS' initiatives. Focusing on the regression including our base controls in Model (2), the PROSPECTIVE initiative, also statistically significant, shows a 2.52pp greater predicted probability of being available at CT for donors invited to this initiative, compared to receiving no invitation (significant at the 1% 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 3.20pp, compared to receiving no request (significant at the 1% level). Considering that participation in the initiative is 27.8% unconditional on getting a CT request, this result is quite large. We also find that the coefficients on STATUS UPDATE-BLOOD and PROSPECTIVE are not statistically different from each other ($p = 0.3768$, Wald test). Being invited to the STATUS UPDATE initiative is associated with a 1.33pp increase, but this is not statistically significant. STATUS UPDATE-BLOOD has a 1.87pp larger impact on availability than STATUS UPDATE ($p = 0.083$, Wald test). STATUS UPDATE is not different from the initiative PROSPECTIVE ($p = 0.2994$, Wald test).

Model (3) of Table 4 shows the predicted CT availability of potential donors by donor participation status in DKMS' initiatives. Participation is defined as the active, voluntary choice by a donor to take part in an initiative, after having received an invitation letter, under the condition that she is medically eligible. Conditional on donors' participation, 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 initiatives we study, and all coefficient tests between participants and non-participants within an initiative are significant at the 1% level.

In detail, donors participating in STATUS UPDATE-BLOOD show a 13.9pp higher predicted CT availability (significant at the 1% level) and STATUS UPDATE participants show a 10.7pp higher availability rate, compared to the average donor that does not receive any invitation. Furthermore, donors participating in the initiative PROSPECTIVE show a 10.1pp higher CT availability. Testing the equality of status update initiatives' coefficients, we find that the coefficient belonging to STATUS UPDATE-BLOOD, YES is not significantly larger than STATUS UPDATE, YES (Wald test: $p = 0.1536$). The coefficient of PROSPECTIVE, YES is about 3.8pp smaller than STATUS UPDATE-BLOOD, YES ($p = 0.0028$), but not different to STATUS UPDATE, YES ($p = 0.7727$).

[19] Table B.3 in the Appendix shows all control variables.

Table 4: Effects of individual initiatives on potential donors' CT availability

Dependent variable:	CT availability			
Method:	Logit	Logit	Logit	2SLS
Model:	(1)	(2)	(3)	(4)
Prospective	0.0236***	0.0252***		
	(0.0057)	(0.0063)		
Status update	0.0354***	0.0133		
	(0.0084)	(0.0097)		
Status update-blood	0.0530***	0.0320***		
	(0.0039)	(0.0050)		
Prospective, no			-0.0524***	
			(0.0083)	
Prospective, yes			0.1005***	0.0427***
			(0.0090)	(0.0105)
Status update, no			-0.0217**	
			(0.0109)	
Status update, yes			0.1069***	0.0383
			(0.0204)	(0.0286)
Status update-blood, no			-0.0100*	
			(0.0055)	
Status update-blood, yes			0.1389***	0.0817***
			(0.0094)	(0.0123)
Controls	No	Yes	Yes	Yes
Observations	91,479	91,479	91,479	91,479
(Pseudo) R^2	0.0019	0.0379	0.0425	0.0445
Wald tests (p-values):				
Prospective = Status update		0.2994		
Prospective = Status update-blood		0.3768		
Status update = Status update-blood		0.0830		
Prospective, yes = Prospective, no			0.0000	
Status update-blood, yes = Status update-blood, no			0.0000	
Status update, yes = Status update, no			0.0000	
Prospective, yes = Status update, yes			0.7727	0.8843
Prospective, yes = Status update-blood, yes			0.0028	0.0120
Status update, yes = Status update-blood, yes			0.1536	0.1594
Prospective, no = Status update, no			0.0235	
Prospective, no = Status update-blood, no			0.0000	
Status update, no = Status update-blood, no			0.3298	

Notes. This table shows average marginal effects from an intention-to-treat logistic regression (models 1 and 2), logistic regressions by participation status (model 3) and LATE using 2SLS (model 4), using a potential donor's availability for first CT request as the dependent variable. The control variables comprise of: 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, previous invitation to initiative 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. The symbols *, **, and *** represent significance levels of 10%, 5%, and 1%, respectively. Constant not shown.

