2014

Saving Lives with Stem Cell Transplants

Damien Sheehan-Connor, *Wesleyan University*
Ted C Bergstrom, *University of California, Santa Barbara*
Rodney Garratt

Saving Lives with Stem Cell Transplants

Damien Sheehan-Connor, Ted Bergstrom, and Rod Garratt[1]

June 6, 2014

Abstract

For patients with certain diseases, blood stem cell transplants can be life-saving. But a transplant is likely to be successful only if the immune systems of the donor and recipient are a close genetic match. Human immune systems are extremely diverse and a patient's chances of finding a matching donor would be small without the ability to search a very large number of possible donors. For this reason, most advanced nations maintain large registries of potential donors who have offered to donate stem cells if they happen to be the best available match for a patient needing a transplant. In recent years, transplantation of stem cells retrieved from umbilical cord blood of newborn infants has emerged as an alternative technology. In addition to maintaining adult donor registries, many nations now collect and store inventories of cord blood to be made available when and if a matching patient appears. Institutions have arisen that allow transfers of adult donations and of cord blood units across international boundaries. Since no one knows in advance whether they will need a transplant in the future, and since larger registries and banks increase the probability of a match and hence of survival, the registries and cord blood banks present an interesting example of a pure public good with benefits that are fairly evenly dispersed. This paper explores the gains in survival probability that arise from increased registry sizes and uses "value of statistical life" methods to estimate expected benefits and compare them to estimated costs of additions to the adult registry and to the cord blood banks. Our analysis takes account of international flows of blood stem cell materials and compares outcomes when nations act separately in their own self interest with those in which they act cooperatively. Our results suggest that for the world as a whole and for large countries, the sum of marginal benefits of an increase in either the adult registry or the cord blood registry exceed marginal costs. However, marginal benefit-cost ratios for the adult registry are 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.

1 Introduction

For many diseases of the blood, a stem cell transplant is the best available, and often life-saving, treatment. There are two sources of blood stem cells: adult donors and umbilical cord blood. Stem cell transplants are likely to succeed only if the donor and recipient have sufficiently similar immunity types. Because of the great diversity of immunity types, finding a match can be difficult. This problem has been addressed by maintaining "registries" of the types of individuals who have agreed to donate if needed and by storing umbilical cord blood for potential later use in "banks." Potential donor registries and umbilical cord blood banks thus are alternative technologies for saving the lives of patients with blood diseases. In the United States, the largest adult donor registry and the national cord blood bank are maintained by the National Marrow Donor Program (NMDP), a non-profit organization funded primarily by the Health Resources and Services Administration, an agency of the US Department of Health and Human Services. The NMDP donor registry includes more than 11.2 million registrants and their cord blood bank has approximately 190,000 units.[1] 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.[2]

Previous research has shown that marginal benefits exceed costs, both for increasing the size of registries and for increasing the amounts of cord blood stored (Bergstrom et al., 2009; Howard et al., 2008), but these studies do not address the joint problem of varying the size of both simultaneously. This matters because it might, for example, be that one of these sources is uniformly more cost effective than the other and hence it would be better to increase the use of that source and decrease the use of the other. But the situation is complicated by the fact that these two sources of stem cells are imperfect substitutes for one another. While cord blood banking is more expensive than maintaining a registry of potential donors, the use of cord blood has several advantages. These include a lower match stringency, more rapid availability, and lower rates of certain complications. This study considers the optimal use of donor registries and cord blood banks as a joint problem in order to gain insight into the best allocation of resources between the two approaches.

Existing economic analyses of stem cell transplantation (Kollman et al., 2004; Bergstrom et al., 2009; Howard et al., 2008) consider United States registries and patients in isolation. But when a matching donor cannot be found in a patient's home country, it is common practice to search for a donor internationally. Bone Marrow Donors Worldwide (BMDW) maintains a clearing house of registry data that facilitates access to a much larger pool of potential donors and cord blood units. International shipment of stem cell products has become increasingly important. 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 and about 31% of all stem cell donations from U.S. residents go to foreign patients.[3] Here we analyze benefits and costs from two perspectives that take into

---

[1] Health Resources and Services Administration (2014)

[2] Bone Marrow Donors Worldwide (2014)

[3] Annual Report of the World Marrow Donor Association (2009).

account international exchanges through the world registry. We will compare the costs of adding new registrants to the world registry with the expected benefits to US citizens and with expected benefits to the world population.

Performing the required calculations required several innovations beyond previous research methods. First, we use much more detailed estimates of immunity type distributions that have recently become available (Gragert et al., 2013), so that the number of possible types to be considered is in the hundreds of millions. This detailed data is critical to evaluating marginal decisions, since those without matches on existing registries are of very rare types. Second, we derived exact mathematical expressions for the probabilities of patients finding less-than-perfect matches on registries of arbitrary size and composition. Previous studies used simulations to calculate marginal cost-effectiveness, Howard et al. (2008), but could not be used to project optimum registry sizes. Our method of direct calculation allows us to calculate optimum registry and bank sizes. Direct calculation is especially useful when simultaneously considering adult registries and cord blood banks, since if one technology is below its optimum level, the marginal benefit-cost ratio for the other technology can exceed one, even when that technology is being used above its optimal level. Operationalizing these innovations required substantial computing resources. The optimum registry calculations were most intensive, requiring approximately 75 Gigabytes of RAM and nearly one week of computer processor time to complete using MATLAB.[4]

We find that the benefit-cost ratios for expanding registries exceed those for expanding cord blood banks. Our baseline results indicate that both registries and banks should be substantially expanded from their current levels. However, this result is sensitive to the method of valuing health benefits and the manner in which clinicians perform searches for stem cell matches. If a transplant could always be performed from an adult donor when one was available and a lower value for health benefits is used, then cord banks are already larger than optimal for whites and Latinos and less than a doubling in size would reach the optimal for African-Americans and Asians. The same sensitivity does not exist for registries: under all scenarios considered, registries for every race need to increase by a factor of three to nearly twenty. These results suggest that given current technology and usage patterns, expansion of registries should be prioritized over expansion of cord blood banks.

