Transplant Immunology 81 (2023) 101917

Contents lists available at ScienceDirect

Transplant Immunology

journal homepage: www.elsevier.com/locate/trim

# Equity matrix for kidney transplant allocation

Bruno A. Lima [a,*], Filipe Reis [a], Helena Alves [a], Teresa S. Henriques [b,c]

[a] Oficina de Bioestatistica, Transplant Open Registry, Ermesinde, Portugal
[b] Department of Community Medicine, Information and Health Decision Sciences - MEDCIDS, Faculty of Medicine, University of Porto, Portugal
[c] Centre for Health Technology and Services Research (CINTESIS), Faculty of Medicine University of Porto, Portugal

ARTICLE INFO

*Keywords:*
Kidney allocation system
Renal transplantation
Equity and utility
Wait-list

ABSTRACT

There is a general agreement that the distribution of kidneys for transplantation should balance utility criteria with justice. Moreover, a kidney allocation system must be based on transparent policies and seen as an ongoing process.

This study aims to present an allocation system grounded on an equity matrix that balances the criteria of utility and justice.

Synthetic data for a waiting list with 2000 transplant candidates and a pool of 280 donors were generated. A color priority system, the Eurotransplant (ET) kidney allocation system, and the proposed Equity Matrix (EQM) allocation system were compared after 1000 iterations of kidney allocations. Distributions of variables like the age difference, Human Leukocyte Antigens (HLA) mismatches (mmHLA), recipients' time on dialysis, cPRA, and a transplant score obtained by different allocation models were compared graphically and with Cohen's d effect size.

For the analyzed variables, when we compare only the selected recipients from ET with the selected recipients from the EQM neutral model, we can conclude that the former model selects more hypersensitized recipients, a higher number of 65+ years' old recipients with 65+ years' old donors and higher number of recipients with 0 mmHLA. While recipients from EQM neutral are slightly older, have a lower age difference with their donors, have a lower number of mmHLA, are less likely to have 6 mmHLA with their donors, and have more time on dialysis.

The proposed EQM model attempts to provide a simple, transparent, and equitable response to a complex question with results that outperform established practices.

## 1. Introduction

Kidney transplantation is the preferred treatment for patients with renal insufficiency once it allows for a better quality of life and prolonged survival compared to patients on dialysis [1,2].

Transplantation is one of the most publicized fields of medicine and, as a result, is constantly exposed to public scrutiny [3]. Organs from deceased donors are the 'gift of life' for patients on the waiting list and can save many lives [4].

Due to demographic changes, the age of patients on dialysis has been constantly increasing, and with the lack of organs for transplant, the waiting time on dialysis has also increased dramatically, decreasing the relative number of patients who can be transplanted [5]. Furthermore, time on dialysis has a negative impact on both wait-list mortality and transplant survival [6].

Besides time on dialysis, age, heart failure, and diabetes are comorbidities of end-stage renal disease (ESRD) patients associated with poor post-transplant survival. Further, increased donor age is associated with reduced graft survival. Alloantigens expressed on the surface of peripheral blood leukocytes called Human Leukocyte Antigens (HLA) and

*Abbreviations:* AM, Acceptable mismatch; cPRA, Calculated Panel Reactive Antibodies; DSA, donor-specific antibodies; ECD, Extended criteria donors; EQM, Equity matrix; EPTS, Estimated Post Transplant Survival; ESRD, End-stage renal disease; ET, Eurotransplant; ETKAS, Eurotransplant Kidney Allocation system; HLA, Human Leucocyte Antigens; KARS, Kidney Allocation Rules Simulator; KAS, Kidney Allocation system; KDPI, Kidney Donor Profile Index; MMP, Mismatch Probability; mmHLA, HLA mismatches; Q2, Median; Q3, 3rd quartile; SCD, standard criteria donors; SP, Senior Program; TmDial, time on dialysis; TxOR, Transplant Open Registry; txScore, Transplant score; UNOS, United Network Organ Sharing.

* Corresponding author at: Rua Miguel Bombarda, 681, 1° Centro Frente, Ermesinde, Portugal.
*E-mail address:* balima78@gmail.com (B.A. Lima).

https://doi.org/10.1016/j.trim.2023.101917
Received 26 July 2023; Accepted 8 August 2023
Available online 9 August 2023

the number of HLA mismatches between donor and recipient are also a factor that influences graft survival and disease [5].

A kidney allocation system should be based on transparent policies and consider the relationship between supply and demand. Thereby, the search for the most suitable system should be seen as an ongoing process [7].

There is a consensus that the distribution of a rare and life-saving treatment, such as organ transplantation, should be fair (principle of justice) and provide value (principle of utility) [8]. Thus, the rules for allocating scarce resources should balance utility (better use of organs) with justice (providing equal access to transplantation) [6,9]. Under the principle of justice, patients on the waiting list should have an equal opportunity to access kidney transplantation. However, by the principle of utility, the distribution of available organs must maximize the benefit of the recipients and efficiently reduce waste [3,10].

In longevity matching, the kidneys of younger donors are prioritized for younger candidates, while the organs of older donors are restricted to the groups of older patients to pair the longevity of the organ with that of the recipient [11]. Kidneys with a more limited expected survival are not likely to work throughout the life of a younger, healthier recipient, so they will have to return to the transplant waiting list [12].

Matching HLA is another utilitarian criterion used in several allocation programs. Despite advances in current immunosuppression, each additional HLA-A, -B, -DR mismatch is associated with decreased graft survival [13].

HLA sensitization can occur due to pregnancy, blood transfusion, or a previous transplant [14]. Although the percent panel reactive antibody (PRA) obtained by Complement-Dependent Cytotoxicity is not a precise way to define the degree of sensitization, a cut-off of 85% is generally used to classify highly sensitized patients [15]. On the other hand, the calculated PRA (cPRA) value [16] reflects the probability of a patient having HLA antibodies reactive to a donor from the donor's population. So, those patients with higher values of cPRA are less likely to find a suitable donor for transplantation.

Waiting time in dialysis can be seen as a utilitarian criterion, and it is also the most globally accepted justice factor in kidney allocation. The time of pre-transplant dialysis is a strong predictor of mortality both in the post-transplant period and in patients on the waiting list. Therefore, a fair allocation system will prioritize candidates with higher dialysis time to prevent further development of complications [13].

## 2. Objective

This study aims to present an allocation system based on an equity matrix that balances the criteria of utility and justice.

## 3. Materials and methods

### 3.1. Data

A simulated waiting list comprising 2000 kidney transplant candidates was generated. The age of these candidates has an $N(45, 15^2)$ distribution trimmed between 18 and 75 years old. Their ABO blood groups were randomly attributed with probabilities 0.44, 0.022, 0.042, and 0.496 for A, AB, B, and O groups, respectively. Sensitization to HLA was randomly assigned with 70% of the candidates having a cPRA of 0%, 10% with cPRA between 1% and 50% (with a distribution $P(\lambda = 30)$), other 10% with cPRA between 51% and 85% (with a distribution $P(\lambda = 70)$), and the last 10% having a cPRA between 86% and 100% (with a distribution $P(\lambda = 90)$). Candidates' HLA antibodies were randomly given according to their respective cPRA values and HLA genotyping. Also, we assume no candidate is clinically urgent. The number of months on dialysis was generated according to candidates' HLA sensitization and blood group O status, i.e., hypersensitized (cPRA >85%) candidates and blood group O have time on dialysis with an $N(75, 20^2)$ distribution, those that have just one of these characteristics (hypersensitized or being group O) have time on dialysis with an $N(60, 20^2)$ distribution, all the remaining transplant candidates have the number of months from a $N(25, 20^2)$ distribution. Those distributions for clinical and demographic variables (Table 1) were described elsewhere by others [17].

For the simulated 280 deceased donors pool, their age was calculated from a $N(60, 20^2)$ distribution trimmed between 18 and 75 years old. Donors' ABO blood groups were randomly attributed with probabilities 0.4658, 0.0343, 0.077, and 0.4229 for A, AB, B, and O groups, respectively, as described by others [18] (Table 1).

Both for candidates and donors, HLA genotyping, was generated according to HLA allelic and haplotypic frequencies from Portuguese bone marrow voluntary donors [19].

All synthetic data on donors and transplant candidates were generated with {simK} [20], an R package developed to generate synthetic data on kidney transplant simulations.

