

ANNUAL REPORT 2019

CENTER FOR CLINICAL EPIDEMIOLOGY

Center for Clinical Epidemiology
Research Unit for Clinical Epidemiology
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Region of
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UNIVERSITY OF SOUTHERN DENMARK

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WELCOME

We welcome everybody with an interest in clinical epidemiology and data analysis. We ask anyone with a project, advisory task or research project, in the need of assistance within clinical epidemiology and data analysis, to contact us:

Bente Mertz Nørgård – bente.noergaard@rsyd.dk,

Susanne Møllerstrøm – susanne.moellerstroem@rsyd.dk.

The vision of Center for Clinical Epidemiology is to be known and respected for projects and research within clinical epidemiology at an international level, and to provide expert knowledge within a wide range of diseases and clinical epidemiological methods to solve issues regarding the prognosis for patients. We want the staff at the Center for Clinical Epidemiology to be desirable collaborators in local, regional, national, and international projects and research activities.

Our mission is to ensure correct diagnosis and treatment of patients through research results and thereby to ensure that all clinical decisions in the treatment processes are evidence based. We want to focus especially on research findings that can be applied and implemented in the daily clinical practice.

Center for Clinical Epidemiology handles the following activities:

1. Special projects and consultancy services within clinical epidemiology and data analysis
2. Clinical epidemiological research and academic work

Apart from the above activities, the center houses and supports tasks for the RKKP (the regional clinical quality program - the Danish Clinical Registries).

In 2019 we published 28 peer reviewed articles in international medical journals, and we have brought external fundraising into a special focus of interest.

Bente Mertz Nørgård

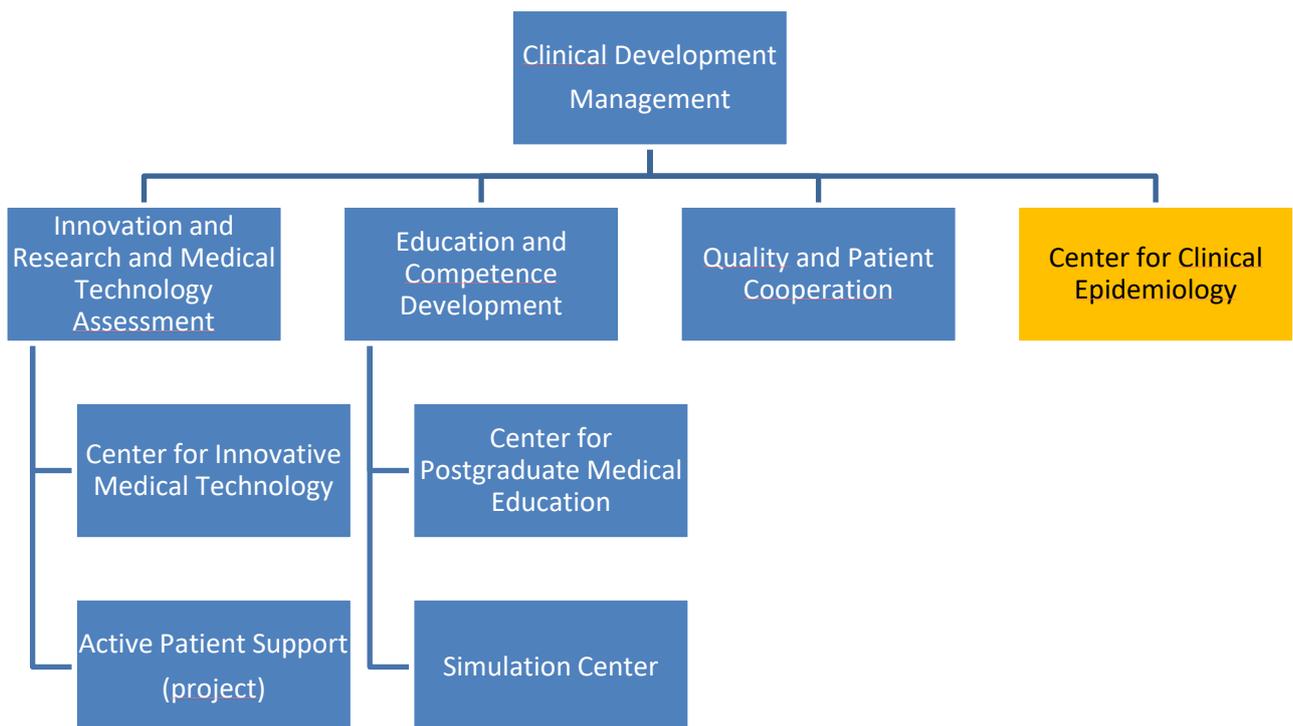
Professor and head of Center for Clinical Epidemiology and the Research Unit of Clinical Epidemiology

