



East Meets West—Impact of Ethnicity on Donor Match Rates in the Ezer Mizion Bone Marrow Donor Registry



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HLA haplotype frequencies in a volunteer bone marrow donor registry should reflect the frequencies of potential transplant recipients served by that registry, a challenge in a country with diverse subethnicities of immigrants from Eastern and Western cultures, such as Israel. We evaluated the likelihood of finding suitable donors for hypothetical patients drawn from defined subethnicities in the Ezer Mizion Bone Marrow Donor Registry (EM BMDR) from donors both within and outside the registry now and during the coming decade. On average, bioinformatics modeling predicts that, given current donor recruitment trends, 6/6 high-resolution HLA match rates for Israelis, which currently stand at 40% to 55% for most subethnicities, will rise by up to 1% per year over the next decade. Subethnicities with historically lower rates of interethnic admixture are less likely to find matches outside of their designated group but will benefit from expansion of the registry, whereas ethnically directed drives will enhance matching rates for currently underrepresented subethnicities. Donor searches for the same cohort using a large extramural registry was of only slight benefit for most of the 19 EM BMDR subethnicities evaluated, confirming that local donor registries that reflect the ethnic diversity of the community being served are best equipped to serve the needs of their respective communities. Contemporary trends of an increasingly multiethnic admixture in Israel may impact the effect of ethnic profiling in assessing future match rates for EM BMDR.

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) can be life-saving for patients with a lethal hematologic malignancy or one of an ever-expanding list of nonmalignant hematologic and immunologic disorders [1,2]. As family size shrinks in many Western countries, patients in need of HSCT must frequently turn to burgeoning bone marrow donor registries to seek a matched unrelated donor (MUD). The growth of donor registries in countries worldwide, their online accessibility, and the improving outcome of unrelated donor HSCT have made this procedure a reality for many patients in need [3,4]. The success of unrelated donor HSCT increases commensurate to the degree of HLA matching between the donor and recipient [5–8]. Because ethnicity affects HLA allele and

haplotype frequency and thus influences the outcome of donor searches, a national registry's donor pool should reflect the ethnicities of that nation's population [9].

The Ezer Mizion Bone Marrow Donor Registry (EM BMDR), established in 1998, is the largest Jewish registry worldwide, with a roster of more than 800,000 volunteer adult donors. From its inception through December 2015, the EM BMDR provided 950 hematopoietic product cells (HPCs) for Israeli patients and 1176 HPCs for patients from outside of Israel. Establishing a comprehensive donor pool for the Israeli population is an immense challenge. Contemporary Jews comprise an aggregate of ethnoreligious communities in Israel and in the Jewish Diaspora. Genetic divergence within the greater Jewish population was caused by admixture with indigenous host populations on a backbone of Mediterranean ancestry, while cultural and religious forces maintained coherence of the Jewish people [10–13]. Israel is a home to the entire genetic spectrum of the Jewish Diaspora, as well as to large minorities composed of non-Jewish ethnic groups, leading to substantial ethnic diversity in a country of only 8

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million individuals. As second-generation Israelis start marrying outside of their ancestral subethnicities, an additional layer of diversity has been introduced into the HLA landscape in Israel, leading to immunogenetic intergenerational differences within the Israeli population [14].

Since 2005, the EM BMDR has enrolled stem cell volunteer donors primarily at the central induction center of the Israel Defense Forces, where military conscripts, at age 18, are offered enrollment as part of the enlistment process. All Israeli teenagers (male and female) of Jewish, Druze, Bedouin, or Circassian descent are required to register at this center on or around their 18th birthday. The EM BMDR's recruitment strategy has increased the number of young, healthy donors in the registry (37% of registered donors are now between 18 and 25 years of age) and has enhanced its HLA diversity to reflect the representation of nearly all of the subethnicities in the Israeli population (according to the 2014 Israeli Census report, Table 2.8) [15]. The EM BMDR also conducts ethnically focused donor drives within Jewish, Arab, and Druze communities in an effort to enhance the ethnic representation of specifically targeted groups. Approximately 10% of the Israeli adult population is registered in the EM BMDR, making it the registry with the highest number of HLA-A, -B, and -DR matched stem cell donors per 10,000 inhabitants worldwide [16].