### 3.2. Models

As a benchmark, we simulate deceased donors' kidney allocation with a system previously suggested by **Lima** et al. [22]. With this model, the patients are prioritized for each available organ according to their clinical urgency (red color) and regarding their time on dialysis and cPRA value. Those patients with a cPRA >85% or with a time on dialysis higher than the 3rd quartile (Q3) of all wait-listed candidates' time on dialysis are classified as orange. Yellow is attributed to patients with a cPRA >50% or with a time on dialysis higher than the median time on dialysis (Q2). Green is the color for all the rest. Also, patients are allocated to donors within the same age group (old to old program), mimicking the EuroTransplant senior program [23]. Within the same color groups, candidates are ordered by the number of HLA mismatches (increasing) and time on dialysis (decreasing).

A simplified version of EuroTransplant (**ET**) Kidney Allocation System (ETKAS) [23] was also simulated. This version only applies to adults who were getting their first kidney, did not have an urgent medical condition, and had not previously donated one of their kidneys. In this simulation for each donor, transplant candidates are ordered as follows:

1. Senior Program (65+ years of old candidates when donor has 65+ years old);
2. Acceptable Mismatch Program (candidates with a cPRA >85% without HLA antibodies against donor's HLA);
3. 000 HLA mismatches (no donor-recipient HLA mismatches);
4. ETKAS points.

The Senior Program prioritizes candidates solely based on their time on dialysis. At the same time, the Acceptable Mismatch (AM) Program allows candidates with compatible blood groups (not only ABO identical) to receive a kidney offer, and then they are ordered according to ETKAS points. All candidates have their Mismatch Probability (MMP) calculated at registration, reflecting their chance of getting a kidney with low HLA mismatch (0 or 1 HLA-A, -B, -DR mismatch based on 1000 kidneys offered). The final points for each eligible candidate are the sum of HLA, dialysis, and MMP points. [24]

Here we present the Equity Matrix (**EQM**) model, applicable to kidney allocation for transplantation. As utility criteria, we consider longevity match and the number of their HLA mismatches (mmHLA), where longevity match is the absolute value between the donor's and recipient's age differences (ageDiff). Then, we built 6 levels of utility for donor-recipient pairs, ordered as ageDiff <9 and mmHLA between 0 and 2; ageDiff <9 and mmHLA 3 or 4; ageDiff ≥9 and mmHLA between 0 and 2; ageDiff <9 and mmHLA 5 or 6; ageDiff ≥9 and mmHLA between 3 or 4; ageDiff ≥9 and mmHLA between 5 or 6.

As criteria of justice, we consider candidates' time on dialysis

**Table 1**
Variables' distributions for the generation of candidates and donors' synthetic data.

| Variable | Distribution | Reference |
|---|---|---|
| Recipients' age (years) | $\sim N(45, 15^2)$ | Tafulo et al, 2016 [17] |
| Recipients' ABO blood group | $\begin{cases} Pr(A) = 0.44 \\ Pr(AB) = 0.022 \\ Pr(B) = 0.042 \\ Pr(O) = 0.496 \end{cases}$ | Tafulo et al, 2016 [17] |
| cPRA values (%) | $\begin{cases} Pr(cPRA = 0\%) = 0.7 \\ Pr(1\% < cPRA \leq 50\%) = 0.1 \\ Pr(51\% < cPRA \leq 85) = 0.1 \\ Pr(cPRA > 85\%) = 0.1 \end{cases}$ | Tafulo et al, 2016 [17] |
| Recipients' time on dialysis in months (according to blood group and cPRA value) | $\begin{cases} O \quad and\ cPRA > 85\% \sim N(75, 20^2) \\ O \quad or\ cPRA > 85\% \sim N(60, 20^2) \\ all\ the\ rest \sim N(25, 20^2) \end{cases}$ | Tafulo et al, 2016 [17] |
| Donors' age (years) | $\sim N(60, 20^2)$ | IPST, 2022 [21] |
| Donors' ABO blood group | $\begin{cases} Pr(A) = 0.4658 \\ Pr(AB) = 0.0343 \\ Pr(B) = 0.077 \\ Pr(O) = 0.4229 \end{cases}$ | Duran et al., 2007 [18] |

cPRA calculated the Panel Reactive Antibody percentage.

(TmDial) and their cPRA values. Likewise, for each candidate, we define 6 levels of justice, ordered as TmDial > Q3 and cPRA >50%; TmDial > Q3 and cPRA ≤50%; TmDial between Q2 - Q3 and cPRA >50%; TmDial between Q2 - Q3 cPRA ≤50%; TmDial ≤ Q2 and cPRA >50%; TmDial ≤ Q2 cPRA ≤50% (where Q2 and Q3 are proxies for the second and third quartile of wait-listed candidates' time on dialysis, respectively).

With those levels, we make a utility/justice matrix with 36 cells ($a_{i,j}$).

Given $a_{1,1} = maximum\ value$:

$$\begin{cases} a_{i,1} = a_{i-1,1} - a_{1,1} \times ratio.just, & i > 1 \\ a_{i,j} = a_{i,j-1} - a_{1,1} \times ratio.util, & i,j > 1 \end{cases}$$

Where

- *ratio.util* – is a value between 0.1 and 0.5 corresponding to the relative weight given to utility criteria.
- *ratio.just* – is a value between 0.1 and 0.5 corresponding to the relative weight given to justice criteria;

For instance, when we assign more weight to the utility ratio (a utility ratio of 0.5 and a justice ratio of 0.1, for example), candidates that fall in the first two columns of the matrix are more likely to be selected for transplantation (Fig. 1 A). On the other hand, when we give more weight to the justice ratio (a utility ratio of 0.1 and a justice ratio of 0.5), those candidates within the first two rows will be more likely the chosen ones (Fig. 1 B).

Within each matrix cell, candidates are ordered by the number of

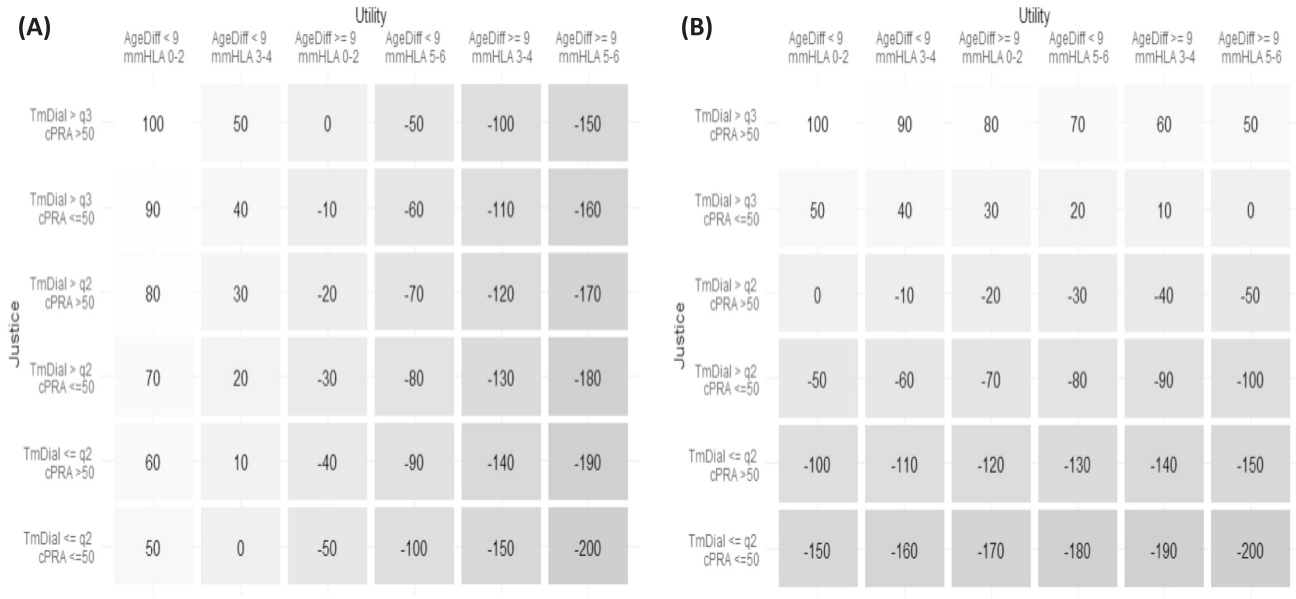


**Fig. 1.** Examples of Utility / Justice matrixes.
(A) maximum value = 100; *ratio.util* = 0.5; *ratio.just* = 0.1.
(B) maximum value = 100; *ratio.util* = 0.1; *ratio.just* = 0.5.