ORGANIZATION

The center is affiliated with the Department of Clinical Development, Odense University Hospital, as an independent unit and all research activities from the research unit refer to the Department of Clinical Research, University of Southern Denmark.

An overview of the staff at the Center for Clinical Epidemiology is available at our web-site: www.ouh.dk/cke

Clinical Development



WORKING RELATIONS

Activities within the following special projects and consultancy tasks in particular have occupied the center's resources in 2019 (the following is not a complete list of consultancy functions):

Center for Clinical Epidemiology has provided the Danish Clinical Registries (RKKP) with a number of consultancy services in 2019. The support has been given within the area of clinical epidemiology to a number of national clinical databases.

The cooperation with Emergency Medicine, Odense University Hospital, concerning the daily operation of "The emergency cohort of Southern Denmark" has been ongoing for several years. The database comprises data on all patients admitted via the Emergency Medicine Units in the Region of Southern Denmark; the project is based on a cooperation with Professor Annmarie Lassen established in 2012 and is to be continued also in 2020.

Many staff members in the Center for Clinical Epidemiology handled consultancy tasks for a number of external parties locally, regionally and nationally, all within clinical epidemiology and data analysis. For instance: A consultancy agreement on a project on antibiotic use, with the Focused Research Unit in Emergency Medicine, Institute of Regional Health Research, University of Southern Denmark, was inaugurated in 2017. Data from all acutely admitted patients were collected, followed by six months of implementing an antibiotic stewardship program, and finalized by another six months of data collection from all acutely admitted patients. Data comprising variables of microbiology, antibiotics, and clinics were compiled and analyzed by our employees.

A consultancy agreement with Jesper Ryg, Department of Geriatrics, is ongoing and we analyze data on the complexity of treatment of elder medical and geriatric patients with multimorbidities. The consultancy agreement has also focused on the analyses of data from The Falls Clinic, a specialized outpatient unit offering systematic evaluation

and treatment of causes of falling and instability. This collaboration will continue in 2020.

Our collaboration with Isik Somuncu Johansen and The Department of Infectious Diseases, Odense University Hospital, was established in 2017. We have an ongoing fruitful collaboration with several researchers from the department on several projects related to tuberculosis, bacteremia, and sepsis biomarkers. This collaboration will continue in 2020.

We have an advisory cooperation with Berit Schiøttz-Christensen, Rygcenter Middelfart (Research Department Spine Centre of Southern Denmark, Hospital Lillebaelt, Middelfart) on a number of projects including two main projects

- 1) Incidence and regional variation of Morbus Bechterew and Spondyloarthritis from 2000-2013: A nationwide cohort study. The aim of the study is to describe the incidence of ankylosing spondylitis and spondyloarthritis in the Danish population from 2000-2013, for the whole nation and for each of the five regions to evaluate if there is a trend over time explained by use of magnetic resonance imaging.
- 2) Prognostic factors of the patients' course when referred to the Spine Centre of Southern Denmark for decision support. The aim of this project is to describe a course of disease and the effect of prognostic factors in the process. Based on the identified prognostic models algorithms are set up to develop individually adapted decision support tools. This collaboration will continue in 2020.

Regarding all working partners related to research projects please see the chapter "Research activities".

RESEARCH ACTIVITIES

The Research Unit of Clinical Epidemiology was established in 2009 with the purpose of handling all research and academic activities in the center. The unit is academically affiliated with the Department of Clinical Research at the University of Southern Denmark.

Several of the employees at the Center for Clinical Epidemiology have a formal academic employment at the Department of Clinical Research. We have a clinical professorship which is also linked to the daily management at the center, and academic affiliations (associate professors) of two biostatisticians and three clinical epidemiologists. One clinical epidemiologist was in 2019 appointed as postdoc. The professor of the department, Bente Mertz Nørgård, is also nominated as Senior Epidemiologist at the Brigham and Women's Hospital, Boston, and lecturer, part-time, at Harvard Medical School.