2   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)

2

Figure 1: Number of Transplants by Stem Cell Source

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. Eight alleles are typically used in evaluating match quality. These include the two alleles at each of four loci: HLA-A, B, C, and DR. 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 made to match six alleles. Cord blood transplants are often 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, while 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, a potential complication of stem cell transplants, graft-versus-host disease, is less common when cord blood is the source of stem cells.

While cord blood has advantages relative to adult donors, it has a major drawback: cost. It is far more expensive to collect, process, and store blood than it is to

collect and store information about a potential donor's HLA type. Initial processing of cord blood costs approximately \$1,000 (Howard et al., 2008), whereas typing a potential donor costs approximately \$105 (personal communication, Martin Maiers, National Marrow Donor Program). Cord blood storage costs approximately \$50 per year, whereas the marginal cost of storing potential donor information in a computer database is negligible.

In an earlier paper (Bergstrom et al., 2009), we provided a benefit-cost analysis of adult donor registries and found that a substantially larger registry than currently exists would be justified. Several papers have suggested sizes for a cord blood registry in various countries, (Querol et al., 2009; Takanashi et al., 2010; Vlachos et al., 2012). These papers provide a cost-effectiveness analysis in which the unit of effectiveness is the percentage of patients who could be matched by a registry of given size, but they do not explicitly value the additional matches. Howard et al. (2008) perform a thorough cost-effectiveness analysis from a US perspective that accounts for the value of life years gained for cord blood banks of various sizes. Writing in 2008, they concluded that an increase in the NMDP cord blood bank size from 50,000 to 150,000 could be justified on benefit-cost grounds and this increase has since occurred.
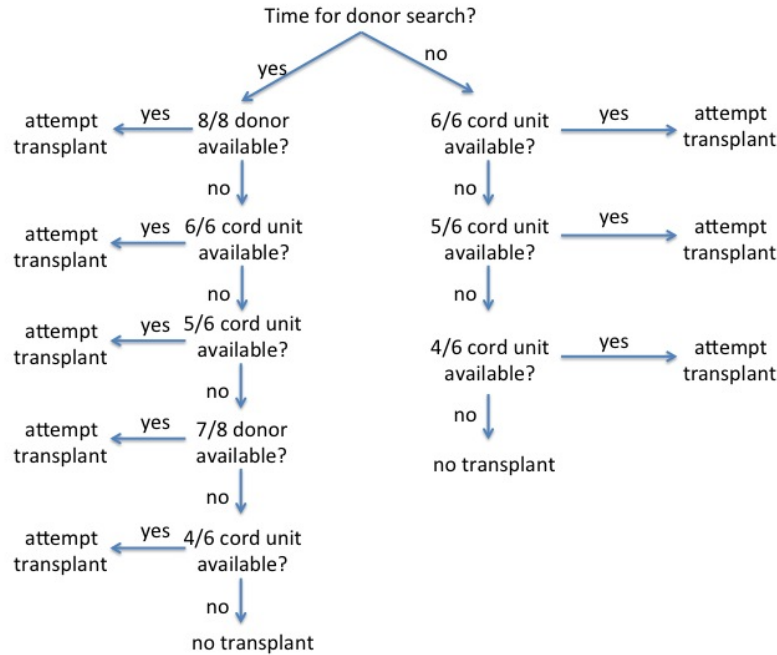
While Bergstrom et al. (2009) and Howard et al. (2008) make a convincing case that the benefits of expanding registries and cord banks exceed the costs, they do so in a partial equilibrium framework. Conditional on the size of the adult donor registry, benefits of increasing cord bank size exceed costs and vice versa. But these analyses do not answer two important questions: (1) Would it be more cost-effective to expand donor registries or cord banks? (2) What would be the optimal registry and bank size when considering expansion of both simultaneously? To illustrate the importance of considering the problem jointly, suppose that it turned out that the benefit-cost ratio for expanding registries exceed those for expanding cord banks and it was decided to increase the size of registries. As registry size increased, more patients could find matches and the marginal benefit to additional *cord units*, as well as additional registrants, would fall. It is possible that the benefit-cost ratio for cord units could fall below one so that the current cord bank size is actually higher than would be optimal, conditional upon registries being at their optimal size. A joint benefit-cost analysis of registries and cord banks will address where the marginal dollar will generate the most benefit and what endpoint should be pursued for both registry and cord bank size. To our knowledge, there has been no other work that addresses the benefits and costs of donor registries and cord banks jointly.

3   Methods

3.1   Registry Search Decision Trees

The impact of an additional adult registrant or cord blood unit on patient outcomes depends upon the search procedure used to match patients with donors or cord blood units when ideal matches are not available. There is no single procedure that is used in all cases (Ballen et al., 2012). The process used for individual patients may depend upon factors specific to that patient and is determined by physicians who may have their own preferences for adult donor versus cord blood transplants.

Figure 2: Baseline Donor search tree

Howard et al. (2008) developed a donor decision tree based on current medical practice in their evaluation of the cost-effectiveness of cord blood registries, which appears in Appendix A, Figure A.1. Patients are first divided into urgent vs. 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 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. It is important to note that the division of patients into "urgent" versus "non-urgent" categories was largely a modelling choice designed to calibrate predicted with observed transplants of various types. As Howard et al. (2008) found, if cord blood were used only when a closer adult match was unavailable, there would be very few cord transplants, because a patient who finds no match in a registry of several million individuals is unlikely to find a match in the much smaller cord blood registry even with less stringent matching standards.

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.[5] In fact, Howard et al. (2008) 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

---

[5]For example, see Eapen et al. (2010) and compare Flomenberg et al. (2004) with Barker et al. (2010).

the preference for 7/8 adult donors in their search algorithm. The donor decision tree used in this analysis, presented in Figure 2 reflects this new effectiveness data and clinical practice by preferring 5/6 and 6/6 cord matches to 7/8 adult donor ones.

3.2 Registry Sizes

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(Health Resources and Services Administration, 2012b). 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 compostion of the "effective" registry. Cord blood units are often too small to be useful for most patients, so the effective size of the cord blood registry is significantly smaller than the number of units it contains. We have not found published estimates of the proportion of cord units that turn out to be useful. 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 transplant would be either because the located cord unit was too small or because 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 for patient side 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, we assume that the portions of stored cord blood units that are large enough for transplant is 20% for adult patients and 40% for children.

