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Saving Lives with Stem Cell Transplants

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Abstract Blood stem cell transplants can be life-saving for some patients, but
the chances of finding a matching donor are small unless a large number of potential donors are evaluated. Many nations maintain large registries of potential
donors who have offered to donate stem cells if they are the best available match
for a patient needing a transplant. An alternative source of stem cells, umbilical
cord blood, is stored in banks. Everyone faces a small probability of needing a
transplant which will increase their likelihood of survival. The registries and cord
blood banks are thus an interesting example of a pure public good with widely
dispersed benefits. This paper explores the gains in survival probability that arise
from increased registry and bank sizes and uses value of statistical life methods
to estimate benefits and compare them to costs. Our results suggest that for the
United States and for the world as a whole, the sum of marginal benefits of an
increase in either the adult registry or the cord blood bank exceeds marginal costs.
However, marginal benefit-cost ratios for the adult registry are much greater than
those for the cord blood banks, which suggests that to the extent that these two
sources of life saving compete for public funds it may be preferable to prioritize
expansion of the adult registry over cord blood banks.

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1 Introduction

1.1 Donor Registries and Cord Blood Banks

For patients suffering from leukemia and other blood diseases, a stem cell transplant is often the best available, and life-saving, treatment. Stem cell transplants are likely to succeed only if the donor and recipient have sufficiently similar immunity types[1]. Because of the great diversity of human immunity types, finding a match can be difficult. The probability that two randomly selected persons of European extraction are of matching type is less than one in 10,000, while about 20 percent of these individuals are of types shared by less than one person in a million.[2]

Current medical technology allows stem cells to be made available by two alternative means. Stem cells may be collected from adult volunteers at the time when they are needed, or they may be obtained from umbilical cord blood collected by hospitals from newborns. These two methods are supported by two different types of "inventory." For adult donors, a registry is maintained of potential donors. Volunteers are asked to submit saliva samples, which are DNA-tested to determine their immunity type. Volunteers agree that if, at some time in the future, they are found to be the best available match for some patient, they will consent to make a donation. In this case, all that the registry needs to store is the volunteer's contact information and immunity type. The collection of cord blood requires storage of actual physical material. With the consent of parents, hospitals collect umbilical cord blood from newborns. This material is kept under refrigeration in anticipation that at some future time it may be the best available match for some patient in need.

In the United States, the largest adult donor registry and the largest cord blood bank are both maintained by the National Marrow Donor Program (NMDP), a non-profit organization funded partially by the U.S. Department of Health and Human Services. The NMDP donor registry includes more than 11.2 million registrants and its cord blood bank has approximately 190,000 units (Health Resources and Services Administration, 2014b). Many other countries also have large donor registries. Currently there are more than 23 million registrants and 580,000 cord blood units maintained by registries around the world (Bone Marrow Donors Worldwide, 2014).

Both the donor registry and the cord blood bank can be viewed as public goods whose benefits take the form of small increments in survival probability for most members of the population. No one knows in advance whether he or she will contract leukemia, and almost no one knows how common or rare their immunity type is. The larger is either of the two inventories, the greater is the chance that someone will have an available match if it is needed, and hence the larger is the survival probability of each population member. This is exactly the kind of environment for which the estimated *value of statistical life* (VSL) is an appropriate tool for measuring the money value of benefits in a benefit-cost analysis.

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[1] Formally, donor and recipient must have compatible human leukocytic antigen (HLA) types.

[2] The African-American population is even more genetically diverse. The probability that two randomly selected individuals are of matching type is less than one in 100,000.

1.2 Related Research

Previous studies have explored the benefits and costs of maintaining adult registries and cord blood banks. In this paper, we introduce some innovations that permit a much more thorough analysis of the economics of stem cell donations. As far as we know, this paper is the first benefit cost analysis that considers the adult registry and the cord blood bank as a simultaneous allocation problem, taking account of substitutability between these resources. It is also the first to account for international exchanges of stem cell material and it is the first benefit-cost study to use the most recently available and highly detailed estimates of the frequencies of immunity type data, which were published by Gragert et al. (2013)[3]

The benefits of registries and banks are realized when a patient in need of a transplant finds a match for her immunity type. The probability that such a match can be found depends upon the distribution of immunity types, which varies by race and ethnicity. Because the type distributions are extremely diffuse, they cannot be determined by simply sampling individuals from the population, but methods have been developed for estimating the prevalence of even very rare types (Mori et al., 1997; Kollman et al., 2007). Evaluating the marginal benefits of expanding registries and cord blood banks requires determining how much the probability of finding a match will increase with further additions of registrants and cord blood units. In addition, matching is not all-or-nothing. There are degrees of match and transplants of imperfectly matched patients have become increasingly common. Registry and bank expansion will lead to higher quality matches as well as a higher quantity of them.

Existing studies of the economic benefits of stem cell transplantation (Kollman et al., 2004; Howard et al., 2008; Bergstrom et al., 2009, 2012) consider United States registries and patients in isolation, ignoring exports and imports of stem cell material. Given the emergence of international stem cell sharing, this is arguably no longer appropriate. An organization called Bone Marrow Donors Worldwide (BMDW) maintains a clearing house of registry data that facilitates access to the pools of potential donors and cord blood units in many nations. When a matching donor cannot be found in a patient's home country, it is now common practice to search for a donor internationally. In 2009, approximately 45% of all adult stem cell transplants and 33% of all cord blood transplants involved donors and recipients living in separate countries. In the United States, about 44% of all stem cell transplants come from foreign donor registries (including those maintained by the NMDP) and about 31% of all stem cell donations from U.S. residents go to foreign patients (World Marrow Donor Association, 2009). Here we analyze benefits and costs from two perspectives that take into account international exchanges through the world registry. We compare the costs of adding new registrants to the world registry with the expected benefits to U.S. citizens and with expected benefits to the world population.

Earlier studies indicate that the marginal social benefits of additions to either the adult registry or to the cord blood bank exceed marginal costs (Bergstrom et al., 2009; Howard et al., 2008). Since these studies were published, the med-

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[3] Gragert et al. (2014) used this data to estimate the likelihood of finding perfect matches and acceptable but less than perfect matches for individuals from several racial groups. They did not, however, conduct a benefit-cost analysis or investigate optimal registry sizes.

ical profession has concluded that matching at a more finely partitioned level is advantageous, and a new data source that presents estimates of the distribution according to this more detailed partition has become available (Gragert et al., 2013). Our benefit cost analysis is based on this new data source. Several technical innovations were required to extend our analysis to incorporate the more detailed immunity type data and to calculate the probability of various partial matches. At this level of detail, the number of possible types to be considered is in the hundreds of millions and the number of acceptable partial matches is also enlarged.[4]

A recent paper by Gragert et al. (2014) also uses the more detailed immunity type data and employs methods conceptually similar to ours to estimate probabilities of finding a matching donor from the US adult registry and/or the US cord blood bank. In addition to estimating match probabilities, our paper presents economic benefit cost analyses of the adult stem cell registry and of the cord blood registry and also takes into account the availability of the world registry. To do so, we need to estimate not only match probabilities, but also the *marginal* effects of small changes in the size of either registry. In addition to calculating marginal effects, we simultaneously estimate optimal sizes for the adult registry and the cord blood bank. Since the adult registry and the cord blood bank are, in part, substitutes, it is important to consider the possibility that even if marginal benefits exceed marginal costs of increasing the size of either resource, while holding the other constant, it might be advantageous to increase the size of one while decreasing that of the other. Our method of direct calculation of match probabilities contingent on the size and racial composition of the adult registry and the cord blood bank allows us to estimate simultaneously the optimal size and composition of the adult registry and of the cord blood bank.

Our estimates, which are displayed in Tables 13 and 14, indicate that marginal benefits exceed marginal costs of expansion both for adult registries and for cord blood banks. However, the ratio of benefits to costs is higher for the adult registries than for the cord banks. Our calculations of optimal registry sizes, shown in Tables 15 and 16, indicate that optimal adult registries would be at least twice as large as current registries, while the optimal cord blood registries, with the exception of that for those of African-American descent, would not be much larger than their current size.

1.3 A Roadmap for Readers

Section 2 summarizes aspects of medical technology and genetics that are central to understanding the purpose of donor registries and cord blood banks. Section 3 presents estimates of the size and racial composition of the adult donor registries and of the cord blood banks for the U.S. and for the world as a whole. In this section, we discuss the way in which physicians prioritize imperfect matches, we calculate the probability that a person of specified race will find a source of stem

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cells at each possible level of match quality, and we assess our method by comparing our calculated results to those obtained in previous work. In Section 4 we estimate the expected number of lives saved in the U.S. and in the entire world by increases in the size of the adult registry and of the cord blood bank. To do so, we estimate the annual number of patients seeking transplants. Using this information and the results on matching probabilities from Section 3, we estimate the expected number of additional stem cell transplants at each level of match quality that result from an increment in the size of the adult registry and of the cord blood bank. We then use medical estimates of survival rates of patients who obtain transplants at each level of match quality to estimate the numbers of lives saved. In Section 5.1 we show how to use existing estimates of the value of a statistical life to evaluate the increases in survival probability that result from adding registrants and cord blood units and we also supply cost estimates of adding to the adult registry and to the cord blood bank. Section 6 compares the costs with the benefits to U.S. citizens and to the world population of expanding the adult registries and the cord blood banks. In this section, we also conduct a sensitivity analysis of the results to alternative assumptions concerning the value of statistical life. Finally, in Section 7 we present estimates of optimal registries of each type and compare these estimates to the existing registries.

2 Some Medical Background

Hematopoietic stem cell transplantation (HSCT) is a procedure used in the treatment of many malignant hematologic disorders, such as leukemias and lymphomas, and non-malignant hematologic diseases, such as aplastic anemia. Treatment proceeds by destroying all of the blood cells in the sick individual and then transplanting hematopoietic stem cells that can re-generate a new set of blood cells, which are hopefully disease free. There are two primary sources of hematopoietic stem cells that can be used for transplantation: (1) the cells can be extracted from *adult donors*, either through bone marrow aspiration or collection from peripheral blood; and (2) the cells are present in umbilical *cord blood*, which can be collected during childbirth. The total number of transplants has been growing rapidly and the share of transplants performed using cord blood has also been increasing (see Figure 1).