HLA mismatches (increasing) and time on dialysis (decreasing).

For this study, we built multiple matrices for different combinations of utility and justice ratios, and with it, we tested different EQM models for kidney allocation. We defined the neutral EQM model (EQM_0.1–0.1), where both ratios have the same value (0.1). In addition, we built some imbalance models where we give more weight to utility than justice (EQM_0.2–0.1, EQM_0.3–0.1, EQM_0.4–0.1, EQM_0.5–0.1) or more weight to justice than utility (EQM_0.1–0.2, EQM_0.1–0.5, EQM_0.1–0.4, EQM_0.1–0.5).

Besides, we also tested EQM models combined with rules similar to the priorities applied to the ET system (EQM_ET), i.e., SP, AM program, and 000 HLA mismatches having priority before applying the utility/justice matrix.

Both for Lima's and EQM's models, we assumed Q2 = 50 months and Q3 = 70 months on dialysis.

For each tested model (Lima, ETKAS, and models derived from EQM), the allocation of the 280 donors selects the two best candidates for the donor without candidate repetition. That is, in each iteration, the two best candidates (according to each allocation model) are assigned to the first donor, to the second donor are assigned the 2 best renaming candidates (i.e., without candidates assigned to previous donors), and so on until a maximum of 560 (2 × 280) candidates are assigned for a poll of donors.

In all the models, eligible candidates for each donor must have a negative virtual crossmatch and must be ABO identical to the donor to be considered for transplantation.

### 3.3. Analysis

To ensure that the ordering of donors does not influence the results of the models, up to 1000 iterations per model have been performed. Further, the order of the donors to which candidates were assigned was randomly defined at each iteration.

Consequently, for each iteration of each model, it was possible to compute summary statistics of the selected recipients' variables (age, age difference for donor-recipients pairs, number of HLA mismatches, time on dialyses, cPRA value and TxScore a predictive score for transplant outcome [25]). The distributions of this summary statistics were plotted and analyzed. We compared mean values between models with Cohen's d-effect size statistic.

Allocation models analyzed here can be simulated using the application KARS [24] from Transplant Open Registry (TxOR) initiative [26]. The KARS user manual [27] contains a more detailed overview of the applicability of each model.

All analysis and simulations were done in R with {histoc} [28], a package for histocompatibility on kidney transplant allocation systems. A GitHub repository with all the data and R code used in this analysis [29] is also available.

## 4. Results

The EQM neutral model (EQM_0.1–0.1) selects slightly older recipients than ET and EQM_ET_0.1–0.1 (EQM_0.1–0.1 applied after SP, AM, and 000 mmHLA) models (Table 2). As the pool of donors has an age distribution with a higher mean than the wait list candidates and the age differences between donors and recipients are one of the criteria used by EQM models, these models chose donor recipients pairs with lower age differences (Fig. 2).

By the same token, TxScores are to some extent higher for EQM models than ET alone (Fig. 3). The Txscore measures transplant outcome efficacy and computes a 5-year probability of death or graft failure [25]. Here, and due to the limitations of our synthetic data, for each recipient, TxScore was calculated taking into account the donor's age, recipient's age, time on dialysis, and mmHLA, for all other variables used to calculate the TxScore constant values were assumed. So, this probability is influenced by the recipients' age. Then, being the recipients selected by ET younger than those selected by EQM models and with more recipients with 0 mmHLA, we observe that the former have slightly lower TxScore values than the latter (Fig. 3).

From the comparison between ET and EQM_ET_0.1–0.1, the higher size effect (with Cohen's d = −17.04) is for the mean age difference between donors and recipients (Table 3). As for the ET model also for EQM_ET_0.1–0.1 allocation is done after the application of SP and AM program. Consequently, we found smaller differences for cPRA and Hypersensitized recipients (with Cohen's d of 0.18 and − 2.26, respectively) as for the comparison of ET vs. Lima (with Cohen's d of −18.9 and − 34.3, respectively) and ET vs EQM_0.1–0.1 (with Cohen's d of −26.5 and − 39.3, respectively).

Regarding the number of HLA mismatches (mmHLA) for selected donor-recipients pairs and comparing to the other models (Fig. 4), EQM_0.1–0.1 presents a lower mean for the total number of mmHLA (EQM_0.1–0.1 = 2.87; ET = 3.34; Lima = 3.04), a lower number of pairs with 6 mmHLA (EQM_0.1–0.1 = 4.98; ET = 43.4; Lima = 17.36) and a higher number of pairs with until 2 mmHLA(EQM = 229.78; ET = 178.44; Lima = 192.73) as reported in Table 2. Both ET and EQM_ET_ models select a higher number of donor-recipient pairs with 0 mmHLA (14.49 and 13.21, respectively) once these models prioritize 0 mmHLA on candidates' selection.

**Table 2**
Descriptive statistics for each allocation model and effect size between models after 1000 iterations.

| | EQM_0.1–0.1 | EQM_ET_0.1–0.1 | ET | Lima | Cohen's d | | |
|---|---|---|---|---|---|---|---|
| Variable | | | | | Lima vs. ET | EQM_0.1–0.1 vs. ET | EQM_ET_0.1–0.1 vs. ET |
| recipients' age | 49.48 (± 0.21) | 50.72 (± 0.21) | 49.21 (± 0.18) | 48.58 (± 0.14) | −1.895 | 2.653 | 7.618 |
| age differences | 6.49 (± 0.22) | 7.69 (± 0.23) | 11.96 (± 0.26) | 11.84 (± 0.24) | −0.841 | −23.744 | −17.044 |
| number of HLA mm | 2.87 (± 0.03) | 3.35 (± 0.03) | 3.34 (± 0.03) | 3.04 (± 0.02) | −9.967 | −14.771 | 1.842 |
| pairs' with 0 HLA mm | 3.30 (± 0.88) | 14.49 (± 2.63) | 13.21 (± 2.69) | 9.27 (± 1.54) | −3.750 | −7.012 | −0.219 |
| pairs with 0 to 2 HLA mm | 229.78 (± 7.38) | 152.06 (± 6.70) | 178.44 (± 6.28) | 192.73 (± 6.72) | 2.468 | 5.986 | −5.873 |
| pairs' with 6 HLA mm | 4.98 (± 1.93) | 31.31 (± 4.01) | 43.40 (± 5.26) | 17.36 (± 3.39) | −5.488 | −8.678 | −2.599 |
| time on dialysis | 59.65 (± 0.28) | 57.80 (± 0.27) | 58.11 (± 0.36) | 59.98 (± 0.21) | 5.523 | 6.018 | −1.122 |
| cPRA | 23.09 (± 0.64) | 38.27 (± 0.53) | 37.35 (± 0.46) | 29.21 (± 0.37) | −18.887 | −26.529 | 0.177 |
| Hypersensitized recipients | 75.52 (± 3.25) | 184.08 (± 2.24) | 189.16 (± 2.12) | 100.53 (± 2.26) | −34.317 | −39.310 | −2.259 |
| transplants with Senior Program | 54.70 (± 3.10) | 108.96 (± 0.20) | 108.38 (± 0.67) | 108.70 (± 0.49) | 1.148 | −20.845 | 1.886 |
| TxScore (%) | 60.17 (± 0.09) | 59.96 (± 0.09) | 59.56 (± 0.09) | 60.32 (± 0.06) | 12.855 | 8.261 | 8.010 |

Summary statistics: mean (± sd).
cPRA calculated the Panel Reactive Antibody percentage.
TxScore predictive score for transplant outcome.
HLA mm mismatches HLA.
age differences given by |donor's age – recipient'sage|.
ET EuroTransplant.
EQM Equity Matrix.