Turning to non-participants, we find a sizable and statistically significant negative correlation with CT availability for all initiatives. The largest negative effect size can be found for non-participation in the PROSPECTIVE initiative with a 5.2pp lower average availability. For status update initiatives, predicted availability of non-participating donors are between 1.0pp (STATUS UPDATE BLOOD, NO) and 2.2pp (STATUS UPDATE, NO) lower than the reference group. The difference between PROSPECTIVE, NO and STATUS UPDATE-BLOOD, NO is significant ($p = 0.0000$), as is the difference between PROSPECTIVE, NO and STATUS UPDATE, NO ($p = 0.0235$), but not significant between STATUS UPDATE-BLOOD, NO and STATUS UPDATE, NO ($p = 0.3298$). Overall, these results show that participants in the registry's initiatives are more likely to be available than non-participants.

Model (4) of Table 4 shows the estimated local average treatment effect for each initiative. STATUS UPDATE-BLOOD has the highest impact on CT availability with an 8.2pp effect size, followed by PROSPECTIVE with an effect size of 4.3pp. However, the coefficient for STATUS UPDATE is not significantly different from zero, which might be partly explained by the lower number of observations for this initiative. These results are largely in line with the intention-to-treat estimates. However, they show a larger impact of initiatives.

These results show that the initiatives do not just sort donors on availability, but actually have an impact on their participation decision. The magnitude of the LATE associated with STATUS UPDATE-BLOOD is about 59% the size of the associated coefficient in the *by participation* specification, suggesting that only 41% of the coefficient from the *by participation* specification is due to a self-selection of potential donors into the initiative, and the rest is an impact on donor availability through the initiative. Similar computations can be made for the PROSPECTIVE initiative, where 43% of the "yes" coefficient in the *by participation* specification is due to a positive impact of the initiative on the participants, and the rest is due to sorting.

In Appendix B, we replicate the main intention-to-treat results using a regression adjustment model. This ensures we only compare the persons receiving the treatment to a comparable control group. Furthermore, we test the proportion of unobserved selection to observed selection that would generate a null result, using the methodology of Oster (2019). The results from this test for unobserved selection are well within reasonable bounds. Together, the results from these robustness tests broadly support our results. Further, to account for the fact that there are relatively more participants to non-participants in initiatives who are invited to CT, we calculate a back of the envelope bias-adjustment. We do this by calculating the difference in the descriptive availability by initiative that would result from re-weighting the participants and non-participants, so that their relative amounts are the same as in the total registry. Then, we subtract this difference from the effect size. For example, for status update blood there are 24.4% participants in the entire registry, and in the sample of CT requests there are 34.7% participants. This suggests the point estimate is over-estimated. Re-weighting observations gives weights 0.7 to the participants and 1.15 to the non-participants. This would lead to a re-weighted descriptive average availability of 81.2%, which is 1.2pp lower. Correcting our point estimate of 3.2pp by this amount would lead to a point estimate of about 2.0pp, which would still reach statistical significance, given the estimated standard error is 0.50pp. Similarly, for the PROSPECTIVE initiative, we see descriptively a 1.1pp lower

availability rate in aggregate when re-weighting the participants and non-participants uniformly. This would lead to an effect size of 1.4pp, which would still reach standard levels of statistical significance, given the estimated standard error is 0.63pp. Thus, even with a substantial reduction in effect size due to the potential endogenous sample selection, we still expect to see a significantly large impact of both initiatives.

5 Discussion and conclusions

We studied the impact of a set of initiatives implemented by DKMS Germany, a large stem cell donor registry, on availability to move forward with the donation process by registered donors who are a match for a patient in need of a transplant. Our results indicate that the initiatives were beneficial for two reasons. First, based on our ITT results, we found that the invitation to participate had a direct positive effect on completing the CT request (and hence, a relatively large relative reduction in attrition). Second, based on the predictive effect in which potential donors sorted themselves into participants and non-participants, the initiatives improved DKMS's ability to identify potential donors who were more likely to follow through with a CT request. Further, we also document a large causal impact on the availability of participants, for whom the reduction in attrition reduces by between 17% (3.8/22.9) and 36% (8.2/22.9).

