

The Epidemiology of Bile Acid Diarrhea in Denmark [Response to Letter]

Martin L Kårhus¹, Anne-Marie Ellegaard¹, Filip K Knop¹⁻³, Line L Kårhus⁴

¹Center for Clinical Metabolic Research, Copenhagen University Hospital – Herlev and Gentofte, Hellerup, Denmark; ²Steno Diabetes Center Copenhagen, Herlev, Denmark; ³Department of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark; ⁴Center for Clinical Research and Prevention, Copenhagen University Hospital – Bispebjerg and Frederiksberg, Frederiksberg, Denmark

Correspondence: Anne-Marie Ellegaard, Center for Clinical Metabolic Research, Copenhagen University Hospital – Herlev and Gentofte, Gentofte Hospitalsvej 7, 3rd floor, Hellerup, DK-2900, Denmark, Email anne.marie.gade.ellegaard@regionh.dk

Dear editor

We read the Letter to the Editor by Nurmawanti et al regarding our recent study investigating the epidemiology of bile acid diarrhea (BAD) in Denmark¹ with interest.

Nurmawanti et al appreciate the importance of our study and the robust design, which we are thankful for. They, then, state that the study “may not reflect the true prevalence of BAD in the Danish population”, which we agree with. As we state in the discussion, our priority was to define and include individuals that we were confident suffered from BAD thereby excluding individuals not diagnosed by ⁷⁵selenium homotaurocholic acid (SeHCAT) test and/or individuals who never redeemed a prescription of bile acid sequestrants. Importantly, our study was not designed to establish the true prevalence of BAD in the Danish population, but to describe the demographic characteristics of individuals suffering from BAD in Denmark.

Next, Nurmawanti et al find that the regional differences in the number of BAD diagnoses are not adequately explained. The reason(s) for these differences is difficult to investigate; however, since Denmark is a small country with low regional variation within demographic characteristics, healthcare utilization, and medication use,² we speculate that these differences are more likely to be explained by differences in clinical practice and traditions rather than differences in the population, as also mentioned in our discussion.¹

Nurmawanti et al suggest that further research is needed to understand the causal relationship between BAD and low income and education levels. We agree that studying this question would be interesting, but it was not in the scope of this study, and has previously been addressed by others, as referenced in our discussion.^{3,4}

Nurmawanti et al highlight the need for further information on the safety and efficacy of using liraglutide to treat BAD. We agree that this is warranted, but we do not find register-based research suitable to address this question. The safety and efficacy of liraglutide have been investigated in a six-week randomized, double-blind, double-dummy clinical trial,⁵ addressed in a registry-based analysis of prescription patterns,⁶ and described in case reports.⁷⁻⁹

Lastly, Nurmawanti et al suggest that our study could have been improved with surveys and interviews to include individuals who had not undergone a SeHCAT test or were not using bile acid sequestrants and to analyze regional differences. We agree that these aspects would be interesting to address in future studies.

Acknowledgment

Filip K Knop is currently employed at Novo Nordisk A/S.

Disclosure

The authors declare no conflicts of interest regarding this communication.

References

1. Kårhus ML, Ellegaard AM, Winther-Jensen M, Hansen S, Knop FK, Kårhus LL. The epidemiology of bile acid diarrhea in Denmark. *Clin Epidemiol*. 2023;15:1173–1181. doi:10.2147/clep.S442054
2. Henriksen DP, Rasmussen L, Hansen MR, Hallas J, Pottegård A. Comparison of the five Danish regions regarding demographic characteristics, healthcare utilization, and medication use—a descriptive cross-sectional study. *PLoS One*. 2015;10(10):e0140197. doi:10.1371/journal.pone.0140197
3. Andrae DA, Patrick DL, Drossman DA, Covington PS. Evaluation of the Irritable Bowel Syndrome Quality of Life (IBS-QOL) questionnaire in diarrheal-predominant irritable bowel syndrome patients. *Health Qual Life Outcomes*. 2013;11:208. doi:10.1186/1477-7525-11-208
4. Paré P, Gray J, Lam S, et al. Health-related quality of life, work productivity, and health care resource utilization of subjects with irritable bowel syndrome: baseline results from LOGIC (Longitudinal Outcomes Study of Gastrointestinal Symptoms in Canada), a naturalistic study. *Clin Ther*. 2006;28:1726–1735. doi:10.1016/j.clinthera.2006.10.010
5. Kårhus ML, Brønden A, Forman JL, et al. Safety and efficacy of liraglutide versus colesevelam for the treatment of bile acid diarrhoea: a randomised, double-blind, active-comparator, non-inferiority clinical trial. *Lancet Gastroenterol Hepatol*. 2022;7(10):922–931. doi:10.1016/S2468-1253(22)00198-4
6. Rahbek MT, Lund LC, Hallas J. A case for screening real-world data for collateral drug benefits: glucagon-like peptide 1 receptor agonists and bile acid diarrhea. *Pharmacoepidemiol Drug Saf*. 2023. doi:10.1002/pds.5673
7. Conley TE, White KL, Bond A, Harrison S, McLaughlin J, Lal S. Emerging uses of glucagon-like peptide 1 (GLP-1) receptor agonists following ileal resection: literature review and case examples. *Front Gastroenterol*. 2023;14(6):521–526. doi:10.1136/flgastro-2023-102402
8. Kårhus ML, Brønden A, Røder ME, Leotta S, Sonne DP, Knop FK. Remission of bile acid malabsorption symptoms following treatment with the glucagon-like peptide 1 receptor agonist liraglutide. *Gastroenterology*. 2019;157(2):569–571. doi:10.1053/j.gastro.2019.04.002
9. Kårhus ML, Knudsen E, Knop FK. Different effects of once-weekly and once-daily administered GLP-1RA semaglutide and liraglutide on bile acid diarrhea. *J Clin Endocrinol Metab*. 2022;1(1):luac004. doi:10.1210/jcemcr/luac004

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Clinical Epidemiology 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Clinical Epidemiology editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Clinical Epidemiology

Dovepress

Publish your work in this journal

Clinical Epidemiology is an international, peer-reviewed, open access, online journal focusing on disease and drug epidemiology, identification of risk factors and screening procedures to develop optimal preventative initiatives and programs. Specific topics include: diagnosis, prognosis, treatment, screening, prevention, risk factor modification, systematic reviews, risk & safety of medical interventions, epidemiology & biostatistical methods, and evaluation of guidelines, translational medicine, health policies & economic evaluations. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use.

Submit your manuscript here: <https://www.dovepress.com/clinical-epidemiology-journal>

<https://doi.org/10.2147/CLEP.S455102>