A critical requirement for performing a transplant is that there be an adequate "match" between the immunity systems of the donor and the recipient. How closely two individuals match is determined by the number of alleles they share in common in a set of genes known as human leukocytic antigens, or HLA.[5] Eight alleles are typically used in evaluating match quality. These include the two alleles at each of four loci, which are known as HLA-A, B, C, and DR. The combination of eight alleles possessed by an individual is called her *phenotype*. When matching adult donors to patients, an attempt is made to match all eight alleles, but transplants may be performed if only seven match. The degree of match is referred to as "eight of eight" and written 8/8 or "seven of eight" and written 7/8. Cord blood matching is less stringent, and usually omits consideration of HLA-C so that an attempt is

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[5] An allele is an alternative form of a gene located at a specific position (genetic locus) in one's DNA strand. Each locus contains two alleles, one inherited from each of the individual's parents.

Fig. 1: Number of Transplants by Stem Cell Source
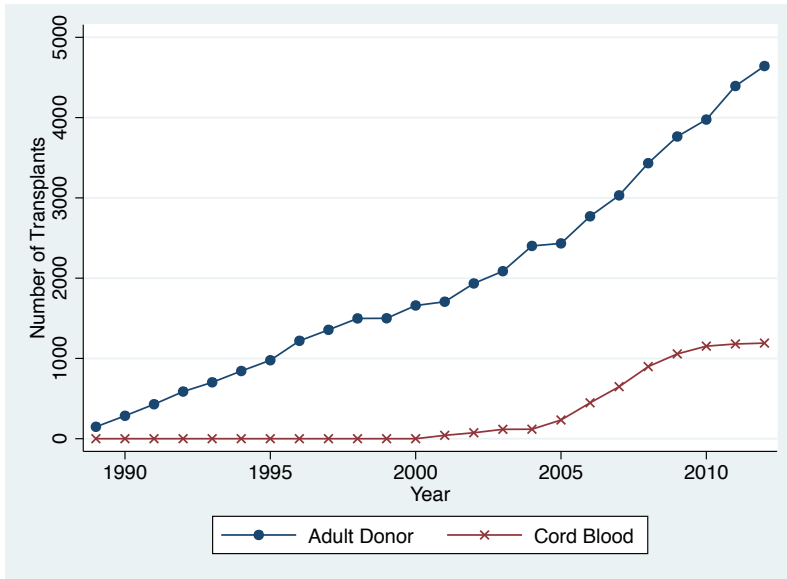
made to match six alleles. Cord blood transplants may be performed for 6/6, 5/6, or 4/6 matches.

Stem cell transplants and cord blood transplants are substitutes for one another, but they are not perfectly substitutable. Cord blood transplants have three important advantages over stem cell transplants (Seitz et al., 2012). First, if a matching cord blood deposit exists, then it is usually available much more quickly than a transplant from an adult donor. When an adult donor is needed, the donor must be contacted, consent must be obtained, confirmatory testing of HLA type must be performed, and the donor must undergo medical preparation for donation, whereas a cord blood unit can simply be retrieved from storage. Second, there is considerable inconvenience and a small probability of harm to an adult donor, but essentially no risk or cost to the donor of cord blood. Finally, it appears that in the absence of a perfect match, an imperfectly matched cord blood transplant is somewhat more likely to succeed than an equivalent match from an adult donor.

While cord blood has advantages over adult donation, it has a major drawback: cost. It is far more expensive to collect, process, and store blood than to collect and store information about a potential donor's HLA type (see Section 5.2).

3 Registry Size, Race, and Match Probabilities

3.1 Effective Registry Size by Race

The probability that a patient will find a match on the registry or in the cord bank depends upon her HLA type and upon the size and composition of these sources. Because the distribution of HLA types varies across racial groups, it is important

to determine the racial composition of each source. Table 1 shows the estimated size and racial composition of the registry and cord bank maintained in the United States by the NMDP as of Fall 2011 as reported by the Health Resources and Services Administration (2012b).[6] Some registrants are not available to donate when needed, because they cannot be found, are not medically eligible to donate, or decline to do so. According to the NMDP (Martin Maiers, personal communication), the percentage of registrants who can be found and are eligible and willing to donate is 57% for whites, 27% for African-Americans, 35% for Asians, and 34% for Hispanics. The total number of registrants is multiplied by these proportions to obtain the size and composition of the "effective" registry.

Table 1: **Effective NMDP Registry and Cord Bank Composition**

Race/ Ethnicity	Donor Registry		Cord Blood Registry		
	No.	Effective No.	No.	Effective No.- Adult	Effective No.- Child
White	7,161,000	4,082,000	110,000	22,000	44,000
Afr-Amer	710,000	192,000	13,000	3,000	5,000
Asian	710,000	249,000	13,000	3,000	5,000
Hispanic	975,000	331,000	32,000	6,000	13,000

Small cord blood units often have too few stem cells to be useful for adult patients, so the effective size of the cord blood bank is significantly smaller than the total number of units that are collected. According to Kurtzberg et al. (2005), all banked units should be large enough for children up to 10kg, but only 2% of units are large enough for an 80kg patient. To overcome this problem it has become common to transplant multiple cord units simultaneously to large adult patients (Ballen et al., 2012), particularly in the United States. In their model, Howard et al. (2008) estimate that only 10% of adult patients and 20% of children who have matching cord units go on to receive a cord blood transplant. The reason for not proceeding with a transplant may be either that the located cord unit was too small or that patient-specific factors led the treating physician to pursue alternative therapies. In our model, we account for the size of cord units by reducing the effective registry size and patient-specific factors using a calibration that ensures that the number of transplants predicted by our model equals the number actually performed. Since the patient-side factors are handled by the calibration, it seems reasonable to assume greater availability of units than Howard, et al. Taking all of these factors into account, our model assumes that 20% of units are large enough for adults while 40% are large enough for children.

Table 2 reports our estimates of the size and racial composition of the world registry.[7] Two sets of imputations were needed to produce the data in Table 2. First,

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[6] Most of the work on HLA type distributions has treated Hispanic as a "race" rather than an "ethnicity." We work with this data because it is what is available and use the term "racial group" or "race" to refer to the categories shown in the table.

[7] A detailed country-by-country listing of the number of transplants performed, the number of adult donors registered, and the number of cord blood units can be found in Table A.1 of Appendix A. Table 2 excludes the Brazilian registry and cord banks. Although Brazil reports more than three million registrants, the country exported only 3 stem cell products in 2009

in order to allocate the registrants and cord units by race, we consulted the World Fact Book 2013-2014 (Central Intelligence Agency, 2013) for the racial/ethnic distribution of each country and assumed that the racial distribution of registrants and cord units in each country reflect the same proportions as the entire population.[8] Second, while we have information on the percentage of registrants available and willing to donate when needed for the NMDP, this information is not available for other registries. For registered donors outside of the United States, regardless of their race, we assume that their availability is equal to that of whites within the U.S., or 57%.

Table 2: **Imputed International Registry and Cord Bank Distribution**

Race/ Ethnicity	Donor Registry		Cord Blood Registry		
	No.	Effective No.	No.	Effective No.- Adult	Effective No.- Child
White	14,333,000	8,170,000	404,000	81,000	161,000
Afr-Amer	840,000	266,000	23,000	5,000	9,000
Asian	2,177,000	1,085,000	114,000	23,000	45,000
Hispanic	987,000	338,000	42,000	8,000	17,000

*Notes:* Registry totals were calculated from the data sources used for Table A.1 as described in the text.

3.2 Physicians' Search Decision Trees

A physician who determines that a patient could benefit from a hematopoietic stem cell transplant will initiate a search of the adult donor registry and/or cord blood bank to find the best available match for this patient. Transplants are normally performed for a patient who has either an 8/8 or 7/8 match with an adult donor or has a 6/6, 5/6, or 4/6 match in the cord blood bank, in which case we say the patient has a "usable" match.

For those patients who do not have an 8/8 adult match or a 6/6 cord blood match, physicians must choose a best available match that follows some order of priority for imperfect matches. Howard et al. (2008) developed a donor decision tree based on then current medical practice. Patients are first divided into urgent versus non-urgent categories. Searches for urgent patients are limited to the cord blood registry because cord units are available more quickly than adult donors. If matching cord blood units can be found, urgent patients are transplanted with a

(World Marrow Donor Association, 2009). We interpret this to mean there are substantial frictions preventing these registrants from being truly available to the remainder of the world. Because Brazil has a large population of African heritage, counting these registrants would have the effect of making the calculated matching probabilities for Africans (and African-Americans) much higher than is actually observed.

[8] Public data on HLA type distributions is divided into the racial/ethnic categories white, African-American, Asian, and Hispanic but only the United States reports registry totals using these categories. To match the registry data with these categories, we included Pacific islanders in the Asian category and Native Americans in the white category. Mixed race individuals were assigned to single races in proportion to the size of each single race group.

Fig. 2: Donor search tree
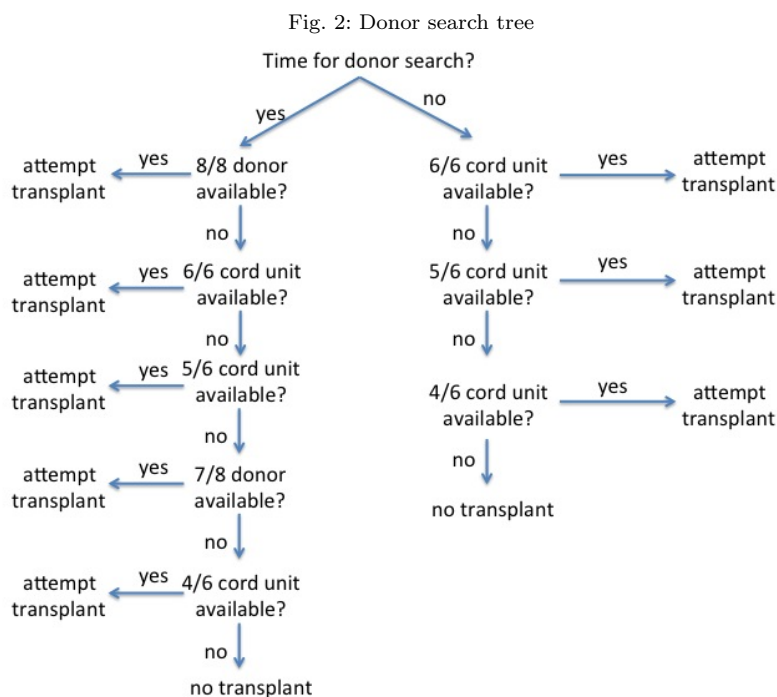
unit with the highest degree of match available. For the non-urgent patients, the adult donor registry is searched first. If an 8/8 or 7/8 match is found, the patient is transplanted from a matching adult donor. If no match is found, the cord blood registry is searched and the best matching unit (if any) is transplanted.

