

Odense, 6. december 2025

Colitis – Crohn Foreningen
Kongensgade 66-68, 2. TH
5000 Odense

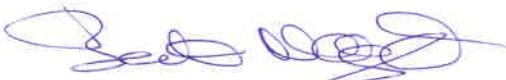
Til Colitis – Crohn Foreningen,

Hermed fremsendes ansøgning om støtte til forskningsprojekt vedrørende graviditets- og fødselsudfald hos kvinder med IBD som samtidig er i medicinsk behandling for psykisk sygdom.

Projektet er et landsdækkende registerstudie forankret ved Center for Klinisk Epidemiologi, Odense Universitetshospital, og udføres i samarbejde med forskere fra ind- og udland.

Vi håber at Colitis – Crohn Foreningen vil finde interesse for projektet hvortil vi søger om midler til dataudtræk og publiceringsafgift.

Venlig hilsen,



Forskningsleder, Professor
Bente Mertz Nørgård
Center for Klinisk Epidemiologi
Bente.noergaard@rsyd.dk



Epidemiolog, Lektor
Line Riis Jølving
Center for Klinisk Epidemiologi
Line.joelving@rsyd.dk

Vedlagt er følgende dokumenter:

- Short-form CV for ansøgere på vegne af forskningsgruppen (Forskningsleder og epidemiolog)
- Forskningsprotokol
- Lægmandsbeskrivelse
- Budget

CV - Bente Mertz Nørgård

Personal data

Bente Mertz Nørgård

Education and authorizations

1989, MD, Aarhus University, Denmark

1997, authorized specialist of internal medicine

2006, International Project Manager Education, organized by International Business College

Academic degrees

Professor, 2014, March 14th

DrMedSci, 2011, September 15th

PhD, 2002, February 18th

Dissertations

DrMedSci (doctor of medical science) thesis, 2011. Title: "Birth outcome in women with ulcerative colitis and Crohn's disease, and pharmacoepidemiological aspects of anti-inflammatory drug therapy".

PhD thesis 2002: Title: "Colitis ulcerosa, coeliaki og graviditet; en oversigt med speciel reference til forløb og sikkerhed af medicinsk behandling".

Present position and professional affiliations

Clinical Professor in clinical epidemiology, and chief physician and head of Center for Clinical Epidemiology, Odense University Hospital, and Department of Clinical Research, University of Southern Denmark. Head of Research Unit of Clinical Epidemiology, Odense University Hospital. Appointed as Lecturer at Harvard Medical School, and Senior Epidemiologist at Brigham and Women's Hospital, Boston, USA.

Appointed as adjunct clinical professor at Tufts, Department of Medicine, University School of Medicine, Boston, USA.

Associate Editor at Journal of Inflammatory Bowel Diseases, USA.

Administrative experience and key areas of research

For the past 20 years, I have been practicing full-time management and research in clinical epidemiology. Since 2007 I have been the chief physician and head of Center for Clinical Epidemiology, and I have extensive administrative experience – including day-to-day management of the department and the head of Research Unit of Clinical Epidemiology. During my research, I have focused on multiple topics related to pharmacoepidemiology, surgery, medical treatments, mental health, and reproduction in patients with autoimmune diseases, in particular inflammatory bowel diseases. I have solid experience in using Danish nationwide health registries.

International collaborations

I am experienced with international research collaborations, mainly in the USA. I have had

collaboration with research institutions and universities in Boston, USA, during the last 15 years. I am appointed as lecturer at Harvard Medical School, Senior Epidemiologist at Brigham and Women's Hospital, Boston, and adjunct clinical professor at Tufts, University School of Medicine.

Teaching and supervising

I have substantial experience in clinical epidemiological teaching. This comprises a total of 264 confrontation lectures and 114 group instruction lessons.

During that last 15 years I have supervised, and examined, more than 150 medical students at the Faculty of Health Science, University of Southern Denmark, bachelor projects.

Ongoing supervisor for three PhD students. I have been main supervisor for ten PhD students (all successful), and co-supervisor for seven PhD student (all successful).

Supervising fellows at Brigham and Women's Hospital, Boston, and Tufts, Department of Medicine, University School of Medicine, Boston, USA: at least 100 hours per year during the last 10 years.

Funding

During the last 10 years I have obtained research funding for 39.949.619 DKK.

Publications

ORCID identifier is 0000-0002-9514-3033

Web of Science ResearcherID: F-9563-2013

Number of citations: 6,110 and H-index: 41 (<https://www.researchgate.net/profile/Bente-Norgard-2/stats/citations>), assessed by April 4, 2025

Total number of published and accepted papers: 194

Total number of published papers in peer-reviewed journals: 181 (first authorships 41 and last authorships 71).

