

Hellerup, 11. december 2025

Sammenhæng mellem galdesyrediarré og knogleskørhed

Formålet med dette projekt er at undersøge, om patienter med galdesyrediarré har højere forekomst af knogleskørhed og knoglebrud, samt om de har ændringer i deres knoglestofskifte, som kan tyde på en højere risiko for at udvikle knogleskørhed.

I en unik samling af blodprøver fra næsten 70 patienter med galdesyrediarré og en tilsvarende kontrolgruppe vil vi analysere og sammenligne biologiske markører for knogleomsætningen og galdesyreniveauerne. Derudover vil i de danske sundhedsregistre undersøge, om knogleskørhed og knoglebrud er hyppigere hos personer med galdesyrediarré i forhold til den generelle befolkning.

Vores præliminære analyser viser en øget forekomst af knogleskørhed blandt personer med galdesyrediarré i forhold til kontroller, samt at disse personer har nedsat D-vitamin-niveau i blodet. Dette kan være en medvirkende årsag, da D-vitamin spiller en stor rolle i sund knogledannelse.

Projektet vil give helt ny viden om en mulig sammenhæng mellem galdesyrediarré og knogleskørhed. Hvis analyserne bekræfter vores præliminære resultater, kan det betyde, at patienter med galdesyrediarré i fremtiden bør screenes og følges tættere for knogleproblemer. Det vil kunne føre til tidligere forebyggelse, bedre behandling og i sidste ende højere livskvalitet for patientgruppen.

Perspektiverne rækker også længere: projektet kan bane vejen for større studier, der mere detaljeret kan undersøge, hvordan galdesyrrer påvirker knoglestofskiftet. Dermed kan resultaterne ikke blot gavne patienter med galdesyrediarré, men også bidrage til ny forståelse af samspillet mellem fordøjelsessystemet og knoglesundheden generelt.

Projektet udføres af medicinstuderende Sólvá Strøm Olsen og læge, ph.d.-studerende Mads Bank Lynggaard på Center for Klinisk Metabolisk Forskning, Gentofte Hospital undervejledning af overlæge, klinisk lektor Asger B. Lund og seniorforsker Anne Marie Gade Ellegaard.

De 75.000 kr vi søger fra Colitis-Crohn Foreningen skal delvist dække udgifter til analyse af de biologiske markører.

Med venlig hilsen



Anne Marie Gade Ellegaard

Seniorforsker og gruppeleder

Center for Klinisk Metabolisk Forskning, Gentofte Hospital

Anne Marie Gade Ellegaard – CV

Arbejdserfaringer og uddannelser

Gæsteforsker , Biomedicinsk Institut, Københavns Universitet	2025 -
Seniorforsker og gruppeleder , Center for Klinisk Metabolisk Forskning, Gentofte Hospital	2022 -
Postdoc og forskningskoordinator , Center for Klinisk Metabolisk Forskning, Gentofte Hospital	2020 - 2022
Klinisk Farmakologisk Forsker , Clinical Pharmacology Obesity, Novo Nordisk	2018 - 2020
Postdoc , Kræftens Bekæmpelses Forskningscenter	2015 - 2017
PhD , Kræftens Bekæmpelses Forskningscenter	2011 - 2015
Forskningsassistent , Kræftens Bekæmpelses Forskningscenter	2010 - 2011
Kandidat i Molekylær Biomedicin, Master of Excellence , Københavns Universitet	2008 - 2010
Praktikophold , Queen's University, Belfast, Nordirland	2008
Bachelor i Molekylær Biomedicin , Københavns Universitet	2005 - 2008
Udvekslingsophold ved Zürich University og ETH Zürich, Schweiz	2007
Studererjob , Regulatorisk afdeling, Lægemiddelstyrelsen	2006 – 2007