Despite the large size of this donor pool, however, many Israeli patients in need of an MUD HSCT cannot find a suitably matched local donor [17]. According to the World Marrow Donor Association's 2014 annual report, 72% of the MUD products required for transplantations in Israel were procured from Israeli BMDRs, of which 68% were provided by the EM BMDR [16].

Haplotype frequency estimation using phenotypic population data can permit, among other things, an estimate of the size of a theoretical donor pool that will meet the needs of a specific patient population [18–20]. In a previous study, we analyzed the HLA alleles and haplotype frequencies of 19 subethnic populations in the EM BMDR [21]. The current report extends our analysis to measure the likelihood of finding donors at different matching stringencies for the population served by the registry. For this purpose, we used hypothetical patients from each subethnicity in the EM BMDR, in an effort to show the ability of the current registry (in terms of size and subethnic representation) to provide stem cell donors for the Israeli population. We also project the effects of donor registry growth on the likelihood of successful donor searches within the registry.

METHODS

Study Population

The initial dataset included all 754,135 adult volunteer donors registered at the EM BMDR from its inception through June 2014. All subjects provided informed consent for registration at recruitment and provided self-reported information regarding the country of origin of each parent, which we used to assign subethnic population designations. Donors were asked to write in the country of parental origin and did not choose from a registry-generated list, so as not to limit their answers. The study was approved by Rabin Medical Center's Ethics Committee. Study subjects were restricted to those individuals who reported the same subethnicity for both parents. Multiethnic or mixed-ethnicity donors were excluded from this analysis. The initial dataset included 67 subethnicities, with an average sample size of 5200 (range, 2 to 69,716) per population; however, only 19 populations, containing a total of 275,699 donors, were large enough for analysis, considering our typing resolution determinations [21] (Table 1). The United States, Argentina, and Ashkenazi (donors who did not specify their parents' geographical origin but reported being of Ashkenazi ancestry) subethnic populations are predominantly emigrants from Eastern and Western Europe. The southeast Europe (SEE) subethnic population includes Jews from Romania, Bulgaria, Moldova, Greece, geographic Yugoslavia, Albania, Serbia, Transyl-

Table 1

The 19 Analyzed Ezer Mizion Populations and Sample Counts

Ezer Mizion Population	Sample Count
Arab	12,300
Argentina*	4,307
Ashkenazi	4,625
Bukhara	2,317
Druze	5,914
Ethiopia	5,928
Georgia	4,471
Iran	8,153
Iraq	13,270
Israel	69,716
Kavkaz	2,840
Libya	3,739
Morocco	36,718
Poland	13,871
SEE†	11,179
Tunisia	9,070
United States*	6,058
USSR‡	45,681
Yemen	15,542
Total	275,699

* The Argentina and United States populations are derived from emigrants of European Jews.

† SEE includes Romania, Bulgaria, Moldova, Greece, Yugoslavia, Albania, Serbia, Transylvania, and Cyprus.

‡ USSR includes Russia, Ukraine, Belarus, Lithuania, Latvia, and East Europe.

vania, and Cyprus. The USSR subethnic population includes Jews from Russia, Ukraine, Belarus, Lithuania, Latvia, and Eastern Europe. Donors who listed "Israel" as their subethnicity reflect a diverse group whose parents do not necessarily share the same ethnic origin; these donors indicated not their parents' ethnicity, but rather their parents' country of birth. For the purpose of this study, all EM BMDR donors who met the foregoing criteria were used as potential patients seeking an unrelated stem cell donor.