Number of published papers in peer-reviewed journals during 2018-2025: 89 (first or last author of 70 publications out of 89 (79%))

Details on all publications can be found here:

<https://portal.findresearcher.sdu.dk/da/persons/bnoergaard/publications/>

CV LINE RIIS JØLVING

December 2025

Center for Clinical Epidemiology and Research Unit of Clinical Epidemiology
OUH Odense University Hospital and University of Southern Denmark
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5000 Odense C.
Mail: line.joelving@rsyd.dk

Education and authorizations

2001, RN, Aarhus, Denmark
2003, BA in Nursing, Aarhus, Denmark
2006, Master of Science in Health, Aarhus University
2008, Certified project management, Implement Consulting Group, Denmark

Academic degree and title

2018, February 2nd, PhD in Epidemiology
2021, August 1st, Associate Professor

Disseetation

PhD thesis 2018: Title: *“Maternal chronic disease during pregnancy and long-term morbidity in the offspring”*
University of Southern Denmark, Department of Clinical Research.

Present position

Clinical epidemiologist at the Center for Clinical Epidemiology, Odense University Hospital, and the Research Unit of Clinical Epidemiology, Odense University Hospital. Associate professor in clinical epidemiology at the Department of Clinical Research.

Professional summary and scientific focus areas

I am a dedicated clinical epidemiologist with a strong focus on reproductive health, particularly the impact of maternal chronic and autoimmune diseases and related conditions on reproductive outcomes. My research encompasses a wide range of topics within clinical epidemiology, including neonatal and child health, maternal mental health, medically assisted reproductive technology, pharmacoepidemiology, and register-based study designs. With a robust academic background and extensive experience in project management, teaching, and international collaboration, I am committed to advancing the field of clinical epidemiology through innovative research and effective knowledge dissemination.

Supervision

Supervisor and examiner for Bachelor's in Medicine, University of Southern Denmark (115 students since 2015). Co-supervisor on PhD project (Mette Louise Andersen, MD, 2022-2025). Co-supervisor in a master's project in public health (Signe Marie Aagaard, MSc, 2023). Co-supervisor in a research stay at the Center for Clinical Epidemiology (Cathrine Budtz, MD, 2025).

Teaching

Data workshop in epidemiology, biostatistics, and STATA software, University of Southern Denmark (2021, 2022). Introduction to epidemiology, pre-PhD course, University of Southern Denmark (2018). Introduction to reproductive epidemiology, Department of Gynecology and Obstetrics at OUH Odense University Hospital (2019).

Board member of academic committees, networks, and the evaluation of scientific work

Representative in OUH's pre-graduate committee (2014-2017). Chair PhD defense (November 2023). Project manager of a clinical epidemiological network, Odense University Hospital, and University of Southern Denmark. Project manager CKE Talks, Center for Clinical Epidemiology (bi-weekly). Appointed censor in epidemiology, National Censor Board (2022-2026). Peer review: Scientific (PhD) protocol, October 2022. Chair of a postdoc position committee, January 2023, and reviewer of a postdoc position, May 2025. Peer reviewer for scientific journals on several occasions.

Selected funding

Independent Research Fund Denmark // 3,791,678 DKK, Aase og Ejnar Danielsens fond // 100.000 DKK, Guldsmid A L Rasmussen og hustrus fond // 48.000 DKK, Region of Southern Denmark // 443.000 DKK, Merck Group // 386.681 DKK (6-month research fellowship) + 180.000 DKK (research fellowship), Kong Christian den Tiendes Fond // 25.000 DKK, Scleroseforeningen // 200.000 DKK, Beckett Fonden // 100.000 DKK + 100.000 DKK, Region of Southern Denmark // 360.000 DKK (postdoc), Else Poulsens Mindelegat // 10.000 DKK, Direktør Jacob Madsen og Hustru Olga Madsens Fond // 10.000 DKK, Colitis-Crohn Foreningen // 50.000 DKK + 42.000 DKK + 50.000 DKK, Odense University Hospital, Free research fund // 93.000 DKK + 100.000 DKK, University of Southern Denmark // One year salary (as a PhD student), Region of Southern Denmark // One year salary (as a PhD student).

