Maximizing Effectiveness and Equity in Kidney Exchange Programs for Novel HLA Mismatch Paradigms

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INTRODUCTION

Living donor kidney transplant is the most (cost-)effective treatment for patients suffering from ESRD. However, patients may be ABO- or HLA-incompatible with their willing living donor. Kidney exchange programs (KEPs) improve access to transplantation by enrolling incompatible donor–recipient pairs and reallocating donors to form more compatible pairs (matching).

The degree of HLA compatibility between matched pairs critically determines transplant effectiveness, and KEP performance. Recent advances in immunological understanding and technology have advanced HLA compatibility paradigms from antigen to allele and eplet levels.

Caution to adopt these advancements has been called for as they may enlarge racial inequities in access to living donor transplant.

OBJECTIVE

To evaluate how antigen-, allele-, and eplet-based compatibility paradigms affect:

RQ1: Efectiveness of KEPs.
RQ2: Equity of transplant access and quality KEPs provide to ethnic subpopulations.

Moreover,

RQ3: Develop and test an equity weighted optimization model to remedy any inequities associated with the paradigms, in particular the adoption of more advanced paradigms.

METHODS

To provide evidence on effects of advancing HLA paradigms we constructed a first large scale Dynamic KEP instance of 990 ethnically diverse pairs. Data are from a set of recipients and donors for whom sufficient allele level data was available in the UNOS/OPTN registry. Allele level data where imputed using haplostats and eplet level data derived using HLA registry conversión tables. A largest possible set of pairs was formed using bipartite matching.

Subpopulation s based KEP Performance Metrics included:

F(s): Transplant Probability
L(s): Probability of leaving the KEP without transplant
W(s): Average waiting time until transplant
HLA(s): Compatibility score (match quality)

Each KEP run covered ten years with quarterly matching rounds solved via the cycle formulation for static KEPs maximizing a hierarchical objective function with F(s) and HLA(s) (in Python/Gurobi).

Three HLA(s) scenarios were analyzed (antigen, allele, eplet) to answer RQ1 and RQ2. An iterative method to minimize objective function differences among subpopulations was used to provide equitable solutions.