Table 2 reports our estimates of the size and racial composition of the world registry.[6]. Two sets of imputations were needed to produce the data in Table 2. First, in order to allocate the registrants and cord units by race, we consulted the CIA World Fact Book 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.[7] Second, while we have information on

---

[6]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 B.1 of Appendix B. 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 (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 matching probabilities for Africans (and African Americans) much higher than is actually observed.

[7]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 cate-

the percentage of registrants available and willing to donate when needed for the NMDP, this information is not available for other registries. Because non-whites in other countries presumably do not face the same obstacles as they do within the United States, we assume that the availabity of all racial/ethnic groups outside the US is equal to the availability of whites within the US, or 57%.

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

	Donor Registry		Cord Blood Registry		
Race/		Effective		Effective	Effective
Ethnicity	No.	No.	No.	No.- Adult	No.- Child
White	7,160,779	4,081,644	110,068	22,014	44,027
Afr Amer	710,271	191,773	13,173	2,635	5,269
Asian	710,271	248,595	13,338	2,668	5,335
Hispanic	974,679	331,391	31,835	6,367	12,734

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

	Donor Registry		Cord Blood Registry		
Race/		Effective		Effective	Effective
Ethnicity	No.	No.	No.	No.- Adult	No.- Child
White	14,332,925	8,169,767	403,670	80,734	161,468
Afr/Afr Amer	839,683	265,535	22,632	4,526	9,053
Asian	2,177,101	1,084,685	113,684	22,737	45,474
Hispanic	987,141	338,478	42,456	8,491	16,982

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

3.3 Matching Probabilities

In Bergstrom et al. (2009), we developed methods for calculating phenotype distributions by racial group and the probability of finding a "perfect" match[8] for individuals of each race, given the size and racial composition of the registry. In this paper we also calculate the probabilities of less exact matches, and the conditional probabilities of matches at each stage in the search tree, given that a patient has not found a match at a higher level. 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

---

gories. 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.

[8]Using the more limited type data available at the time, this meant a 6/6 match. The corresponding calculation in this paper is for an 8/8 match.

but not an 8/8 match. We also estimate the probability that someone will have a 6/6 match in 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, 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 estimates are found in Appendix C.

Since the the cord blood and adult registries 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 possible point of the donor search tree. Taking derivatives of the expressions for the probability of a given level of match allows the computation of marginal changes in the probability of each match level with respect to the size and racial composition of the registry and cord bank. Further details of these calculations are presented in Appendix C.

We use the estimated changes in match probability to compute the number of additional transplants at each level of match that will result from registry or bank expansion. Finally, the results of medical studies of the impact of transplant on survival probability allow us to calculate the expected number of statistical lives saved by adding either an adult to the registry or a unit of cord blood to the cord blood bank.

4 Results

4.1 Estimated Match Probabilities

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.

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 ?? shows the estimated probability that an adult patient of given race will find a "perfect" match and a "usable" match from searching ponly the U.S. NMDP registries and from searching the entire world registry. [9]

Table ?? 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.[10] Access

---

[9]Table D.1 of Appendix D reports detailed matching probabilities for each usable type of match by race and shows matching probabilities for children as well as adults. Children have somewhat better prospects than adults of finding a suitable match in the cord blood registry because some cord blood units are large enough for a child patient but not for an adult patient.

[10]The estimated matching probabilities that we find for the U.S. registries are similar to those

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

	Race of patient			
Quality of Match	Caucasian	African	Asian	Hispanic
From US 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

to the world registry improves probabilities of finding a usable match only slightly. But being able to search the world registry significantly improves the probability of finding a perfect match. For Americans of Caucasian extraction, access to the entire world registry improves the probability of finding a perfect match from 72% to 79% and for those of Asian extraction, access to the world registries improves the probability of finding a perfect match from 36% to 48%.

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 registry for adults and for children by race.[11]

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

	Outcomes for Adults				Outcomes for Children			
Match	Cauc	African	Asian	Hisp	Cauc	African	Asian	Hisp
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

4.2 Estimated Number of Searches

The total benefits of expanding an adult registry or cord blood bank depends on the number of patients who seek a transplant. This number, however, can not be obtained directly from the number of searches initiated at the world's registries.

---

estimated in a separate study conducted by the NMDP and are also similar to those found in empirical studies of the frequency with which actual patients are able to find matches. Comparisons of our results with the results of these studies are shown in Table E.1 of Appendix E.

[11]Estimates of these probabilities from a search the U.S. registry alone are found in Table D.1 in Appendix D.

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 he 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.

Detailed information about the number of transplants facilitated by the U.S. NMDP registry and cord blood bank is available from the Health Resources and Services Administration (Health Resources and Services Administration, 2012a). The data includes the numbers of patients, by age and race, receiving transplants from adult donors and from cord blood. In the year, 2011, 4,415 patients received transplants form adult donors and 1158 received cord blood transplants. Futher details of the composition by age, race, and source of donation can be found in Table F.1 of the Appendix. In 2011, there were 14,209 adult donor and 4,093 cord blood transplants performed worldwide (World Marrow Donor Association, 2012). By subtracting those performed in the US, this implies that there were 9,816 transplants from adult donors and 2,913 from cord blood performed outside the United States. We do not have information of the age distribution, nor of the racial distribution of those who received transplants outside of the United States. We assume that the fraction of searches performed for children matches that estimated for the United States. For each country outside the United States, we assume that the racial distribution of transplant recipients is the same as that of the country's population. DAMIEN, IF ANYTHING GOES HERE, I WOULD SUGGEST A TABLE SHOWING THE estimated number of patients of each race seeking adult and cord blood transplants.

4.3 Benefits and Costs of Increases in Number of Registrants and of Cord Blood Units

When we estimate the effects of small changes in the size of the adult registry and the cord blood registry, we do not need to be concerned about interactions between the two registries. Table 5 estimates the 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, while Table 6 estimates the effects on number of transplants received by U.S. citizens of the addition of 100 cord blood units.[12] Expanding the registries and cord blood banks increases both the average quality of best available matches as well as the total number of usable matches. Additional adult registrants result in only a very small increase in the number of transplants performed, but lead 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 G.1 and G.2 of

---

[12]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 registrants by 1,000 and of adding a single cord blood unit by 100.

the Appendix.