Modeling and Definitions

Match rate projection tools were developed by the National Marrow Donor Program (NMDP)/Be The Match Bioinformatics Research Department and were previously applied to the Be The Match (US) registry [22]. For the purpose of this study, HLA-matching models were based on donor–recipient 3-loci (HLA-A, -B, and -DRB1) high-resolution haplotype frequencies of the EM BMDR subethnicities [21]. Matching at all 3 loci is termed a 6/6 HLA match. A $\geq 5/6$ allele match includes matches of all 6 alleles of the donor–recipient pairs or allows for a single mismatched allele (5/6 or better). In addition, we analyzed the probability of identifying donors from within and outside of the patient's subethnic group accounting for current donor availability rates. The match rate for searches outside the donor's ethnic group is calculated by subtracting the within match rate from the cumulative match rate using the entire registry, and thus represents the matches that could not be found on an initial search within the given population.

Availability of Donors

Many factors affect the availability of registered volunteer donors [23,24]. Availability rates of potentially HLA-matched donors are given for the 3 stages of the MUD search process: confirmatory typing (CT), donor validation, and medical clearance. At the CT stage, a blood sample is obtained from identified potentially matching volunteers to confirm HLA typing. Preliminary serologic testing for infectious agents is performed as well. Donor unavailability at this stage may result from failure to locate the donor, donor health-related issues, or scheduling conflicts. At the donor validation stage, the initially inferred HLA typing at the preliminary search is compared with the CT results; discrepancies might invalidate the donor. Finally, MUDs receive detailed information about the donation process, and their medical eligibility is determined; at this stage, a donor may decline to continue or may be deemed medically unfit to donate stem cells. Donor availability rates were similar among the various subethnic populations in the EM BMDR registry, and the cumulative availability factor was calculated by multiplying the percentages of availability at the 3 respective stages, treating each stage as provisional for each subsequent event (Table 2). Match rates were adjusted for availability in our model by multiplying the number of donors in each analyzed population by this cumulative availability factor [21].

Table 2
Adult Donor Availability in 2015 Requested from EM BMDR

Confirmatory Typing Available, %*	Typing Not Discrepant, %†	Workup Available, %‡	Available Overall, %
80	99.4	94	75

* Data for donors who can be contacted and who have a DNA sample collected for confirmatory HLA typing.

† Data for donors whose confirmatory HLA typing was consistent with HLA typing performed at recruitment.

‡ Data for donors who were cleared as healthy by means of a medical examination and who agreed at this stage to proceed toward donation.

Statistical Analysis

In our analysis we included only donors who had been genotyped by DNA methods at HLA-A, -B and -DRB1 loci. Owing to progressive changes in HLA genotyping technology, the registry data contains donors at varying levels of resolution. Only subethnicities with a minimum of 200 high-resolution (first 2 nomenclature fields) typed samples at HLA-A, -B, and -DRB1 were included in this study; 19 subethnic populations met this selection criterion (Table 1). We used the expectation maximization (EM) algorithm, which is designed to handle mixed resolution data and to resolve both allelic and phase ambiguity [25–28], to estimate HLA A–B–DRB1 haplotype frequencies for each population [21]. We entered the haplotype frequencies and effective donor registry sizes for each population into a matching model [29–31] and assessed deviations from Hardy–Weinberg equilibrium (HWE) at the allele family level [21]. We used the model to calculate the population-specific HLA match rates for the given registry size and match definitions. Match rates were defined as the likelihood at which each individual from a given subethnic population would find an allele-matched adult donor by searching the same subethnic population, other subethnic populations, or the entire EM BMDR donor list. The adult donor match rate was modeled for each subethnic population over a range of potential registry sizes that predicted growth proportional to the initially reported subethnic population size. Based on annual growth of the registry during the previous decade, a projected annual registry growth rate of 6% over the next 10 years was selected for this analysis. We assumed a proportional expansion of each subethnicity from its current representation based on this growth rate, and did not account for future ethnically driven donor recruitment drives.