International collaborations

Ongoing collaboration with researchers at Brigham and Women's Hospital in Boston and Tufts Medical Center, Massachusetts, USA, and Harvard Medical School and Boston University, including exchange visits to Boston. Close and fruitful collaboration with associate professor Michael Due Larsen at the Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Science, Norwegian University of Science and Technology, Trondheim,

Norway, and with professor Jens Fedder from Aarhus University. Lately, I have initiated a collaboration with Professor Kenny Rodriguez-Wallberg from the Karolinska Institute in Stockholm.

Presentations

Oral presentation, Open Research Day, Region of Southern Denmark, several occasions. Poster, Advances in Inflammatory Bowel Diseases IBD, Crohn's & Colitis Foundation of America's Clinical & Research Conference, Orlando, Florida, December 2016. The poster won the best poster award in the clinical pediatric category. Article in Best Practice Rheumatology, August 2018. Poster presentation at the European Society of Human Reproduction, ESHRE congress, Vienna, June 2019. Virtual study presentation at Scleroseforeningen, October 2020.

Link to the University of Southern Denmark at PURE

[http://findresearcher.sdu.dk/portal/da/persons/line-riis-joelving\(524924f0-2e37-4535-9dd3-59630ea8c815\)/info.html?uri=cv](http://findresearcher.sdu.dk/portal/da/persons/line-riis-joelving(524924f0-2e37-4535-9dd3-59630ea8c815)/info.html?uri=cv)

Publications with peer review – published and accepted

ORCID: 0000-0002-7433-7656.

H index: 15 (Scopus). Number of citations: 573, assessed by December 2, 2025.

The total number of papers published and accepted in peer-reviewed medical journals is 39 (10 with first authorship and 2 with last authorship).

Selected papers below:

1. S. Friedman, O.S. Garvik, J. Nielsen, **Line Riis Jølvig**, M.L. Andersen, B.M. Nørgård. 2025. The consequences of preterm birth in the children of mothers with inflammatory bowel disease: A nationwide cohort study. *Inflamm Bowel Dis.* 2025 Feb. Doi: 10.1093/ibd/izaf010.
2. **Jølvig, L. R.**, Zegers, F. D., Lund, K., Wod, M., Nielsen, J., Qvist, N., Nielsen, R. G. & Nørgård, B. M. 2024. Children and Adolescents Diagnosed With Inflammatory Bowel Disease Are at Increased Risk of Developing Diseases With a Possible Autoimmune Pathogenesis. *Inflammatory Bowel Diseases.* 2025 Jan. Doi: 10.1093/ibd/izae047.
3. A. M-C., **L. R. Jølvig**, P. L. Anru, J. A. Murray, R. G. Nielsen, N. Qvist, S. Laurberg, H. Engberg, J. Kjeldsen and B. M. Nørgård. A population-based nationwide study on total colectomy for ulcerative colitis and risk of ten prevalent inflammatory or autoimmune diseases. *Scandinavian Journal of Gastroenterology.* 2023 Jul-Dec. Doi: 10.1080/00365521.2023.2231586.
4. **L.R. Jølvig**, J. Nielsen, M.L. Andersen, S. Friedman, B. M. Nørgård. 2023. Adverse birth outcomes and early life infections after in utero exposure to corticosteroids for inflammatory bowel disease: A Danish nationwide cohort study. *BMC Medicine.* 2023 Apr. Doi: 10.1186/s12916-023-02817-7.
5. S. Friedman, F. D. Zegers, **L. R. Jølvig**, J. Nielsen, B. M. Nørgård. 2022. Increased risk of postpartum infections after caesarian and vaginal delivery in women with inflammatory bowel disease: A Danish nationwide cohort study. *Inflammatory Bowel Disease.* 2023 Feb. Doi: 10.1093/ibd/izac088.
6. S. Friedman, F. D. Zegers, **L. R. Jølvig**, J. Nielsen, B. M. Nørgård. 2022. Postpartum Surgical Complications in Women with Inflammatory Bowel Disease After Caesarian Section: A Danish Nationwide Cohort Study. *Journal of Crohn's and Colitis.* 2022 May. Doi: 10.1093/ecco-jcc/jjab187.
7. **L. R. Jølvig**, P.L. Anru, J. Nielsen, S. Friedman, B. M. Nørgård. 2021. The risk of chronic diseases and congenital malformations during childhood and adolescence after in utero drug exposure to thiopurines. *Alimentary Pharmacology & Therapeutics.* 2021 Oct. Doi: 10.1111/apt.16578.
8. B. M. Nørgård, M. Wod, M. D. Larsen, S. Friedman, **L. R. Jølvig**, J. Fedder. 2021. The impact of medical therapies and factors related to treatment procedures in women with rheumatoid arthritis and inflammatory bowel disease receiving assisted reproduction: a nationwide cohort study. *Fertility and Sterility.* 2021 Dec. Doi: 10.1016/j.fertnstert.2021.07.1198.
9. **Jølvig LR**, Erb K, Nørgård BM, Fedder J, Larsen MD. 2021. The Danish National Register of assisted reproductive technology – Content and research potentials. *European Journal of Epidemiology.* 2021 Apr;36(4):445-452. doi: 10.1007/s10654-021-00742-8.
10. S. Friedman, J. Nielsen, **L. R. Jølvig**, E. A. Nohr, B. M. Nørgård. 2020. Long-term motor and cognitive function in the children of women with inflammatory bowel disease. *Journal of Crohn's and Colitis.* 2020 Dec. Doi: 10.1093/ecco-jcc/jjaa106.
11. Nørgård BM, **Jølvig LR**, Larsen MD, Friedman S. 2019. Parental IBD and Long-term Health Outcomes in the Offspring. *Inflamm Bowel Dis.* 2019 Jul. Doi: 10.1093/ibd/izy396.
12. Friedman S, Nielsen J, Nøhr EA, **Jølvig LR**, Nørgård BM. 2019. Comparison of Time to Pregnancy in Women With and Without Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol.* 2020 Jun. Doi: 10.1016/j.cgh.2019.08.031.
13. **Jølvig LR**, Nielsen J, Beck-Nielsen SS, Nielsen RG, Sonia Friedman, Kesmodel US, Nørgård BM. 2017. The Association Between Maternal Chronic Inflammatory Bowel Disease and Long-term Health Outcomes in Children – A nationwide Cohort Study. *Inflamm Bowel Dis.* 2017 Aug. Doi: 10.1097/MIB.0000000000001146.
14. **Jølvig LR**, Nielsen J, Kesmodel US, Nielsen RG, Beck-Nielsen SS, Nørgård BM. 2016. Prevalence of maternal chronic diseases during pregnancy - a nationwide population based study from 1989 to 2013. *Acta Obstet Gynecol Scand.* 2016 Nov. Doi: 10.1111/aogs.13007.