Table 5: Changes in Expected Annual Number of US 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
African	.0277	-.0006	-.0151	.0091	-.0198	.0014
Asian	.0130	-.0007	-.0100	.0005	-.0028	.0001
Hispanic	.0323	-.0013	-.0209	.0056	-.014.7	.0010

Table 6: Changes in Expected Annual Number of US 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	.01186	.04128	-.04774	-.00458	.00082
African	0.0	.00785	.14816	-.10564	-.01841	.03197
Asian	0.0	.00379	.03001	-.02872	-.00384	.00125
Hispanic	0.0	.01238	.09565	-.07881	-.01545	.01378

4.4 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. Howard et al. (2008) and Bergstrom et al. (2009) examined this medical literature and use a consensus 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 taken from study by Barker et al. (2010) of the outcomes of more than 1,000 cord transplants with match levels of 4/6, 5/6, or 6/6. The resulting estimates for all matching types appear in Table 7.

4.5 Valuing the Benefits

DAMIEN. I THINK THAT ABOUT HERE WE SHOULD HAVE A TABLE(S) SHOWING EXPECTED NUMBER OF LIVES SAVED BY ADDING 10,000 ADULT DONORS AND 10,000 CORD BLOOD DONORS.

Table 7: 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

I WILL TRY TO REWRITE THIS PARAGRAPH WITH SOME MORE REFERENCES There are two common methods for valuing improvements to survival probability and length of life. Many economists prefer to use the "value of statistical life" or VSL approach (Mishan, 1971; Bergstrom, 1982; Drèze and Dehez, 1982), which is based on estimates of the amount of money people would be willing to pay to reduce their probability of death by a small amount. This approach seems well-suited to the current analysis: the benefit of adding a registrant is a small reduction in the probability of death for every member of society since anyone might need a transplant someday. A second approach, favored by many in the medical community, is to place a value on additional length of life, typically by placing a value on life years, often adjusted for quality of life (Gold et al., 1996). There are pros and cons to this approach. As noted above, marrow or cord blood recipients do have shorter expected lives conditional on surviving their transplant, a fact that the VSL approach does not account for explicitly. On the other hand, even though older people have fewer years to live, economists have found that they are willing to pay comparable amounts to young people, though less than middle-aged people, to reduce the probability of death (Aldy and Viscusi, 2008), so it is not clear that length of life conditional upon survival is a valid measure of benefit. We use the VSL approach as our baseline specification and present results from the life years approach in our sensitivity analysis. Viscusi and Aldy (2003) provide a thorough survey of the literature estimating the appropriate VSL to use and note that most estimates cluster in the $4 million to $9 million range; we use the mid-point of this range, $6.5 million.

4.6   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.[13] 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.

---

[13]Martin Maiers of NMDP, personal communication.

This means that the average cost per year of availability of an additional adult registrant is roughtly $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 peforming 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 $1,000 and the annual storage cost at $50.

DAMIEN, IT SEEMS TO ME THAT HERE WE NEED A NUMBER FOR THE ESTIMATED COST OF INCREASING THE STEADY STATE BANK SIZE BY ONE (OR PERHAPS 10,000) UNITS . i.e. if the steady state bank is 1 unit larger, what is the increase in the annual number of deposits that need to be made?

In addition, since only a fraction of units is large enough to use for transplants, multiple units must be collected to replace those that are used. The figures in the table reflect the additional annual cost of replacing expiring units and those used for transplants that would result from a permanent increase in the size of the cord bank of one unit. DAMIEN, CAN YOU ELABORATE A LITTLE ON WHAT YOU DID HERE.

Note that the additional annual costs attributable to expanding the cord bank are higher than for expanding the donor registry. This is due in part to the fact that collecting and storing cord blood is more expensive than collecting and storing information about registrants HLA type but also to the much higher number of additional transplants expected to be performed when cord units are added.

4.7 Comparing Benefits and Costs

Table 8 shows estimates of the expected benefits and costs to citizens of the United States that arise from an increase in the size of the registry of adult donors under the assumption that US patients have access to the worldwide donor registry. The first column of each 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 $6,500,000. The direct costs column shows the estimated direct cost of maintaining a registry or cord blood bank with an additional 1,000 units. 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 value of benefits and the total costs of adding 1,000 units to the registry or cord blood bank. Similarly, Table 9 shows benefits and costs of

adding 100 cord blood units.

Table 8: Benefits and Costs to US citizens of 1,000 Additional Adult Registrants

Race of Registrants	Expected US Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	.00232	$15,080	$4,200	$10	$10,800
African	.00344	$22,330	$4,200	$420	$17,710
Asian	.00130	$8,460	$4,200	$20	$4,240
Hispanic	.00361	$23,460	$4,200	$300	$18,960

Table 9: Benefits and Costs to US citizens of 100 Cord Blood Units

Race of Registrants	Expected US Lives Saved	Value of Lives Saved	Direct Costs	Medical Costs	Benefits Minus Costs
Caucasian	.002640	$17,200	$9,100	$300	$7,800
African	.009009	$58,600	$9,300	$9,800	$39,500
Asian	.001419	$9,200	$9,100	$400	−$300
Hispanic	.005910	$38,400	$9,200	$4,200	$24,800

Tables 8 and 9 estimate and evaluate the expected number of lives of US citizens that would be saved by increased registry sizes. The reduction in number of US deaths is the sum of such changes for each individual in the US population. Since no one knows in advance whether they will ever need a transplant, these probabilities the reduction in mortality risk is spread fairly evenly across the population. Thus if total benefits of an increased registry exceed total costs and if costs are divided fairly equally, we would expect it to be in the interest of most US citizens to have a larger registry, even if they are entirely selfish. Because of international sharing, however, an increase in the size of the US registry will save lives in other countries and increases in the size of foreign registries will save foreign 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. Since the preponderance of transplants occur in wealthy industrialized countries, using the same valuation for all lives saved by stem cell transplants seems a reasonable approximation. Tables 10 and 11 estimate lives saved in the entire world by adding 10,000 registrants adult registrants and cord blood units, respectively.