Three adjunct professors

The Research Unit of Clinical Epidemiology has affiliated an adjunct professor in clinical epidemiology (Sonia Friedman, MD, Visiting Professor Harvard Medical School and Brigham and Women's Hospital, Boston). Sonia Friedman is an expert within chronic inflammatory bowel disease and reproduction issues. At the same time Sonia Friedman is an associated professor at Harvard University, Boston.

The Research Unit of Clinical Epidemiology has also affiliated Pedro Manuel Sarmento Rodrigues Póvoa, Unidade de Cuidados Intensivos Polivalente, MD, Hospital de São Francisco Xavier, Lisbon, as an adjunct professor. Pedro Póvoa is an expert researcher within areas related to intensive care and patients suffering from sepsis. Pedro Póvoa has especially focused on the importance of C-reactive protein of which daily records exceed a single count in monitoring the patient's condition.

In 2019, the Research Unit of Clinical Epidemiology has further affiliated Fernando Godinho Zampieri, MD, HCor-Hospital do Coração, São Paulo, Brazil, as an adjunct

professor. Fernando Zampieri is an expert researcher within critical care medicine and will especially focus on critically ill patients and enhanced statistical models.

Research areas

The employees at Center for Clinical Epidemiology conduct their own initiated and funded research projects in collaboration with domestic and foreign researchers. Our research is mainly within the following areas (for the specific publications please refer to the last chapter 'Publications'):

- Cancer
- Acute medicine and intensive care
- Sepsis
- Bowel diseases and chronic inflammatory bowel disease
- Human reproduction
- Chronic diseases
- Obstetrics
- Gynecology
- Psychiatry
- Geriatrics
- Social medicine

Regarding research areas we kindly refer to our research strategy:

<http://www.ouh.dk/wm220632>

Presentations and congresses

- February. At Center for Innovative Medical Technology, CIMT academy. Topic: Center for Clinical Epidemiology, Big data, Machine learning, Real World Data. Invited speaker
- Poster presentation, ECCO Congress, 7-9 March 2019, Copenhagen: Anti-TNF α therapy, use of corticosteroids, and colectomy among pediatric and adolescent patients with ulcerative colitis – nationwide study

- Oral presentation. Open Research, 25 April 2019, Region of Southern Denmark, Fredericia: Reassuring results on the chance of a live born child in women with multiple sclerosis receiving assisted reproduction
Oral presentation: The impact of anti-TNF α therapy on colectomy rates and corticosteroid treatment among 3001 pediatric and adolescent patients with ulcerative colitis – a nationwide study from 1995-2015
- Falk Forum IBD conference. Royal College of Physicians of Ireland. Pregnancy, surgery and sexual dysfunction in inflammatory bowel disease, 26th April 2019.
Oral presentation: What the Danish IBD databases/registries have taught us about IBD?
- Oral presentation and a poster presentation. ESHRE 35th Annual Meeting June 23-26, 2019 – European Society of Human Reproduction and Embryology in Vienna, Austria: No decreased chance of a live born child in women with epilepsy after assisted reproduction treatment: a nationwide cohort study
Poster presentation: Reassuring results on the chance of a live born child in women with multiple sclerosis receiving assisted reproduction
- 12th Annual Inflammatory Bowel Disease: The Art and Science in the Diagnosis and Treatment, 13-14 September, Boston
- NorPEN congress, 12-13 November 2019, Aarhus
- Poster presentation, Nordic IBD congress, 28-29 November 2019, Malmø: Anti-TNF α alone or as combination therapy with immunomodulators in pediatric and adolescent patients with Crohn's disease – a nationwide cohort study

International work stays

Three day visit from Lisbon, February 2019 (adjunct professor Pedro Póvoa)

One week visit in Boston, March 2019 (Bente Mertz Nørgård)

One week visit from São Paulo, Brazil, April 2019 (adjunct professor, Fernando Zampieri)

Three day visit from Lisbon, July 2019 (adjunct professor Pedro Póvoa)

One week visit in Boston, August 2019 (Line Riis Jølving, Ken Lund)

One week visit from Boston, October 2019 (adjunct professor Sonia Friedman)