Barselsorlov

Okt 2016 – Okt 2017; Feb 2019 – Mar 2020; Okt 2021 – Nov 2022

Opnåede bevillinger

Savværksejer Jeppe Juhl og Hustru Ovita Juhls Mindelegat	1.000.000 kr	2025
Ekspeditionssekretær Torkil Steensbecks Legat	180.000 kr	2025
Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat Dagmar Marshalls Fond	500.000 kr	2024
150.000 kr	2024	
Prosektor Dr. Med. Axel Søeborg Ohlsen og Hustrus Legat	40.000 kr	2024
Fabrikant Einar Willumsens Mindelegat	100.000 kr	2024
Valborg og Edit Larsens Æreslegat til fremme af kvinders forskningsmulighed	15.000 kr	2024
Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat	650.000 kr	2023
Aage og Johanne Louis-Hansens Fond	2.900.000 kr	2023
Læge Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat	550.000 kr	2022
Savværksejer Jeppe Juhl og Hustru Ovita Juhls Mindelegat	1.000.000 kr	2022

Vejledning

Primær medvejleder for en succesfuld ph.d.-studerende, medvejleder for to succesfulde ph.d.-studerende og en succesfuld kandidatstuderende. Aktuelt primær medvejleder for en ph.d.-studerende og en medicinstuderende og medvejleder for tre ph.d.-studerende.

Konferencedeltagelse

Deltaget med poster og/eller oral præsentation i >30 danske og internationale konferencer. Inviteret taler (indenfor de sidste fem år): Digestive Disease Week (2026), United European Gastroenterology Week 2024, Symposium on Clinical Metabolic Physiology (2023), Bile Acids in the Small Intestine and Colon (2023).

Publikationer

H-index: 10 (kilde: Google Scholar); citationer: 1211; publikationer: 38; peer-reviewed: 30; bogkapitler: 2; første-forfatterskaber (peer-reviewed): 14; sidste-forfatterskaber: 1; korresponderende forfatter: 10. ORCID: [0000-0002-4389-3908](https://orcid.org/0000-0002-4389-3908)

Udvalgte, relevante publikationer

Eget navn med fed skrift

1. Gilliam-Vigh H, **Ellegaard AM**, Madsen MR, Lund AB, Jensen BAH, Vilsbøll T, Rigbolt K, Knop FK. Mucosal transcriptomic landscape along the small and large intestines in individuals with and without type 2 diabetes. *Gut*, accepted for publication July 2025
2. **Ellegaard AM**†, Winther-Jensen M, Kårhus LL, Knop FK, Kårhus ML. Bile acid diarrhea is associated with an increased risk of type 2 diabetes and cardiovascular disease: a nationwide cohort study. *Clinical and Translational Gastroenterology* May 23, 2025
3. Gilliam-Vigh H, Suppli MP, Heimbürger SMN, Lund AB, Knop FK, **Ellegaard AM**†. Cholesin mRNA Expression in Human Intestinal, Liver, and Adipose Tissues. *Nutrients* 17 (4), 619.
4. **Ellegaard AM**†, Kårhus ML, Winther-Jensen M, Lund AB, Knop FK. Treatment of bile acid diarrhea with GLP-1 receptor agonists: A Promising Yet Understudied Approach. *Clinical and Translational Gastroenterology* 16(3):p e00815, March 2025.
5. Nerild HH, Gilliam-Vigh H, **Ellegaard AM**, Forman JL, Vilsbøll T, Sonne DP, Brønden A, Knop FK. Expression of bile acid receptors and transporters along the intestine of patients with type 2 diabetes and controls. *Journal of Clinical Endocrinology and Metabolism*, 2024;., dgae261.
6. Lange AH, Pedersen MG, **Ellegaard AM**, Nerild HH, Brønden A, Sonne DP, Knop FK. The bile-gut axis and metabolic consequences of cholecystectomy. *European Journal of Endocrinology* 2024 Mar 30;190(4):R1-R9.
7. Nerild HH, Brønden A, Haddouchi AE, **Ellegaard AM**, Hartmann B, Rehfeld JF, Holst JJ, Sonne DS, Vilsbøll T, Knop FK. Elucidating the Glucose-Lowering Effect of the Bile Acid Sequestrant Sevelamer. *Diabetes, Obesity, and Metabolism*. 2024; 26(4), 1252–1263.
8. **Ellegaard AM**†, Kårhus ML, Winther-Jensen M, Knop FK, Kårhus LL. Bile acid diarrhea is associated with increased incidence of gastrointestinal cancers. *American Journal of Gastroenterology*, 2024 Oct 1;119(10):2107-2113.
9. **Ellegaard AM**†, Kårhus ML, Krych L, Sonne DP, Forman JL, Hansen SH, Dragsted LO, Nielsen DS, Knop FK. Liraglutide and Colesevelam Changes Serum and Fecal Bile Acid Levels in a Randomized Trial with Patients with Bile Acid Diarrhea. *Clinical and Translational Gastroenterology*. September 23, 2024.
10. Kårhus ML*, **Ellegaard AM***†, Winther-Jensen M, Hansen S, Knop FK, Kårhus LK. The epidemiology of bile acid diarrhoea in Denmark. *Clinical Epidemiology* 2023, 15, 1173-1181. * delt forfatterskab
11. Lewinska M*, Kårhus ML*, **Ellegaard AM**, Romero-Gómez M, Macias RIR, Andersen JB, Knop FK. Serum lipidome unravels a diagnostic potential in bile acid diarrhoea. *Gut* 2023 Apr 18;gutjnl-2022-329213. * delt forfatterskab