Since the Howard et al. (2008) paper was written, cord blood transplants have increased as a fraction of all stem cell transplants. This reflects the fact that studies have increasingly found that 5/6 and 6/6 cord blood transplants are more beneficial than 7/8 transplants from an adult donor.[9] In this analysis, we will use the donor decision tree Figure 2, which reflects the new effectiveness data and clinical practice and thus prefers 5/6 and 6/6 cord matches to 7/8 adult donor ones.

3.3 Match Probabilities

For a registry of given size and racial composition, we estimate the probability that a person of specified race will have an 8/8 match in the adult registry and the conditional probability that someone will have a 7/8 match but not an 8/8 match. We also estimate the probability that someone will have a 6/6 match in

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[9] For example, see Eapen et al. (2010) and compare Flomenberg et al. (2004) with Barker et al. (2010). Howard et al. (2008) also presented effectiveness scenarios in their sensitivity analysis in which the benefits of 5/6 and 6/6 cord blood transplants were greater than 7/8 adult donor ones, but maintained the preference for 7/8 adult donors in their search algorithm.

the cord blood bank, the conditional probability that someone without a 6/6 cord blood match will have a 5/6 cord blood match, and the probability that someone with neither a 6/6 nor a 5/6 match will have a 4/6 match in the cord blood bank. Because each phenotype has a large number of less-than-perfect matches,[10] calculation of these conditional probabilities is much more computation-intensive than calculation of probabilities of 8/8 matches. Details of the methods used to compute these probabilities are found in Appendix B.

Given the size and the composition of the registries and the conditional matching probabilities, we can estimate the probability that a patient of specified race will find a match of given quality in the U.S. NMDP registries and in the entire world registry. Table 3 shows the estimated probability that an adult patient of given race will find a "perfect" match and a "usable" match from searching only the U.S. NMDP registries and from searching the world registry. A more comprehensive table of match probabilities by racial group, degree of match, and age group is presented in Appendix C.

Table 3: Probability of Finding a Match for Adult Patients by Source and Race

| Quality of Match | Race of patient | | | |
	Caucasian	Afr-Amer	Asian	Hispanic
From U.S. Registry only				
8/8 adult or 6/6 cord blood	0.72	0.20	0.36	0.39
Some usable match	0.95	0.86	0.90	0.90
From World Registry				
8/8 adult donor or 6/6 cord blood	0.79	0.23	0.48	0.40
Some usable match	0.95	0.89	0.92	0.91

Table 3 indicates that 86% of patients of African extraction and 90% or more of persons of other races can find some usable match in the U.S. registries. Access to the world registry improves probabilities of finding a usable match only slightly, but the ability to search the world registry significantly improves the probability of finding a perfect match. Access to the world registry improves the probability of finding a perfect match from 72% to 79% for Americans of Caucasian ancestry and from 36% to 48% for those of Asian extraction.

For some patients, the delays involved in obtaining a transplant from an adult donor mean that the only viable source of a transplant is the cord blood bank. Table 4 shows estimates of the probabilities of finding a match in the world cord blood banks for adults and for children by race.[11]

3.4 Comparison with Other Estimates of Match Probabilities

Three recent studies use three different methods of estimating the probability of finding a match in the U.S. NMDP registry. The study by Gragert et al. (2014), like

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[10] Each phenotype can match as many as 8 others at a 7/8 match level; 6 others at a 5/6 match level; and 15 others at a 4/6 match level.

[11] Estimates of these probabilities from a search of U.S. banks alone are found in Appendix C.

Table 4: Probability of Match Availability from World Cord Blood Banks

	Outcomes for Adults				Outcomes for Children			
Match	**Cauc**	**Afr-Amer**	**Asian**	**Hisp**	**Cauc**	**Afr-Amer**	**Asian**	**Hisp**
6/6	0.38	0.03	0.13	0.12	0.46	0.05	0.19	0.16
5/6	0.51	0.32	0.54	0.45	0.45	0.42	0.57	0.50
4/6	0.08	0.52	0.25	0.33	0.04	0.43	0.16	0.26
None	0.05	0.12	0.08	0.10	0.05	0.11	0.08	0.09

Notes: Table entries are the fraction of patients for whom the given match level will be the best available match. Some columns do not sum to one due to rounding.

ours, is based on a genetic model of matching using the estimated haplotype distributions found by Gragert et al. (2013) for each race. A study by Dehn et al. (2010) estimates matching probabilities by a more direct method. In this study, 1344 individuals were randomly selected without replacement from the 2009 NMDP donor registry. The remaining registry was then searched for an 8/8 match for each of these individuals. An even more direct method of estimation, by Anasetti et al. (2010), is based on the experience of actual patients seeking transplants. For 398 consecutive hospital patients in search of transplants, this study reports the numbers and proportions of patients of each race who found 8/8 matches and also the number who found matches of either 7/8 or 8/8. Comparison of these estimates offers a good check on the validity of each of these methods. It is reassuring to see in Table 5 that the more direct estimations by Dehn et al. (2010) and Anasetti et al. (2010) produce similar results to the theoretically-based genetic models found in Gragert et al. (2014) and in this paper. The theoretically-founded estimates in our paper allow us to make predictions about marginal effects and about optimal registry size that are not available from direct estimation. The fact that the theoretically-based models predict matching rates similar to those found in direct empirical studies, gives us reason to expect that the additional predictions of our model have a sound basis.

4 Counting Expected Lives Saved

4.1 Estimated Number of Searches

The total benefit of expanding an adult registry or cord blood bank depends on the number of patients seeking transplants. This number, however, cannot be obtained directly from the number of searches performed by the world's registries. Many searches are initiated "just in case" a transplant becomes necessary, but do not lead to transplants even when suitable matches are available. For this reason, we estimate the number of "true" searches by calibration, assuming that the number of transplants actually performed is the product of the number of searches by patients who will undergo a transplant if matched times the probability that a patient will find a usable match in the registry. Using this approach, we impute that 6,347 U.S. searches and 13,491 world searches (including the U.S. ones) would

Table 5: Comparison of Calculated Match Probabilities

	*This paper	**Gragert et al	Anasetti et al	Dehn et al
Adult Donor Matches				
Caucasian - 8/8	0.72	0.75	0.62	0.68
Afr-American - 8/8	0.20	0.19	0.15	0.27
Asian - 8/8	0.32	0.27-0.42		0.45
Hispanic - 8/8	0.38	0.34-0.40	0.34	0.42
Caucasian - 7/8 or 8/8	0.95	0.97	0.89	
Afr-American - 7/8 or 8/8	0.72	0.76	0.63	
Asian - 7/8 or 8/8	0.8	0.72-0.88		
Hispanic - 7/8 or 8/8	0.81	0.80-0.87	0.77	
Cord Blood Matches				
Caucasian 4/6 or better	0.95	0.96		
Afr-Amer 4/6 or better	0.88	0.84		

Notes: *The results reported for this paper are taken from a list of detailed results found in Table C of the Appendix. **The Gragert et al. (2014) paper uses more finely grained racial groupings and report multiple match rates for Asian and Hispanic groups. The range given in the table corresponds to the minimum and maximum match rates among the relevant subgroups.

be required to lead to the observed number of transplants. The details of these imputations are described in Appendix D.

4.2 Additional matches

Since the cord blood and adult registries are assumed to constitute independent draws from the population, the probability of any combination of outcomes from the two registries is simply the product of the probability of the outcome from each registry. Thus we can calculate the probability that a person of a given race will find her best donor match at each node of the donor search tree. By taking derivatives of the expressions for the probability of a given level of match, we can calculate the marginal effect of an additional adult registrant or cord blood unit of specified race on the expected number of matches at each level of matching for persons of each race.[12] We can then use these estimates, together with the results of medical studies of the impact of transplant on survival probability, to calculate the expected number of statistical lives saved by adding either an adult of specified race or a unit of cord blood from a person of specified race to the stock of potential donors.

Table 6 presents the estimated effect on the expected annual number of transplants received by U.S. citizens if 1,000 registrants of specified race are added to the adult registry. Similarly, Table 7 provides estimates of the effects on number

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[12] Appendix B shows the detailed calculations used to make these estimates.

of transplants received by U.S. citizens of the addition of 100 cord blood units.[13] Expanding the registries and cord blood banks increases the average quality of best available matches, as well as the total number of usable matches. Adding adult registrants results in only a very small increase in the number of transplants performed, but leads to a substantial shift toward higher quality matches. The negative entries represent the fact that the number of less desirable matches decreases as better matches become available. Comparable estimates of the effect of additional registrants on the number of transplants performed in the entire world are reported in Tables E.1 and E.2 of Appendix E.

Table 6: Changes in Expected Annual Number of U.S. Transplants by Match Type Resulting From Addition of 1,000 Adult Registrants

Race of donors	8/8 adult	6/6 cord blood	5/6 cord blood	7/8 adult	4/6 cord blood	Usable total
Caucasian	.0248	-.0016	-.0200	-.0020	-.0012	.0000
Afr-Amer	.0277	-.0006	-.0151	.0091	-.0198	.0014
Asian	.0130	-.0007	-.0100	.0005	-.0028	.0001
Hispanic	.0323	-.0013	-.0209	.0056	-.0147	.0010

Table 7: Changes in Expected Annual Number of U.S. Transplants by Match Type Resulting From Addition of 100 Cord Blood Units

Race of donors	8/8 adult	6/6 cord blood	5/6 cord blood	7/8 adult	4/6 cord blood	Usable total
Caucasian	0.0	.0119	.0413	-.0477	-.0046	.0008
Afr-Amer	0.0	.0076	.1482	-.1056	-.0184	.0320
Asian	0.0	.0038	.0300	-.0287	-.0038	.0013
Hispanic	0.0	.0124	.0957	-.0788	-.0155	.0138

4.3 Survival probability by type of match

A substantial medical literature compares 5-year survival rates for those who have received transplants with that of patients who have not.[14] Howard et al. (2008) and Bergstrom et al. (2009) examined this literature and separately arrived at a

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[13] These figures are based on our estimates of the effects of adding a single registrant or cord blood unit. To make the tables more readily interpretable, we report estimated effects of adding 1,000 adult registrants or 100 cord blood units. The figures in the tables are calculated by multiplying the estimated effects of adding a single adult registrant by 1,000 and of adding a single cord blood unit by 100.