Two day visit from Lisbon, October 2019 (adjunct professor Pedro Póvoa)

PHD-STUDENTS

Phd-students supervised by Center for Clinical Epidemiology staff members, 2019

- Majken Munk Brønserud: Patientrapporteret livskvalitet hos lungecancer patienter – Anvendelse af patientrapporterede oplysninger (PRO) som kvalitetsindikator (Patient reported quality of life in patients with lung cancer – Applied patient reported information as a quality indicator). Defended October 2019
- Ken Lund: Disease control in pediatric and adolescent patients with inflammatory bowel disease: aspects of Anti-TNF- α and physical activity. Ongoing.
- Pernille Sanberg Ljungdahl: Psychiatric comorbidity in Back Pain Disorders – Risk, treatment and pharmaco-epidemiological analysis. Ongoing.
- Sara Bønløkke Simonsen: Project description for the study "Risk of cancer among women with prior cervical precancer: a register-based study". Ongoing.
- Line Holdgaard Thomsen: Risk factors of epithelial ovarian cancer among women with endometriosis: An epidemiologic study based on Danish registries and an endometriosis specific questionnaire. Ongoing.

Future PhD-students at the center:

- Christina Gaarslev: Fathers' use of medications and risks related to reproduction.
- Mette Louise Andersen: Women with multiple sclerosis and pregnancy and child outcomes
- Simone Faurholt Simonsen: Pivmecillinam in the treatment of community-acquired lower urinary tract infections in women – short and long term implications

ACADEMIC ASSESSMENT

In 2019 the staff at the Center for Clinical Epidemiology has

- worked as reviewers for scientific journals
- evaluated research protocols for local, national, and international scientific foundations
- participated in scientific congresses nationally and internationally
- given scientific oral presentations nationally and internationally
- undertaken assessments of PhD protocols and dissertations for the Faculty of Health Sciences at the University of Southern Denmark and other universities in Denmark
- acted as chairman of the evaluation committee of PhD dissertations
- acted as board member of the evaluation committee for a clinical professorship
- been appointed as censors
- undertaken censorship tasks for the medical educations in Denmark
- supervised PhD students
- acted as member of OUH's Forskningsråd (Odense University Hospital Research council)

TEACHING

The staff at the center has trained, supervised, and examined a large number of bachelor students and master's thesis students at the Faculty of Health Sciences at University of Southern Denmark.

FUNDINGS

The following foundations have supported a number of projects:

Helsefonden: Social inequality and lung cancer treatment

Augustinusfonden: Assisted reproduction, steroid treatment and inflammatory bowel disease. Scleroseforeningen: Participation in congress, ESHRE

OUH innovationspulje: Project in machine learning

Pharmadanmark: Assisted reproduction and epilepsy

OUH (Odense University Hospital), free funds: Assisted reproduction and child outcomes

OUH (Odense University Hospital), free funds: Medications in pregnancy and child outcomes

Brigham and Women's Hospital, Boston: Studies on women with inflammatory bowel disease and reproduction.

PUBLICATIONS

Scientific publications

In 2019, 28 papers were published in peer-reviewed journals (extracted date: 18 December 2019). Please refer to **the list below** or our web-site

[http://findresearcher.sdu.dk/portal/en/organisations/klinisk-epidemiologi\(ad64bacf-78d9-4b18-84a3-53070d6bc23a\)/publications.html?filter=researchhttp%3A%2F%2F](http://findresearcher.sdu.dk/portal/en/organisations/klinisk-epidemiologi(ad64bacf-78d9-4b18-84a3-53070d6bc23a)/publications.html?filter=researchhttp%3A%2F%2F)