Regarding the underlying mechanisms behind our results, we observe a much larger relative impact for the initiative STATUS UPDATE-BLOOD than for the initiative PROSPECTIVE on the participants in the LATE specification. One plausible reason for the higher availability among the STATUS UPDATE-BLOOD than the PROSPECTIVE initiative could be due to the higher participation burden (i.e., higher costs due to a blood draw) that could have served as a stronger commitment device for follow through with the donation. In the initiative STATUS UPDATE-BLOOD, donors must first give a blood draw, then participate in a health questionnaire, and are further asked to update the registry about their future unavailability periods, whereas in PROSPECTIVE, they only do either a blood draw or hand in a buccal swab.

The letters to the initiative PROSPECTIVE ask donors to send in buccal swabs or 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. At the same time, the action-requiring PROSPECTIVE letters can be seen as costly by the registered donors, because the expected benefits from fulfilling the required task might be small from the donor's point of view, while the upfront costs of retyping might be perceived as substantially larger. The costs could be even larger if donors have strong time preferences.

There are a few channels through which the status update initiatives could have increased CT availability. First, the request for unavailability dates worked as intended. Specifically, to the extent that registered donors participating in these initiatives provided their unavailability dates, DKMS was able to successfully reduce the likelihood to ask these individuals when they were unavailable. Second, the additional requirement of reporting periods of absence, which might at a first glance be perceived as too much of a burden for potential donors, turned out to increase availability, on average, for the STATUS UPDATE-BLOOD initiative. This interpretation is supported by the fact that participation rates for status

update initiatives are far lower than for retyping initiatives. Here, a foot-in-the-door mechanism might be effective, since STATUS UPDATE-BLOOD donors are required to provide blood samples, which costs some time and effort. However, this may not be the only reason for differences. For instance, the wording of letters substantially changed from STATUS UPDATE-BLOOD to STATUS UPDATE. Letters of the initiative STATUS UPDATE-BLOOD are emphasizing the recruitment of "quickly available team members". This could potentially nudge STATUS UPDATE-BLOOD invitees to participate, whereas in STATUS UPDATE, the letter is more neutrally framed. Thus, the overall 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.

One mechanism potentially driving the CT availability, due to the initiatives, is the time between invitation to an initiative and the CT request. Here, a few channels may play a role. First, the memory of participating or being invited may fade over time. Second, participants in STATUS UPDATE-BLOOD and STATUS UPDATE may initially report unavailability, thus leading to less CT requests for those unavailable initially, but over time, if participants forget to report unavailability in advance, they may be more likely to be unavailable when called to CT.

Another potential mechanism driving the effects is that, participants in PROSPECTIVE and STATUS UPDATE-BLOOD are more likely to be matched with a patient, since they have, per definition better HLA resolution and are thus more likely to be discovered in donor searches by doctors as a matching donor. Thus, we might see more donors that participated in retyping in the sample of CT requests. If participants are more motivated, as we have shown, then retyping can also positively behaviorally influence CT availability on top of providing better match information to search coordinators.

The results provide some practical implications for donor registries. We show that information on CT availability is contained in the participation choice of potential donors in an initiative. This information from participation decisions could be used to identify committed donors, since participants are more available than non-participants. Thus, given two biologically matched donors for a patient, all other things equal, one would prefer to always ask a potential donor participating in an initiative for a CT if faced with the constraint of only being able to invite one donor. 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 start the work-up process over again. From a health policy perspective, these results have important 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 to make such information available to search coordinators, which is currently not feasible.

This study has strengths and limitations. First, we were able to analyze a rich data set of 91,479 CT requests with initiatives that either retyped patients or asked them about their future unavailability. This is fairly unique given that the probability of getting a CT request is, on average, rather low, and thus a large number of invitations were sent out to registered donors beforehand. Also, the data is unique in that there is a potentially long time frame from registration, and the initiatives, to CT request. This

is helpful, since it can potentially offer insights applicable to other areas of volunteering, where people are called 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 call to duty. This shows that similar settings that ask people to once again refresh their status as a member, or continually provide updates, can help increase the endline commitment toward the cause.