Table 10: 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	.00669	$43,046	$4,200	$10	$38,836
African	.00668	$43,400	$4,200	$790	$38,510
Asian	.01940	$126,009	$4,200	$310	$121,499
Hispanic	.00538	$34,960	$4,200	$330	$30,430

Table 11: 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	.008319	$54,100	$9,100	$500	$44,500
African	.015003	$97,500	$9,500	$16,000	$72,000
Asian	.015076	$98,000	$9,200	$3,400	$85,400
Hispanic	.009494	$61,470	$9,200	$5,200	$47,070

We see from these tables that the benefits to US citizens exceed the costs of increasing the number of registrants of any race. Benefits to US 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 registry is generally more than it costs, even if only takes into account the benefits to US citizens and becomes significantly more valuable if benefits to persons outside the US are also accounted for. These facts can be useful for encouraging an expansion of the registries, but the fact that efficient sizes have not yet been achieved suggests that expansion of the registries is constrained by budgets. Thus it becomes interesting to inquire whether the data suggests 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 8 -11 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 avail-

able 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 12 and 13 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 H.1 and H.2 of the Appendix.

Table 12: Ranked Ratios of US Benefits to Total Costs

Registrant Race Registry type	Ratio of Benefits to Total Cost
Hispanic adult registry	5.2
African adult registry	4.8
Caucasian adult registry	3.6
African cord blood bank	3.1
Hispanic cord blood bank	2.9
Caucasian cord blood bank	2.0
Asian adult registry	2.0
Asian cord blood bank	1.0

Table 13: Ranked Ratios of World Benefits to Total Costs

Race and Registry type	Ratio of Benefits to Total Cost
Asian adult registry	27.9
Caucasian adult registry	10.3
African adult registry	8.7
Asian cord blood bank	7.8
Hispanic adult registry	7.7
Caucasian cord blood bank	5.6
Hispanic cord blood bank	4.3
African cord blood bank	3.8

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 4.9.

4.8   Sensitivity Analysis

The benefit-cost analysis was repeated under alternative assumptions to test the sensitivity of the main results. First, as discussed in Section 4.3, an alternative to the VSL approach to valuing survival benefits is to value years of life. A typical value attributed to a year of life by US researchers and policy makers is $100,000 dollars (Ubel et al., 2003). The mean number of years of life for a transplant recipient was calculated using data on the age distribution of transplant recipients (Health Resources and Services Administration, 2012a) and life tables from the CDC (Arias, 2012) under the assumption that death rates for transplant recipients are three times average(Socié et al., 1999). The resulting value was 31.9 years, so that the benefit to a survivor of a transplant would be approximately $3.2 million. The benefit-cost ratios in Columns (2) and (4) of Table 14 use this value in calculating benefits. The second alternative assumption is that there are no cord-only searches, but rather all searches start by looking for a donor on the registry. The use of cord only searches was a modeling choice by Howard et al. (2008) to account for the fact that there were more cord transplants than they could otherwise account for, but we have been unable to find good estimates of how common this practice actually is. The assumption of no cord only searches is used in calculating the benefit-cost ratios in Columns (3) and (4) of Table 14.

Under either or both alternative specification presented in Table 14, most of the benefit-cost ratios for adding registrants remain greater than one. The main exception involves searches for US Asians. As noted above, the world cord bank size is approximately optimal given the number of searches by US Asians, so the benefit cost ratios fall below one for each of the alternative specifications in panel (b). Considering world searches, however, benefit cost ratios are greater than one for both registrants and cord units and for all races under each of the alternative scenarios. The ratios continue to be considerably higher for adding registrants than for addng cord units.

4.9   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 BC ratios are higher; and (2) increase both registry and bank sizes since all of the BC ratios are considerably above one. It is necessary 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 blook bank can be determined using the benefit-cost framework above. With the optimal registry, R_{opt}, and cord bank, C_{opt}, 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 in Table 15.

Whether one takes the US or world perspective our base specification and all of

Table 14: Benefit-Cost Ratios Under Alternative Assumptions

(a) US Searches, World Registry

	Baseline	Life Years	No Cord Only	Life Years and No Cord Only
donor race				
Caucasian	3.6	1.8	3.7	1.8
African	4.8	2.4	5.6	2.8
Asian	2.0	1.0	2.1	1.0
Hispanic	5.2	2.6	5.9	2.9
cord race				
Caucasian	1.8	0.9	1.3	0.6
African	3.1	1.5	2.4	1.2
Asian	1.0	0.5	0.8	0.4
Hispanic	2.9	1.4	2.1	1.0

(b) World Searches, World Registry

	Baseline	Life Years	No Cord Only	Life Years and No Cord Only
donor race				
Caucasian	10.3	5.1	10.7	5.3
African	8.7	4.3	9.5	4.7
Asian	27.9	13.8	29.1	14.3
Hispanic	7.7	3.8	8.5	4.2
cord race				
Caucasian	5.6	2.8	3.8	1.9
African	3.8	1.9	3.3	1.6
Asian	7.8	3.8	6.5	3.2
Hispanic	4.3	2.1	3.3	1.6

Notes: The table shows the benefit-cost ratio "BC Ratio 1." under alternative assumptions. Column (1) repeats the baseline specification from Table **??**. Column (2) values life years at $100,000 rather than using a VSL of $6.5 million. Column (3) assumes that there are no urgent, cord-only searches. Column (4) combines the assumptions of Columns (2) and (3).

Table 15: Optimal Registry Under Various Assumptions

(a) US Searches Only

	Current Registry		Optimal Registry			
	NMDP	**World**	**VSL**	**QALY**	**No CO**	**QALY/No CO**
donor registry						
Caucasian	7,160,779	14,332,925	38,300,000	22,717,000	40,593,000	23,905,000
African	710,271	839,683	4,658,000	2,198,000	6,599,000	3,168,000
Asian	710,271	2,177,101	3,897,000	1,985,000	4,481,000	2,311,000
Hispanic	974,679	987,141	6,420,000	3,293,000	8,992,000	4,523,000
cord bank						
Caucasian	110,068	403,670	485,000	288,000	273,000	177,000
African	13,173	22,632	156,000	75,000	72,000	21,000
Asian	13,338	113,684	79,000	36,000	46,000	15,000
Hispanic	31,835	42,456	257,000	120,000	92,000	27,000

(b) World Searches

	Current Registry		Optimal Registry			
	NMDP	**World**	**VSL**	**QALY**	**No CO**	**QALY/No CO**
donor registry						
Caucasian	7,160,779	14,332,925	81,267,000	49,163,000	87,369,000	52,638,000
African	710,271	839,683	9,789,000	5,012,000	11,519,000	6,004,000
Asian	710,271	2,177,101	43,142,000	25,222,000	46,432,000	27,123,000
Hispanic	974,679	987,141	7,121,000	3,672,000	8,819,000	4,613,000
cord bank						
Caucasian	110,068	403,670	1,316,000	772,000	545,000	363,000
African	13,173	22,632	183,000	92,000	91,000	38,000
Asian	13,338	113,684	590,000	329,000	287,000	171,000
Hispanic	31,835	42,456	223,000	103,000	98,000	39,000

Notes: The table shows the current and optimal size and racial distribution of registrants and cord units.