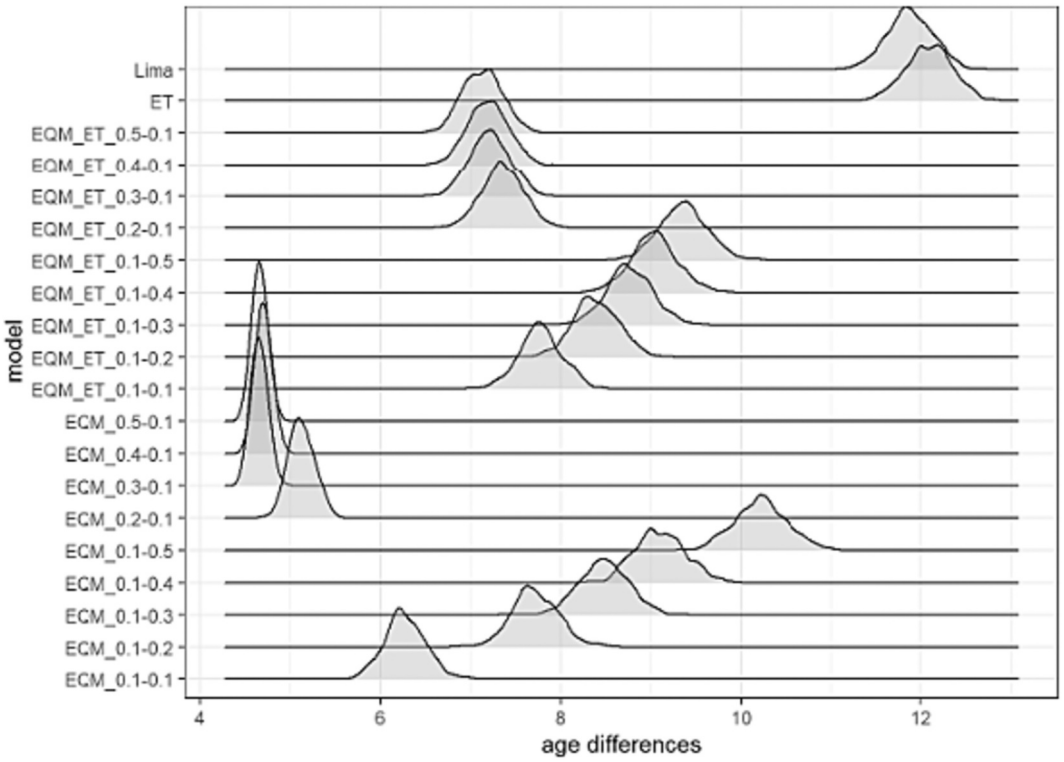


**Fig. 2.** Age differences distribution from donor-recipient pairs obtained from 1000 iterations.

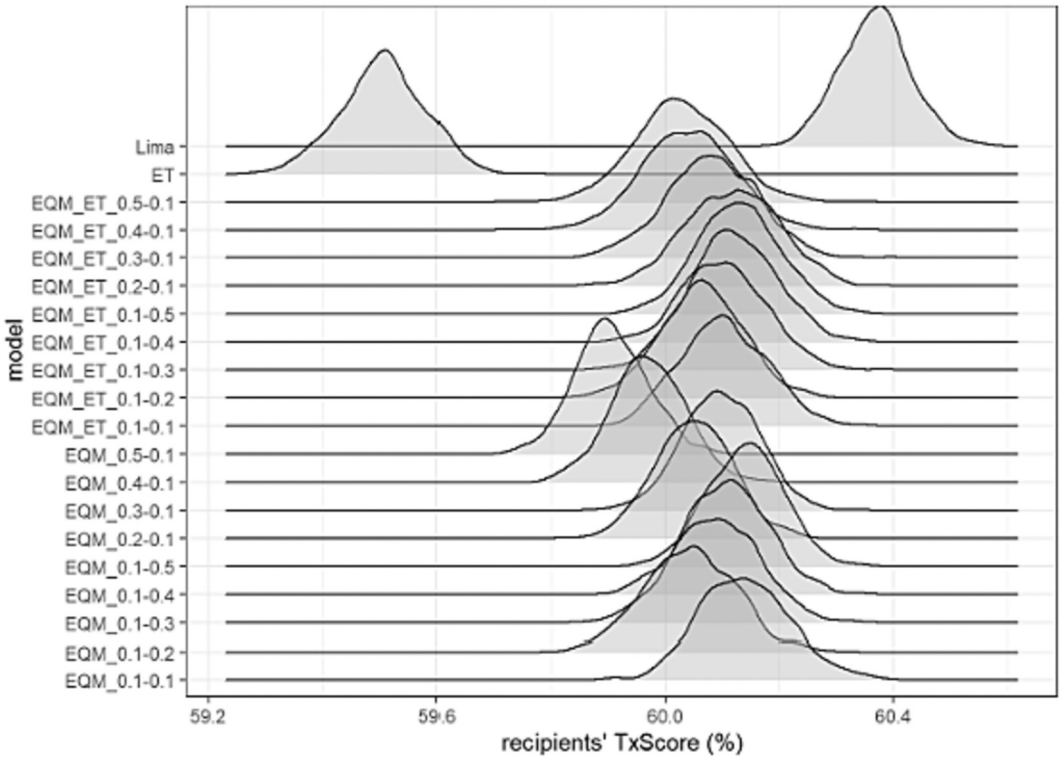


**Fig. 3.** TxScore % (predictive score for transplant outcome) distribution obtained from 1000 iterations.

**Table 3**
Ranked models for best performance by variable.

| Variable | Lima | ET | EQM_0.1–0.1 | EQM_ET_0.1–0.1 | Best model |
|---|---|---|---|---|---|
| age differences | 3rd | 4th | 1st | 2nd | EQM_0.5–0.1 |
| number of HLA mm | 2nd | 3rd | 1st | 3rd | EQM_0.5–0.1 |
| pairs' with 0 HLA mm | 3rd | 1st | 4th | 1st | EQM_ET_ |
| pairs with 0 to 2 HLA mm | 2nd | 4th | 1st | 3rd | EQM_0.5–0.1 |
| pairs' with 6 HLA mm | 2nd | 4th | 1st | 3rd | EQM_0.5–0.1 |
| time on dialysis | 2nd | 3rd | 1st | 4th | EQM_0.1–0.5 |
| cPRA | 4th | 1st | 3rd | 1st | EQM_ET_0.1–0.5 |
| Hypersensitized recipients | 3rd | 1st | 4th | 2nd | ET |
| transplants with Senior Program | 1st | 1st | 4th | 1st | ET |
| TxScore (%) | 4th | 1st | 2nd | 2nd | ET |

cPRA calculated the Panel Reactive Antibody percentage.
TxScore predictive score for transplant outcome.
HLA mm mismatches HLA.
age differences given by |donor's age – recipient'sage|.
ET EuroTransplant.
EQM Equity Matrix.