Marginal Benefit Analysis

We modeled the allele-level 6/6 and $\geq 5/6$ adult donor match rates for patients utilizing the donor pools of both EM BMDR and Be the Match

registries, in order to assess the effect conferred by the existence of EM BMDR on finding donors for potential patients drawn from the study populations enumerated above. We used previously published A–B–DRB1 haplotype frequencies for 21 race groups for modeling the Be the Match registry. The number of donors in individual race groups ranged from 1,469 for Alaskan Native to 2,899,081 for European. A donor availability factor could not be assessed for some ethnicities owing to the low number of transplantations performed in minority patients in Be the Match registry. We accounted for donor availability in the models by multiplying the number of donors in each of the 21 populations in the Be the Match registry by the donor availability of their corresponding broad race group. We calculated match rates attained from searching only the Be the Match registry for all individuals from each of the 19 subethnic populations analyzed from the EM BMDR at the 6/6 and $\geq 5/6$ levels, and termed this a marginal benefit [27].

RESULTS

Adult Donor Match Rates

Figure 1 shows the 5/6 and 6/6 overall match rates for the subethnic populations analyzed in the EM BMDR considering a 75% cumulative donor availability rate. Most patients will have a 6/6 or $\geq 5/6$ HLA MUD available from within the registry. For the majority of subethnic populations, 6/6 match rates were 40% to 55%; exceptions were the Tunisia (36%) Kavkaz (33%), Druze (33%), Yemeni (31%), Arab (17%), and Ethiopian (12%) populations. When allowing for a single HLA allele-mismatched donor, potential transplant candidates from all subethnic populations had a match rate $\geq 80%$ with the exception of the Arab (77%) and Ethiopian (66%) subethnic populations. Although 6/6 and $\geq 5/6$ loci HLA match rates are greatest within most subethnic populations (with the exception of Argentina, Ashkenaz, SEE, and United States, relatively small and very heterogenous groups) (Table 3), exploiting potential donors from other ethnic groups may enhance the chances of finding suitably matched donors (Supplementary Table S1). Individuals belonging to subethnic populations with a high level of genetic admixture (Ashkenazi and European [Argentina, Poland, United States]) have a 6/6 match rate of 21% to 31% with donors identified outside their

