Financial support

The authors received no financial support to produce this manuscript.

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

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

Authors' contributions

CR and AZ had the idea to write the letter. CR developed the letter. JB and AZ provided important intellectual input. All authors have approved the final manuscript.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2022.07.031.

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Reply to: "SEAL: Why was this approach not effective?"

To the Editors:

We would like to thank Professor Ripoll and colleagues for their interest and their commentary on our SEAL study published in the *Journal of Hepatology*.[1,2] Ripoll *et al.* raise some important points and potential limitations of SEAL that we would like to take the opportunity to reply to.

We agree with our colleagues who point out that people of lower socioeconomic status are less likely to participate in a preventive health care program such as the German Check-up 35 program, as targeted in SEAL. This is a non-negligible circumstance that leads to a potential selection bias and should be taken into account when interpreting the results of SEAL. However, it should be noted that all SEAL participants were members of AOK, the largest general medical insurance in Germany, excluding patients from alternative insurance companies and all with private insurance, who have in general higher socioeconomic status.

Notwithstanding this shortcoming, it is an important finding for the hepatology community that screening for compensated advanced chronic liver disease (cACLD) even in a population with a potentially higher degree of health awareness is feasible and provides benefit. On the other hand, SEAL suggests that future studies could specifically target populations at highest risk of chronic liver disease. Though, these populations may be more difficult to approach, since the awareness of liver health in these populations is lower than in Check-up 35 participants, and appointments with a liver specialist in SEAL were only attended by about 50% of cases. Therefore, we agree that awareness of liver health needs to be raised in all parts of our society.

Ripoll *et al.* proposed the recently published CLivD score to identify a high-risk population in the general population that deserves detailed screening for cACLD.[3] We argue that a stepwise approach with defined strategies that help primary care physicians to identify patients at high risk for liver disease might indeed improve the care for patients with cACLD. Because this is another lesson that SEAL and other studies have taught us: Screening in the general population using traditional and simple non-invasive tests may not be sufficient and lacks positive predictive value.[1,4,5] However, it has to be acknowledged that scores such as the CLivD are frequently developed in retrospective cohorts. Therefore, studies testing the benefits of these algorithms as well as alternative methods (*e.g.*, transient elastography) prospectively are needed before implementation. In this context, we believe that SEAL can serve as a blueprint for these studies by demonstrating not only what is possible in terms of patient recruitment and involvement of multiple levels of care, but also the future needs.

In summary, we believe that we have only reached the tip of the iceberg in the early detection of cACLD and are eagerly awaiting the results of additional screening studies.

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Received 20 September 2022; Accepted 22 September 2022; Available online 27 September 2022
https://doi.org/10.1016/j.jhep.2022.09.016

Financial support

This project was funded by the Innovationsausschuss beim Gemeinsamen Bundesausschuss from 2016 to 2021 (G-BA 01NVF16026).

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.
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.2022.09.016.

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Author names in bold designate shared co-first authorship.

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Cirrhosis is an independent predictor for COVID-19 mortality: A meta-analysis of confounding cofactors-controlled data

To the Editor:
We read with great interest the excellent paper by Marjot *et al.* titled "Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study".[1] In this paper, the authors reported that cirrhosis was significantly associated with coronavirus disease 2019 (COVID-19) mortality on multivariable analysis. Meanwhile, other studies have reported that cirrhosis is not significantly associated with the risk for COVID-19 mortality on multivariable analysis.[2–4] This suggested that the association between cirrhosis and COVID-19 mortality remains inconclusive. Therefore, we performed this meta-analysis to clarify the association between cirrhosis and COVID-19 mortality based on confounding cofactors-controlled effect estimates.

A systematic search was performed in PubMed, Web of Science, EMBASE, Springer Link, Wiley Library, Elsevier ScienceDirect and Cochrane Library to identify all relevant studies as of August 12, 2022. The search terms were: "coronavirus disease 2019", "COVID-19", "severe acute respiratory syndrome coronavirus 2", "SARS-CoV-2", "mortality", "cirrhosis" and "liver cirrhosis". We included the articles reporting the confounding cofactors-controlled effect estimates on the association between cirrhosis and COVID-19 mortality. We excluded preprints, reviews, duplications, errata, case reports and studies reporting the confounding cofactors-uncontrolled effect estimates. We also examined the reference lists of reviews and retrieved original literature to identify all relevant articles. Two authors independently performed literature search and data extraction. Any discrepancy was resolved by consulting the third author. This meta-analysis was reported following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.[5]

Heterogeneity was assessed by using the I^2 statistic and Cochran's Q test. The pooled effects and 95% CIs were