RESULTS

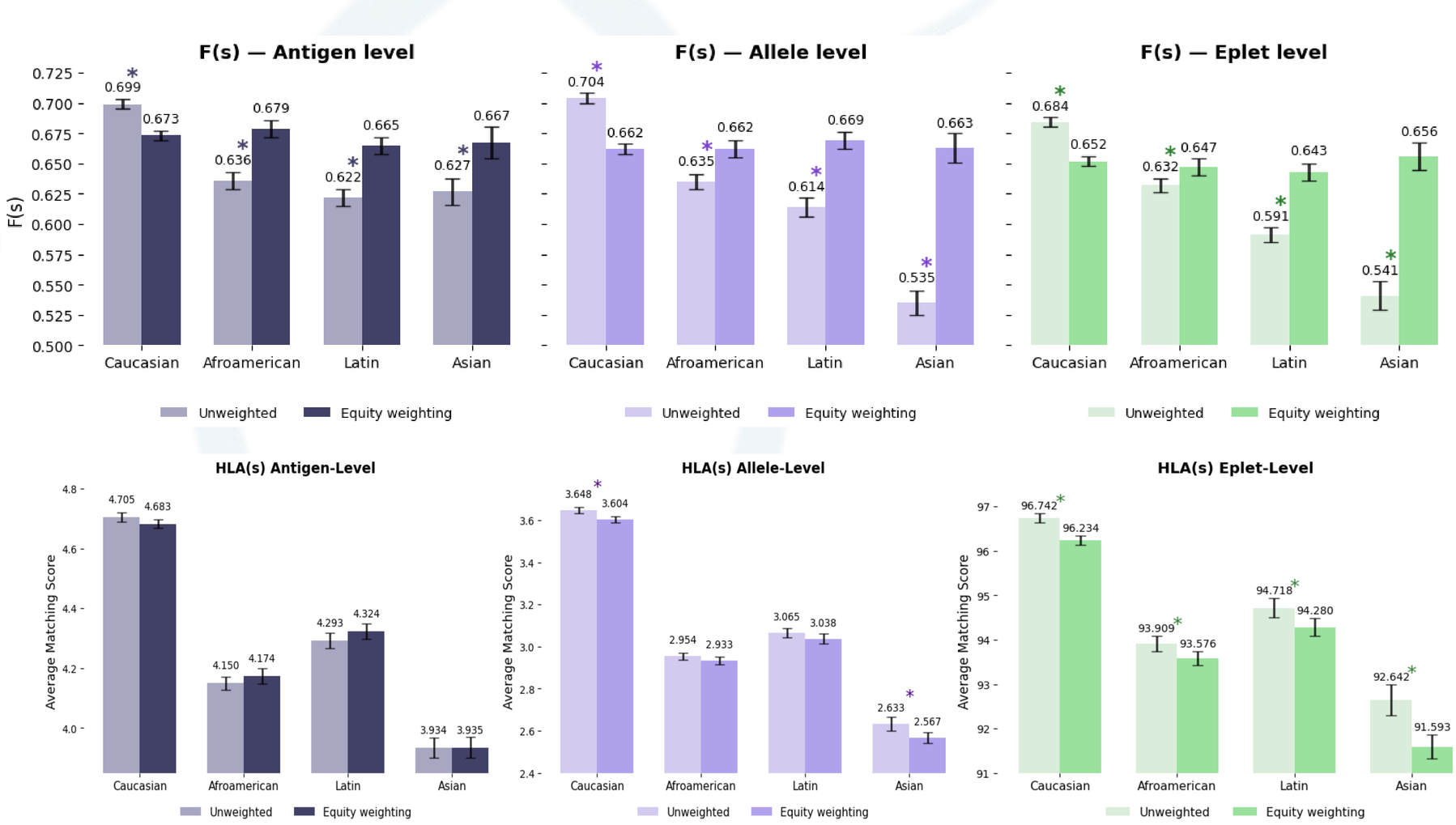
Effectiveness
F(s) ≈ 0.67 across paradigms.
HLA(s) score per paradigm improves significantly when considered explicitly in objective function (details in [1]).

Equity
Substantial and significant differences across subpopulations for antigen based HLA(s).

Differences increase when moving to allele and eplet level. Especially Asian recipients have lower access and longer waiting times when moving from antigen to allele level HLA matching.

Equity weighting
The equity-weighted model eliminated disparities in transplant probability while maintaining overall effectiveness (<0.5% loss).
The equity weighted model increase differences in HLA(s); in expected outcomes

Equity weights need to align with the HLA(s) weights in the hierarchical objective function.



Note: (*) indicate non-overlapping 95% confidence intervals.
*In the **upper panels**, they mark subpopulations whose F(s) confidence interval does not overlap with the overall mean F(s) interval.*
*In the **lower panels**, they indicate cases where the unweighted and equity-weighted confidence intervals for the same subpopulation do not overlap.*

CONCLUSIONS

Choice of antigen, allele, and eplet paradigm in HLA match score matters! Change of paradigm has significant effects on match probability and match quality.

Without counter measures, advancing from antigen to allele to eplet levels enlarged inequity in transplant access in the case study KEP.

Equity weighting resolved differences in transplant access for all three HLA paradigms, however at the cost of differences in HLA match quality.

Equity weights need to be finely tuned with HLA(s) weights in the objective function to balance equity of transplant access with match quality.

Future research can consider real-world KEPs as data become available and incorporate health outcomes (LYFT/QALYs) to assess KEP effectiveness and equity.

REFERENCES

Peralta Clarke, V., de Ferrante, H., Pérez Galarce, F., & van de Klundert, J. (2025). *Maximizing Effectiveness and Equity in Kidney Exchange Programs for Novel Compatibility Paradigms.* arXiv:2510.14013. https://doi.org/10.48550/arXiv.2510.14013

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