[14] Conditional on surviving five years, transplant recipients have life expectancy similar to that of the healthy population (Majhail and Rizzo, 2013). The importance of this fact to valuing benefits is discussed in Section 5.1.

value of 0.21 for the gain in survival probability from having a perfectly matched adult donor rather than no donor at all. Howard et al. (2008) estimated the benefit of a 6/6 cord transplant to be as beneficial as an 8/8 adult donor one and a 7/8 transplant to be about half as beneficial. These estimates seem to be consistent with more recent literature. Our estimates of the gains in survival probability for recipients of cord blood transplants with 5/6 and 4/6 matches are computed using the relative risk values obtained by Barker et al. (2010) in a study of more than 1,000 cord transplants with match levels of 4/6, 5/6, or 6/6. The resulting estimates for all degrees of match appear in Table 8.

Table 8: Increased Survival Probability Resulting from Transplants

Degree of Match	Increase in Survival Probability	
	Adult Patient	Child Patient
8/8 adult donor	0.21	0.34
6/6 cord blood	0.21	0.34
5/6 cord blood	0.12	0.22
7/8 adult donor	0.10	0.19
4/6 cord blood	0.08	0.16

5 Evaluating Benefits and Costs

5.1 Valuing Lives Saved

Bone marrow registries and cord blood banks are usefully viewed as pure public goods whose benefits are dispersed widely throughout the population. No one knows in advance who will contract leukemia or other blood diseases that can be cured only by a match from the bone marrow registry, nor does anyone know whether he or she would find a match in existing registries. The larger the registries, the greater is one's chance of finding a match. An increase in the size of the registry results in a very small reduction in the probability of an early death for each of a large number of people. As Mishan (1971) observed, this kind of situation lends itself well to a cost-benefit analysis that determines whether expenditures on public safety result in a "potential Pareto improvement."

People frequently make choices that implicitly trade small risks of life for goods or pleasure. To the extent that these decisions are consistent and rational, it is possible to define an individual's marginal rate of substitution between annual survival probability and wealth. The amount of money that person i will be willing to pay for small changes $\Delta \pi_i$ in survival probability is approximately $m_i \Delta \pi_i$ where m_i is person i's marginal rate of substitution between survival probability and wealth. The sum of the willingnesses-to-pay of all community members for the improved survival probability resulting from the project is then $\sum_i m_i \Delta \pi_i$. If individual gains in survival probability π_i are uncorrelated with the marginal valuations m_i, then the total willingness to pay is approximately equal to $\bar{m} \sum_i \Delta \pi_i$,

where $\bar{m}$ is the mean value of the m_i's. Since $\sum_i \Delta\pi_i$ is the expected number of lives saved, it follows that the total willingness to pay is equal to the expected number of lives saved, times the mean value of the marginal rates of substitution between survival probability and wealth. Thus, this marginal rate of substitution has come to be known as the "Value of a Statistical Life."[15]

Economists have conducted dozens of studies that attempt to estimate the value of statistical life and its correlates by means of a variety of methods and for many countries. Jones-Lee et al. (1985) initiated a line of research in which carefully devised questionnaires are used to elicit subjects' subjective values of small changes in survival probability. Blomquist (1979) and others used consumers' willingness to pay for safety-enhancing products, such as automobile seat belts to estimate the VSL. Thaler and Rosen (1975) and Viscusi (1978) proposed estimating the VSL by means of compensating wage differentials for hazardous occupations. These labor market based studies have become increasingly sophisticated as better data has become available, and at least for the United States, seem to be the most influential among policy makers. Recent developments in this area are well summarized by Knieser et al. (2010) and Viscusi (2013).

The many efforts to estimate the VSL have been been jointly evaluated in meta-analyses by Viscusi and Aldy (2003), de Blaeij et al. (2003), Alberini (2005), and Miller (2000). While there is wide variation among the estimates of VSL under different methodologies, a rough consensus seems to be emerging. According to Viscusi (2013), recent labor market based studies based on the best available data indicate a value of $9.1 million. Estimates from contingent valuation studies found in the survey by Miller (2000) for the developed countries of Europe and North America tend to be somewhat lower, with mean and median estimates of about $5.3 million in current U.S. dollars.

In 2013, the U.S. Department of Transportation (2013) published a memorandum stating that "on the basis of the best available evidence," analyses assessing the benefits of preventing fatalities will use $9.1 million as the value of a statistical life. The DOT memorandum also suggests using a sensitivity analysis of the effects of using alternative VSL values with a low value of $5.2 million and and a high of $12.9 million. The U.S. Environmental Protection Agency recommends a VSL of $8.55 million current dollars for evaluating public policy options.[16]

Conceptually, the VSL measures a person's willingness to pay to avoid a risk of death in the current period, while retaining the survival prospects of a healthy individual of one's age. In the short term, the survival probability of patients who receive successful stem cell transplants is lower than that of healthy individuals. Recent research, as summarized by Majhail and Rizzo (2013), suggests that conditional upon surviving for 2 to 5 years after a transplant, mortality rates for stem cell recipients approach those of the general population. Differences in mortality and health paths within the first few years after transplant are more difficult to ascertain. In the absence of more detailed short-term survival data, our calculations are made assuming that patients who survive for at least five years after a transplant face normal mortality risks, while attributing no additional survival for those

[15] Further discussions of this theory are found in Jones-Lee (1976), Drèze and Dehez (1982), Bergstrom (1982), and Hammitt (2007)

[16] The EPA website U.S. Environmental Protection Agency (2014) states a VSL of $7.4 million 2006 dollars, which equates to $8.55 million 2013 dollars.

who survive for less than five years. This is the basis for using changes in five-year survival rates as a measure of clinical benefit in the discussion of Section 4.3.

An alternative approach, favored by many in the medical community, is to measure the effectiveness of a policy measure by estimating the expected number of years of life the policy adds and applying a valuation to each life-year. This approach focuses attention on the observation that a reduction of risks to young people adds more expected years of life than a reduction of risk to older people and also focuses on the fact that the value of a treatment depends not only on its effects on immediate survival, but also its effects on long term survival. If subjective values of expected additional life years are independent of one's age, the life-year approach would imply that willingness to take risks would decline continuously with age, roughly in proportion to the reduction in one's expected remaining lifetime. Hammitt (2007), Aldy and Viscusi (2008), and Krupnick (2007) investigate this hypothesis using evidence from labor-market-based revealed preference studies and contingent valuation studies. Their evidence indicates that willingness to pay for survival probability does not decline steadily with age, but rather increases with age for persons in their 20's, reaches a plateau, and then begins to decline for those in their 50's and 60's. Thus, it seems more reasonable to apply different VSLs to different ages than to consider additional life years for a case such as transplants that, when successful, return the recipients to the survial prospects of a healthy individual.

The $9 million VSL used by the U.S. Department of Transportation is an estimate of the average VSL of persons in the labor force. The age distribution of the population of transplant recipients differs from the age distribution of the labor force since it includes children under 18 years of age and since the population of adult transplant recipients tends to be somewhat older than the population in the labor force. To account for this, we use estimates of the age distribution of VSLs among 18 to 62 year-olds provided by Aldy and Viscusi (2008). We assume that children's survival probability is valued by their parents at the same level the parents value their own survival probability. Furthermore, we use the VSL estimated for 54 to 62 year-olds for individuals over 62 as well. Combining these estimates with the age distribution of the general population (United States Census Bureau, 2014) and transplant recipients (Health Resources and Services Administration, 2014a), we find that it may be appropriate to reduce the $9 million figure downward to $7.5 million per statistical life. This adjustment is considered among the sensitivity analyses below.

5.2 Calculating Costs

The costs of an expanded adult registry include the direct cost of recruiting new donors, determining their immunity type by DNA testing, and storing their contact information. The NMDP estimates that the marginal cost of adding an additional person to the registry is $105 (Martin Maiers of NMDP, personal communication). The mean age of persons added to the registry is 35 years. Registrants remain eligible to make donations until they reach the age of 60. Thus the average new registrant will be available for approximately 25 years. This means that the average cost per year of availability of an additional adult registrant is roughly $105/25=$4.20. An increase in the size of the donor registry will also result in a

larger number of usable matches and hence in more transplants, which, in turn, lead to additional costs for hospitalization and medical care. Howard et al. (2008) estimates that in the United States, the total medical costs incurred in performing a transplant average roughly $308,000. We will use this estimate in our cost calculations.

By the cost of adding a unit to the cord blood bank, we mean the annual cost of maintaining a steady-state stock of cord blood that is one unit larger. For each unit of cord blood stored, there is an annual cost of keeping the blood in cold storage. Moreover, in order to maintain an inventory of constant size, cord blood units must be replaced when they are withdrawn, either to be transplanted to a matching patient or because they have exceeded their 20 year shelf life. We follow Howard et al. (2008) in estimating the collection cost for a unit of cord blood at $2,000 and the annual storage cost at $50.[17]

It is worth noticing that the costs of expanding the cord bank are higher than for expanding the donor registry for several reasons. First, collecting and storing cord blood is more expensive than collecting and storing information about registrants' HLA types. Second, an addition to the cord blood bank is more likely to increase the number of transplants performed and hence to increase hospitalization costs than is an addition to the adult registry. Finally, adult donors remain on the registry after donation whereas cord units cannot be reused and so must be replaced.

6 Comparing Benefits and Costs

6.1 Own-country benefits and costs for the U.S.

Given the fact that nearly half of the adult stem cell and cord blood transplants performed in the United States have come from foreign registries, a benefit cost analysis that ignores the availability of the world registry would be far from realistic. However, it is of some interest to calculate the more narrow benefits to U.S. citizens who value donor registries and cord blood banks only for their effects on their own survival probabilities. Table 9 shows estimates of the expected benefits and costs to United States citizens that arise from an increase in the size of the registry of adult donors under the assumption that U.S. patients have access to the worldwide donor registry. The first column of the table specifies the race of the hypothesized new registrants. The second column shows the expected number of lives saved by adding 1,000 registrants. The third column indicates a money value for the improved survival probability of patients who have access to the resulting larger pool of registrants, where this value is calculated under the assumption that the value of a statistical life is $9 million. The direct costs column shows the estimated direct cost of maintaining a registry with an additional 1,000 registrants. The medical costs column shows the expected physician and hospitalization cost resulting from the additional transplants that become possible with the larger registry. The final column shows the difference between the estimated

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[17] Howard et al. (2008) provide estimates from cord banks that: (1) 50% of collected units are too small and must be discarded; (2) the cost of processing a unit that is ultimately discarded is $500; and (3) the cost of processing a unit that is ultimately added to the bank is $1500. Together, these figures imply spending $2,000 for each newly banked unit.

value of benefits and the total costs of adding 1,000 units to the registry. Table 10 presents analogous estimates of the benefits and costs of adding 100 cord blood units. The variation in direct costs across races is due to the necessity of replacing cord units used for new transplants. Since registrants remain on the registry after donation, there is no similar variation in costs evident in Table 9.