Budget	Haves/søges andet sted	Søges fra CCF
Løn		
Seniorforsker (10%, 12 mdr)	70.000	
Ph.d.-studerende (20%, 12 mdr)	150.000	
Forskningsårsstuderende (100%, 7 mdr)	42000	
Analyser		
Analyse af biomarkører for knogle- og galdesyremetabolisme	400.000	75.000
Analyse af registerdata	125.000	
Offentliggørelse		
Publikationsudgifter	30000	
Præsentation af resultater på internationale konferencer	15000	
Total	832.000	75.000



Gentofte, 24. september 2025

Vedr. Anne Marie Gade Ellegaards ansøgning til projektet ”Har personer med galdehyrediarré øget risiko for knogleskørhed?”

Jeg bekræfter hermed min støtte til ansøgningen fra seniorforsker Anne Marie Gade Ellegaard, cand.scient., ph.d., fra Center for Klinisk Metabolisk Forskning til ovennævnte projekt.

Galdehyremetabolisme og galdehyrediarré har længe været et fokusområde i Center for Klinisk Metabolisk Forskning, og vi er internationalt anerkendt for vores ekspertise inden for kliniske studier af bl.a. galdehyrediarré. Med mere end 35 videnskabelige artikler inden for galdehyremetabolisme og galdehyrediarré har vi etableret os som internationalt førende på området.

I dette studie vil Anne Maries gruppe undersøge, om personer med galdehyrediarré har øget forekomst af osteoporose, og i så fald om det kan skyldes ændringer i knoglemetabolismen. Galdehyrer kan påvirke knogleomsætningen, og det er derfor relevant at undersøge, om den ændrede galdehyresammensætning hos patienterne, resulterer i en påvirket knogleomsætning. Projektet indeholder to dele, en biokemisk analyse af blodprøver fra patienter og en register-baseret analyse. Projektet vil således med to forskellige men komplementerende forskningsdiscipliner prøve at besvare samme spørgsmål; nemlig om patienter med galdehyrediarré har øget risiko for osteoporose. En sådan tilgang vil give langt stærkere resultater, som kan danne grundlag for øget opmærksomhed i klinikken samt mere forskning i dette krydsfelt mellem knogle- og galdehyremetabolisme.

Anne Marie har været ansat som forsker i Center for Klinisk Metabolisk Forskning siden 2020 og har arbejdet med klinisk forskning indenfor galdehyremetabolisme og galdehyrediarré. Hun har startet sin egen gruppe, som forsker i galdehyrediarré, og har tidligere modtaget flere store bevillinger samt for nyligt et æreslegat til *kvinder i forskning* for sit store bidrag til centerets aktiviteter og hendes engagement i de ph.d.-studerendes læring og udvikling. Med hendes entusiastiske projektlederevner og ihærdige gåpåmod er jeg sikker på, at hun og hendes team sikrer en succesfuld gennemførelse af projektet.

Jeg bekræfter hermed, at Gentofte Hospital vil sikre rammerne for projektet samt administration af en eventuel bevilling.

