Matching probabilities of eight Indian population groups in the donor pool of DKMS Foundation India

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ISBMT
Indian Society for Blood & Marrow Transplantation

Objective

For patients with severe hematopoietic diseases, allogeneic hematopoietic stem cell transplantation (HSCT) is often the last option for a cure. An optimal transplantation outcome is achieved when patient and donor match in the alleles of particular population-specific human leucocyte antigen (HLA) genes. Since in many cases no suitable related donor is found, registries of voluntary unrelated HSCT donors have been established worldwide.

DKMS Foundation India is a Bangalore-based donor registry with nationwide donor recruitment activities. We assessed the benefits of the current registry's donor pool for Indian patients and analysed the need for future donor recruitment based on a data set of n=130,518 registered potential stem cell donors[1].

Methods

Eight subpopulations with sample sizes of n>5,000 DKMS India donors were defined by combining information on geographical origin and native language of both parents of the donors:

Sample short	Native language	State of origin
BEN	Bengali	West Bengal
GUJ	Gujarati	Gujarat
HIN	Hindi	Uttar Pradesh
KAN	Kannada	Karnataka
MAL	Malayalam	Kerala
MAR	Marathi	Maharashtra
TAM	Tamil	Tamil Nadu
TEL	Telugu	Andhra Pradesh
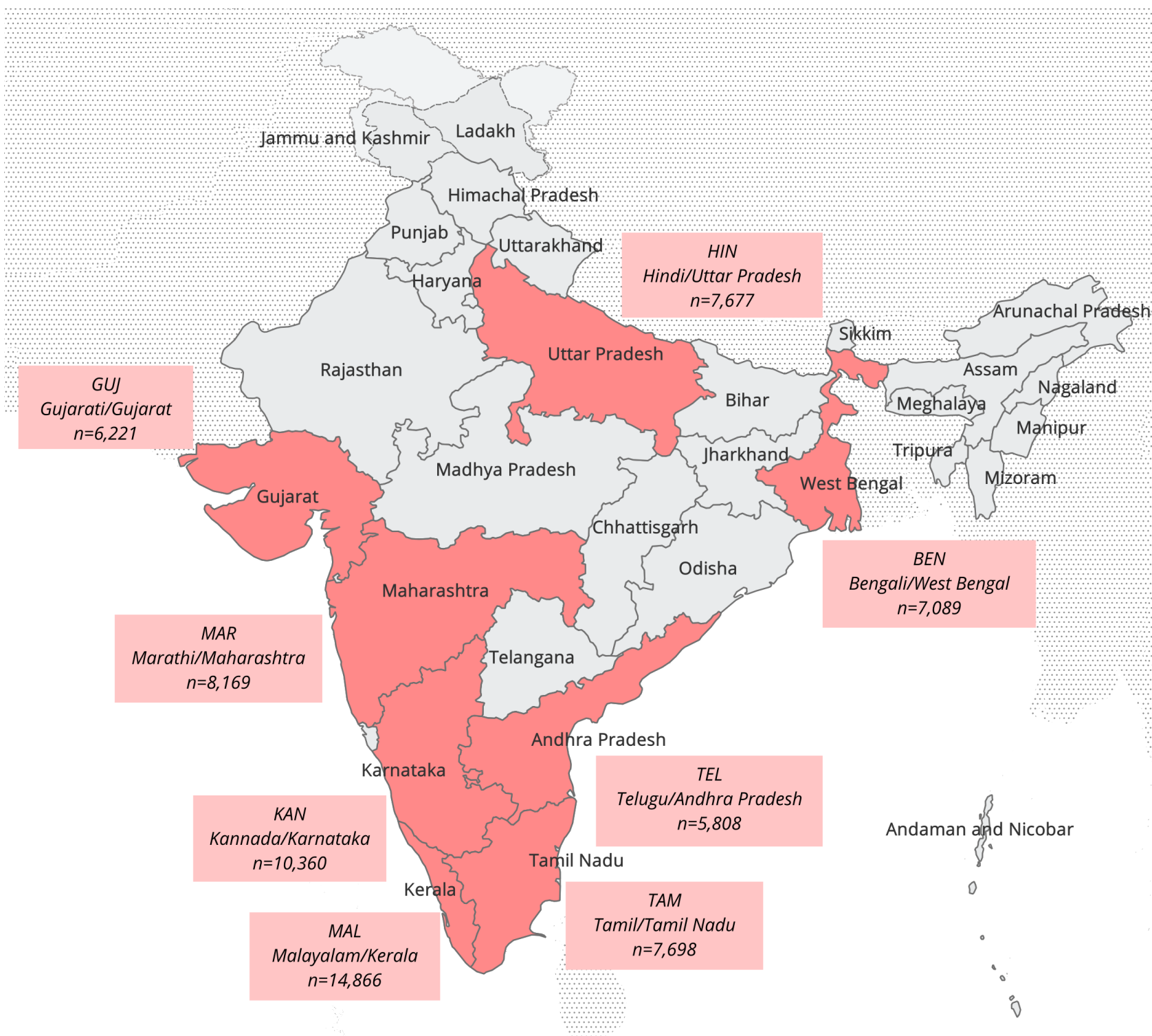
The subsample drawn for the frequency estimation of the 8 subpopulations sums up to a size of n=67,888, corresponding to 52% of the total sample.