Table 9: Benefits and Costs to U.S. citizens of 1,000 Additional Adult Registrants

Race of Registrants	Expected U.S. Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	0.00232	$20,877	$4,200	$5	$16,671
Afr-Amer	0.00344	$30,918	$4,200	$420	$26,298
Asian	0.00130	$11,709	$4,200	$18	$7,491
Hispanic	0.00361	$32,481	$4,200	$301	$27,981

Table 10: Benefits and Costs to U.S. citizens of 100 Cord Blood Units

Race of Registrants	Expected U.S. Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	0.00264	$23,760	$15,010	$253	$8,496
Afr-Amer	0.00901	$81,085	$15,399	$9,845	$55,840
Asian	0.00142	$12,773	$15,015	$383	-$2,626
Hispanic	0.00591	$53,189	$15,172	$4,243	$33,774

6.2 Worldwide benefits and costs

Because of international sharing, an increase in the size of the U.S. registry will save lives in other countries and increases in the size of foreign registries will save U.S. lives. If the total value to citizens of all nations of an increased registry exceeds its costs, and if nations could reach efficient agreements, then there would be possible ways for all to benefit if any of the world's registries were expanded. For this reason, it is of interest to compare the total benefits to persons in the entire world to the costs of increased registry size. If we do so, we must confront the issue that the appropriate value of a statistical life need not be the same in all countries. A survey by Miller (2000) suggests that across countries, values of statistical life are roughly proportional to income and are roughly similar across the wealthy industrialized countries of Europe and North America. Currently, however, there are substantial differences between the values used by regulatory agencies with the U.K. Department for Transport using a value of approximately $3 million, which is only one-third the value used by the U.S. Department of Transportation, but in line with other European nations (UK Department for Transport, 2011). For comparability, we present the results of world benefit-cost analyses using the same

$9 million figure we used for the U.S., but will check the sensitivity of the results to this assumption in Section 6.3. Tables 11 and 12 show the benefits and costs associated with adding 1,000 adult registrants or 100 cord blood units, respectively.

Table 11: Benefits and Costs to World Population of 1,000 Additional Adult Registrants

Race of Registrants	Expected Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	0.00669	$60,171	$4,200	$13	$55,958
Afr-Amer	0.00668	$60,092	$4,200	$794	$55,098
Asian	0.01940	$174,581	$4,200	$312	$170,069
Hispanic	0.00538	$48,408	$4,200	$333	$43,876

Table 12: Benefits and Costs to World Population of 100 Additional Cord Blood Units

Race of Registrants	Expected Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	0.00832	$74,867	$15,020	$488	$59,359
Afr-Amer	0.01500	$135,024	$15,650	$16,010	$103,364
Asian	0.01508	$135,681	$15,139	$3,424	$117,118
Hispanic	0.00949	$85,446	$15,212	$5,220	$65,014

We see from Tables 9-12 that the benefits to U.S. citizens exceed the costs of increasing the number of registrants of any race. Benefits to U.S. citizens exceed costs for adding cord bank units of all races except for those of Asian extraction. When we consider the benefits to the entire world, the difference between benefits and costs becomes much larger. In the case of Asian cord blood units, the difference between benefits and costs not only becomes positive, but exceeds that for all other races.

A simple message from these tables is that adding persons of any race to the adult registry or to the cord blood banks generally has benefits that exceed costs, even if one only takes into account the benefits to U.S. citizens and becomes significantly more valuable if benefits to persons outside the U.S. are also accounted for. These facts can be useful for encouraging an expansion of registries and banks, but the fact that efficient sizes have not yet been achieved suggests that such expansion is constrained by budgets. Thus it becomes interesting to inquire whether the data suggest that current budgets could be used more efficiently if redirected between adult registries and cord blood or between recruitment of alternative races. Similarly, in case modest increments in funding for registries becomes available, it is of interest to explore where such increments would be best expended.

If the constraint that leads to suboptimal registries and cord blood banks is a limitation on total expenditures, including hospitalization and medical care as well as the establishment and maintenance of the registries, then it is appropriate to determine priorities by the ratios of benefits to total cost, where benefits are as reported in the third columns of Tables 9 -12 and costs include both direct and

medical costs as measured in the fourth and fifth column of these tables. If, on the other hand, the constraint that leads to suboptimal registries is a limitation only of money available for recruitment and maintenance of the registries, then the appropriate measure would be the ratio of net benefits of transplants to direct costs of maintaining the registries and/or cord banks, where net benefits is the difference between the value of the increased survival probability and the increased total medical costs that result from increased registry sizes.

Tables 13 and 14 rank alternative increments to the registry or cord bank by ratios of benefits to total costs. Rankings of these alternatives by the ratio of net benefits to direct costs are similar, but not identical, and can be found in Tables F.1 and F.2 of Appendix F.

Table 13: Ranked Ratios of U.S. Benefits to Total Costs

Registrant Race Registry type	Ratio of Benefits to Total Cost
Hispanic adult registry	7.2
African-American adult registry	6.7
Caucasian adult registry	5.0
African-American cord blood bank	3.2
Asian adult registry	2.8
Hispanic cord blood bank	2.7
Caucasian cord blood bank	1.6
Asian cord blood bank	0.8

Table 14: Ranked Ratios of World Benefits to Total Costs

Race and Registry type	Ratio of Benefits to Total Cost
Asian adult registry	38.7
Caucasian adult registry	14.3
African-American adult registry	12.0
Hispanic adult registry	10.7
Asian cord blood bank	7.3
Caucasian cord blood bank	4.8
African-American cord blood bank	4.3
Hispanic cord blood bank	4.2

These results suggest that, on the margin, expansions of the adult registry offer greater returns per dollar spent than increases in the cord blood inventory. As registries are expanded, the benefit-cost ratios for cord blood will fall and could even fall below one, which would imply that current cord blood banks are larger than optimal. This illustrates why the optimal size of the cord and adult donor registries cannot be determined in isolation. The interaction between these two alternative production technologies must be accounted for, a subject taken up in Section 7.

6.3 Sensitivity Analysis

The benefit-cost ratios presented in Tables 13 and 14 assume a value of statistical life of $9 million. While this value has significant support from labor market studies and is the value used by some U.S. agencies, as discussed in Section 5.1, there have been a wide range of estimates for the appropriate VSL to use in benefit-cost analyses. Western European countries use a value closer to $3 million; contingent valuation studies suggest a value closer to $5 million; and the U.S. Department of Transportation advocates using a low value of $5.2 million in sensitivity analyses. Figure 3 shows the sensitivity of the own-country benefit-cost ratios for the U.S. to VSLs ranging from $0 to $12 million. At the low end of the range of VSLs discussed for the U.S. (represented in the figure by the "U.S. DOT VSL (min)" of $5.2 million), adding registrants of any race would still have benefits exceeding costs. Cord blood units, however, would only have benefits exceeding costs for African-Americans and Latinos, but not Caucasians and Asians.

Figure 4 shows a similar sensitivity analysis taking into account potential transplant recipients from anywhere in the world. The figure indicates the VSLs suggested by the U.S. Department of Transportation and U.K. Department for Transport. Even at the lower U.K. threshold, benefits exceed costs for both registrants and cord units of any racial group.

7 Toward Optimal Registries and Banks

The benefit cost results suggest that benefits exceed costs for adding either registrants or cord units on the margin, but this does not imply that the optimal registry and cord bank size will both be larger than they currently are for all races. Benefit-cost ratios are higher for registrants than cord units. If we expand the registry, the benefit-cost ratios for cord units will fall and could even fall below one before the registry reaches its optimal size. Two possible policy approaches are: (1) prioritize increasing the registry size since the benefit-cost ratios are higher; and (2) increase both registry and bank sizes since all of the benefit-cost ratios are considerably above one. It is helpful to consider the optimal registry and bank sizes to decide which of these options is to be preferred.

The optimal sizes and racial composition of the adult donor registry and cord blood bank can be determined using the benefit-cost framework above. At the optimal registry and cord bank, the marginal benefits of adding registrants or cord units of any race will equal the marginal costs. MATLAB was used to find these optimal values under various assumptions and the results are presented from the U.S. own-country perspective in Table 15 and from a world perspective in Table 16. Both tables show a baseline specification in the left panel using $9 million as the VSL for U.S. patients and $3 million as the VSL for non-U.S. patients, values consistent with those used by the U.S. Department of Transportation and U.K. Department for Transport. The right panel presents optima using half these values for the VSL to assess the results' sensitivity to this parameter.

Whether one takes the U.S. or world perspective our base specification and sensitivity results suggest that current world registries are substantially smaller than optimal. On the other hand, the current world inventory of cord units is actually super-optimal for Asians and Caucasians in three of the four cases considered.

Fig. 3: Sensitivity of U.S. own-country benefit-cost ratio to the VSL

(a) Adult Registrants

(b) Cord Blood Units
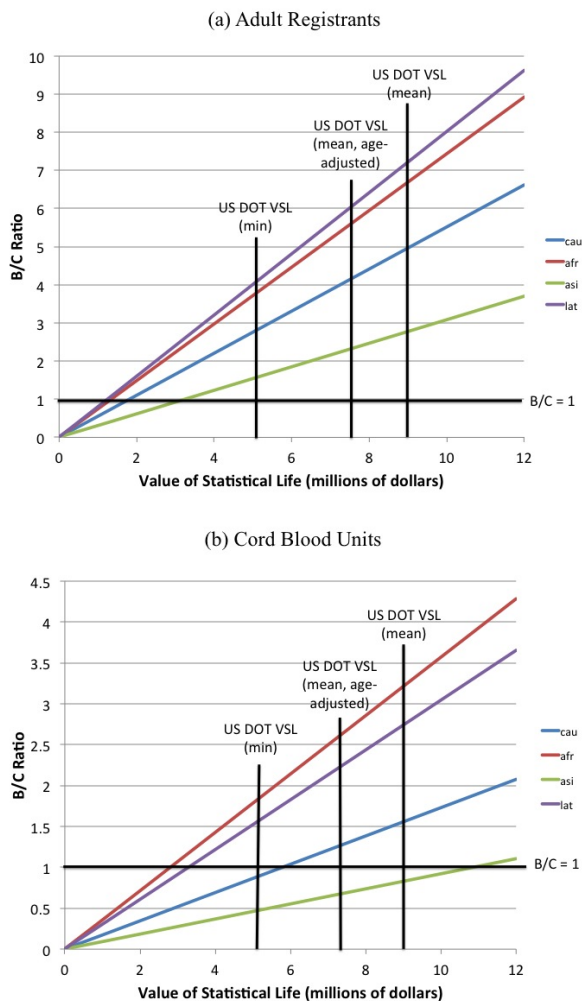
Notes: The figures illustrate the sensitivity of U.S. benefit-cost ratios by racial group to the value of statistical life. The mean and minimum values suggested for use by the U.S. Department of Transportation are highlighted as is the mean VSL adjusted for the age distribution of transplant recipients.