Maternal and neonatal outcomes in vulnerable women with inflammatory bowel disease and treatment-requiring psychiatric comorbidities

Specific Aims

Our study objective is to investigate adverse reproductive health outcomes in the childbirths of women with inflammatory bowel disease (IBD) who have treatment-requiring psychiatric comorbidities. We hypothesize that women with IBD who have treatment-requiring psychiatric comorbidities prior to conception experience a higher risk of adverse maternal and neonatal outcomes compared to women with IBD but without such psychiatric comorbidities.

Significance and background

Women with IBD constitute a vulnerable obstetric population with higher risks of miscarriage, preterm birth, fetal growth restriction, and maternal complications than the background population.¹⁻⁹ Women with IBD represent a high-risk obstetric population, yet the overlap between IBD and psychiatric comorbidity during pregnancy remains critically understudied. IBD and psychiatric comorbidity (e.g., depression, anxiety, bipolar disorder) may independently and interactively influence pregnancy and childbirth outcomes, influencing fertility, pregnancy course, and neonatal outcomes through biological, behavioral, and pharmacological pathways.¹⁰⁻¹² The systematic exclusion of pregnant women from clinical trials and the persistent male bias in biomedical research have created critical evidence gaps, leading to inequitable care and uncertainty in clinical decision-making.^{13,14} Moreover, psychiatric comorbidity may exacerbate IBD disease activity, reduce medication adherence, and alter health-seeking behaviors, potentially worsening maternal and fetal prognosis.¹⁵⁻¹⁷ Existing studies¹⁸ have shown that psychiatric disorders are indeed more prevalent in women with IBD compared to the general population, with depression affecting approximately 15% and anxiety affecting 21% of patients,¹⁹ and that women with IBD face increased risk of developing new-onset psychiatric conditions in the postpartum period.²⁰ According to the State of Health in the EU – Denmark Country Health Profile (2023), the estimated prevalence of depressive disorders in the Danish background population is 4.4% and anxiety disorders 5.4%.²¹ However, no studies have investigated how pre-existing, treatment-requiring psychiatric comorbidities influence childbirth outcomes within this group. Clarifying this association is essential for identifying high-risk patients and optimizing multidisciplinary care that involves gastroenterologists, obstetricians, and psychiatric health care professionals. This research addresses a significant clinical gap by investigating how treatment-requiring psychiatric comorbidity influences maternal and neonatal reproductive outcomes in women with IBD. This study will generate evidence to stratify risk better and tailor care for women with IBD and treatment-requiring psychiatric comorbidities, ultimately improving shared decision-making and clinical management. Examining psychiatric comorbidity before conception addresses a critical gap in balancing maternal mental health with fetal safety and may inform clinical guidelines on medication continuation or modification during pregnancy. The findings will also support the development of integrated care models involving gastroenterologists, obstetricians, and psychiatric health care professionals, ensuring coordinated and