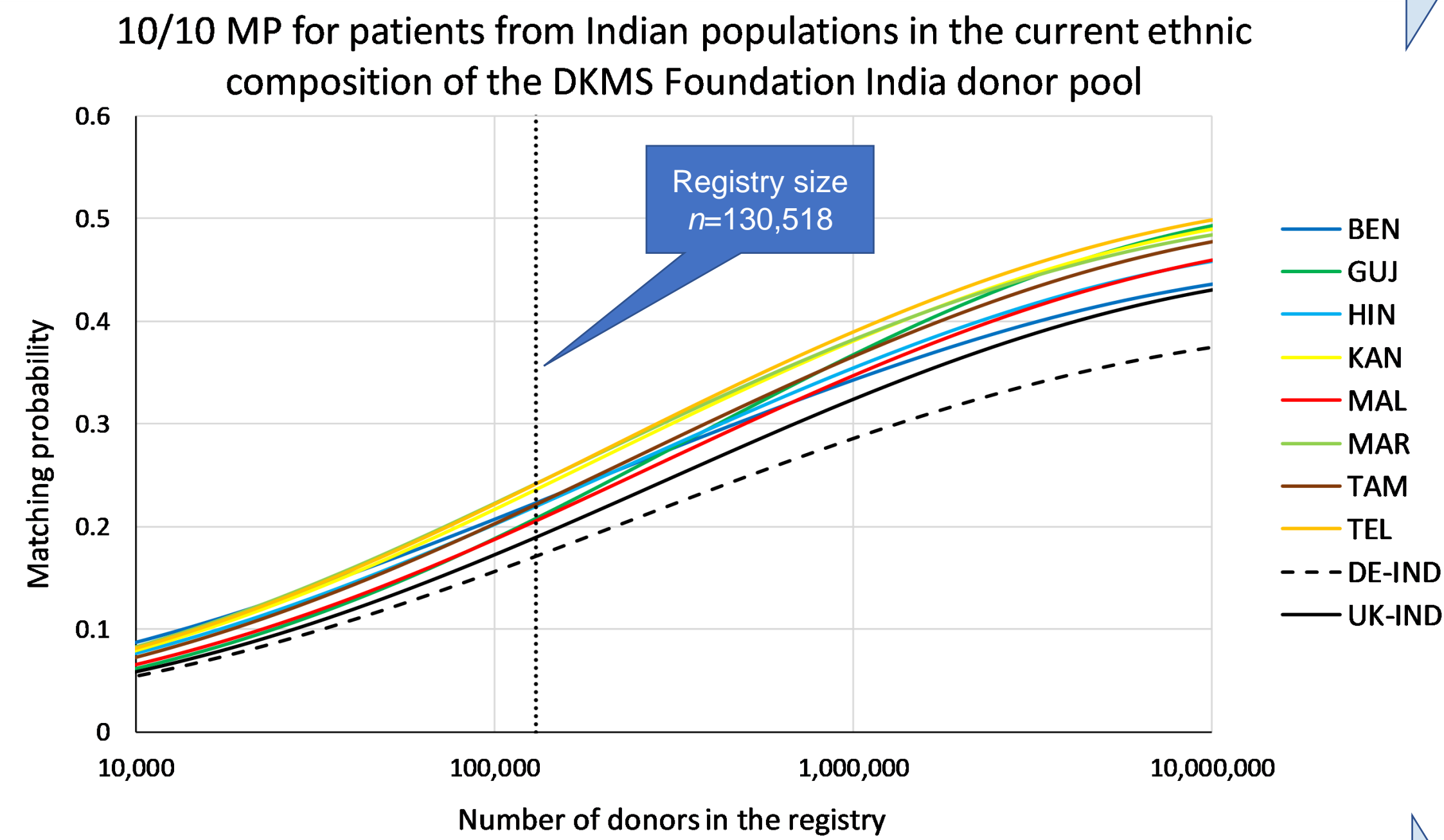Donors of Indian origin from DKMS UK (UK-IND; n=57,218) and Germany (DE-IND; n=4,703) served as reference populations.