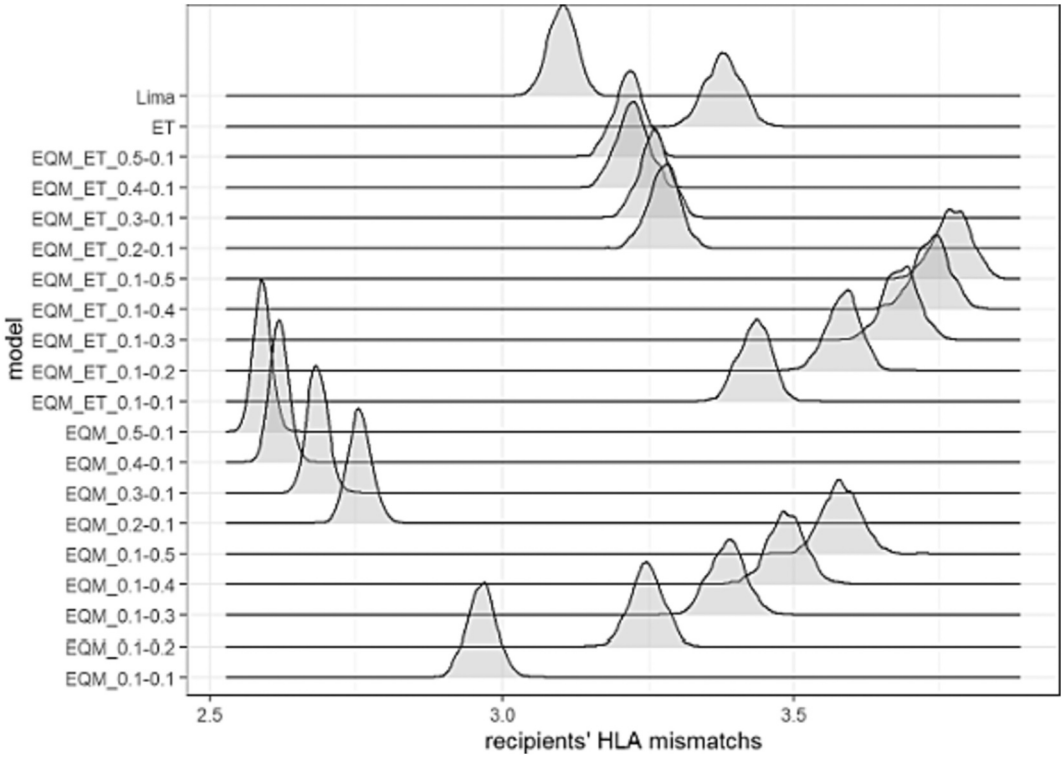


**Fig. 4.** Number of HLA mismatches for donor-recipient pair; distribution obtained from 1000 iterations.

The EQM models that give a higher weight to justice (EQM_0.1–0.2 to EQM_0.1–0.5) are those that select recipients with higher time on dialysis (Fig. 5). Recipients' time on dialysis from the ET model and from the EQM model, even with higher weight for justice but with ET prioritization (EQM_ET_0.1–0.2 to EQM_ET_0.1–0.5) are lower than those of selected recipients both by the neutral EQM model and Lima's model.

Models that apply the AM program (ET and EQM_ET_) (Table 3) select a higher number of hyperimmunized recipients (ET = 189.16; EQM_ET_0.1–0.1 = 184.08; EQM_0.1–0.1 = 75.52; Lima = 100.53) and have higher means of cPRA values than Lima and the neutral EQM (ET = 37.35; EQM_ET_0.1–0.1 = 38.27; EQM_0.1–0.1 = 23.09; Lima = 29.21). Only the EQM with the higher weight to justice (EQM_0.1–0.5) has a higher mean cPRA value than ET but fewer hyperimmunized recipients (Fig. 6A).

Similarly, for the models that apply the Senior Program (Lima, ET, and EQM_ET), the number of 65+ recipients transplanted with 65+ years old donors is way higher than for the remaining models.

Suppose we apply the Senior program, the AM program, and the priority of 0 mmHLA to a neutral EQM (results given by EQM_ET_0.1–0.1 model). In that case, we obtain similar results to the ET allocation regarding the number of hypersensitized recipients (Fig. 6A), the number of 65 + recipients with a 65+ donor (Fig. 6B), the number of pairs with 0 mmHLA (Cohen's d = −0.22), the number of total mmHLA (Fig. 4) and mean time on dialysis (Fig. 5). In contrast, recipients selected from the EQM_ET_0.1–0.1 model have a lower age difference with their donor (Fig. 2), lower mean for the total number of HLA mismatches (Fig. 4), and are less likely to have 6 mmHLA than the recipients selected from the ET model (31.31 and 43.4, respectively) (Table 3).

When we compare the performance of the models Lima, ET, EQM_0.1–0.1, and EQM_ET_0.1–0.1 and rank them for the obtained results by each of the analyzed variables (table 4), both ET and

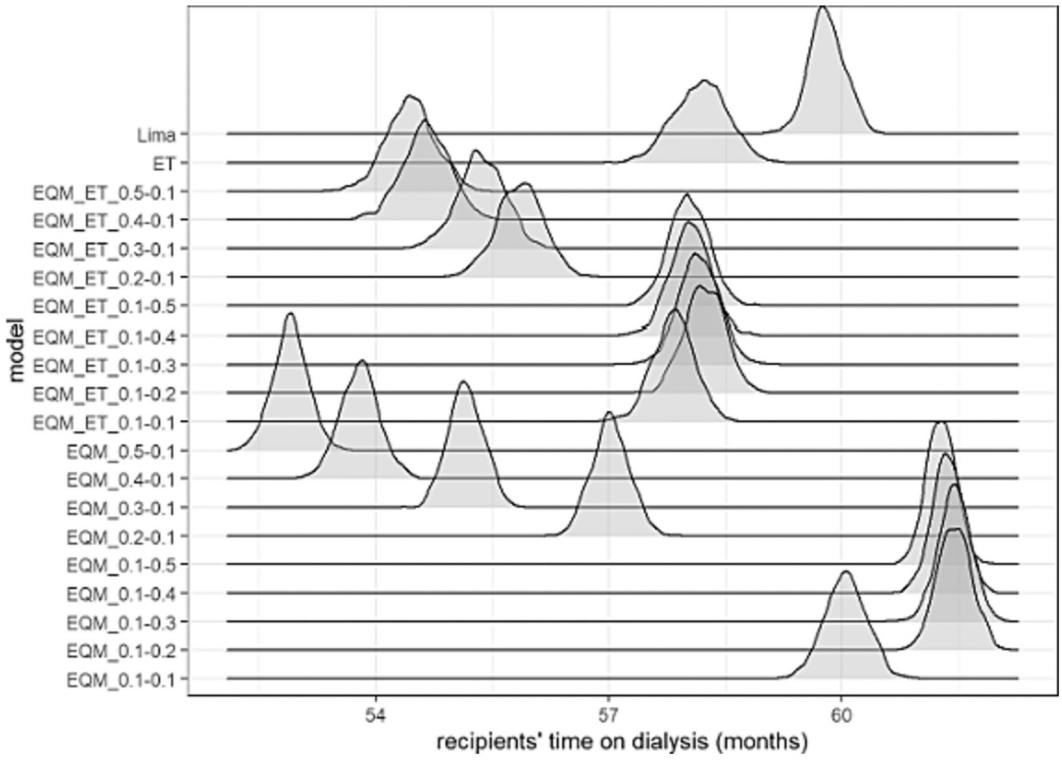


**Fig. 5.** Mean recipients' time on dialysis distribution from 1000 iterations.

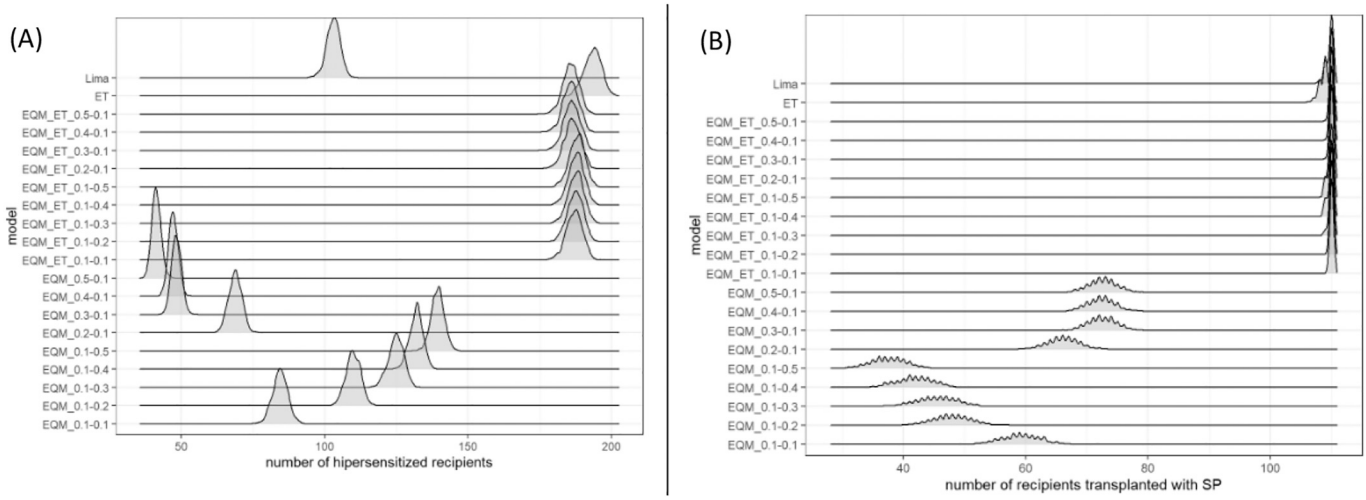


**Fig. 6.** Results from Senior Program and acceptable Mismatch program (distributions from 1000 iterations).
(A) number of hypersensitized recipients.
(B) number of recipients transplanted according to the Senior Program.

EQM_0.1–0.1 ranked 1st for 5 different variables. The models' ET and EQM_ET_0.1–0.1 ranked 1st on variables that measure the number of recipients with 0 mmHLA, mean cPRA, number of hypersensitive recipients, and recipients transplanted with SP. Obviously, this is a clear result of the priorities inherent to the ET allocation program.