equitable care for a vulnerable patient group often excluded from clinical trials, and addressing outcomes that are, in fact, preventable when appropriate initiatives are applied. By promoting more inclusive and personalized approaches to IBD care, the project aligns with current priorities in precision medicine and health equity. Improved understanding of risk factors and effective management strategies can enable earlier interventions, tailored counseling, and safer treatment plans, reducing complications such as preterm birth, miscarriage, and postpartum morbidity. Healthier pregnancies and better maternal outcomes also translate into long-term benefits for children, including reduced risk of developmental complications and chronic disease, contributing to societal well-being and reduced healthcare costs. Overall, our vision is to build a robust evidence base that supports safe, individualized, and equitable reproductive care for women with IBD and psychiatric comorbidities.

Pilot Data

The studies are expected to have adequate statistical power based on prior research, preliminary data, and access to nationwide birth data (~60,000 births annually in Denmark over 28 years, 1995–2023). We know from previous studies in our research group that from 1995-2015, 6986 women with IBD underwent pregnancy in Denmark.²² Psychiatric comorbidity and psychotropic medication-treatment, such as for depression and anxiety, is a common consequence of living with IBD, and previous studies have estimated the prevalence of IBD patients diagnosed with depression to be 15.2% and 20.7% diagnosed with anxiety.¹⁹ In our preliminary data, we have examined the use of psychotropic medications prior to conception, and we find that the prevalence has been increasing since 1997 (Figure 1). In the most recent years, approximately 8% of all the women in our IBD birth cohort used psychotropic medications within 12 months prior to conception, and this use is mainly driven by the use of antidepressant medications (Figure 1). For the background population of women without IBD, it was 5.5%, as presented in Figure 2.

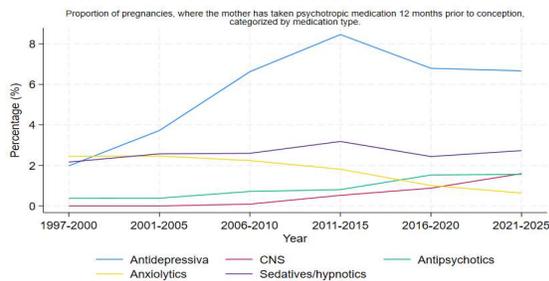


Figure 1. The proportion of pregnancies in Denmark where the mother has taken psychotropic medication, categorized by medication type, 12 months before conception from 1997 to 2025.

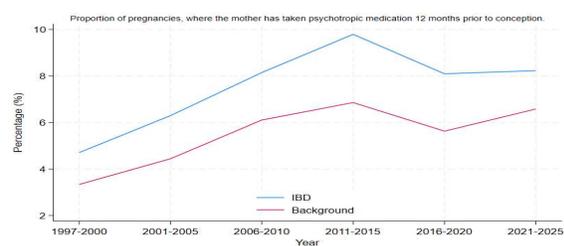


Figure 2. The proportion of pregnancies in Denmark where the mother has taken psychotropic medication 12 months before conception from 1997 to 2025. Women with inflammatory bowel disease and women in the background population.

Research Plan

The proposed project aims to investigate how psychiatric comorbidity influences maternal and neonatal outcomes in women with IBD, using high-quality, population-wide data from Danish national health registers. By linking data on diagnoses, prescriptions, and birth outcomes, we will compare outcomes between IBD pregnancies with and without recent psychotropic medication use. Outcomes include hypertensive disorders, gestational diabetes, cesarean section deliveries, preterm birth, small for gestational age (SGA), low Apgar scores, neonatal intensive care unit admission, and perinatal mortality. The study leverages Denmark's unique data infrastructure, ensuring complete follow-up and robust statistical power.