19

the sensitivity analyses suggest that current world registries are substantially smaller than optimal. If one only considers US searches, the current world inventory of cord units is actually super-optimal for Asians and near optimal for whites. When accounting for world searches, cord banks are suboptimal for the baseline specification, but the sensitivity analysis includes the possibility that current cord banks are super-optimal for some races and near optimal for the others. The percentage increase in size required to reach the optimum is higher for registries than cord banks for all specifications. The benefit-cost results and optimal registry results both suggest that expanding registries should be prioritized over increasing inventories of cord blood units.

5   Discussion

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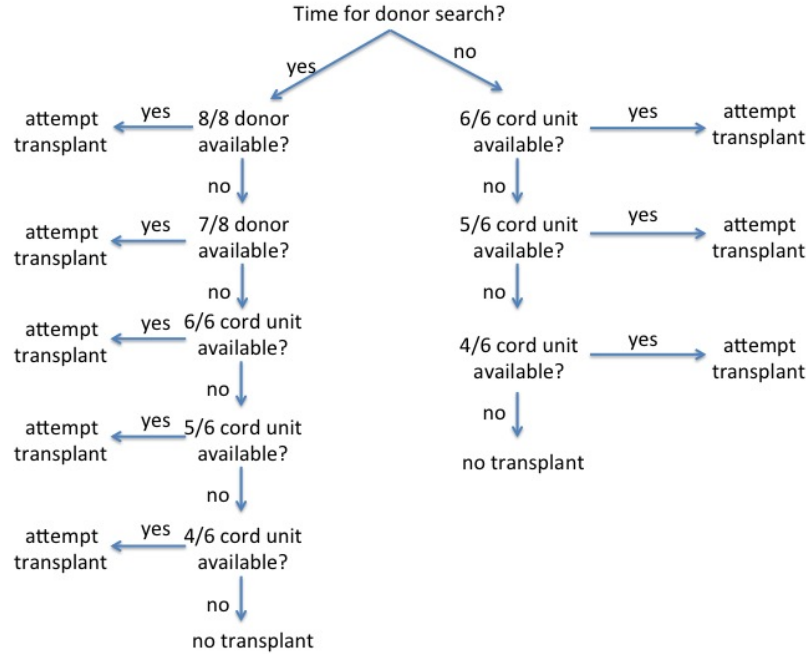
There are three features of the results that support the notion that expansion of adult donor registries should be prioritized over growing cord blood banks. First, the marginal benefit-cost ratios for registries are substantially higher than those for cord banks. Second, adult donor registries are further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

These results are, of course, contingent upon current technology and usage patterns. If costs of cord banking are likely to fall with continued growth or the benfits of cord blood relative to adult donors is likely to increase over time, it may be that continued emphasis on 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.

Appendices

A   Howard, et al. Donor Search Tree

Figure A.1: Donor search tree used in Howard, et al. (2008)

The donor search tree used in Howard et al. (2008) is shown in Figure A.1. It prioritized adult donor transplants over cord blood transplants as shown in the left pathway. The search tree used in the current analysis prioritized 6/6 or 5/6 cord transplants above 7/8 donor transplants. It is shown in Figure 2 and discussed in Section 3.1.

B   National Registries

The size of many of the larger national registries and the number of transplants performed in each of these countries is presented in Table B.1.

C   Detailed Methods

C.1   Phenotype Frequencies

Because the distribution of HLA phenotypes is far too diffuse to estimate directly, researchers have used statistical techniques to estimate haplotype distributions (Mori et al., 1997; Kollman et al., 2007; Maiers et al., 2007; Gragert et al., 2013) under the assumption that all mating is within racial groups but otherwise uncorrelated with

Table B.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
Croatia	6	33,551	2,381
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
India	3	21,430	0
Iran	0	2,608	3,492
Ireland	30	21,110	0
Israel	138	794,305	10,676
Italy	552	340,409	28,518
Japan	1,203	432,318	4,698
Korea	417	0	24,022
Mexico	2	12,349	303
Netherlands	213	43,035	3,285
Norway	32	29,940	0
Poland	191	464,488	1,201
Portugal	47	327,774	0
Russia	85	8,122	4,657
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: The number of transplants for each country was obtained from World Marrow Donor Association (2009) while the reistry and bank sizes were found at **?**.

HLA type. We use the haplotype distribution estimates of Gragert et al. (2013)[14] 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 freqency 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, consisting 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.[15] 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

---

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

[15]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.

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.

C.2 Registry Composition

The quantities calculated in Section C.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:

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

C.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

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

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

$$p_{\bar{6}54,i}^M(C) = p_{5or6,i}^M(C) - p_{6,i}^M(C) \tag{10}$$

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

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

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

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

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 probabilties, and the corresponding "best" match given the search algorithm described in Section 3.1 are presented in Table C.1.

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

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

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

<div align="center">**Table C.1**: **Possible Search Outcomes**</div>

8/8	7/8	6/6	5/6	4/6	Probability	Best 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	$p^M_{\overline{87}\,\overline{654},i}(R,C) = p^M_{\overline{87},i}(R) * p^M_{\overline{654},i}(C)$	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.