So, for the analyzed variables, when we compare only the selected recipients from ET with the selected recipients from the EQM neutral model (EQM_0.1–0.1), we can conclude that the former model selects more hypersensitized recipients, a higher number of 65+ recipients with a 65+ donor and higher number of recipients with 0 mmHLA. While recipients from EQM neutral are slightly older, have a lower age difference with their donors, have a lower number of mmHLA, are less likely to have 6 mmHLA with their donor, and have more time on dialysis.

## 5. Discussion

The presented Equity Matrix neutral model (EQM_0.1–0.1) can outperform not only the Lima model (used as a benchmark) but also the EuroTransplant kidney allocation algorithm in some of the measured variables. The EQM model not only selects recipients with more time on dialysis but also donor-recipient pairs with a lower number of HLA mismatches and lower age differences.

There is a significant longevity mismatch with consequent loss of

graft years when kidneys from young donors are transplanted into older recipients who die with functioning kidneys and when younger candidates receive older kidneys and consequently need a re-transplant [6]. The EQM model prioritized transplants that minimize age differences between donors and their recipients as a proxy for a longevity match.

If it has proven challenging to increase the number of available donors for transplantation, then the few available organs should be optimized to ensure their best utilization. In other words, efforts should be made to allocate the right kidney to the right patient. Nevertheless, there is evidence that virtually all renal transplant recipients live longer than similar patients on dialysis; there are also clear differences in survival rates among groups of transplanted patients based on their underlying disease, comorbidities, race, gender, and age. So, to ensure that the maximum amount of renal function is recovered from a deceased donor kidney, this should be allocated to the recipient who would benefit the most from it [3].

The shortage of organs for transplantation is increasing with the growing number of ESRD patients in aging societies, resulting in longer waiting times for transplantation. Theoretically, a more efficient program for kidney allocation would avoid assigning kidneys with a high expected survival rate to patients with a low post-transplant life expectancy. Similarly, kidneys with limited expected survival should not be allocated to younger patients or those with a longer life expectancy who would require a re-transplant [12].

In EuroTransplant, most kidneys are allocated according to the ETKAS score based on HLA mismatches, the probability of matching, the waiting time, the distance between recipient and donor, and the trade-off between the participating countries [12]. Whereas the EuroTransplant Senior Program (ESP) is applied to candidates and donors over 65 years of age to use the organs of older donors [5]. With ESP, organ allocation is done locally based on ABO compatibility and waiting time without necessarily considering the donor's HLA. The rejection rates of the ESP program are higher than those of transplants from elderly patients with young donors. However, it should be noted that despite the risk factors for this increased mortality after transplantation, ESP transplantation results in increased life expectancy and better quality of life compared to 65+ patients who remain on dialysis [5]. While by ESP, a 64 years old candidate will not be an option for a 65+ donor, by the EQM model, this transplant candidate will have more points for all donors aged between 56 and 72 (age difference $< 9$).

In contrast to standard criteria donors (SCD), extended criteria donors (ECD) are those aged 60 years or older or over 50 with 2 or more of the following criteria: death from stroke, history of hypertension, and terminal creatinine $>1.5$ mg/dL. The Kidney Donor Risk Index (KDRI) was developed as an alternative to the dichotomous classification of donors between SCD vs ECD. Constructed from 10 variables, KDRI expresses a hazard ratio on a gradual, continuous scale that reflects the risk of graft failure. Proposed by Rao et al. [30], this score is based on some donors' characteristics associated with graft survival: age, height, weight, ethnicity, history of hypertension and/or diabetes, cause of death, serum creatinine, HCV, and donation after cardiac death. Based on the KDRI, the Kidney Donor Profile Index (KDPI) is calculated, which expresses the quality of a donor relative to other kidney donors. The Estimated Post Transplant Survival (EPTS) score was proposed to predict how long a patient will survive after kidney transplantation and is based on only 4 variables: age, time on dialysis, number of previous transplants, and diabetes status [6,31]. So, in the Kidney Allocation System (KAS) from United Network Organ Sharing (UNOS), patients with EPTS $<20\%$ are prioritized for donors with KDPI $<20\%$ as a longevity matching criterion, i.e., pairing kidneys that are expected to last longer (top 20% KDPI) with patients with a longer life expectancy (top 20% EPTS). The 20% cut-off could be reasonable when KAS was initially implemented, although it probably should be revisited now. Thus, a continuous distribution based on a scoring system has been suggested to replace the current KAS, which is based on a classification.

In this study, we could not test a longevity match based on KDPI and EPTS values as done by UNOS' KAS, mainly due to the limitations of our simulated data. Although, we believe that age difference between donor and recipient is a good proxy for the mentioned longevity match. Nevertheless, using KDPI in the decision-making process for organ acceptance from deceased donors could also help increase transplant rates and outcomes [32].

With the identification of the different HLA antigen groups, it was quickly concluded that the peaceful acceptance of grafts in humans depended on the HLA identity between the donor and the recipient [33]. Despite the relevance of HLA matching in kidney transplantation being questioned in favor of other non-immunological factors, HLA factors are still important in many kidney allocation systems. Since it is considered that HLA mismatches influence transplant outcomes, as proven by the results of large patient registries [33]. Another utilitarian criterion utilized in various allocation methods is HLA matching, including ET and our proposed EQM. There is no consensus on its use, although prioritizing kidneys with zero-mismatches is a common practice [13].

Highly sensitized transplant recipients may have worse outcomes than non-sensitized recipients due to a higher risk of delayed graft function, acute rejection, and graft failure [34]. The presence of anti-HLA antibodies in the circulation of a candidate for kidney transplantation negatively impacts their access to transplantation and graft survival, especially if the antibody is specific to their donor [35]. Besides, the calculated PRA (cPRA) value [16] indicates the likelihood that a patient may have HLA antibodies reactive to the next donor available. Moreover, since the reliability of cPRA values depend on the donor pool from which they are calculated, it is very important that this pool represents those who are potential organ donors [36].

With more sensitive techniques for anti-HLA antibody detection and the identification of hypersensitized patients through cPRA, the number of these patients on the waiting list for kidney transplantation has increased. With the careful immunological characterization of transplant candidates, it is possible to implement a virtual crossmatch in organ allocation systems with the identification of donor-specific antibodies (DSA) and thus increase the pool of available donors for hypersensitized patients [37]. Despite this, not all DSA are equally harmful, nor does the absence of DSA detected at the time of transplantation mean that the patient cannot develop a humoral memory cell response against the graft [35].

The success of kidney transplantation depends on the genetic and immunological compatibility between donor-recipient pairs, and HLA sensitization is a barrier to possible transplantation. The combined use of sensitization measures such as cPRA and virtual crossmatch is crucial in managing hypersensitized patients for their access to kidney transplantation [38]. The EQM algorithm also depends on candidates' cPRA and the application of a virtual crossmatch, although it does not prioritize hypersensitized (cPRA $>85\%$) patients.

The Acceptable Mismatch (AM) program of EuroTransplant has been proven to be an efficient way to increase the transplantation of highly sensitized patients with great outcomes [39]. Although hypersensitized patients have a lower graft survival than others, justice for these patients competes with the principle of utility.

It is well known that kidney transplantation in highly sensitized patients through regular allocation rules is associated with a high risk of graft rejection. In contrast, patients transplanted through the AM program of ET have significantly lower rejection rates [14] due to three factors: the absence of HLA specificity is determined for patients in the AM program both in current serum and historical serum; there is evidence that neonatal tolerance explains a portion of acceptable antigens, as acceptable antigens often include non-inherited maternal antigens; both antigens may include low-level epitope mismatches, or the present epitope mismatch is of low immunogenicity [14].

In KAS from UNOS, candidates with cPRA $\geq 99\%$ are allocated at a national level with a large increase in their priority points. Therefore, these patients also receive organs from donors with lower KDPI values (better organs), reducing access to these kidneys for less sensitized

candidates [6]. The increased use of kidneys with lower KDPI values in hypersensitized patients reduces the availability of these organs for the remaining candidates on the waiting list, many of whom have a much higher expected post-transplant survival than hypersensitized patients [40].