Cord unit inventories are suboptimal for African-Americans and Hispanics in all cases, but far less so than are the registries. To reach the world optimum using the higher VSL value, registries would have to increase by a factor of six from their current size whereas cord banks would need to less than double. The benefit-cost results and optimal registry results both suggest that expanding registries should be prioritized over increasing inventories of cord blood units.

Fig. 4: Sensitivity of world benefit-cost ratio to the VSL

(a) Adult Registrants

(b) Cord Blood Units
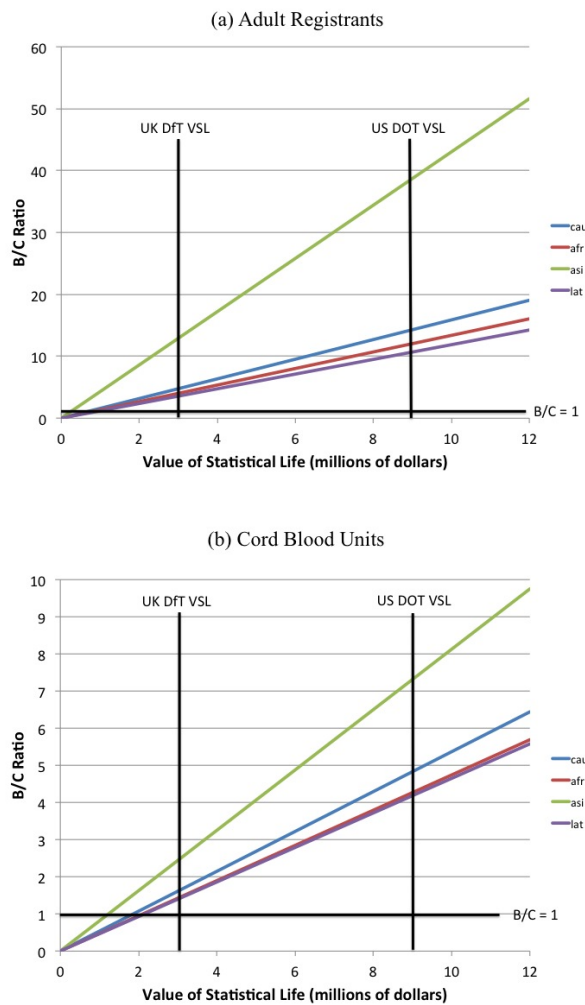
Notes: The figures illustrate the sensitivity of world benefit-cost ratios by racial group to the value of statistical life. Values suggested for the VSL by the U.S. Department of Transportation and the U.K. Department for Transport are highlighted.

8 Discussion

This paper has presented several innovations that allow us to perform a more thorough analysis of the economics of stem cell donations than has been possible before. It is the first benefit-cost study that we are aware of to (1) take an international perspective; (2) approach registries and cord banks jointly in order

Table 15: U.S. own-country optimal registry and bank

	VSL of $9m		VSL of $4.5m	
	Optimal Registry	Required Increase (%)	Optimal Registry	Required Increase (%)
donor registry				
cau	49,884,115	248%	30,168,792	110%
afa	7,332,880	773%	3,751,095	347%
asi	5,795,243	166%	3,126,902	44%
lat	9,406,840	853%	5,039,182	410%
cord bank				
cau	358,596	-11%	212,131	-47%
afa	101,051	346%	48,157	113%
asi	40,655	-64%	18,305	-84%
lat	171,617	304%	81,031	91%

Table 16: World optimal registry and bank

	VSL of $9m / $3m		VSL of $4.5m /$1.5m	
	Optimal Registry	Required Increase (%)	Optimal Registry	Required Increase (%)
donor registry				
cau	70,074,747	389%	42,762,861	198%
afa	9,525,426	1034%	4,965,249	491%
asi	26,845,481	1133%	15,610,414	617%
lat	9,570,409	870%	5,135,235	420%
cord bank				
cau	613,557	52%	361,097	-11%
afa	111,594	393%	51,081	126%
asi	192,967	70%	94,649	-17%
lat	167,702	295%	77,810	83%

to compute their optimal use; and (3) use the most recently available and highly detailed HLA type data in computing benefits.

Both donor registries and cord blood banks have been shown to be cost-effective in previous research, conditional upon the current size of the other, but this study is the first to consider the optimal way to allocate resources between these two alternative production technologies as a joint problem. The results suggest that the two technologies are complementary, at least to a point: the optimal size for both registries and cord banks is non-zero. The lower matching stringency required for cord blood results in more matches for patients with rare types and this benefit outweighs the higher cost of maintaining a cord blood bank.

There are three features of the results that support the notion that expansion of adult donor registries should be prioritized over growing cord blood banks. First, the benefit-cost ratios for adding adult donors to the registries are substantially higher than those for adding units to the cord banks. Second, adult donor registries are further below their optimal size than are cord banks. Finally, all sen-

sitivity analyses suggest that registries are far less than optimal whereas for some reasonable values of the model parameters we find that cord banks are currently close to optimal.

The welfare implications of moving to optimum registries are substantial. From a U.S. perspective, moving to the optimum registry would increase annual costs by $244 million, which is large relative to the $360 million annual budget of the NMDP. Annual benefits are calculated to increase by $522 million, however, so that net benefits would increase by $278 million, a return of 114% on the additional spending. The NMDP receives less than 15% of its funding from government sources. Increasing government spending on registries has the potential to lead to a substantial social return.

One limitation of the approach taken here is the reliance on type distributions for very broadly defined racial groups. HLA type distributions vary across countries. A country whose type distribution differs substantially from that of the patients from which the current registries are drawn might have a much higher benefit to adding registrants and cord units locally than in having them added to the world total. Schmidt et al. (2014) demonstrate the potentially large impact of local recruitment on match rates for some smaller countries. Because these countries are small, however, there are few potential beneficiaries of transplants so that total benefits may still be low relative to costs. A thorough benefit-cost analysis remains to be done.

Our results are, of course, contingent upon current technology and usage patterns. If costs of cord banking are likely to fall with continued bank growth or the benefits of cord blood relative to adult donors is likely to increase over time, it may be that continued emphasis on expanding cord banks is a reasonable option. Finally, it may be possible to lower the cost of cord banking by improving inventory management. Since much of the cost of cord banking is incurred by storing collected cord units, it may be optimal to discard units that have little probability of being used. These issues warrant further research and the results of this work could tip the balance toward favoring cord banks. But on current evidence, a policy of emphasizing expansion of donor registries over cord banks is strongly indicated.

Appendices

A National Registries

Table A.1: Transplants, Registrants, and Cord Units by Country

Country	Transplants	Registrants	Cord Units
Australia	162	174,960	25,716
Austria	118	63,328	1,712
Belgium	128	62,673	17,363
Brazil	87	3,065,249	0
Canada	231	347,258	7,605
China	462	385,854	0
China Hong Kong	38	77,023	0
Cyprus	8	126,342	1,977
Czech Republic	160	63,796	3,971
Denmark	67	42,698	0
Finland	61	21,228	3,362
France	653	213,450	27,305
Germany	1,749	4,999,925	33,820
Greece	56	40,950	2,007
Israel	138	794,305	10,676
Italy	552	340,409	28,518
Japan	1,203	432,318	4,698
Netherlands	213	43,035	3,285
Poland	191	464,488	1,201
Portugal	47	327,774	0
Singapore	43	34,998	0
South Africa	25	65,256	0
Spain	223	118,252	56,980
Sweden	135	40,241	2,788
Switzerland	75	45,544	3,927
Taiwan	101	310,128	62,174
Thailand	5	139,727	2,040
Turkey	44	37,117	679
United Kingdom	722	864,715	20,053
United States	3,142	7,456,218	221,223

Notes: Numbers of transplants were obtained from World Marrow Donor Association (2009) while the registry and cord bank sizes were found at Bone Marrow Donors Worldwide (2013).

B Detailed Methods

B.1 Phenotype Frequencies

Because the distribution of HLA phenotypes is far too diffuse to estimate directly, researchers have used statistical techniques to estimate haplotype[18] distributions Mori et al. (1997); Kollman et al. (2007); Maiers et al. (2007); Gragert et al. (2013) under the assumption that all

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[18] A *haplotype* is a list of four HLA alleles located on a single chromosome. An individual's phenotype is determined by two haplotypes, one inherited from each biological parent.

mating is within racial groups but otherwise uncorrelated with HLA type. We use the haplo-type distribution estimates of Gragert et al. (2013)[19] to estimate the phenotype distribution for each racial group, also by assuming reproduction is within race but otherwise unrelated to HLA type. Similar estimates of phenotype distributions have been employed in much of the research on the economics of HLA matching Bergstrom et al. (2009, 2012); Howard et al. (2008), but, to our knowledge, this is the first use of the most recent, and much more detailed, data made available by NMDP in 2013. This is important because the new estimates allow more precise estimation of the frequencies of rare types that are important on the margin when starting with a large registry.

Gragert et al. (2013) estimate the frequencies of more than 67,000 different haplotypes. There are thus nearly 4.5 billion haplotype pairs corresponding to hundreds of millions of phenotypes that could, in principle, be considered. While substantial computing resources were available for this project, working with all of these combinations would not be feasible. However, many of the haplotypes pairs are of a frequency so low that they can be ignored without seriously distorting the results. We considered all haplotype pairs with a density of greater than 10^{-10} to construct estimates of all phenotypes with a density greater than 10^{-9}. This procedure used more than 97% of the density available in the original haplotype estimates and only omits types so rare that fewer than six people in the world would be predicted to match them. The analyses below include consideration of the more than 110 million distinct HLA types resulting from this process.