Based on the population-specific 5-locus (HLA-A, -B, -C, -DRB1 and -DQB1) haplotype frequencies[2,3], we estimated the probabilities for patients from the different Indian subpopulations to find a suitable donor in their own donor pool or in the donor pool of the growing DKMS Foundation India registry[1,4].

Results

The estimated matching probabilities (MP) reflect inter- and intra-population HLA haplotype diversity of the included Indian populations.
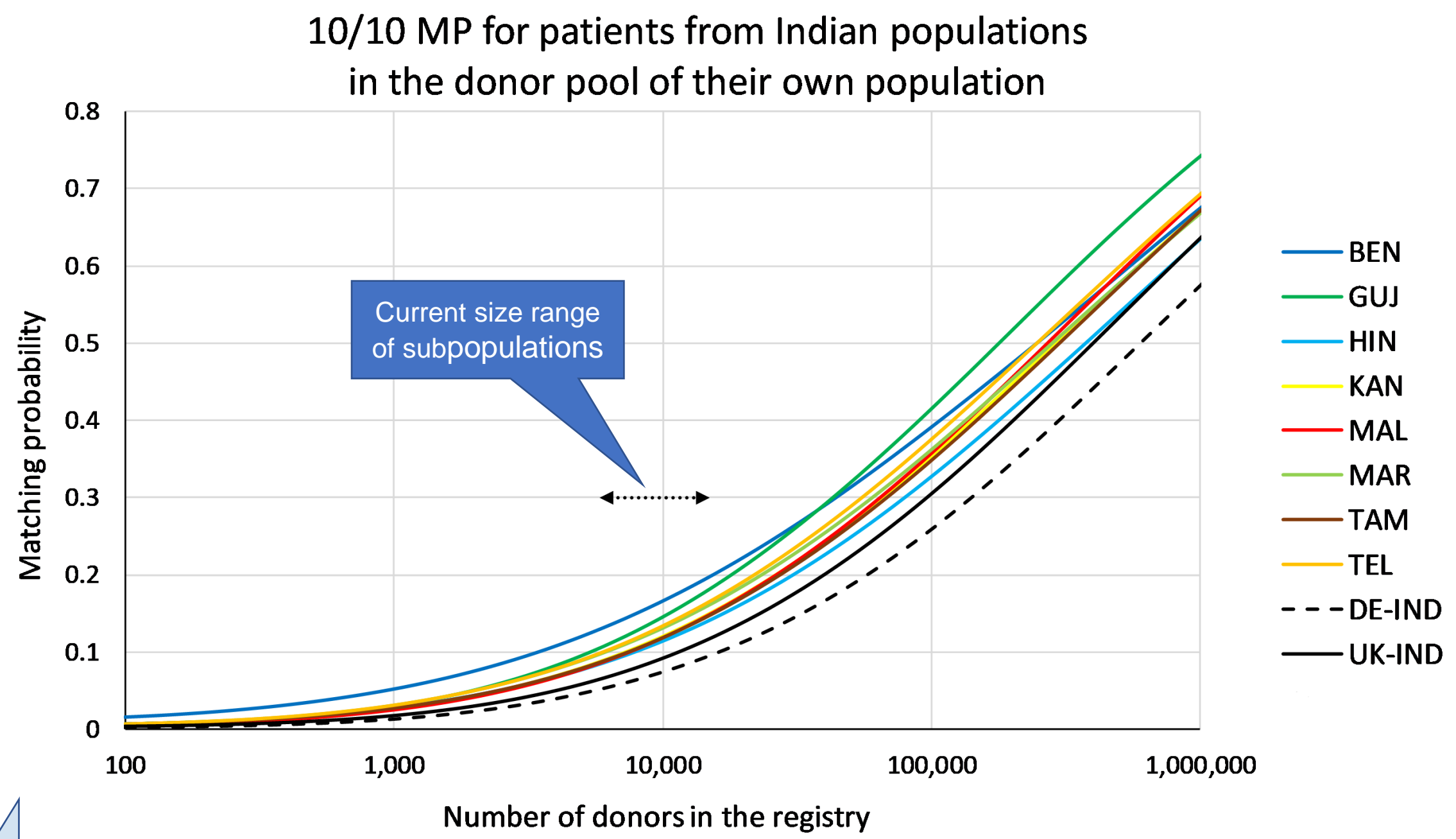
In the following, MP values are compared using the exemplarily assumed register size n=100,000.