The use of a program like AM in combination with the EQM model can be considered depending on a detailed characterization and analysis of the patients on the waiting list for transplantation. Furthermore, there is a survival advantage for patients transplanted as HLA incompatible compared to those who remain on dialysis. So, deceased donors' kidney allocation programs should also consider the additional waiting time to which hypersensitized patients are subject.

Other factors may be considered for some candidates on the waiting list to achieve fairness in allocation. For instance, candidates who have donated a kidney in the past may get priority, as their current condition may be related to their donation. Similarly, children are prioritized due to the negative impact of dialysis and the unique benefits of transplantation on growth and development. In addition, kidney transplantation becomes an urgent life-saving treatment for patients for whom it is impossible to obtain adequate access to dialysis. Thus, most allocation programs define medical urgency as eligible for prioritization [13]. Additionally, it is customary to allocate the kidneys to identical ABO candidates instead of compatible ABO to prevent candidates from group O of increasing waiting times [41].

We must be able to look for different answers to the necessary distribution of deceased donor kidneys, compare them and evaluate the best measures to improve that distribution [42]. In order to measure the desired evolution and improvements in kidney transplantation, systematic metrics, and tools must be defined to evaluate established practices [26]. The definition of such objective and systematic measures for analyzing and evaluating the activities inherent to kidney transplantation is even more necessary when it is intended to make informed decisions to suggest new health policies [43].

Allocation systems that are assumed to work well may fail to do so due to changes in the donor pool, the demographics of transplant candidates, or due to societal changes in perceptions about the allocation of scarce goods [8].

In the search for a more straightforward, more transparent, and more equitable allocation system, the principles of Equal Opportunity Matrix [10], previously proposed, as well as the 4 conditions of 'accountability for reasonableness' [44] can and should be observed. The suggested EQM model tries to be a simple, transparent, and equitable answer to a complex question. Thus, any new proposal for a new kidney allocation system must be subject to the public scrutiny of its merits and should be assessed with data from different sources [45].

## Authors' contributions

Conception and design: BL.
Analysis and interpretation of data: BL, TH.
Drafting the article and revising it: BL, FR, HA, TH.
Providing intellectual content: BL, FR, HA, TH.
Approval of final version: BL, FR, HA, TH.

## Funding

This project received the "António Morais Sarmento" research grant from the Portuguese Society of Transplantation. This funding had no role in: the study design; collection, analysis, or interpretation of data; in the writing of the report; neither in the decision to submit the article for publication.

## Declaration of Competing Interest

The authors declare that they have no conflicts of interest to disclose.

## Data availability

Data will be made available on request.

## References

[1] C. Medin, C. Elinder, B. Hylander, B. Blom, H. Wilczek, Survival of patients who have been on a waiting list for renal transplantation, Nephrol. Dial. Transplant. 15 (2000) 701–704.
[2] M. Tonelli, N. Wiebe, G. Knoll, A. Bello, S. Browne, D. Jadhav, S. Klarenbach, J. Gill, Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes, Am. J. Transplant. 11 (2011) 2093–2109, https://doi.org/10.1111/j.1600-6143.2011.03686.x.
[3] E.S. Baskin-Bey, S.L. Nyberg, Matching graft to recipient by predicted survival: can this be an acceptable strategy to improve utilization of deceased donor kidneys? Transplant. Rev. 22 (2008) 167–170, https://doi.org/10.1016/j.trre.2008.02.005.
[4] R. Girlanda, Deceased organ donation for transplantation: challenges and opportunities, World J. Transplant. 6 (2016) 451, https://doi.org/10.5500/wjt.v6.i3.451.
[5] N.D. Eklou, B.M. Jänigen, P. Pisarski, G. Walz, J. Schneider, Evaluation of deceased donor kidney transplantation in the Eurotransplant senior program in comparison to standard allocation, Ann. Transplant. 27 (2022) 1–12, https://doi.org/10.12659/AOT.936514.
[6] J.M. Glorioso, Kidney allocation policy: past, present, and future, Adv. Chronic Kidney Dis. 28 (2021) 511–516, https://doi.org/10.1053/j.ackd.2022.01.006.
[7] B.A. Lima, M. Mendes, H. Alves, Kidney transplant allocation in Portugal, Port. J. Nephrol. Hypert. 27 (2013) 313–316.
[8] M.E. Shapiro, The development of new allocation policy for deceased donor kidneys, Curr. Opin. Nephrol. Hypertens. 16 (2007) 512–515, https://doi.org/10.1097/MNH.0b013e3282f08638.
[9] D.J. Norman, The kidney transplant wait-list: allocation of patients to a limited supply of organs, Semin. Dial. 18 (2005) 456–459, https://doi.org/10.1111/j.1525-139X.2005.00088.x.
[10] B.A. Lima, H. Alves, Access to kidney transplantation: a bioethical perspective, Port. J. Nephrol. Hypertens. 34 (2020) 76–78, https://doi.org/10.32932/pjnh.2020.07.070.
[11] S. Senanayake, N. Graves, H. Healy, K. Baboolal, A. Barnett, M.P. Sypek, S. Kularatna, Deceased donor kidney allocation: an economic evaluation of contemporary longevity matching practices, BMC Health Serv. Res. 20 (2020) 1–11, https://doi.org/10.1186/s12913-020-05736-y.
[12] K. Schulte, V. Klasen, C. Vollmer, C. Borzikowsky, U. Kunzendorf, T. Feldkamp, Analysis of the Eurotransplant kidney allocation algorithm: how should we balance utility and equity? Transplant. Proc. 50 (2018) 3010–3016, https://doi.org/10.1016/j.transproceed.2018.08.040.
[13] D. Lee, J. Kanellis, W.R. Mulley, Allocation of deceased donor kidneys: a review of international practices, Nephrology. 24 (2019) 591–598, https://doi.org/10.1111/nep.13548.
[14] S. Heidt, G.W. Haasnoot, M.D. Witvliet, M.J.H. van der Linden-van Oevelen, E. G. Kamburova, B.W. Wisse, I. Joosten, W.A. Allebes, A. van der Meer, L. B. Hilbrands, M.C. Baas, E. Spierings, C.E. Hack, F.E. van Reekum, A.D. van Zuilen, M.C. Verhaar, M.L. Bots, A.C.A.D. Drop, L. Plaisier, M.A.J. Seelen, J.S. Sanders, B. G. Hepkema, A.J.A. Lambeck, L.B. Bungener, C. Roozendaal, M.G.J. Tilanus, C. E. Voorter, L. Wieten, E.M. van Duijnhoven, M.A.C.J. Gelens, M.H.L. Christiaans, F. J. van Ittersum, S.A. Nurmohamed, N.M. Lardy, W. Swelsen, K.A.M.I. van der Pant, N.C. van der Weerd, I.J.M. ten Berge, F.J. Bemelman, A. Hoitsma, P.J.M. van der Boog, J.W. de Fijter, M.G.H. Betjes, H.G. Otten, D.L. Roelen, F.H.J. Claas, Allocation to highly sensitized patients based on acceptable mismatches results in low rejection rates comparable to nonsensitized patients, Am. J. Transplant. 19 (2019) 2926–2933, https://doi.org/10.1111/ajt.15486.
[15] N. Mamode, O. Bestard, F. Claas, L. Furian, S. Griffin, C. Legendre, L. Pengel, M. Naesens, European guideline for the Management of Kidney Transplant Patients with HLA antibodies: by the European society for organ transplantation working group, Transpl. Int. 35 (2022) 1–16, https://doi.org/10.3389/ti.2022.10511.
[16] J.M. Cecka, Calculated PRA (CPRA): the new measure of sensitization for transplant candidates: special feature, Am. J. Transplant. 10 (2010) 26–29, https://doi.org/10.1111/j.1600-6143.2009.02927.x.
[17] S. Tafulo, J. Malheiro, L. Dias, C. Mendes, E. Osório, L.S. Martins, J. Santos, S. Pedroso, Low transplantability of 0 blood group and highly sensitized candidates in the Portuguese kidney allocation algorithm : quantifying an old problem in search of new solutions, HLA. 88 (2016) 232–238, https://doi.org/10.1111/tan.12895.
[18] J. Duran, T. Chabert, F. Rodrigues, D. Pestana, Distribuição dos grupos sanguíneos na população portuguesa, AB0. 29 (2007) 5–17.
[19] B.A. Lima, H. Alves, HLA-A, -C, -B, AND -DRB1 allele ic and haplotypic diversity in bone marrow volunteer donors from northern Portugal, organs, Tissue Cell (2013) 19–26. https://12f11c1f-960a-f627-594d-b8ce276384f7.filesusr.com/ugd/3e838e_dc548dede99a4db5869c3d2c20c2d16f.pdf?index=true.
[20] B.A. Lima, simK: Synthetic Data on Kidney Transplantation, Transpl. Open Regist., 2022. https://txopen.github.io/simK/index.html (accessed July 13, 2022).
[21] IPST, Doação e Transplantação de Órgãos, Tecidos e Células. https://www.ipst.pt/files/TRANSPLANTACAO/DOACAOETRANSPLANTACAO/DadosAnuaiAtividadeDoacaotransplantacao_2022.pdf, 2022.