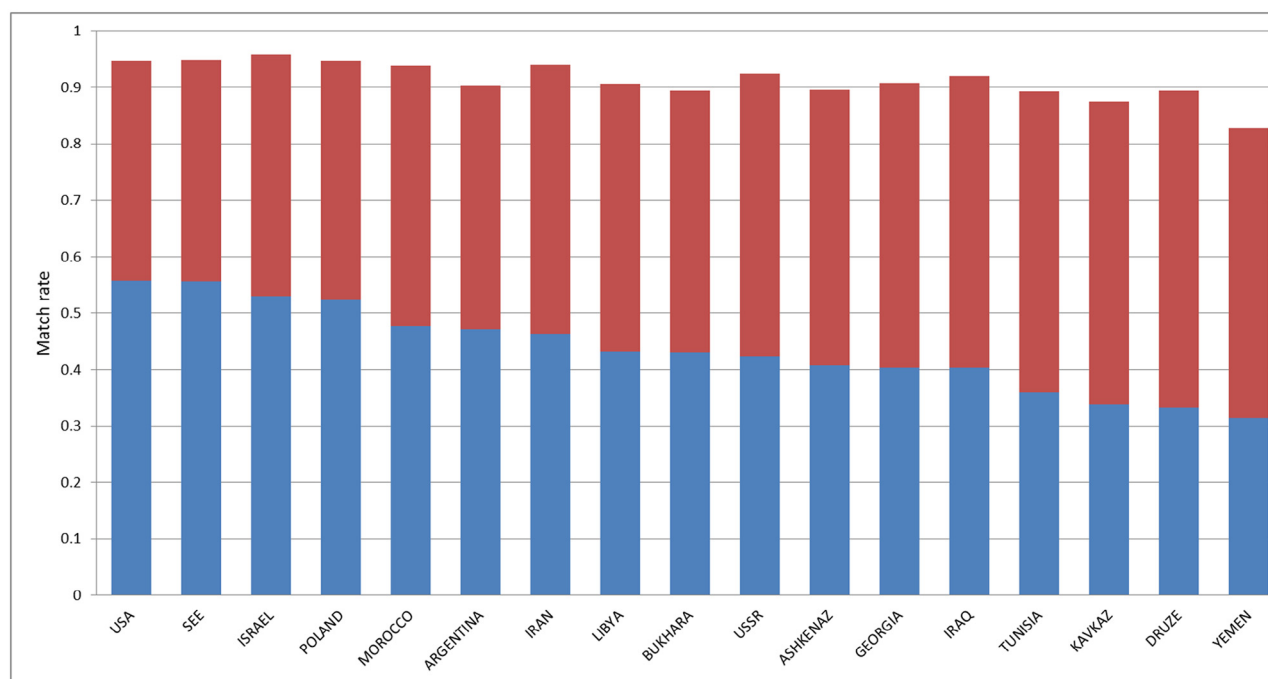


Figure 1. 6/6 and 5/6 stacked HLA match rates using a donor availability factor of 75%. For each population, the match rate shown represents the rate at which patients from this population would find an allele-matched donor by searching the entire EM BMDR.

Table 3
Probability of Identifying Adult Donors From Within and Outside the Patient's Subethnic Group Considering Donor Availability

Ethnicity	Cumulative 6/6	Within Population 6/6	Outside Population 6/6	Cumulative ≥5/6	Within Population ≥5/6	Outside Population ≥5/6
Arab	.170	.069	.101	.774	.543	.231
Argentina*	.471	.163	.309	.904	.594	.310
Ashkenaz	.407	.164	.243	.895	.595	.301
Bukhara	.431	.355	.076	.895	.751	.144
Druze	.333	.256	.077	.894	.762	.132
Ethiopia	.122	.114	.008	.667	.565	.101
Georgia	.404	.314	.091	.908	.768	.141
Iran	.463	.381	.082	.940	.834	.105
Iraq	.404	.318	.086	.919	.820	.100
Israel	.530	.446	.084	.959	.918	.041
Kavkaz	.338	.217	.122	.875	.610	.265
Libya	.432	.280	.152	.907	.720	.187
Morocco	.477	.420	.057	.939	.884	.055
Poland	.525	.309	.216	.948	.797	.151
SEE†	.555	.275	.281	.948	.766	.182
Tunisia	.361	.205	.155	.892	.716	.176
United States	.558	.239	.319	.947	.708	.239
USSR‡	.424	.327	.097	.923	.852	.072
Yemen	.314	.291	.023	.827	.753	.074

* Argentina and United States populations are derived from emigrants of European Jews.

† SEE includes Romania, Bulgaria, Moldova, Greece, Yugoslavia, Albania, Serbia, Transylvania, and Cyprus.

‡ USSR includes Russia, Ukraine, Belarus, Lithuania, Latvia, and East Europe.

ethnic group. In contrast, potential patients from subethnicities with lower levels of genetic admixture and unique allele representations [21] rarely find extramural 6/6-matched donors (Bukhara, 7.6%; Druze, 7.7%; Yemen, 2.3%; Ethiopia, 0.8%). It should be noted that patients belonging to subethnicities of large sample size (eg, Israel, Morocco, USSR) also have a low rate of extramural matching because they have a better chance of finding matched donors from within their own population.

Donor Registry Growth

We projected the expansion of the registry roster from 2016 to 2026. Projected match rates were calculated based on an anticipated growth of 6% cumulatively each year and 75% donor availability. We forecasted that aggregate 6/6 (Figure 2) match rates will improve by 0.5% to 1% per population per year

through 2026. We compared changes in match rates for specific subethnicities and found that Druze (9.8%) and Georgia (9.3%) populations experienced the most rapid growth in this metric. As expected, populations with already high match rates using the current registry donor roster and high levels of genetic admixture (Ashkenazi and European) will reap lower benefits from projected registry growth (6% to 7.5%). We also modeled 6/6 and ≥5/6 HLA allele donor match rates given a doubling of the total registry roster from 750,000 to 1,500,000 donors (Supplementary Figure S1). The 6/6 allele aggregate match rate rose from 52% to 62% for the entire registry cohort. The increase of donor-recipient matches by subethnicity ranged from 6.8% to 12.3%, with highest levels among the Druze community. The aggregate increase in match rate for ≥5/6 donor-recipient pairs with doubling of the registry size was