Med venlig hilsen

Asger Bach Lund

Speciallæge, ph.d. klinisk lektor



Assessment of bone metabolism in patients with bile acid diarrhoea

the BAD-BONE study

Background

Bile acids are traditionally recognised for their role in lipid digestion and fat-soluble vitamin absorption. However, recent evidence has shown they are also potent signalling molecules with effects on metabolism (reviewed in ¹). The bile acid receptors farnesoid X receptor (FXR) and G-protein-coupled bile acid receptor 1 (GPBAR1/TGR5) are expressed in bone cells and influence both osteoblast and osteoclast activity²⁻⁴. Generally, studies indicate that bile acids stimulate bone formation over bone resorption, however, the composition of the bile acid pool and the population seem to matter⁵⁻⁷. A study with pre-menopausal Caucasian women showed a positive correlation between bone mineral density and serum levels of cholic acid, ursodeoxycholic acid and taurine-ursodeoxycholic acid⁸. Similarly, a retrospective study on Chinese pre-menopausal women found a positive correlation between bone mineral density and serum total bile acid levels⁹. In contrast, in postmenopausal women, serum total bile acids and the bile acid-absorption related fibroblast growth factor 19 (FGF19) were significantly decreased in those with osteoporosis and osteopenia compared with healthy women, and both correlated positively with bone mineral density¹⁰. Collectively, these studies indicate a regulatory role of circulating bile acids on bone metabolism but the mechanism and (patho)physiological significance of this remains elusive.

Bile acid diarrhoea (BAD) is a chronic, socially debilitating disease, affecting up to 2% of the population¹¹. The primary symptoms are diarrhoea, abdominal pain, urgency and uncontrollable bowel movements. Apart from the physical effects, it impairs quality of life¹² and is associated with lower income and more co-morbidities¹³. Normally, bile acids are absorbed in the small intestine, however, in BAD a spillover of bile acids from the small intestine into the large intestine results in irritation of the colonic mucosa, water influx and stimulation of peristalsis¹⁴. The spillover can be caused by increased synthesis of bile acids in the hepatocytes and/or reduced re-absorption in the small intestine. BAD can arise secondary to other conditions impairing bile acid absorption, or it can arise idiopathically. Whether individuals with BAD have altered circulating bile acid levels is still under debate; however, despite normal levels, the composition of the bile acid pool might be altered^{15,16}, which greatly affects the potency of receptor activation.

Despite the plausible link between bile acids and bone homeostasis, no study has yet investigated possible bone metabolism changes or the incidence of osteoporosis in individuals with BAD. This is the aim of this study. We hypothesise that individuals with BAD show changes in circulating biomarkers indicative of bone loss and that individuals with BAD have increased incidence of osteoporosis and fractures typical to osteoporosis.

Research plan and methods

Part I: Biochemical changes in individuals living with BAD compared to individuals living with similar symptoms without having BAD

Study material: At Center for Clinical Metabolic Research, we have recently finished the data collection in a clinical study involving patients referred to the diagnostic test for BAD. Thus, we have a collection of plasma samples from 69 patients with BAD and 63 patients with non-BAD diarrhoeal diseases.

Sample analyses: The collected fasting plasma samples will be analysed for biomarkers relevant for assessing bone metabolism, including C-terminal telopeptide of type I collagen (CTX), procollagen type 1 N-terminal propeptide (P1NP), parathyroid hormone, calcium, phosphate, 25-hydroxyvitamin D. Furthermore, the levels of biomarkers of bile acid metabolism, 7 α -Hydroxy-4-cholesten-3-one (C4) and FGF19.

Preliminary results: We see a significantly altered circulating bile acid composition in individuals with BAD compared to individuals with similar symptoms not having BAD (see figure 1)

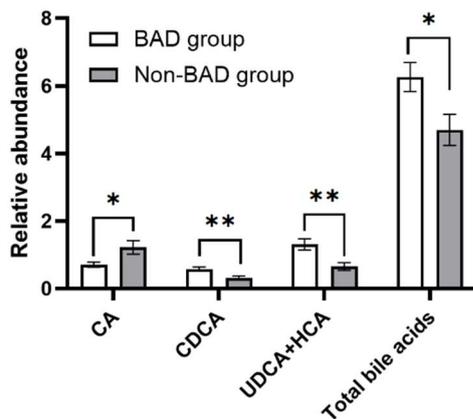


Figure 1: The relative abundance of some of the bile acids important in metabolic signaling as well as total bile acid levels in individuals living with BAD (n = 69) and individuals with similar symptoms without BAD (Non-BAD group, n = 63).