Haplotype Frequencies of the Top5 Haplotypes in the DMKS Foundation India Donor Pool

	BEN	GUJ	HIN	KAN	MAL	MAR	TAM	TEL	Total
A*33:03g~B*44:03g~C*07:01g~DRB1*07:01g~DQB1*02:01g	7.1%	2.1%	4.2%	3.1%	3.1%	3.3%	2.0%	2.3%	3.2%
A*01:01g~B*57:01g~C*06:02g~DRB1*07:01g~DQB1*03:03g	2.2%	2.3%	1.9%	1.9%	1.9%	1.5%	4.0%	4.1%	2.2%
A*01:01g~B*37:01g~C*06:02g~DRB1*10:01g~DQB1*05:01g	0.9%	1.1%	1.0%	1.5%	0.8%	1.1%	2.3%	1.7%	1.2%
A*33:03g~B*58:01g~C*03:02g~DRB1*03:01g~DQB1*02:01g	1.1%	0.7%	1.2%	1.7%	0.8%	1.1%	1.4%	1.1%	1.2%
A*02:11g~B*40:06g~C*15:02g~DRB1*15:01g~DQB1*06:01g	0.8%	0.6%	1.5%	1.3%	0.5%	2.0%	0.8%	1.4%	1.1%

The highest 10/10 matching probabilities (patient and donor match in 10 out of 10 HLA alleles) were achieved by searching the donor pool of the patient's own population. Assuming 100,000 donors of one population, the 10/10 MP were between 33% (HIN) and 42% (GUJ). At the sizes of the populations in DKMS Foundation India's current donor pool, 10/10 MP ranged between 10% (HIN, TEL) and 15% (MAL).

10/10 MP for patients from Indian populations in the donor pool of their own population

10/10 MP for patients from Indian populations in the current ethnic composition of the DKMS Foundation India donor pool