The Gragert et al. (2013) haplotype estimates employed here are at the 4 loci level, consist-ing of a frequency for each possible HLA-A, B, C, DR combination. The resulting phenotypes are thus a list of eight alleles, two each for HLA-A, B, C, and DR, along with an associated frequency. These phenotypes are henceforth referred to as "8-types" to enable us to distinguish between matches of different numbers of alleles. We record the phenotype distribution for a particular race, r, with a vector of probabilities, f_8^r, in which the ith component, $f_{8,i}^r$, gives the probability that a randomly selected individual of race r is of HLA 8-type i. For each 8-type i and for each race r, we calculate the fraction $f_{7,i}^r$ of all individuals of race r who are of a type that is a 7/8 match for type i.[20] Note that $f_{7,i}^r$ is not a pdf like $f_{8,i}^r$ as it will sum to more than one.

Cord blood matches are determined by the alleles in three loci, HLA-A, B, and DR, instead of four. We make a list of "6-types," indexed by k, simply by taking the list of 8-types and omitting the two HLA-C alleles. The value for $f_{6,k}^r$, the fraction of race r that is of 6-type k, is obtained by summing the values of $f_{8,i}^r$ for each of the 8-types that corresponds to 6-type k. The fraction of race r that is at least a 5/6 match for 6-type k, $f_{5,k}^r$, is obtained using a procedure directly analogous to that used to calculate $f_{7,i}^r$. Finally, $f_{4,k}^r$, the fraction of race r that is at least a 4/6 match for 6-type k is obtained by summing the frequency of all of the 6-types corresponding to each possible combination of 4 alleles.

When calculating match probabilities, it will be useful to match the 6-type distributions back to the corresponding 8-types. Because each 8-type i maps to a single 6-type k, the new variable $f_{6,i}^r$ simply takes on the value of $f_{6,k}^r$ for the corresponding 6-type. Note that $f_{6,i}^r$ is not a pdf as it will sum to more than one. The interpretation of $f_{6,i}^r$ is that it gives the fraction of the population of race r that has a 6-type that is a match for 8-type i. An analogous procedure is used to calculate $f_{5,i}^r$, the fraction of the population of race r that is at least a 5/6 match for 8-type i and $f_{4,i}^r$, the fraction of the population of race r that is at least a 4/6 match for 8-type i. The variable $f_{8,i}^r$ is a pdf that describes the distribution of HLA types among members of race r. The variables $f_{n,i}^r$ with $n \in (4, 5, 6, 7)$ are not pdfs, but give the proportion of the population of race r that matches an individual of type i at the given level of stringency.

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[19] The haplotype data was downloaded from http://frequency.nmdp.org/NMDPFrequencies2011/ in September of 2013.

[20] We do this by listing all of the 8-types that have at least seven alleles in common with the original 8-type and summing the probabilities of these 8-types.

B.2 Registry Composition

The quantities calculated in Section B.1 can be used to calculate the probability that individuals of particular types will find matches on the registries. First considering the registry of adult donors, let R_r be the number of persons of race r on the registry and R be the vector that contains the number of registrants of each race. The probability that there is no individual of 8-type i on a registry containing R_r members of race r is given by $(1 - f_{8,i}^r)^{R_r}$. The probability that there will be an individual of 8-type i of *some* racial group on the registry R is given by:

$$p_{8,i}^M(R) = 1 - \prod_r (1 - f_{8,i}^r)^{R_r}. \tag{1}$$

Similarly, the probability that there will be an individual of some race who is at least a 7/8 match for 8-type i is:

$$p_{7or8,i}^M(R) = 1 - \prod_r (1 - f_{7,i}^r)^{R_r}. \tag{2}$$

Analogous quantities can be calculated for the cord blood registry. Define C_r as the number of cord blood units from race r and C as the vector of cord blood units from each race. The probability that there is a cord unit that is a 6/6 match for an individual of type i in the cord bank C is:

$$p_{6,i}^M(C) = 1 - \prod_r (1 - f_{6,i}^r)^{C_r}, \tag{3}$$

and the probability that there is a cord unit in the bank that is at least a 5/6 match for 8-type i is:

$$p_{5or6,i}^M(C) = 1 - \prod_r (1 - f_{5,i}^r)^{C_r}. \tag{4}$$

Finally, the probability that there is a cord unit in the bank that is at least a 4/6 match for 8-type i is:

$$p_{4or5or6,i}^M(C) = 1 - \prod_r (1 - f_{4,i}^r)^{C_r}. \tag{5}$$

B.3 Calculating Match Probabilities

When the adult donor registry, R, is searched for a match for an individual of type i, there are three mutually exclusive and collectively exhaustive outcomes that can occur. These outcomes, along with their probabilities are:

1. There are 8/8 and 7/8 matches for i

$$p_{87,i}^M(R) = p_{8,i}^M(R) \tag{6}$$

2. There is a 7/8 match for i, but no 8/8 match

$$p_{\overline{87},i}^M(R) = p_{7or8,i}^M(R) - p_{8,i}^M(R) \tag{7}$$

3. There is no 8/8 or 7/8 match for i

$$p_{\overline{87},i}^M(R) = 1 - p_{7or8,i}^M(R) \tag{8}$$

Similarly, when the cord blood registry, C, is searched for matches to type i, the possible outcomes are:

1. There are 6/6, 5/6, and 4/6 matches for i

$$p_{654,i}^M(C) = p_{6,i}^M(C) \tag{9}$$

2. There are 5/6 and 4/6 matches for i, but no 6/6 match

$$p^M_{\overline{6}54,i}(C) = p^M_{5or6,i}(C) - p^M_{6,i}(C) \tag{10}$$

3. There is a 4/6 match but no 6/6 or 5/6 match for i,

$$p^M_{\overline{65}4,i}(C) = p^M_{4or5or6,i}(C) - p^M_{5or6,i}(C) \tag{11}$$

4. There is no 6/6, 5/6, or 4/6 match for i

$$p^M_{\overline{654},i}(C) = 1 - p^M_{4or5or6,i}(C) \tag{12}$$

The two registries are independent draws from the population, so the probability of each combination of outcomes from searching the two registries is simply the product of the probabilities of the constituent outcomes. The possible outcomes, their probabilities, and the corresponding "best" match given the search algorithm described in Section ?? are presented in Table B.1.

Table B.1: **Possible Search Outcomes**

| **Type of Match** | | | | | | **Best** |
8/8	7/8	6/6	5/6	4/6	**Probability**	**Match**
yes	yes	yes	yes	yes	$p^M_{87654,i}(R,C) = p^M_{87,i}(R) * p^M_{654,i}(C)$	8/8
yes	yes	no	yes	yes	$p^M_{87\overline{6}54,i}(R,C) = p^M_{87,i}(R) * p^M_{\overline{6}54,i}(C)$	8/8
yes	yes	no	no	yes	$p^M_{87\overline{65}4,i}(R,C) = p^M_{87,i}(R) * p^M_{\overline{65}4,i}(C)$	8/8
yes	yes	no	no	no	$p^M_{87\overline{654},i}(R,C) = p^M_{87,i}(R) * p^M_{\overline{654},i}(C)$	8/8
no	yes	yes	yes	yes	$p^M_{\overline{8}7654,i}(R,C) = p^M_{\overline{8}7,i}(R) * p^M_{654,i}(C)$	6/6
no	yes	no	yes	yes	$p^M_{\overline{8}7\overline{6}54,i}(R,C) = p^M_{\overline{8}7,i}(R) * p^M_{\overline{6}54,i}(C)$	5/6
no	yes	no	no	yes	$p^M_{\overline{8}7\overline{65}4,i}(R,C) = p^M_{\overline{8}7,i}(R) * p^M_{\overline{65}4,i}(C)$	7/8
no	yes	no	no	no	$p^M_{\overline{8}7\overline{654},i}(R,C) = p^M_{\overline{8}7,i}(R) * p^M_{\overline{654},i}(C)$	7/8
no	no	yes	yes	yes	$p^M_{\overline{87}654,i}(R,C) = p^M_{\overline{87},i}(R) * p^M_{654,i}(C)$	6/6
no	no	no	yes	yes	$p^M_{\overline{87}\overline{6}54,i}(R,C) = p^M_{\overline{87},i}(R) * p^M_{\overline{6}54,i}(C)$	5/6
no	no	no	no	yes	$p^M_{\overline{87}\overline{65}4,i}(R,C) = p^M_{\overline{87},i}(R) * p^M_{\overline{65}4,i}(C)$	4/6
no	no	no	no	no	$p^M_{\overline{87654},i}(R,C) = p^M_{\overline{87},i}(R) * p^M_{\overline{654},i}(C)$	none

Notes: "Type of Match" refers to whether 8/8 and/or 7/8 matches are found on the adult donor registry and whether 6/6 and/or 5/6 and/or 4/6 matches are found on the cord blood registry. The final column indicates the "best" match for this search outcome given the search algorithm described in Figure 2.