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

$$p^*_{5,i}(R,C) = p^M_{\overline{8}7\overline{6}54,i}(R,C) + p^M_{\overline{87}\overline{6}54,i}(R,C) \tag{15}$$

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

$$p^*_{7,i}(R,C) = p^M_{\overline{8}7\overline{65}4,i}(R,C) + p^M_{\overline{8}7\overline{654},i}(R,C) \tag{16}$$

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

$$p^*_{4,i}(R,C) = p^M_{\overline{87}\overline{65}4,i}(R,C) \tag{17}$$

6. There is no match for type i

$$p^*_{0,i}(R,C) = p^M_{\overline{87}\overline{654},i}(R,C) \tag{18}$$

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:

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

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

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

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

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

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

C.3.1 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,

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

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

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

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

D   Detailed Table of Matching Probabilities

The details of matching probability for patients of each race searching the NMDP or world registries are presented in Table D.1.

Table D.1: Search Outcomes

(a) Best Match Distribution using US (NMDP) Registry Alone

	Outcomes for Adults				Outcomes for Children			
Best	**Donors or Cord Blood**				**Donors or Cord Blood**			
Match	**cau**	**afa**	**api**	**his**	**cau**	**afa**	**api**	**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

	Cord Blood Only				Cord Blood Only			
Best								
Match	**cau**	**afa**	**api**	**his**	**cau**	**afa**	**api**	**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

(b) Best Match Disribution using World Registry

	Outcomes for Adults				Outcomes for Children			
Best	**Donors or Cord Blood**				**Donors or Cord Blood**			
Match	**cau**	**afa**	**api**	**his**	**cau**	**afa**	**api**	**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

	Cord Blood Only				Cord Blood Only			
Best								
Match	**cau**	**afa**	**api**	**his**	**cau**	**afa**	**api**	**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

Notes: The table gives the probability that the best match for the given age and racial group falls into each category when using when searching the indicated registry using the search algorithm described in panel (b) of Figure 2. Key for racial groups: "cau" is Caucasian; "afa" is African/African-American; "api" is Asian/Pacific Islander; "lat" is Latino.

E Comparison of Calculated Match Probabilities to Previous Work

The match probabilities calculated in this paper are similar to those computed using different methods (**?**) and found empirically (Anasetti et al., 2010; Dehn et al., 2010) as shown in Table E.1.

Table E.1: Comparison of Calculated Match Probabilities

	This paper	NMDP	Anasetti et al	Dehn et al
Adult Donor Matches				
Caucasian - 8/8	0.72		0.62	0.68
African - 8/8	0.2		0.15	0.26
Asian - 8/8	0.32			
Hispanic - 8/8	0.38		0.34	
Caucasian - 7/8 or 8/8	0.95	0.97	0.89	
African - 7/8 or 8/8	0.72	0.76	0.63	
Asian - 7/8 or 8/8	0.8	0.84		
Hispanic - 7/8 or 8/8	0.81	0.83	0.77	
Cord Blood Matches				
Caucasian 4/6 or better	0.95	0.96		
African 4/6 or better	0.88	0.84		

F Details of Estimating Number of Persons Seeking Matches

The ten entries in this table can be used 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

Table F.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 faciliated by the NMDP in 2011.

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 pedicted number of transplants of each type would exactly match the values given in Table F.1. These parameter values obtained are presented in Table F.2 and are used as the base model for determining the distribution of searches in the United States in all future calculations. Note that the required fraction of searches that are cord only is much lower than in Howard et al. (2008) due to the algorithm preferring 6/6 and 5/6 cord blood to 7/8 adult donor transplants.

Table F.2: Search Calibration Parameters

(a) 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

(b) 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.

G   Effects of Larger Registries on Expected Number of World Transplants

Table G.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
African	.0544	-.0013	-.0300	.0168	-.0373	.0026
Asian	.01921	-.0094	-.01446	.0077	-.0448	.0010
Hispanic	.0500	-.0010	-.0345	.0056	-.0179	.0011

Table G.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
African	.0000	.01366	.26436	-.20914	-.01690	.05198
Asian	.0000	.03957	.33707	-.32753	-.03799	.01112
Hispanic	.0000	.02337	.16690	-.15123	-.02208	.01695

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

References

ALDY, J. E. AND W. K. VISCUSI (2008): "Adjusting the value of a statistical life for age and cohort effects," *The Review of Economics and Statistics*, 90, 573–581.

ANASETTI, C., R. HILLGRUBER, V. NYE, E. AYALA, ET AL. (2010): "Patient Ethnicity markedly affects the probability of finding an HLA-A, -B,-C amd DRB 1 allele matched unrelated donor for hemopoietic cell transplantation," *Biology of blood and marrow transplantation*, 16, S172.

ARIAS, E. (2012): "United States Life Tables, 2008," *CDC/NCHS National Vital Statistics Reports*, 61.

Table H.1: Ranked Ratios of US Net Benefits to Direct Registry Costs

Race and Registry type	Ratio of Benefits to Total Cost
Hispanic adult registry	5.2
African adult registry	4.8
Caucasian adult registry	3.6
African cord blood bank	3.1
Hispanic cord blood bank	2.9
Caucasian cord blood bank	2.0
Asian adult registry	2.0
Asian cord blood bank	1.0

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

Race and Registry type	Ratio of Benefits to Total Cost
Asian adult registry	29.9
Caucasian adult registry	10.3
Asian cord blood bank	10.3
African adult registry	10.1
African cord blood bank	8.6
Hispanic adult registry	8.2
Hispanic cord blood bank	6.1
Caucasian cord blood bank	5.9

Ballen, K. K., J. Koreth, Y.-B. Chen, B. R. Dey, and T. R. Spitzer (2012): "Selection of optimal alternative graft source: mismatched unrelated donor, umbilical cord blood, or haploidentical transplant," *Blood*, 119, 1972–1980.

Barker, J. N., A. Scaradavou, and C. E. Stevens (2010): "Combined effect of total nucleated cell dose and HLA match on transplantation outcome in 1061 cord blood recipients with hematologic malignancies," *Blood*, 115, 1843–1849.

Bergstrom, T. (1982): "When is a man's life worth more than his human capital?" in *The Value of Life and Safety*, ed. by M. W. Jones-Lee, North Holland, 3–26.

Bergstrom, T. C., R. Garratt, and D. Sheehan-Connor (2009): "One Chance in a Million: Altruism and the Bone Marrow Registry," *American Economic Review*, 99, 1309–1334.

——— (2012): "Stem Cell Donor Matching for Patients of Mixed Race," *The B.E. Journal of Economic Analysis and Policy*, 12.

