



## Reply to: “An individualized cirrhosis screening strategy might be more cost-effective in the general population”

To the Editor:

We thank Dr. Zhao, Dr. Liao and Dr. Fan for their commentary on our SEAL study funded by the Federal Joint Committee, the highest decision-making body of the self-government of physicians, hospitals and health insurance funds in Germany, and published in the *Journal of Hepatology*.<sup>1,2</sup> In SEAL (Structured Early detection of Asymptomatic Liver cirrhosis), we were able to demonstrate that screening for cirrhosis and advanced fibrosis in the general population is feasible and that our approach has the potential to increase the early detection rate of these patients.

Zhao *et al.* raised some important points on non-invasive tests (NITs) for hepatic fibrosis and cirrhosis that we address as follows. We fully agree with our colleagues who point out the importance of age and comorbidities on the discriminative power of NITs such as the APRI score. Above all, of course, this also has relevant implications for general population screening, as performed in SEAL. Unfortunately, all of the evidence cited by Zhao *et al.* on these topics was published after the start of the SEAL study, so these observations could not be considered for this initiative, and due to the prespecified design of our study, we are not able to perform these *post hoc* analyses. Nonetheless, it would be interesting to examine the performance of age-adjusted cut-offs in similar settings.

On another note, Zhao *et al.* suggested that the rate of missed diagnoses of cirrhosis in patients with underlying chronic liver disease could be further reduced by using a lower cut-off value of the NIT. We have also considered this, but it is unlikely to be more (cost-)effective because most patients in our population did not have liver disease at inclusion. Actually, this may be a hidden strength of the SEAL study, since our results also suggest that screening in the general population might increase the early detection rate not only of advanced fibrosis and cirrhosis, but also of chronic liver disease *per se*. In this setting, “liver screening” – independent of the test applied – may have beneficial effects by inducing lifestyle changes, as recently highlighted by a study in Denmark.<sup>3</sup>

Taken together, we believe that – regardless of the NIT or cut-offs used – it is of pivotal importance to start screening for advanced liver diseases in the general population. In this context, SEAL should represent an initial blueprint that can now be built on to bring chronic liver disease more into the (public health) spotlight. Because that’s another important lesson SEAL has taught us: awareness of liver diseases in the general population is still low, and therefore better care for patients with liver diseases should be our joint aim.

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### Conflicts of interest

The authors have read guidance on competing interests, and they declare no competing interests.

Please refer to the accompanying ICMJE disclosure forms for further details.

### Authors’ contributions

All authors contributed equally on conceptualization, drafting and writing of this reply.

### Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhep.2022.08.006>.

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Author names in bold designate shared co-first authorship

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