anatomy alone is insufficient to capture the complexities of tumour biology. A one-size-fits-all approach to therapeutic options is ineffective, highlighting the key need for biomarkers capable of guiding treatment sequencing (upfront surgery or neoadjuvant treatment), determining the optimal chemotherapy regimens and duration, and ideally facilitating the adoption of targeted therapies of improved efficacy.[5]

We declare no competing interests.

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Validating the new nomenclature of steatotic liver disease in patients with excessive alcohol intake

We read with interest the Article by Mads Israelsen and colleagues[1] that aimed to validate prognostic distinctions among steatotic liver disease subclasses, including metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic dysfunction and alcohol-related steatotic liver disease (MetALD), and alcohol-related liver disease (ALD). Patients with steatotic liver disease had a significantly higher risk of hepatic decompensation and overall mortality compared with those without steatotic liver disease. Risk increased progressively from MASLD to MetALD and then to ALD, emphasising the need for precise risk stratification and management subclassification.

We congratulate the authors on this study, but further research is needed to examine several aspects. First, the validity of nomenclature based only on the Danish population is limited. The authors should account for differences between the general population and the Danish population. They might therefore consider generalising their effect estimates to the general population, which would better validate the new nomenclature.

Second, there are statistically significant correlations between per capita annual alcohol consumption and the alcohol-attributable fraction.[2] Therefore, when categorising steatotic liver disease by alcohol consumption, merely using average alcohol intake from the past 3 months before inclusion might introduce bias, because a person's average alcohol intake from the past 3 months and that from the past year can be very different. Moreover, the effect of alcohol consumption on hepatic decompensation and overall mortality might vary across different timepoints, especially when considering long time periods. Thus, we suggest using average alcohol intake or a weighted average from the past year.

Third, the authors use multivariable Cox regression to show that the risk of hepatic decompensation increases gradually with the level of alcohol intake from MASLD, through MetALD, to ALD, independent of age, sex, and liver stiffness. However, to fully show this point, the interaction terms consisting of sex, age, and strata of liver stiffness should be included in the Cox regression.

Finally, the fact that only one pathologist performed the histological scoring during the study period raises concerns, as a single-reader approach could be subject to temporal bias and intrareader variability.[3] Therefore, we suggest that a panel of several trained pathologists independently scoring histology parameters would produce high consensus rates.[4]

We declare no competing interests.

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Authors' reply

We thank Yu Wu and Fei Fang for their interest in and comments on our Article.[1] First, we acknowledge that the Danish population might not represent the global population entirely. However, the applicability of the nomenclature for steatotic liver disease across diverse populations worldwide, including in the USA,[2] has been shown. In our study and others, increasing alcohol use has been shown to markedly affect the prognosis of liver disease.[3] Consequently, the accuracy of reporting alcohol use is