Letter to the Editor

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Towards optimally replacing the current version of MELD

To the Editor:

I was delighted to read Ge *et al.*'s review (2022)[1] published in the *Journal of Hepatology* that included a summary of the leading liver allocation models and computational methodologies, including model for end-stage liver disease (MELD)-Plus, a model which was developed as a collaboration between Massachusetts General Hospital and IBM Research in 2017.[2] The authors also highlighted MELD 3.0, which was proposed to replace the current version of MELD, the MELD-Na score.[3] The methodology of developing MELD 3.0 involved evaluating and using additional variables that were not included in the MELD-Na model. The performance of MELD 3.0 seems promising, especially because it correctly reclassified a net of 8.8% of decedents to a higher MELD tier, resulting in a simulated model with fewer waitlist deaths compared to MELD-Na. Although MELD 3.0 seems promising as a potential top candidate to replace MELD-Na, I would like to raise a few points for further consideration.

The development of MELD 3.0 included the evaluation of additional variables on top of MELD-Na's, including measurable variables such as albumin and height; however, the evaluation did not include components of other leading models, such as lactate (MELD-lactate),[4] blood urea nitrogen (MELD-GRAIL-Na),[5,6] and MELD-Plus's white blood cells, and total cholesterol.[2] The rationale behind excluding these variables should be discussed.

Note that the limitation specified in Table 1,[1] that MELD-Plus can only be calculated after a cirrhosis-related hospital admission is found to be incorrect. It is true that MELD-Plus was developed based on analyzing electronic health records of cirrhosis-related admissions; however, there is no limitation to using the model at any given time point, while considering the most recent value of each variable *e.g.*[7,8] MELD-Plus has not been studied in patients exclusively registered on the liver transplant waitlist.[3] Note, however, that all patients of the MELD-Plus study had cirrhosis at the time of their admission and an average MELD score of 14.2 (6.1), only slightly lower than the value calculated in the MELD 3.0 cohort.[3] Additionally, the prevalence of liver-related comorbidities, including ascites (37.9%), hepatic encephalopathy (28.6%), hepatocellular carcinoma (4.3%), and hepatorenal syndrome (3.2%), as well as chronic conditions not directly related to the liver, such as diabetes (57.0%), hypertension (58.9%), and heart failure (36.7%), was high in the MELD-Plus study. A cohort with such a high burden of comorbid conditions may be comparable with one that exclusively contains candidates for liver transplantation.

Note also that MELD-Plus has a version with 7 variables that has comparable performance to the 9-variable full version and does not rely on admission length of stay.[2,9] Furthermore, while MELD 3.0 was indeed found to be more discriminating compared to MELD-Na (by approximately 0.8%), MELD-Plus was consistently found to be more discriminating compared to MELD-Na in two large independent databases (by 11.4% and 16.9% in the Mass General Brigham and IBM Explorys repositories, respectively[2]). I therefore encourage all members of the scientific community to assess further well-validated and well-calibrated[10] leading hepatic risk models, as well as their individual components, as we work toward optimally replacing the current version of MELD.

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Author names in bold designate shared co-first authorship

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