Materials and Methods

The outlined project is based on the unique Danish national health registers and covers the entire population of approximately 6 million inhabitants, and not just insured or health-system-connected individuals. The registers, including the National Prescription Register,²³ the Medical Birth Register,²⁴ and the National Patient Register²⁵ are all validated and widely used in research, and all hospital contacts must be documented. By linkage, we will be using the unique personal identification number assigned to all inhabitants in Denmark at birth or immigration, which ensures no loss to follow-up.²⁶ The different registers collectively hold comprehensive data on filled and redeemed prescriptions, surgical procedures, diagnoses, and pregnancies/childbirths from the past decades. Consistency in data coding and healthcare delivery ensures high temporal reliability. Furthermore, uniform national clinical guidelines reduce variability in diagnostic and treatment practices across the country. Medication use is classified using Anatomical Therapeutic Chemical (ATC) codes. The ATC system, a hierarchical classification system developed by the World Health Organization.²³ Diagnoses are classified according to the International Classification of Diseases System in the 8th revision (ICD-8) until 1994 and the 10th revision thereafter, and surgical procedures are classified according to the Nordic Medico-Statistical Committee (NOMESCO) codes. Because the data covers the entire population, Denmark is uniquely suited to research on rare diseases, rare exposures (e.g., specific medications before or during pregnancy), and uncommon but serious outcomes. This produces statistical power that is generally unattainable in single-hospital or insurance-based datasets.

Study population: To investigate both maternal and neonatal outcomes, two study populations will be established: one including all IBD pregnancies and one including all births by IBD patients. The IBD populations will consist of all women in Denmark with at least two recorded diagnoses of IBD, including both prevalent and incident cases, registered in The Danish National Patient Register from January 1, 1977, to the present.²⁷ For valid assessment of Crohn's disease, we will require at least two diagnoses of Crohn's disease (ICD-8 code: 56301, and ICD-10 code: K50), and for ulcerative colitis (ICD-8 codes 563.19; 569.04, and ICD-10 code: K51) registered in the National Patient Register at any

given time before conception. The exposure of psychotropic medication will be identified in the National Prescription Register using ATC classification codes as follows: Antidepressants (ATC: N06A), Central nervous system (CNS) stimulating agents (ATC: N06B), Antipsychotics (ATC: N05A), Anxiolytics (ATC: N05B), Sedatives/hypnotics (ATC: N05C).

Exposed and unexposed cohorts: Women with IBD having treatment-requiring psychiatric comorbidities before conception will constitute the exposed cohorts. Treatment-requiring psychiatric comorbidities will be defined as having at least one redeemed prescription for psychotropic medication within a period of i) 6 months and ii) 12 months preceding conception. Women with IBD without redeemed prescriptions for psychotropic medication in the same period will constitute the unexposed cohort. In the study of neonatal outcomes, exposure will be defined based on maternal status (psychiatric comorbidity or not). Children born to mothers with IBD who had a treatment-requiring psychiatric comorbidity before conception or during pregnancy (as defined above) will constitute the exposed group. Children born to mothers with IBD without treatment-requiring psychiatric comorbidities in the same period will constitute the unexposed group. Based on the above, two sub-studies will be conducted.

Study I. Adverse maternal outcome during pregnancies in women with IBD having treatment-requiring psychiatric comorbidities: The study outcomes include hypertensive disorders of pregnancy (including gestational hypertension and preeclampsia), gestational diabetes, and mode of delivery (vaginal/cesarean section).

Study II. Adverse child outcomes in women with IBD having treatment-requiring psychiatric comorbidities: SGA, preterm birth (<37 weeks), low Apgar score (<7 at 5 minutes), neonatal intensive care unit admission, and perinatal or neonatal mortality (includes stillbirth > 22 weeks of gestation or death within the first 28 days of life).

Statistics: Multivariable logistic regression adjusting for age, parity, assisted reproduction, IBD disease characteristics (subtype, duration of disease, IBD-related surgery), medication use, comorbidities, body mass index, smoking, and obstetric history. Risk estimates will be reported as odds ratios (OR) with 95% confidence intervals (CI). The most frequent outcomes of interest are cesarean section, with a prevalence in Denmark of 20-21%, and the rarest outcome is low Apgar score, with a prevalence of <1%.²⁸ Power analyses show sufficient power ($\geq 80\%$) to detect a relative risk of 1.2 for cesarean section and 2.02 for low Apgar score.