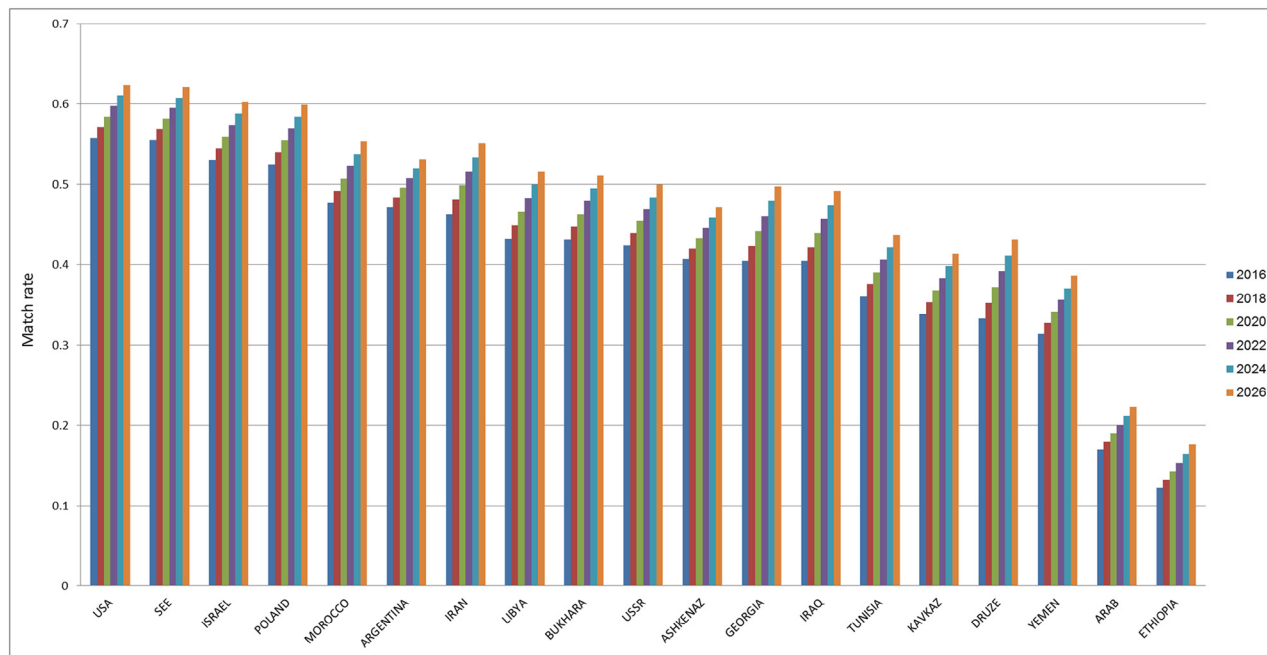


Figure 2. Adult donor 6/6 projected match rates based on current donor availability projected from 2016 to 2026. Calculations were based on an anticipated cumulative growth of 6% per year.

a more modest 2.5% (from 94.2% to 96.7%), with Ethiopian, Arab, and Yemeni match rates rising 7.9%, 5.3% and 4%; all other groups showed only nominal increases.