Another strength of the data is that we can control for the selection criteria employed by DKMS to invite donors into the initiatives. This enables us to get closer to a causal impact of the initiatives than would have been the case without knowledge of assignment. Also, since the selection criteria are predetermined and cannot easily be affected by the donors themselves, there is unlikely to be self-selection to being invited. We also have information on participation in the initiatives, which enables us to go beyond the ITT effect and test how large the initiative impact on participants is, relative to the self-selection effect. This is useful, as it shows whether initiatives sort donors, and whether there is an *impact* on donor availability for participants.

While we have been able to identify a causal link between invitation to participate in the initiatives and subsequent CT availability, we are unable to go further to identify the precise channel(s) through which the initiatives had their effects. For example, for the initiative STATUS UPDATE-BLOOD, we cannot exactly identify the channels, since we have no simultaneous random assignment of a similar letter. This is why a randomized controlled field experiment could help identify the behavioral channels, by appealing to different preferences or psychological constructs that can crowd in donors more likely to donate, and lead them to commit to donation. Here, we have some first evidence that the STATUS UPDATE-BLOOD initiative can serve as a commitment device, hence crowding-in potential donors with appeals to identity-related preferences may tend more to participate. Sorting could have been driven by an appeal indicated in the letter to the initiative to join a team. We are unable, however, to exactly identify this potential channel.

In sum, our paper shows that the retyping and status update initiatives can be meaningful to enhance donor availability at the CT stage and may help to sort potential donors. Further, the evaluation of retyping and status update schemes and potential donor characteristics may help to optimize the donor recruitment process and thereby increase the chances that donors requested will be available. This should help to reduce delays in the donation process and, ultimately, improve patient outcomes. Insights from our results shed light on how to optimally design the recruitment and status update initiatives of a registry for two-stage volunteer markets in order to maintain a high commitment rate, so that donors positively respond to donation requests. This will help to enable a fast and efficient donor search, which is essential for many patients in need of a transplant. Finally, our results highlight the importance of carefully designing initiatives and to leverage the potential of insights from the behavioral sciences.

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A Additional table(s)

Table A.1: Descriptive statistics of categorical variables

A. Registry-related characteristics			
Variable name	**Variable value**	**Number of cases**	**Rate of CT availability (%)**
Recruitment method	Non-patient-centered public community drive	21,425	77.2
	Patient-centered public community drive	20,042	77.2
	Company drive	4,442	73.8
	Special projects	14,264	74.6
	Online registration	31,259	82.5
	Missing	47	80.6
Sample collection	Blood draw	34,123	76.3
	Buccal swab	48,038	79.6
	Unknown	9,318	75.9
Month of request	January	7,546	78.0
	February	7,231	78.0
	March	7,851	78.8
	April	7,420	78.1
	May	7,457	77.9
	June	7,929	77.7
	July	8,042	77.7
	August	8,100	78.0
	September	7,501	78.4
	October	8,001	77.6
	November	7,235	77.7
	December	7,166	77.7
B. Donor-related characteristics			
Sex	Female	34,853	73.8
	Male	56,626	80.5
Age categories	17 to 25 (years old)	34,636	79.7
	26 to 30	20,330	77.7
	31 to 35	12,749	75.8
	36 to 40	8,542	77.9
	41 to 45	6,347	79.4
	46 to 50	5,238	76.8
	51 to 55	2,809	72.2
	56 to 61	828	61.5
Ancestry	German	77,801	80.2
	Non-German	10,947	62.5
	Missing	3,431	75.8
Federal state	Baden-Württemberg	14,358	78.4
	Bavaria	15,118	79.3
	Berlin	3,009	76.2
	Brandenburg	1,424	78.7
	Bremen	766	75.7
	Hamburg	2,052	77.4
	Hesse	6,663	77.1
	Lower Saxony	21,028	77.1
	Mecklenburg-Western	1,180	76.0