Description of the research environment

The study will be conducted within the collaborative research environment at Odense University Hospital, Odense, Denmark, in the Department of Clinical Epidemiology and under the leadership of an interdisciplinary team with both clinical and epidemiological expertise. We are very familiar with the

use of the Danish nationwide health registries and the application of relevant epidemiological methods to clinical research questions. Our research group is qualified to perform these studies, and we have data managers, biostatisticians, and epidemiologists who are experienced in performing pharmacoepidemiologic studies. The preliminary data confirm sufficient sample size and exposure prevalence to ensure adequate statistical power. Ethical approvals and data access procedures are well-established, further supporting timely and successful project execution. We have a productive and long-lasting collaboration between the Division of Gastroenterology at Tufts Medical Center in Boston, Massachusetts, and the Center for Clinical Epidemiology at Odense University Hospital in Odense, Denmark. The main investigators of this project are Professor Bente Nørgård MD, PhD, DMSc, and colleagues. Dr. Nørgård will contribute expert oversight in epidemiological design and data interpretation, ensuring the robustness of registry analyses and statistical methodology, and will offer international expertise and cross-disciplinary input, enhancing study design, interpretation, and global contextualization of results. Co-investigators, PhD Line Riis Jølving, MD, PhD Mette Louise Andersen, MD, Sonia Friedman, Tuft Medical Center in Boston, will provide clinical obstetric perspectives, guiding patient selection, clinical data interpretation, and the translation of findings into obstetric care recommendations, and biostatistician Pavithra Laxsen Anru will lead the biostatistical analysis. Professor Jens Kjeldsen from the Department of Gastroenterology at Odense University Hospital will contribute his extensive clinical and research experience in IBD, providing clinical interpretation and relevance of findings. His involvement ensures that the project is closely aligned with current gastroenterological practice in Denmark and facilitates translation of results into evidence-based gastroenterological recommendations. This coordinated interdisciplinary project, with strong international anchoring, ensures clinically relevant research.

Approvals

There are no legal or ethical obstacles associated with these studies. The protocol is approved by the health research in the Region of Southern Denmark (journal no. 22/45337), and the conducted studies will follow all currently applicable Danish laws regarding scientific research. According to Danish law, research based on registries can be performed without patient consent and approval from the ethical committee.

References

1. Friedman S, Nielsen J, Qvist N, et al. Does Surgery Before Pregnancy in Women With Inflammatory Bowel Disease Increase the Risk of Adverse Maternal and Fetal Outcomes? A Danish National Cohort Study. *The American journal of gastroenterology*. Mar 25 2024;doi:10.14309/ajg.0000000000002732
2. Friedman S, Zegers FD, Riis Jolving L, Nielsen J, Norgard BM. Postpartum Surgical Complications in Women with Inflammatory Bowel Disease After Caesarian Section: A Danish Nationwide Cohort Study. *J Crohns Colitis*. May 10 2022;16(4):625-632. doi:10.1093/ecco-jcc/jjab187
3. Norgard BM, Friedman S, Kjeldsen J, Nielsen J. The safety of paternal and maternal use of 5-aminosalicylic acid during conception and pregnancy: a nationwide cohort study. *Alimentary pharmacology & therapeutics*. Nov 2022;56(9):1349-1360. doi:10.1111/apt.17189
4. Kammerlander H, Nielsen J, Kjeldsen J, et al. Fecal Calprotectin During Pregnancy in Women With Moderate-Severe Inflammatory Bowel Disease. *Inflammatory bowel diseases*. Feb 28 2018;doi:10.1093/ibd/izx055
5. Friedman S, Larsen PV, Fedder J, Norgard BM. The Efficacy of Assisted Reproduction in Women with Inflammatory Bowel Disease and the Impact of Surgery-A Nationwide Cohort Study. *Inflamm Bowel Dis*. Feb 2017;23(2):208-217. doi:10.1097/MIB.0000000000000996
6. de Silva PS, Hansen HH, Wehberg S, Friedman S, Norgard BM. Ectopic pregnancy in women with inflammatory bowel disease - a 22 year nationwide cohort study. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association*. Jul 07 2017;doi:10.1016/j.cgh.2017.06.054
7. Winter RW, Larsen MD, Magnussen B, Friedman S, Kammerlander H, Norgard BM. Birth outcomes after preconception paternal exposure to methotrexate: A nationwide cohort study. *Reprod Toxicol*. Dec 2017;74:219-223. doi:10.1016/j.reprotox.2017.10.004
8. Jolving LR, Nielsen J, Beck-Nielsen SS, et al. The Association Between Maternal Chronic Inflammatory Bowel Disease and Long-term Health Outcomes in Children-A Nationwide Cohort Study. *Inflamm Bowel Dis*. Aug 2017;23(8):1440-1446. doi:10.1097/MIB.0000000000001146
9. Norgard BM, Larsen PV, Fedder J, de Silva PS, Larsen MD, Friedman S. Live birth and adverse birth outcomes in women with ulcerative colitis and Crohn's disease receiving assisted reproduction: a 20-year nationwide cohort study. *Gut*. May 2016;65(5):767-76. doi:10.1136/gutjnl-2015-311246
10. Nillni YI, Wesselink AK, Gradus JL, et al. Depression, anxiety, and psychotropic medication use and fecundability. *Am J Obstet Gynecol*. Oct 2016;215(4):453 e1-8. doi:10.1016/j.ajog.2016.04.022
11. Momen NC, Chatwin H, Holde K, et al. Maternal mental disorders and neonatal outcomes: Danish population-based cohort study. *Br J Psychiatry*. Jan 2025;226(1):31-38. doi:10.1192/bjp.2024.164
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Lægmandsbeskrivelse af registerforskningsprojekt omhandlende graviditets- og fødselsudfald hos kvinder med kronisk inflammatorisk tarmsygdom og medicinsk behandlet psykiatrisk sygdom