[22] B.A. Lima, M. Mendes, H. Alves, Kidney transplant allocation in Portugal, Port. J. Nephrol. Hypert. 27 (2013) 313–316. http://www.bbg01.com/cdn/clientes/spnefro/pjnh/46/artigo_14.pdf.
[23] EuroTransplant, ETKAS and ESP. https://www.eurotransplant.org/wp-content/uploads/2020/01/H4-Kidney-2021.2-April-2021.pdf, 2020.
[24] B.A. Lima, T.S. Henriques, H. Alves, Kidney allocation rules simulator, Transpl. Immunol. 72 (2022), 101578, https://doi.org/10.1016/j.trim.2022.101578.
[25] M.Z. Molnar, D.V. Nguyen, Y. Chen, V. Ravel, E. Streja, M. Krishnan, C.P. Kovesdy, K. Kalantar-zadeh, T. Science, E. Segundo, M. Veterans, A. Medical, Predictive score for Posttransplantation outcomes, Transplantation. 101 (2018) 1353–1364, https://doi.org/10.1097/TP.0000000000001326.Predictive.
[26] B.A. Lima, T. Henriques, F. Reis, H. Alves, Transplant open registry initiative, Port. J. Nephrol. Hypertens. 36 (2022) 201–206, https://doi.org/10.32932/pjnh.2022.10.204.
[27] B.A. Lima, KARS users' Manual, Transpl. Open Regist., 2021. https://kars-manual.netlify.app (accessed May 9, 2023).
[28] B.A. Lima, F.P. Reis, Histoc: histocompatibility analysis performed by kidney allocation systems, J. Open Source Softw. 7 (2022) 4807, https://doi.org/10.21105/joss.04807.
[29] B.A. Lima, eq-mtx. https://github.com/balima78/eq-mtx, 2023.
[30] P.S. Rao, D.E. Schaubel, M.K. Guidinger, K.A. Andreoni, R.A. Wolfe, R.M. Merion, F.K. Port, R.S. Sung, A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index, Transplantation. 88 (2009) 231–236, https://doi.org/10.1097/TP.0b013e3181ac620b.
[31] R.N. Formica, A critical assessment on kidney allocation systems, Transplant. Rev. 31 (2017) 61–67, https://doi.org/10.1016/j.trre.2016.10.002.
[32] E. Philipse, A.P.K. Lee, B. Bracke, V. Hartman, T. Chapelle, G. Roeyen, K. De Greef, D.K. Ysebaert, G. Van Beeumen, M.M. Couttenye, A.H. Van Craenenbroeck, R. Hellemans, J.L. Bosmans, D. Abramowicz, Does kidney donor risk index implementation lead to the transplantation of more and higher-quality donor kidneys? Nephrol. Dial. Transplant. 32 (2017) 1934–1938, https://doi.org/10.1093/ndt/gfx257.
[33] H. Sá, R. Leal, M.S. Rosa, Renal transplant immunology in the last 20 years: a revolution towards graft and patient survival improvement, Int. Rev. Immunol. 36 (2017) 182–203, https://doi.org/10.1080/08830185.2016.1225300.
[34] K.R. Jackson, J. Chen, E. Kraus, N. Desai, D.L. Segev, N. Alachkar, Outcomes of cPRA 100% deceased donor kidney transplant recipients under the new kidney allocation system: a single-center cohort study, Am. J. Transplant. 20 (2020) 2890–2898, https://doi.org/10.1111/ajt.15956.
[35] O. Bestard, L. Couzi, M. Crespo, N. Kessaris, O. Thaunat, Stratifying the humoral risk of candidates to a solid organ transplantation: a proposal of the ENGAGE working group, Transpl. Int. 34 (2021) 1005–1018, https://doi.org/10.1111/tri.13874.
[36] B.A. Lima, H. Alves, Portuguese calculated panel reactive antibodies online estimator, HLA. 93 (2019) 445–450, https://doi.org/10.1111/tan.13516.
[37] M.O. Valentin, J.C. Ruiz, R. Vega, C. Martín, R. Matesanz, J.J. Gimeno Lozano, A. Gutiérrez Dalmau, C. Moreno Parado, P.L. Martín Moreno, A.F. Maside, M. L. Perez Tamajón, A. Bosch Martínez, E.F. Tagarro, M.L. Hoyos, D. San Segundo, J. C. Ruiz San Millán, M.N. Colón, A. Mendiluce Herrero, L.A. Marín Rubio, G. Tabernero Fernández, J. Ontañón Rodríguez, I.L. Gonzalez, C. Canal, J.M. Pons, F. Diekmann, A. García Martínez, M. Crespo Barrio, F. Moreso Mateos, O. Bestard, L.C. Sole, N.P. Alcaraz, I.B. Castello, J.K. Berga, C.G. Roiz, M.I. Alcala Peña, J. G. Rial, C.D. Rodríguez, J.C. Fernandez, A.A. Hernández, A.F. García, N.M. Pomar, J.R. Valeriano, I.P. Flores, J.L. Castañer Alabaud, A.M. Fernández Rodríguez, E. M. Sierra, A.A. Belmonte, C.J. Martín, A.A. Melgar, A.A. Gutierrez, G.G. Erauzkin, A.L. Vázquez, M.L. Suarez Fernández, M.M. Amador, M.J. González Soriano, R. V. Pinto, C.M. Delagebasala, M. de la Oliva Valentín Muñoz, Implementation of a national priority allocation system for hypersensitized patients in Spain, based on virtual crossmatch: initial results, Transplant. Proc. 48 (2016) 2871–2875, https://doi.org/10.1016/j.transproceed.2016.09.024.
[38] B.A. Lima, M. Mendes, H. Alves, Hypersensitized candidates to kidney transplantation in Portugal, Port. J. Nephrol. Hypert. 27 (2013) 77–81.
[39] L. Mumford, S.V. Fuggle, J. Martorell, A. Slavcev, A. Iniotaki, G.W. Haasnoot, S. Heidt, F.H.J. Claas, A Europe wide acceptable mismatch program will enable transplantation of long waiting highly sensitised patients with a compatible donor, Transpl. Immunol. 64 (2021), 101354, https://doi.org/10.1016/j.trim.2020.101354.
[40] S. Sethi, R. Najjar, A. Peng, J. Mirocha, A. Vo, S. Bunnapradist, S.C. Jordan, E. Huang, Allocation of the highest quality kidneys and transplant outcomes under the new kidney allocation system, Am. J. Kidney Dis. 73 (2019) 605–614, https://doi.org/10.1053/j.ajkd.2018.12.036.
[41] B.A. Lima, H. Alves, Selection of donor-recipient pairs in renal transplantation: comparative simulation results, Acta Medica Port. 30 (2017) 854–860.
[42] B.A. Lima, H. Alves, Evaluation of the Portuguese kidney transplant allocation system: comparative results from a simulation, Port. J. Nephrol. Hypert. 32 (2018) 201–207.
[43] B.A. Lima, M. Mendes, H. Alves, Measuring kidney transplantation activity, Port. J. Nephrol. Hypert. 28 (2014) 171–176. http://www.bbg01.com/cdn/clientes/spnefro/pjnh/49/artigo_13.pdf.
[44] N. Daniels, J. Sabin, The ethics of accountability in managed care reform, Health Aff. 17 (1998) 50–64, https://doi.org/10.1377/hlthaff.17.5.50.
[45] B.A. Lima, H. Alves, Looking for proposals on a new kidney allocation system, Port. J. Nephrol. Hypertens. 33 (2019) 75–76, https://doi.org/10.32932/pjnh.2019.04.015.