of residence	Pomerania		
	North Rhine-Westphalia	10,841	78.9
	Rhineland-Palatinate	4,708	78.2
	Saarland	1,014	77.0
	Saxony	2,964	77.0
	Saxony-Anhalt	960	77.8
	Schleswig-Holstein	3,880	78.1
	Thuringia	1,456	77.6
	Missing	58	72.4
Population of place of residence	$<$ 50,000	54,470	79.3
	50,000-99,999	8,777	77.5
	100,000-199,000	6,048	76.1
	200,000-499,000	8,259	76.0
	$>$ 500,000	13,925	77.5
Year registered	until end 2006	8,279	74.3
	2007-2010	16,355	74.6
	2011-2014	38,960	79.2
	2015-2018	27,855	79.3
Information letter	No	83,097	78.3
	Yes	8,382	74.4
Multiple invitations	No	89,966	77.9
	Yes	1,513	81.22

B Robustness checks

B.1 Average treatment effects on the treated

In a next test, we use a regression adjustment approach with a logistic outcome model to estimate average treatment effects on the treated, where "treated" denotes all individuals invited to an initiative (not just participants). This asks the question, how the CT availability of those persons in the registry who were invited to an initiative would have changed, had they not been invited.

This approach has multiple advantages. First, we only need to assume that the covariates for the individuals invited to the initiative have a positive probability of not being invited, and not a positive probability of invitation for the covariate values for all of those who were not invited, except for those with similar individual characteristics. For example, it would not make sense to only look at the average treatment effect, if there were many individuals in the group not invited that had covariates making them very unlikely to be invited (e.g. age over 45, or too high BMI) (Heckman, 1997). The ATET regression adjustment estimator thus compares potential outcomes for the group of treated individuals, conditional on their covariates, weighted by the probability of being invited (Abadie and Cattaneo, 2018), i.e.

$$\tau_{ATET} = E\left[E[Y|X = x, W = 1] - E[Y|X = x, W = 0]\right] Pr(X = x|W = 1),$$

where Y is the estimated probability of being available for CT, X are covariates, and W is an indicator for being invited to an initiative of interest. We model the probability of being available for both treated and untreated with a logistic model using all controls. Since only a sub-population of potential invitees actually receives an invitation, we can be relatively sure that the reduced overlap assumption is fulfilled. We have a large number of individuals with heterogeneous BMI and age categories in the group not invited to any initiative.

The results of average marginal effects from logistic ATET estimates are shown in Table B.1. We use robust standard errors in all estimates. Column 1 of Table B.1 shows the ATET of PROSPECTIVE, where we find a 2.77 pp increase on CT availability for the invited. The STATUS UPDATE-BLOOD initiative has a slightly larger effect size of 3.22 pp. Again, in column 3, the STATUS UPDATE shows a 1.29 pp effect size, which is not significantly different from zero.

Regarding the plausibility of results, note that the potential outcome mean of availability for not being treated is about 2.5pp higher for the status update initiatives than for retyping initiatives (0.77 for PROSPECTIVE in column 1, 0.79 for STATUS UPDATE-BLOOD and STATUS UPDATE in Table B.1. This is likely because those invited to status update initiatives are younger and more likely to be male, who have a higher CT availability. Also, overall, the ATET results show consistent estimates, suggesting that no individual model is significantly biased, and that the logistic regression models can be interpreted

similarly to the ATET estimates.

Table B.1: Regression adjustment: ATET

Dep. variable:	CT availability		
Model:	(1)	(2)	(3)
Prospective	0.0277***		
	(0.0061)		
Status update blood		0.0322***	
		(0.0041)	
Status update			0.0129
			(0.0091)
Potential outcome mean	0.7674***	0.7922***	0.7938***
(no invitation)	(0.0030)	(0.0021)	(0.0035)
Observations	78,430	84,142	75,381

Notes. This table shows average treatment effects on the treated (ATET), estimated using regression adjustment with a logistic outcome model and robust standard errors. The dependent variable is a potential donor's availability for first CT request. The control variables comprise of: 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, multiple requests, information letter, and month of request. Robust standard errors in parentheses. The symbols *, **, and *** represent significance levels of 10%, 5%, and 1%, respectively.