Marginal Benefit Analysis with the Be the Match Donor Registry

Allele-level 6/6 match rates for patients searching both the Ezer Mizion and Be the Match registries ranged from 16.9% to 65.4% for Ethiopia and Poland sub-ethnicities, respectively (Table 4). Cumulative 6/6 match rates in Table 3 represent the sum of the cumulative 6/6 match rates from Table 2 (using the EM BMDR pool alone) plus the marginal benefit added by searching the Be the Match pool of donors. For most potential patients searching both registries, the likelihood of finding a 6/6 matched donor exceeds 46%; exceptions include Ethiopian, Druze, Yemeni and Arab individuals. On average, potential patients from the Ethiopia, Druze, Yemen, and Arab sub-ethnic populations are 22% less likely to find a 6/6 matched donor in both registries than individuals from other populations. When allowing for a single HLA-allele mismatch (5/6 or better), most sub-ethnic populations have match rates exceeding 94%, with the exception of the Yemen and Ethiopia sub-ethnic populations.

The average marginal benefit achieved for potential patients from EM BMDR by searching the Be the Match donor pool for a 6/6 matched donor was 9%, but it varied by subethnicity. Specifically, marginal benefits of this extramural search ranged from 3% for Yemeni patients to 22% for Arab patients. The likelihood of finding a 6/6 matched donor for potential EM BMDR recipients only in the Be the Match registry was < 10% for most patients, except for Poland (13%), Kavkaz (14%), USSR (14%), and Arab (22%) subethnic populations. Comparative values for equivalent match rates in EM BMDR were 52%, 33%, 42%, and 17% for these same populations, respectively. The Arab population was the only population more likely to find a 6/6 matched donor in the Be the Match registry than in the EM BMDR. The likelihood of finding a $\geq 5/6$ matched donor only

in the Be the Match registry for EM BMDR potential patients was <8%, except in the Ethiopian (15%) and Arab (17%) subethnic populations.

CONCLUSIONS AND DISCUSSION

Analysis of a target population's HLA profile is integral to strategic planning for the establishment and expansion of stem cell donor registries that will provide an optimal representation of the population that they are meant to serve. We used HLA-A, -B, and -DRB1 haplotype frequencies from 19 subethnic populations of adult volunteer donors from within our registry to estimate match rates for hypothetical domestic patients given the current size of the EM BMDR. We assessed the effects of nondirected short-term growth of the registry (expansion of the donor pool without ethnicity-directed donor drives) on matching frequencies for Israelis patients of these subethnicities who seek a stem cell donor. Using a population-based genetic model [22] with selection criteria that predict the likelihood of finding a 6/6 or $\geq 5/6$ HLA-matched donor and accounting for our current rate of donor availability, we charted the effect that enlarging the registry would have on HLA match rates over the next decade. Each donor with both parents of the same subethnicity was considered a potential HSCT recipient for the purpose of this analysis.

Our results show that 40% to 55% of potential transplant recipients from most of the subethnic populations studied will find a 6/6 HLA allele-matched donor within the EM BMDR registry. Searches performed at lower stringency ($\geq 5/6$ matching stringency), resulted in match rates of $\geq 80%$ for patients from most of the subethnic populations. Some subethnic populations continue to have lower match rates within the EM BMDR because of lower representation in the registry (eg, Arab and Druze donors) or due to distinct HLA allele frequencies, likely the result of limited admixture with the greater Jewish Diaspora (eg, Ethiopian, Kavkazi, and Yemen).

Given projected donor enrollment rates, we anticipate adding approximately 500,000 donors to the EM BMDR by 2026. We predict an aggregate improvement in 6/6 match rates of 0.5% to 1% per population per year during this period (Figure 2). Although directed donor recruitment will alter this dynamic for currently underrepresented groups, all other populations in our registry will benefit from ongoing recruitment efforts. More importantly, our model does not account for future shifts in the immigration patterns or for multiethnic admixtures in Israeli society over the coming decade. Assuming that the discrete subethnicities on whom we have reported maintain their unique HLA haplotype frequencies, we forecast improved match rates for some currently underrepresented subethnicities that are moderately higher than the effects of registry growth on the EM BMDR population as a whole. A registry's mandate is to expeditiously identify the best available donor [32]. Our findings are consistent with those reported by Gragert et al. [22], and point to the futility of delaying transplant for a patient who does not find a donor in the hope that one will be identified in the near future.