A search in a donor pool of the current ethnic composition of the DKMS Foundation India registry yielded 10/10 MP between 19% (MAL) and 23% (MAR, TEL) at a registry size of n=100,000 (20-24% at registry size n=130,518, indicated as vertical dotted line).
Patients from Southern Indian populations would be the main beneficiaries from further growth of the donor file in its current ethnic composition.
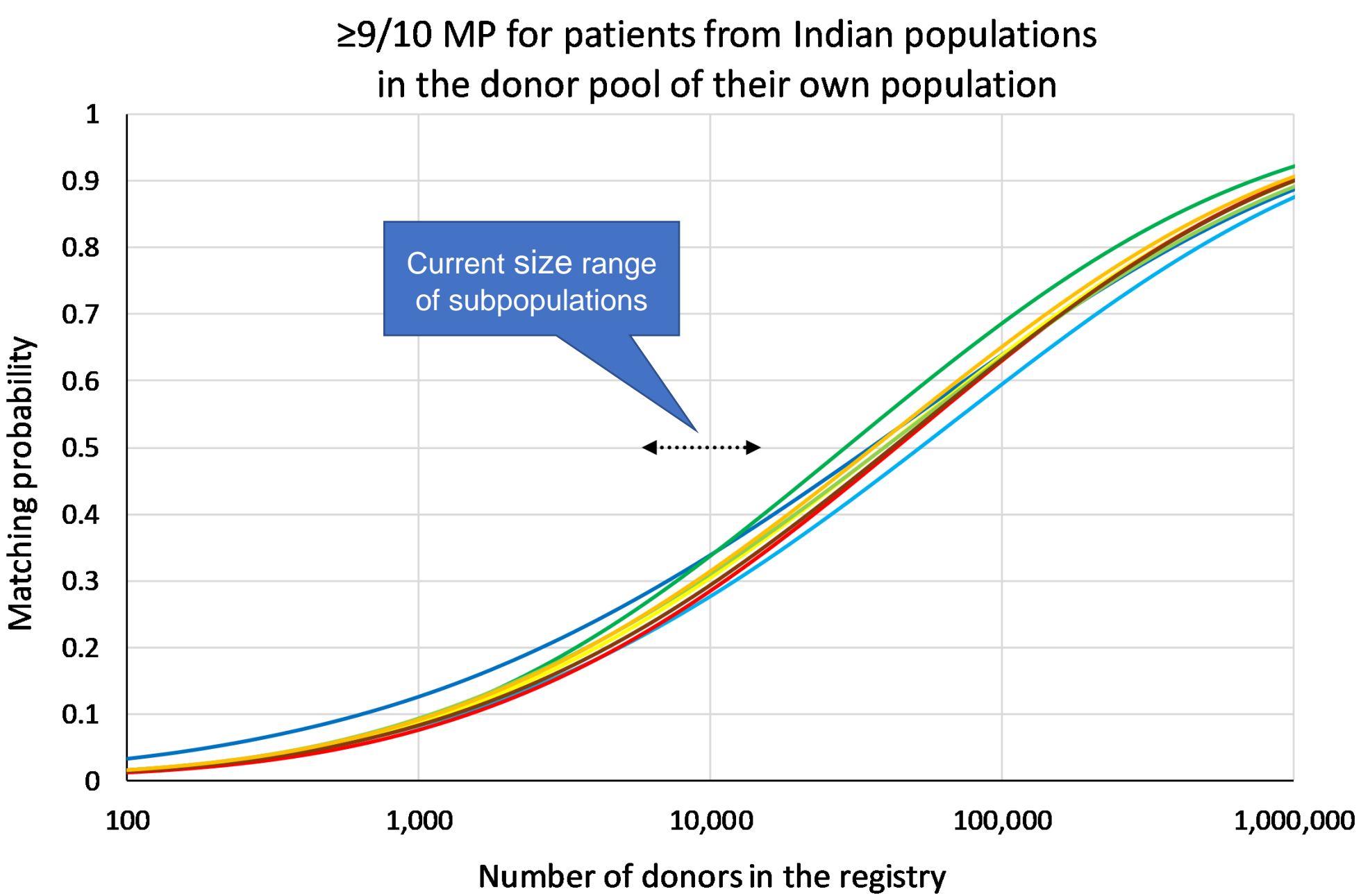
The permission of one single mismatch (9/10 or 10/10) between patient and donor in the scenario of a donor search in the pool of the patient's own population increased MP to considerably higher values.
Assuming a registry size of n=100,000 for each population, ≥9/10 MP ranged between 60% (HIN) and 69% (GUJ). At the sizes of the populations in the current donor pool, ≥9/10 MP ranged between 25% (HIN, TEL) and 34% (MAL).

≥9/10 MP for patients from Indian populations in the donor pool of their own population

Conclusion

Our findings support DKMS Foundation India's strategy to achieve nationwide coverage by opening local donor recruitment offices in different parts of India to address the needs of Indian patients.

Increased acceptance of mismatches in donor selection, fostered by the use of post-transplant cyclophosphamide (PTCy)-based prophylaxis for graft-versus-host disease (GVHD) in unrelated mismatched HSCT, may provide a chance for patients from populations with high genetic diversity and, more generally, populations that are underrepresented in global volunteer donor registries.

References

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(2) Schäfer C et al. Hapl-o-Mat: open-source software for HLA haplotype frequency estimation from ambiguous and heterogeneous data. BMC Bioinf. (2017) 18:284. doi: 10.1186/s12859-017-1692-y.

(3) https://github.com/DKMS/Hapl-o-Mat

(4) Schmidt AH et al. Toward an optimal global stem cell donor recruitment strategy. PloS One. (2014) 9:e86605. doi: 10.1371/journal.pone.0086605

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