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# Correcting the sex disparity in access to liver transplantation: Lest perfect be the enemy of better

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The implementation of the model for end-stage liver disease (MELD) as the backbone of liver allocation policy in the United States in 2002 has overall improved waitlist outcomes and standardized access to liver transplantation for patients with end-stage liver disease. However, women experience higher waitlist mortality and lower transplant rates compared with men, attributed in part to underestimation of renal dysfunction by the use of serum creatinine in MELD and MELD-Na.[1–3] Alternative models have been proposed to reduce this gap, including replacement of serum creatinine with estimated glomerular filtration rate or granting additional MELD points to women, but what has been lacking in the literature has been quantification and comparison of the potential impact of these models on the sex disparity itself.

In this issue of AJT, Wood et al. compare four scores to determine waitlist priority—the existing MELD-Na, the previously proposed MELD-Na-MDRD and MELD-Na-GRAIL, and a new MELD-Na-Shift—and consider their effect on waitlist outcomes and transplant rates.[4] The authors apply robust statistical methods in a data set spanning from 2003 to 2019 to estimate 90-day without-transplant survival, incorporating all MELD updates during the waiting period (not only at listing) and taking into account the occurrence of transplantation utilizing probability censoring weights. Corrections to replace the serum creatinine with eGFR (by MDRD or GRAIL) did not optimally improve sex disparity. A new score, MELD-Na-Shift, which the investigative team developed by adding points for women to approximate the MELD where they would be at similar mortality risk compared with men, equalized both the 90-day without-transplant survival and the simulated transplant rates between men and women. In LSAM modeling, the implementation of MELD-Na-Shift eliminated the difference in the transplant and mortality rates between women and men.

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DISCLOSURE

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Is MELD-Na-Shift the solution to the sex disparity in liver transplant waitlist outcomes? MELD-Na-Shift is "reverse-engineered", adding 1 point for women with certain MELD-Na scores (16, 18–26, 28–31, 33, 35, 37, 38), and 0 points for the remainder—a relatively simple modification that does not alter the underlying MELD formula or coefficients. The idea to artificially boost MELD may be relatively easy to understand, but it is not grounded in the biologic underpinnings of the sex disparity. This, in and of itself, is not a fatal flaw; the liver transplant community has deemed this concept of "granting" points acceptable, such as is standard for eligible patients with hepatocellular carcinoma (HCC). However, since this type of correction focuses on transplant probability rather than biologic values, it is susceptible to changes in allocation policy and the shifting demographics and distribution of liver disease on the waitlist. Such a correction would have to be validated with contemporary data, and if implemented, then continually recalibrated. Frequent adjustments of MELD score calculations for women on the waitlist could lead to a sense of uncertainty, lack of transparency, and distrust in the system.

Is there a better way? A forced shift in the MELD-Na for women is a pragmatic strategy, but the more ideal solution would be to replace the serum creatinine in MELD-Na with a more accurate representation of kidney function unaffected by demographic factors such as race or sex. At this time, however, no such biomarker is readily available for implementation on a nationwide scale. A compromise may be to refit MELD coefficients to more accurately weight creatinine in its prediction of 90-day mortality *and* to incorporate sex as a component that contributes to this outcome. Such a strategy is less than perfect, as it does not fully account for the root causes of the sex disparity. However, it would allow for more accurate waitlist prioritization of both women and men within the current MELD-based national allocation scheme and, therefore, be the strategy that could be realistically implemented in a timely manner.

Fair and equitable organ distribution is a mandate of the National Organ Transplant Act, and the sex disparity is a priority for ongoing efforts at the United Network of Organ Sharing to refine and improve upon the liver allocation system. By nature of organs being a scarce resource, if one group is advantaged, another group may in turn be disadvantaged. Rigorous analysis and testing are needed to safeguard against the unintended effects of any new policy. This comparative analysis and modeling exercise by Wood et al. is an important contribution to the debate regarding the best strategy to address the sex disparity in liver transplantation. As we approach nearly 2 decades of women experiencing inferior waiting list outcomes compared with men, we need to be wary of falling into the trap of "perfect being the enemy of better." We urge the liver transplant community to come together to address this disparity as soon as possible.

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