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Reply to ‘The 50 shades of bilirubin’. Letter regarding the article ‘Liver tests and outcomes in heart failure with reduced ejection fraction: findings from DAPA-HF’

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We would like to thank Drs Krawczyk and Böhm for their interesting comments. We fully agree that some of the participants in DAPA-HF may have had Gilbert's syndrome, although not necessarily only those in the highest third of baseline bilirubin levels as bilirubin is not elevated all of the time in everyone with this syndrome.¹ Moreover, the characteristics of patients in the upper third of bilirubin concentrations (lower ejection fraction and blood pressure; higher N-terminal pro-B-type natriuretic peptide level; worse New York Heart Association class and Kansas City Cardiomyopathy Questionnaire scores) suggest that they were, in the main, patients with more advanced heart failure, as of course does their worse outcomes which cannot be explained by a benign condition like Gilbert's syndrome.² It is of course true that patients with hyper-bilirubinaemia due to Gilbert's syndrome may have 'diluted' the strength of the association between elevated bilirubin concentration and adverse clinical outcomes in our analyses, serving to reinforce the prognostic value of this readily available and inexpensive biomarker.^{2,3}

References

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3. Suzuki K, Claggett B, Minamisawa M, Packer M, Zile MR, Rouleau J, et al. Liver function and prognosis, and influence of sacubitril/valsartan in patients with heart failure with reduced ejection fraction. *Eur J Heart Fail.* 2020;22:1662–71.