1. On behalf of the Nine-i Investigators (2019). Expert statement on the ICU management of patients with thrombotic thrombocytopenic purpura. *Intensive Care Medicine*, 45(11), 1518-1539. <https://doi.org/10.1007/s00134-019-05736-5>
2. Bay-Richter, C., Buttenschøn, H. N., Mors, O., Eskelund, A., Budac, D., Kærlev, L., & Wegener, G. (2019). Latent toxoplasmosis and psychiatric symptoms – A role of tryptophan metabolism? *Journal of Psychiatric Research*, 110, 45-50. <https://doi.org/10.1016/j.jpsychires.2018.12.016>
3. Brønserud, M. M., Iachina, M., Green, A., Groenvold, M., Dørflinger, L., & Jakobsen, E. (2019). Patient-reported outcomes (PROs) in lung cancer: Experiences from a nationwide feasibility study. *Lung Cancer*, 128, 67-73. <https://doi.org/10.1016/j.lungcan.2018.12.014>
4. Brønserud, M. M., Iachina, M., Green, A., Groenvold, M., & Jakobsen, E. (2019). Patient reported outcome data as performance indicators in surgically treated lung cancer patients. *Lung Cancer*, 130, 143-148. <https://doi.org/10.1016/j.lungcan.2019.02.010>
5. Eriksson, M., Kaerlev, L., Johansen, P., Afonso, N., Ahrens, W., Costa-Pereira, A., ... Sabroe, S. (2019). Tobacco smoking and alcohol consumption as risk factors for thymoma - A European case-control study. *Cancer Epidemiology*, 61, 133-138. <https://doi.org/10.1016/j.canep.2019.06.008>
6. Froes, F., Pereira, J. G., & Póvoa, P. (2019). Outpatient management of community-acquired pneumonia. *Current Opinion in Pulmonary Medicine*, 25(3), 249-256. <https://doi.org/10.1097/MCP.0000000000000558>
7. Hansen, M. F., Lose, G., Sigurdardóttir, H. B., & Gradel, K. O. (2019). A Danish national population-based cohort study of synthetic midurethral slings, 2007–2011. *International Urogynecology Journal*, 30(5), 733-741. <https://doi.org/10.1007/s00192-018-3719-y>
8. Husby, K. R., Larsen, M. D., Lose, G., & Klarskov, N. (2019). Surgical treatment of primary uterine prolapse: a comparison of vaginal native tissue surgical techniques. *International Urogynecology Journal*, 30(11), 1887-1893. <https://doi.org/10.1007/s00192-019-03950-9>
9. Iachina, M., Ljungdalh, P. M., Sørensen, R. G., Kaerlev, L., Blaakær, J., Trosko, O., ... Nørgård, B. M. (2019). Influence of Prior Psychiatric Disorders on the Treatment Course of Gynaecological Cancer – A Nationwide Cohort Study. *Clinical Oncology*, 31(2), 115-123. <https://doi.org/10.1016/j.clon.2018.11.006>