Kvinder med inflammatorisk tarmsygdom (IBD) har en øget risiko for at opleve komplikationer under graviditet og fødsel. Denne risiko kan være endnu mere udpræget hos kvinder, der samtidig har psykiske lidelser som depression, angst eller bipolar sygdom, som kræver medicinsk behandling. Dette registerforskningsprojekt undersøger, hvordan disse psykiske lidelser, som behandles medicinsk sideløbende med IBD, påvirker både mødres og børns helbred i forbindelse med graviditet og fødsel. Vi ved fra tidligere forskning, at IBD og psykiske lidelser hver for sig kan påvirke graviditetsforløb, fødsel og barnets sundhed. Når tilstandene optræder samtidig, kan de forværre sygdomsaktivitet, mindske medicin-efterlevelse og ændre patienternes sundhedssøgende adfærd. Alligevel er denne gruppe kvinder ofte udeladt fra kliniske studier, hvilket skaber betydelige videns huller og ulighed i sundhed. Projektet vi her søger om forskningsstøtte til, anvender de nationale danske sundhedsregistre med data fra næsten 30 års fødsler og inkluderer alle kvinder med IBD der har født et eller flere børn i perioden, og hvoraf nogle har fået behandling for psykiske lidelser før graviditeten. Vi undersøger, om disse kvinder har øget risiko for komplikationer som svangerskabsforgiftning, fødsler med kejsersnit og for tidlig fødsel, samt hvordan det påvirker barnets helbred – fx som lav Apgar-score, indlæggelse på neonatalafdeling og dødfødsel. Resultaterne vil hjælpe sundhedsprofessionelle i et tværfagligt perspektiv, med bedre rådgivning og behandling af gravide med IBD og psykiske lidelser. Dette kan føre til tidligere indsatser, mere målrettet pleje og bedre sundhed for både mor og barn. Projektet fremmer også lighed i sundhed ved at fokusere på en gruppe, som ofte overses i forskning og er af yderste relevans da der stadig kommer flere patienter med IBD i Danmark.

Reproductive health in VU IBD patients

All costs are listed in DKK

All project years, budget headings	Application CCF	Applied from other funds	Own-Financing	Total
VIP-SALARY-EXPENSES:				
Senior clinical epidemiologist, 3 months salary (a)		206.035		206.035
Senior data management and biostatistician, 3 months salary (a)		206.035		206.035
Senior clinical expertise, professor in clinical epidemiology (Odense)			89.022	89.022
Senior clinical expertise, professor in gastroenterology			44.511	44.511
Senior clinical expertise gynecology and obstetrics			44.511	44.511
TAP-SALARY-EXPENSES:				
Laboratory technician				
Projectmanager/coordinator				
Secretary				
Student associate				
APPARATUS:				
Data from central datasources	50.000			50.000
Datastorage at Sundhedsdatastyrelsen		30.000		30.000
Software license (Stata and Stattransfer)		5.000	5.000	10.000
TRAVEL & MEETING ACTIVITIES:				
Travel				
Workshop and meeting representation				
Dissemination of study results				
OTHER OPERATIONAL EXPENSES:				
Involvement of patient and relative representatives (meeting expenses/"thank you")				
Open Access publication expenses	20.000			20.000
Facilities			20.000	20.000
Assistance for writing, language and proofreading				
Materials for dissemination				
Course - leader courses for main applicant				
TOTAL EXPENSES BEFORE OVERHEAD	70.000	447.070	203.044	720.114
OVERHEAD EXPENSES:				
Cost for accounting, administration, financial reporting and legal consulting				
5% overhead expenses	3.500	22.353		25.853
TOTAL EXPENSES	73.500	469.423	203.044	745.967

a) 2026, total budget-load (DKK)

68.678