B.2 Unobserved selection and coefficient stability

Next we use the methodology of Oster (2019) to assess the potential extent of unobserved confounding factors that could lead to a null result. Although we control for all selection criteria used by DKMS, the controls may be proxies of variables that do not perfectly measure the underlying variable. To do this, we use the approximate formula for the bias-corrected coefficient β^*, assuming proportionate selection of observables and unobservables according to δ (on page 193 of Oster (2019))[20]

$$\beta^* \approx \tilde{\beta} - \delta \left[\mathring{\beta} - \tilde{\beta} \right] \frac{R_{max} - \tilde{R}}{\tilde{R} - \mathring{R}} \tag{5}$$

where $\mathring{\beta}$ and $\mathring{R}$ are the coefficient estimate and R-squared from a regression of the dependent on the explanatory variable of interest without controls, $\tilde{\beta}$ and $\tilde{R}$ with controls, and $R_{max} = \Pi\tilde{R}$ is the maximum R-squared from a hypothetical regression with observed controls and unobserved factors.

We do two assessments of coefficient stability using this formula. First, how large would δ, the ratio of selection on unobservables to observables have to be, for the true β to move to zero. This is done assuming a value of $\Pi = 1.3$, as suggested by Oster, since about 90% of findings from randomized data would survive this. In studies with non-random data, less than 40% of studies assessed in Oster (2019)

[20] This is deemed by the author as an ex post valid test of robustness of results. Although we estimate an average marginal effects logit model, we see very similar results when testing the results of IV regressions, which are linear. This suggests that our test results are not driven by the non-linearity of the coefficient estimation.

survive this threshold. Second, we ask how much larger the explanatory power of a regression including the unobserved elements could become for the coefficient to move to zero, i.e. we estimate the Π s.t. $\beta = 0$ assuming $\delta = 1$.

We use results from Table 4 and untabulated results from LATE estimations without controls, to calculate the results. Results are shown in Table B.2. For PROSPECTIVE, the coefficient becomes larger when taking controls into account, which means that the δ is negative. This means that if observables are positively correlated with the initiative, the unobservables would have to be very strongly negatively correlated with the initiative for $\beta = 0$. Here it seems that the results are very robust. The STATUS UPDATE-BLOOD initiative shows at least a three (LATE) to four times (ITT) larger amount f selection on unobservables, relative to observables, that would be needed to drive to coefficients to zero, and $\Pi > 2$, indicating the R-squared would need to be at least twice as large to drive the coefficients to zero. This strongly suggests that the positive impact of status update initiative with retyping is not entirely the result of unobserved selection. This exercise, all in all, validates the findings from ITT and LATE specifications. We do not assess the *by participation* specification, as this is intentionally analyzing self-selection on unobserved factors.

Table B.2: Selection on unobservable parameters

Initiative		**ITT**	**LATE**
PROSPECTIVE	δ	-49.87	-104.48
	Π	-13.96	-30.34
STATUS UPDATE-BLOOD	δ	4.82	3.32
	Π	2.44	2.00

This table shows the results from tests for selection on unobservables based on Oster (2019). We report $\delta(\beta^* = 0, R_{max} = 1.3\tilde{R})$ and $\Pi(\beta^* = 0, \delta = 1)$ to test whether the result is robust to unobserved selection. We only include ITT and LATE estimates that were significant in Table 4.

Table B.3: Effects of individual initiatives on potential donors' CT availability reporting all covariates