10. Jølvig, L. R., Larsen, M. D., Fedder, J., Friedman, S., & Nørgård, B. M. (2019). The chance of a live birth after assisted reproduction in women with thyroid disorders. *Clinical Epidemiology*, 11, 683-694. <https://doi.org/10.2147/CLEP.S208574>
11. Jørgensen, S. L., Mogensen, O., Wu, C., Korsholm, M., Lund, K., & Jensen, P. T. (2019). Survival after a nationwide introduction of robotic surgery in women with early-stage endometrial cancer: A population-based prospective cohort study *EJC*, 109, 1-11. <https://doi.org/10.1016/j.ejca.2018.12.004>
12. Jørgensen, S. L., Mogensen, O., Wu, C., Lund, K., Iachina, M., Korsholm, M., & Jensen, P. T. (2019). Nationwide Introduction of Minimally Invasive Robotic Surgery for Early-Stage Endometrial Cancer and Its Association With Severe Complications. *JAMA Surgery*, 154(6), 530-538. <https://doi.org/10.1001/jamasurg.2018.5840>
13. Korzenik, J., Larsen, M. D., Nielsen, J., Kjeldsen, J., & Nørgård, B. M. (2019). Increased risk of developing Crohn's disease or ulcerative colitis in 17 018 patients while under treatment with anti-TNF α agents, particularly etanercept, for autoimmune diseases other than inflammatory bowel disease. *Alimentary Pharmacology and Therapeutics*, 50(3), 289-294. <https://doi.org/10.1111/apt.15370>
14. Larsen, M. D., Guldberg, R., & Lose, G. (2019). Perioperative cardiovascular complications following urogynecological operations. *Acta Obstetrica et Gynecologica Scandinavica*, 98(1), 61-67. <https://doi.org/10.1111/aogs.13457>
15. Lund, K., Larsen, M. D., Knudsen, T., Kjeldsen, J., Nielsen, R. G., & Nørgård, B. M. (2019). The impact of anti-TNF α therapy on colectomy rates and corticosteroid treatment among 3001 paediatric and adolescent patients with ulcerative colitis—a nationwide study from 1995 to 2015. *Alimentary Pharmacology and Therapeutics*, 50(10), 1077-1085. <https://doi.org/10.1111/apt.15510>
16. TAVeM study Group (2019). The association of cardiovascular failure with treatment for ventilator-associated lower respiratory tract infection. *Intensive Care Medicine*, 45(12), 1753-1762. <https://doi.org/10.1007/s00134-019-05797-6>
17. Nørgård, B. M., Magnussen, B., Fedder, J., de Silva, P. S., Wehberg, S., & Friedman, S. (2019). The Risk of Elective Abortion in Women With Crohn's Disease and Ulcerative Colitis: A Nationwide Cohort Study. *Inflammatory Bowel Diseases*, 25(3), 561–567. <https://doi.org/10.1093/ibd/izy263>
18. Nørgård, B. M., Larsen, M. D., Friedman, S., Knudsen, T., & Fedder, J. (2019). Decreased chance of a live born child in women with rheumatoid arthritis after assisted reproduction treatment: a nationwide cohort study. *Annals of the Rheumatic Diseases*, 78(3), 328-334. <https://doi.org/10.1136/annrheumdis-2018-214619>
19. Nørgård, B. M., Jølvig, L. R., Larsen, M. D., & Friedman, S. (2019). Parental IBD and Long-term Health Outcomes in the Offspring. *Inflammatory Bowel Diseases*, 25(8), 1339-1348. <https://doi.org/10.1093/ibd/izy396>
20. Nørgård, B. M. (2019). Fædres brug af azathioprin/6-mercaptopurin/methotrexat og sygelighed hos børnene. *Best Practice Nordic. Psykiatri*.
21. Póvoa, P., Coelho, L., & Bos, L. J. (2019). Biomarkers in Pulmonary Infections. *Clinical Pulmonary Medicine*, 26(4), 118-125. <https://doi.org/10.1097/CPM.0000000000000322>

22. Thønnings, S., Jansåker, F., Gradel, K. O., Styrishave, B., & Knudsen, J. D. (2019). Cefuroxime compared to piperacillin/tazobactam as empirical treatment of *Escherichia coli* bacteremia in a low extended-spectrum beta-lactamase (ESBL) prevalence cohort. *Infection and Drug Resistance*, 12, 1257-1264. <https://doi.org/10.2147/IDR.S197735>
23. Vammen, M. A., Mikkelsen, S., Forman, J. L., Hansen, Å. M., Bonde, J. P., Grynderup, M. B., ... Thomsen, J. F. (2019). Emotional demands and exhaustion: cross-sectional and longitudinal associations in a cohort of Danish public sector employees. *International Archives of Occupational and Environmental Health*, 92(5), 639-650. <https://doi.org/10.1007/s00420-018-01398-w>
24. Friedman, S., & Nørgård, B. M. (2019). Confirming Complexity: Assessing Environmental and Genetic Risk Factors for Inflammatory Bowel Disease. *Gastroenterology*, 156(8), 2124-2125. <https://doi.org/10.1053/j.gastro.2019.04.030>
25. Korzenik, J., Larsen, M. D., Nielsen, J., Kjeldsen, J., & Nørgård, B. M. (2019). Editorial: anti-TNF therapy-a double-edged sword? Authors' reply. *Alimentary Pharmacology and Therapeutics*, 50(7), 823-824. <https://doi.org/10.1111/apt.15459>
26. Póvoa, P., & Coelho, L. (2019). Clinical significance of viral detection in critically ill patients more questions than answers. *American Journal of Respiratory and Critical Care Medicine*, 199(4), 411-413. <https://doi.org/10.1164/rccm.201809-27>
27. Taniguchi, L. U., & Póvoa, P. (2019). Leptospirosis: one of the forgotten diseases. *Intensive Care Medicine*, 45(12), 1816-1818. <https://doi.org/10.1007/s00134-019-05839-z>
28. Friedman, S., & Nørgård, B. M. (2019). Response to Zhao et al. *The American Journal of Gastroenterology*, 114(2), 358-359. <https://doi.org/10.14309/ajg.000000000000119>