The probability that the best available match for type i will be of each degree is found by summing probabilities from Table B.1:

1. Best match for type i is 8/8 adult donor

$$p^*_{8,i}(R,C) = p^M_{87654,i}(R,C) + p^M_{87\overline{6}54,i}(R,C) + p^M_{87\overline{65}4,i}(R,C) + p^M_{87\overline{654},i}(R,C) \tag{13}$$

2. Best match for type i is 6/6 cord blood

$$p^*_{6,i}(R,C) = p^M_{\overline{8}7654,i}(R,C) + p^M_{\overline{87}654,i}(R,C) \tag{14}$$

3. Best match for type i is 5/6 cord blood

$$p_{5,i}^*(R,C) = p_{\overline{87}654,i}^M(R,C) + p_{87\overline{6}54,i}^M(R,C) \tag{15}$$

4. Best match for type i is 7/8 adult donor

$$p_{7,i}^*(R,C) = p_{8\overline{7}654,i}^M(R,C) + p_{\overline{87654},i}^M(R,C) \tag{16}$$

5. Best match for type i is 4/6 cord blood

$$p_{4,i}^*(R,C) = p_{876\overline{5}4,i}^M(R,C) \tag{17}$$

6. There is no match for type i

$$p_{0,i}^*(R,C) = p_{8765\overline{4},i}^M(R,C) \tag{18}$$

By summing over all possible 8-types, it is now possible to calculate the probability that a randomly selected member of race r will have a best match of degree $n \in 8, 6, 5, 7, 4, 0$ when searching adult donor registry R and cord blood registry C. These probabilities are:

$$p_8^{*,r}(R,C) = \sum_i f_{8,i}^r p_{8,i}^*(R,C) \tag{19}$$

$$p_6^{*,r}(R,C) = \sum_i f_{8,i}^r p_{6,i}^*(R,C) \tag{20}$$

$$p_5^{*,r}(R,C) = \sum_i f_{8,i}^r p_{5,i}^*(R,C) \tag{21}$$

$$p_7^{*,r}(R,C) = \sum_i f_{8,i}^r p_{7,i}^*(R,C) \tag{22}$$

$$p_4^{*,r}(R,C) = \sum_i f_{8,i}^r p_{4,i}^*(R,C) \tag{23}$$

$$p_0^{*,r}(R,C) = \sum_i f_{8,i}^r p_{0,i}^*(R,C) \tag{24}$$

B.4 Changes in Match Probabilities

The probability of finding a match of a particular degree is a function of the size and racial composition of the adult donor and cord blood registries. To assess the benefit of growing the registries requires partially differentiating equations 19 to 24 with respect to the number of registrants of, or cord units obtained from, each racial group. The number of registrants or cord units enter the calculations in equations 1 to 5 so that the desired partial derivatives are simply functions of the derivatives of these four equations. Starting with equation 1, the change in the probability that there is an 8/8 match for an individual of type i on adult donor registry R by adding an individual of race s to the registry is given by:

$$\frac{dp_{8,i}^M(R)}{dR_s} = -\ln(1 - f_{8,i}^s) \prod_r (1 - f_{8,i}^r)^{R_r} \tag{25}$$

Similarly,

$$\frac{dp_{7or8,i}^M(R)}{dR_s} = -\ln(1 - f_{7,i}^s) \prod_r (1 - f_{7,i}^r)^{R_r} \tag{26}$$

$$\frac{dp_{6,i}^M(C)}{dC_s} = -\ln(1 - f_{6,i}^s) \prod_r (1 - f_{6,i}^r)^{C_r} \tag{27}$$

$$\frac{dp_{5or6,i}^M(C)}{dC_s} = -\ln(1 - f_{5,i}^s) \prod_r (1 - f_{5,i}^r)^{C_r} \tag{28}$$

$$\frac{dp_{4or5or6,i}^M(C)}{dC_s} = -\ln(1 - f_{4,i}^s) \prod_r (1 - f_{4,i}^r)^{C_r} \tag{29}$$

C Detailed Table of Matching Probabilities

The probability that the best match when searching the U.S. (NMDP) registry/bank is of given quality is given by race, age, and search strategy in Table C.1. Match probabilities when searching the world registry are given in Table C.2.

Table C.1: Search outcomes using U.S. (NMDP) registry alone

Best	**Outcomes for Adults**				**Outcomes for Children**			
	Donors or Cord Blood				**Donors or Cord Blood**			
Match	**cau**	**afa**	**asi**	**his**	**cau**	**afa**	**asi**	**his**
8/8 ld	0.721	0.202	0.322	0.381	0.721	0.202	0.322	0.381
6/6 cb	0.004	0.002	0.003	0.004	0.007	0.005	0.006	0.007
5/6 cb	0.109	0.132	0.141	0.151	0.139	0.204	0.208	0.215
7/8 ld	0.115	0.397	0.340	0.282	0.082	0.331	0.276	0.220
4/6 cb	0.005	0.132	0.088	0.076	0.005	0.144	0.095	0.080
None	0.046	0.135	0.107	0.106	0.046	0.114	0.093	0.096
Best	**Cord Blood Only**				**Cord Blood Only**			
Match	**cau**	**afa**	**asi**	**his**	**cau**	**afa**	**asi**	**his**
6/6 cb	0.247	0.020	0.038	0.073	0.317	0.031	0.061	0.105
5/6 cb	0.534	0.237	0.326	0.386	0.526	0.331	0.416	0.455
4/6 cb	0.172	0.584	0.506	0.423	0.111	0.518	0.422	0.340
None	0.047	0.158	0.131	0.119	0.046	0.121	0.101	0.100

Table C.2: Search outcomes using world registry

Best	**Outcomes for Adults**				**Outcomes for Children**			
	Donors or Cord Blood				**Donors or Cord Blood**			
Match	**cau**	**afa**	**asi**	**his**	**cau**	**afa**	**asi**	**his**
8/8 ld	0.778	0.222	0.474	0.398	0.778	0.222	0.474	0.398
6/6 cb	0.006	0.004	0.007	0.006	0.010	0.008	0.013	0.011
5/6 cb	0.114	0.190	0.229	0.203	0.132	0.273	0.286	0.265
7/8 ld	0.055	0.343	0.176	0.216	0.033	0.267	0.116	0.157
4/6 cb	0.002	0.126	0.034	0.079	0.002	0.127	0.031	0.077
None	0.045	0.114	0.081	0.098	0.045	0.103	0.079	0.091
Best	**Cord Blood Only**				**Cord Blood Only**			
Match	**cau**	**afa**	**asi**	**his**	**cau**	**afa**	**asi**	**his**
6/6 cb	0.379	0.033	0.131	0.115	0.458	0.049	0.186	0.156
5/6 cb	0.501	0.324	0.541	0.448	0.454	0.421	0.572	0.496
4/6 cb	0.075	0.520	0.246	0.334	0.042	0.425	0.163	0.256
None	0.046	0.123	0.082	0.102	0.045	0.105	0.080	0.093

D Details of Estimating Number of Persons Seeking Matches

Table D.1: Transplants Performed in United States, 2011

Trans. by Age		Trans by Race and Source			
Age	**No.**	**Race**	**No. ld**	**No. cb**	**Total**
<18	1115	cau	3897	749	4646
≥18	4458	afr	140	135	275
Total	**5573**	asi	134	75	208
		lat	244	199	443
		Total	4415	1158	**5573**

Notes: The table summarizes data available from Health Resources and Services Administration (2012a) about the number of transplants facilitated by the NMDP in 2011.

Table D.1 presents data on the number of transplants performed in the United States by race, age, and stem cell source. The ten entries in this table can be used to estimate the calibration parameters for a simple model of the search process. The parameters of the search model are:

- s_{tot}, the total number of patients searching the registry who would receive a transplant if a match were found
- f_{ch}, the fraction of searches by children
- f_{race}, a vector giving the fraction of searches by individuals of each race
- f_{cord}, a vector giving the fraction of searches that are cord blood only searches for each race

These parameters can be used to calculate the total number of searches by age, race, and search strategy. For example, the number of African-American children searching for cord blood only would be $s_{tot} * f_{ch} * f_{afr} * f_{cord,afr}$. For any given set of parameter values, the matching model described above will predict how many matches, and thus transplants, will occur. A MATLAB routine was used to calculate the parameter values for which the predicted number of transplants of each type would exactly match the values given in Table D.1. The parameter values obtained are presented in Table D.2 and are used as the base model for determining the distribution of searches in the United States in all future calculations.

A similar approach is used to calibrate the number of searches from other countries that would be required to predict the observed number of transplants performed outside the U.S. in 2011 according to the WMDA: 9,816 transplants from adult donors and 2,913 from cord blood. Because there is no age and racial distribution reported for the transplants outside the U.S., the only parameters required are s_{tot} and f_{cord} which is now a scalar applied to all racial groups. It was assumed that the fraction of searches performed for children matched the calibrated value for the United States. The racial distribution was determined by the racial/ethnic distribution of the countries listed in Table A.1 weighted by the number of transplants performed in each country, as reported in column (2) of that table. The calibrated values used to generate searches for non-U.S. countries are also reported in Table D.2.

Table D.2: Search Calibration Parameters for the United States

			Frac of All Searches	Frac of Cord Only Searches
Total Searches	6,347	cau	0.826	0.033
Fraction Children	0.200	afr	0.053	0.178
		asi	0.039	0.074
		lat	0.083	0.175

Table D.3: Search Calibration Parameters for the Rest of World

Total Searches	13,491
Fraction Cord Only	0.055

Notes: The table presents values for the search calibration parameters which lead the matching model to predict the exact number and distribution of transplants observed in 2011. Note, that these values assume that the the entire world registry and cord banks were searched.

E Effects of Larger Registries on Expected Number of World Transplants

Table E.1: Changes in Expected Annual Number of World Transplants by Match Type Resulting From Addition of 1,000 Adult Registrants

Race of donors	8/8 adult	6/6 cord blood	5/6 cord blood	7/8 adult	4/6 cord blood	Usable total
Caucasian	.0715	-.0045	-.0579	-.0059	-.00032	.000
Afr-Amer	.0544	-.0013	-.0300	.0168	-.0373	.0026
Asian	.01921	-.0094	-.01446	.0077	-.0448	.0010
Hispanic	.0500	-.0010	-.0345	.0056	-.0179	.0011

Table E.2: Changes in Expected Annual Number of World Transplants by Match Type Resulting From Addition of 100 Cord Blood Units

Race of donors	8/8 adult	6/6 cord blood	5/6 cord blood	7/8 adult	4/6 cord blood	Usable total
Caucasian	.0000	.04080	.11712	-.14141	-.01493	.00158
Afr-Amer	.0000	.01366	.26436	-.20914	-.01690	.05198
Asian	.0000	.03957	.33707	-.32753	-.03799	.01112
Hispanic	.0000	.02337	.16690	-.15123	-.02208	.01695

F Rankings of alternatives by ratio of net benefits to direct costs

Table F.1: Ranked Ratios of U.S. Net Benefits to Direct Registry Costs

Race and Registry type	Ratio of Benefits to Total Cost
Hispanic adult registry	7.7
African-American adult registry	7.3
Caucasian adult registry	5.0
African-American cord blood bank	4.6
Hispanic cord blood bank	3.2
Asian adult registry	2.8
Caucasian cord blood bank	1.6
Asian cord blood bank	0.8

Table F.2: Ranked Ratios of World Net Benefits to Direct Registry Costs

Race and Registry type	Ratio of Benefits to Total Cost
Asian adult registry	41.5
Caucasian adult registry	14.3
African-American adult registry	14.1
Hispanic adult registry	11.4
Asian cord blood bank	8.7
African-American cord blood bank	7.6
Hispanic cord blood bank	5.3
Caucasian cord blood bank	5.0

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