Dependent variable:	CT availability			
Method:	Logit	Logit	Logit	2SLS
Model:	(1)	(2)	(3)	(4)
Prospective	0.0236***	0.0252***		
	(0.0057)	(0.0063)		
Status update	0.0354***	0.0133		
	(0.0084)	(0.0097)		
Status update-blood	0.0530***	0.0320***		
	(0.0039)	(0.0050)		
Prospective, no			-0.0524***	
			(0.0083)	
Prospective, yes			0.1005***	0.0427***
			(0.0090)	(0.0105)
Status update, no			-0.0217**	
			(0.0109)	
Status update, yes			0.1069***	0.0383
			(0.0204)	(0.0286)
Status update-blood, no			-0.0100*	
			(0.0055)	
Status update-blood, yes			0.1389***	0.0817***
			(0.0094)	(0.0123)
Information letter		-0.0128**	-0.0074	-0.0121*
		(0.0064)	(0.0065)	(0.0071)
Multiple invitations		0.0253**	0.0336***	0.0342***
		(0.0126)	(0.0126)	(0.0114)
Recruitment method:				
Missing		0.0839	0.0891	0.0850
		(0.0619)	(0.0615)	(0.0552)
Special projects		-0.0171***	-0.0163***	-0.0174***
		(0.0054)	(0.0054)	(0.0059)
Company drive		-0.0071	-0.0071	-0.0091
		(0.0070)	(0.0069)	(0.0077)
Online		0.0648***	0.0621***	0.0609***
		(0.0053)	(0.0053)	(0.0055)
Patient-rel. public drive		0.0224***	0.0229***	0.0231***
		(0.0047)	(0.0047)	(0.0049)
Sex: Female dummy		-0.0541***	-0.0558***	-0.0561***
		(0.0029)	(0.0029)	(0.0030)
Federal state of residence:				
Baden-Württemberg		0.0853*	0.0873*	0.0911
		(0.0504)	(0.0501)	(0.0583)
Bavaria		0.0827	0.0849*	0.0881
		(0.0504)	(0.0501)	(0.0583)
Berlin		0.0614	0.0641	0.0668
		(0.0510)	(0.0508)	(0.0589)
Brandenburg		0.0602	0.0628	0.0668
		(0.0514)	(0.0512)	(0.0592)
Bremen		0.0664	0.0695	0.0712
		(0.0524)	(0.0522)	(0.0603)
Hamburg		0.0634	0.0654	0.0685
		(0.0513)	(0.0510)	(0.0591)
Hesse		0.0718	0.0740	0.0774
		(0.0505)	(0.0503)	(0.0584)
Mecklenburg-Western Pomerania		0.0393	0.0411	0.0444
		(0.0515)	(0.0513)	(0.0595)
North Rhine-Westphalia		0.0782	0.0796	0.0835
		(0.0504)	(0.0502)	(0.0583)
Lower Saxony		0.0694	0.0711	0.0747
		(0.0503)	(0.0501)	(0.0583)
Rhineland-Palatinate		0.0764	0.0792	0.0820

	(0.0506)	(0.0504)	(0.0585)
Saarland	0.0573	0.0624	0.0644
	(0.0518)	(0.0516)	(0.0597)
Saxony	0.0424	0.0447	0.0480
	(0.0508)	(0.0506)	(0.0588)
Saxony-Anhalt	0.0489	0.0508	0.0551
	(0.0519)	(0.0516)	(0.0597)
Schleswig-Holstein	0.0651	0.0669	0.0709
	(0.0507)	(0.0504)	(0.0586)
Thuringia	0.0520	0.0535	0.0576
	(0.0513)	(0.0511)	(0.0592)
Ancestry: German	0.1426***	0.1396***	0.1684***
	(0.0037)	(0.0037)	(0.0049)
Missing ancestry	0.1382***	0.1335***	0.1648***
	(0.0087)	(0.0087)	(0.0099)
Population of place of residence:			
50,000-99,999 inhabitants	-0.0046	-0.0040	-0.0042
	(0.0048)	(0.0047)	(0.0048)
100,000-199,000 inhabitants	-0.0150***	-0.0149***	-0.0152***
	(0.0054)	(0.0054)	(0.0057)
200,000-499,999 inhabitants	-0.0145***	-0.0144***	-0.0150***
	(0.0049)	(0.0049)	(0.0051)
Above 500,000 inhabitants	0.0032	0.0034	0.0036
	(0.0050)	(0.0050)	(0.0051)
Body mass index:			
BMI	0.0584***	0.0574***	0.0634***
	(0.0043)	(0.0043)	(0.0049)
BMI squared	-0.0010***	-0.0010***	-0.0011***
	(0.0001)	(0.0001)	(0.0001)
Age:			
Under 26 years old	0.0560***	0.0567***	0.0563***
	(0.0044)	(0.0044)	(0.0045)
26-30 years old	0.0223***	0.0232***	0.0233***
	(0.0045)	(0.0045)	(0.0047)
36-40 years old	0.0261***	0.0261***	0.0272***
	(0.0056)	(0.0056)	(0.0057)
41-45 years old	0.0455***	0.0456***	0.0464***
	(0.0063)	(0.0063)	(0.0063)
46-50 years years old	0.0208***	0.0225***	0.0226***
	(0.0066)	(0.0066)	(0.0070)
51-55 years years old	-0.0197**	-0.0169**	-0.0226**
	(0.0081)	(0.0080)	(0.0093)
56-61 years old	-0.0961***	-0.0918***	-0.1230***
	(0.0128)	(0.0127)	(0.0174)
Year registered			
Registered from 2007 to 2010	0.0001	0.0059	0.0023
	(0.0071)	(0.0071)	(0.0077)
Registered from 2011 to 2014	0.0380***	0.0449***	0.0418***
	(0.0077)	(0.0077)	(0.0084)
Registered from 2015 to 2018	0.0381***	0.0460***	0.0423***
	(0.0081)	(0.0081)	(0.0087)
Sample collection:			
Buccal swab	-0.0079	-0.0068	-0.0073
	(0.0050)	(0.0050)	(0.0053)
Typing method unclear	0.0249***	0.0231***	0.0240***
	(0.0063)	(0.0063)	(0.0066)
Month of CT request:			
CT request in February	-0.0003	-0.0012	-0.0006
	(0.0067)	(0.0067)	(0.0067)
CT request in March	0.0057	0.0056	0.0056
	(0.0066)	(0.0066)	(0.0065)
CT request in April	0.0002	0.0008	0.0006