Bone Marrow Donors Worldwide (2014): "Total Number of stem cell donors," Available at https://www.bmdw.org/index.php?id=statistics_stemcell, Accessed, June 20, 2014.

Dehn, J., K. Buck, S. Yang, S. Schmidt, et al. (2010): "8/8 high-resolution match rate: caucasian and African American patients," *Biology of blood and marrow transplantation*, 17, S170–171.

Drèze, J. H. and P. Dehez (1982): "State-dependent utility, the demand for insurance and the value of safety," in *The Value of Life and Safety*, ed. by M. W. Jones-Lee, North Holland, 41–65.

Eapen, M., V. Rocha, G. Sanz, A. Scaradavou, M.-J. Zhang, W. Arcese, A. Sirvent, R. E. Champlin, N. Chao, A. P. Gee, et al. (2010): "Effect of graft source on unrelated donor haemopoietic stem-cell transplantation in adults with acute leukaemia: a retrospective analysis," *The lancet oncology*, 11, 653–660.

Flomenberg, N., L. A. Baxter-Lowe, D. Confer, M. Fernandez-Vina, A. Filipovich, M. Horowitz, C. Hurley, C. Kollman, C. Anasetti, H. Noreen, et al. (2004): "Impact of HLA class I and class II high-resolution matching on outcomes of unrelated donor bone marrow transplantation: HLA-C mismatching is associated with a strong adverse effect on transplantation outcome," *Blood*, 104, 1923–1930.

Gold, M. R., J. E. Siegel, L. B. Russell, and M. C. Weinstein (1996): *Cost-Effectiveness in Health and Medicine*, Oxford University Press.

Gragert, L., A. Madbouly, J. Freeman, and M. Maiers (2013): "Six-locus high resolution HLA haplotype frequencies derived from mixed-resolution DNA typing for the entire US donor registry," *Human immunology*, 74, 1313–1320.

Health Resources and Services Administration (2012a): "Detailed Description of Donor Registry Data," http://bloodcell.transplant.hrsa.gov/research/transplant_data/registry_tx_data/longdesc/index.html (accessed March 12, 2013).

——— (2012b): "Donor Registry Data," http://bloodcell.transplant.hrsa.gov /RESEARCH/Registry_Data/index.html (accessed July 26, 2012).

——— (2014): "Donor Registry Data," http://bloodcell.transplant.hrsa.gov /RESEARCH/Registry_Data/index.html (accessed June 10, 2014).

Howard, D. H., D. Meltzer, C. Kollman, M. Maiers, B. Logan, L. Gragert, M. Setterholm, and M. M. Horowitz (2008): "Use of cost-effectiveness analysis to determine inventory size for a national cord blood bank," *Medical Decision Making*, 28, 243–253.

Kollman, C., E. Abella, R. Baitty, P. Beatty, R. Chakraborty, C. Christiansen, R. Hartzman, C. Hurly, E. Milford, J. Nyman, T. Smith, G. Switzer, R. Wada, and M. Setterholm (2004): "Assessment of Optimal Size and Composition of the U.S. National Registry of Hematopoietic Stem Cell Donors," *Transplantation*, 78, 89–95.

Kollman, C., M. Maiers, L. Gragert, C. Müller, et al. (2007): "Estimation of HLA-A -B -DRB1 Haplotype Frequencies Using Mixed Resolution Data from a National Registry with selective retyping of volunteers," *Human Immunology*, 68, 950–958.

Maiers, M., L. Gragert, and W. Klitz (2007): "High-resolution HLA alleles and haplotypes in the United States population," *Human immunology*, 68, 779–788.

Miller, T. R. (2000): "Variations between Countries in Values of Statistical Life," *Journal of Transport Economics and Policy*, 34, 169–188.

Mishan, E. (1971): "Evaluation of Life and Limb: A theoretical approach," *Journal of Political Economy*, 79, 687–705.

Mori, M., P. Beatty, M. Graves, K. Boucher, and F. Milford (1997): "HLA gene and haplotype frequencies in the North American population: the National Marrow Donor Program Donor Registry." *Transplantation*, 64, 1017–1027.

Querol, S., G. J. Mufti, S. G. Marsh, A. Pagliuca, A.-M. Little, B. E. Shaw, R. Jeffery, J. Garcia, J. M. Goldman, and J. A. Madrigal (2009): "Cord blood stem cells for hematopoietic stem cell transplantation in the UK: how big should the bank be?" *haematologica*, 94, 536–541.

Seitz, R., A. Hilger, and M. Heiden (2012): "Bone Marrow, Peripheral Blood, or Umbilical Cord Blood: Does the Source of Allogeneic Hematopoietic Progenitor Cells Matter?" *Journal of Blood Disorders & Transfusion*, S1.

Socié, G., J. V. Stone, J. R. Wingard, D. Weisdorf, P. J. Henslee-Downey, C. Bredeson, J.-Y. Cahn, J. R. Passweg, P. A. Rowlings, H. C. Schouten, et al. (1999): "Long-term survival and late deaths after allogeneic bone marrow transplantation," *New England Journal of Medicine*, 341, 14–21.

Takanashi, M., H. Tanaka, M. Kohsaki, K. Nakajima, K. Tadokoro, and M. Nakabayashi (2010): "A suggested total size for the cord blood banks of Japan," *Bone marrow transplantation*, 46, 1014–1015.

Ubel, P., R. Hirth, M. Chernew, and A. Fendrick (2003): "What is the price of life and why doesn't it increase at the rate of inflation?" *Archives of Internal Medicine*, 163, 1637–1641.

Viscusi, W. K. and J. E. Aldy (2003): "The Value of a Statistical Life: A Critical Review of Market Estimates throughout the World," *Journal of Risk and Uncertainty*, 27, 5–76.

Vlachos, D., E. Iakovou, C. Keramydas, and A. Anagnostopoulos (2012): "On the estimation of the necessary inventory for hellenic public cord blood banks using simulation," *Operational Research*, 12, 57–68.

World Marrow Donor Association (2009): "Stem Cell Donor Registries Annual Report 2009," WMDA Publications.

——— (2012): "Annual Report 2011," Http://www.agence-biomedecine.fr/IMG/pdf/donnees_wmda.pdf (accessed June 20, 2014).