Data analysis: Groups will be compared using the Student's t-test or Mann-Whitney test depending on normality. Correlation between bile acid metabolism biomarkers and bone metabolism biomarkers will be calculated using Spearman correlation. A linear regression will be modelled and adjusted for age, sex, BMI and menopausal status.

Sample size justification: Based on the standard deviation and expected difference between the groups in CTX (primary endpoint) from previously published studies^{17,18}, a sample size of 52 patients in each group would provide an statistical significance of 0.05 and power of 80%. Thus, having n >60 in each group should suffice.

Part II: Incidence of osteoporosis and osteoporosis-related fractures in individuals with BAD compared to matches

Study design and analyses: In an already established cohort of individuals with BAD and a matched control cohort derived from the Danish health registries, we will investigate the incidence of osteoporosis and osteoporosis-related fractures. Dataset, methodologies, and collaborative partners resemble our previous registry-based investigations into BAD^{13,19,20}.

Preliminary results: Preliminary analyses indicate that there is a higher incidence of osteoporosis diagnoses and fractures among individuals with BAD compared to among age- and sex-matched controls during a follow-up of up to 15 years. Furthermore, the level of vitamin D is significantly lower in individuals with BAD compared to controls, which might suggest a mechanistic link between BAD and osteoporosis.

Expected timeline

Q4 2025: Study setup (Part II, registry-based analyses)

Q1 2026: Sample analyses (Part I, biochemical analyses), Data analyses (Part II)

Q2 2026: Data analyses (Part I), Data analyses (Part II)

Q3 2026: Interpretation and dissemination (Part I and II)

Ethical aspects

This project includes analysis of biomarkers as a posthoc analysis to an already conducted clinical trial. The participants in the trial voluntarily consented to their samples and data to be used in future related research projects. The results from this study will not benefit the participants but will shed light on an aspect of BAD not previously investigated. The concern that an association between BAD and bone metabolism disorders (such as osteoporosis) might exist has been raised by both a BAD patient involved in one of our research projects and by a gastroenterologist.

Feasibility and research environment

Part I will be carried out as a bachelor thesis project by medical student Sólva Strøm Olsen and PhD student Mads Lynggaard, MD under the supervision of Associate Professor Asger Lund, MD PhD, senior scientist and group leader Anne Marie Ellegaard, MSc PhD. The project will be carried out at Center for Metabolic Research at Gentofte Hospital, where we conduct innovative and groundbreaking research within BAD, which has previously led to changes in clinical management of this disease. Center for Clinical Metabolic Research has a well-established research infrastructure and relevant collaborations readily available for Sólva and Mads to carry out part I of this project. Part II will be carried out in close collaboration with the Center for Clinical Research and Prevention, Frederiksberg Hospital, with whom we have conducted several similar studies previously^{13,19,20}.

Perspectives

BAD is a common yet underdiagnosed, and its systemic effects remain poorly understood. Bile acids are now recognised as endocrine regulators that influence bone metabolism via FXR and TGR5 pathways. Disruption of bile acid signalling in BAD may therefore contribute to altered bone turnover and increased osteoporosis risk, but this has never been systematically studied.

By assessing bone and bile acid biomarkers in individuals with BAD and controls, this project will clarify whether BAD patients represent a high-risk group for impaired bone health. These findings could directly inform clinical monitoring and management, and lay the groundwork for future trials into this potential connection.

References

1. Lange AH, Pedersen MG, Ellegaard AM, et al. The bile–gut axis and metabolic consequences of cholecystectomy. *European Journal of Endocrinology*. 2024;190(4):R1-R9. doi:10.1093/ejendo/lvae034
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