The EM BMDR is supported by charitable and personal contributions, and donor recruitment is a costly process. As the stewards of philanthropic funds, we must allocate the resources of the registry responsibly. As such, we assessed the need for registry expansion by looking at the match rates from extramural donors, taken in this case from the Be the Match registry. The results of this analysis show that existence of the EM BMDR adds substantial benefit for Israelis who would require an unrelated stem cell transplant. Of interest, the Arab

Table 4
6/6 and $\geq 5/6$ Adult Donor Match Rates and Marginal Benefit for EM BMDR Patients Using the Donor Pools of the EM BMDR and Be the Match®

Ethnicity	Cumulative 6/6	Marginal Benefit 6/6	Cumulative $\geq 5/6$	Marginal Benefit $\geq 5/6$
Arab	.394	.225	.945	.171
Argentina*	.542	.071	.954	.050
Ashkenaz	.499	.091	.948	.053
Bukhara	.487	.056	.937	.042
Druze	.389	.056	.950	.057
Ethiopia	.169	.046	.822	.155
Georgia	.469	.065	.946	.038
Iran	.544	.082	.978	.039
Iraq	.504	.100	.965	.045
Israel	.599	.069	.983	.024
Kavkaz	.479	.140	.954	.079
Libya	.502	.070	.954	.048
Morocco	.560	.084	.975	.036
Poland	.654	.130	.987	.039
SEE †	.629	.074	.977	.029
Tunisia	.460	.099	.948	.056
USA	.643	.085	.977	.030
USSR ‡	.568	.143	.975	.052
Yemen	.343	.029	.878	.051

* Argentina and USA population are derived from emigrants of European Jews.

† SEE include Romania, Bulgaria, Moldova, Greece, Yugoslavia, Albania, Serbia, Transylvania and Cyprus.

‡ USSR include Russia, Ukraine, Belarus, Lithuania, Latvia and East Europe.

population in our country gained most from searching the extramural registry. We project that directed donor drives in this community will be required to improve local match rates for Arab patients.

Our model calculated match rates using 6 HLA alleles typed at high resolution. Searches at higher levels of stringency, such as inclusion of typing at HLA-C, will likely result in reduced match rates [33]. Additionally, our models assume HWE and were solely conducted using donors who listed both of their parents as belonging to the same sub-ethnicity. Recent data suggests that contemporary Israel is undergoing profound ethnic changes [34]; East is meeting West and are bearing children. As such, models assuming HWE might not be valid. The results of subethnic admixture in contemporary Israeli society are already apparent in the lower numbers of fully HLA MUDs actually found for children as compared with adult transplant recipients in Israel [14]. Exploring haplotype frequencies and match rates for the growing multi-ethnic population base in the EM BMDR will set the foundation for elaborating strategies for recruitment and expansion of the registry, and will highlight the value added to the international community through the contributions of multiethnic donors in an increasingly globalized community.

This study relied on donor self-reporting of subethnicity, which has been shown to be less than completely reliable [35]. A good example for the drawback of this ethnicity collection method is the reporting of Yugoslavia and Serbia as different countries by the donors, and the large number of donors who indicated USSR as their parents' country of origin. In an ever-changing global landscape, fluidity is required for analysis of these populations. Moreover, a large group of donors was excluded from analysis owing to the absence of data on parental ethnicity or due to multithnic lineages. As noted above, changes in reproductive patterns in contemporary Israel will likely change the subethnic landscape in the coming decades. A changing subethnic admixture will likely result in changes in the representation of HLA-allele frequencies in our populations. We have begun to collect data on grandparental subethnicities in an effort to guide future analyses.

Our data-driven approach will help plan the expansion and recruitment policies of the EM BMDR and aid Israeli and non-Israeli patients worldwide in their search for a stem cell donor.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at [doi:10.1016/j.bbmt.2017.04.005](https://doi.org/10.1016/j.bbmt.2017.04.005).

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