		(0.0067)	(0.0067)	(0.0066)
CT request in May		-0.0033	-0.0026	-0.0033
		(0.0066)	(0.0066)	(0.0066)
CT request in June		-0.0045	-0.0035	-0.0042
		(0.0065)	(0.0065)	(0.0065)
CT request in July		-0.0045	-0.0041	-0.0047
		(0.0065)	(0.0065)	(0.0065)
CT request in August		-0.0042	-0.0042	-0.0044
		(0.0065)	(0.0065)	(0.0065)
CT request in September		0.0004	0.0010	0.0005
		(0.0067)	(0.0067)	(0.0066)
CT request in October		-0.0084	-0.0076	-0.0083
		(0.0065)	(0.0065)	(0.0065)
CT request in November		-0.0020	-0.0021	-0.0020
		(0.0067)	(0.0066)	(0.0067)
CT request in December		-0.0021	-0.0020	-0.0019
		(0.0067)	(0.0067)	(0.0067)
Constant				-0.3896***
				(0.0861)
Observations	91,479	91,479	91,479	91,479
(Pseudo) R^2	0.0019	0.0379	0.0425	0.0445
Wald tests (p-values):				
Prospective = Status update		0.2994		
Prospective = Status update-blood		0.3768		
Status update = Status update-blood		0.0830		
Prospective, yes = Prospective, no			0.0000	
Status update-blood, yes = Status update-blood, no			0.0000	
Status update, yes = Status update, no			0.0000	
Prospective, yes = Status update, yes			0.7727	0.8843
Prospective, yes = Status update-blood, yes			0.0028	0.0120
Status update, yes = Status update-blood, yes			0.1536	0.1594
Prospective, no = Status update, no			0.0235	
Prospective, no = Status update-blood, no			0.0000	
Status update, no = Status update-blood, no			0.3298	

Notes. This table shows average marginal effects from an intention-to-treat logistic regression (models 1 and 2), logistic regressions by participation status (model 3) and LATE using 2SLS (model 4), using a potential donor's availability for first CT request as the dependent variable. All controls reported. Base categories comprise: no invitation (initiatives), non-patient-centered public community drive (recruitment method), missing (federal state), non-German (ancestry), smaller than 50,000 inhabitants (population place of residence, 31-35 years (age), until end of 2006 (year of registration), blood draw (typing method), January (month of CT request). Robust standard errors are reported in parentheses. The symbols *, **, and *** represent significance levels of 10%, 5%, and 1%, respectively. Constant not shown.