

ANNUAL REPORT 2020

CENTER FOR CLINICAL EPIDEMIOLOGY

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**Center for
Clinical Epidemiology**

OUH
Odense
University Hospital

Region of
Southern Denmark

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 all patients through research results and thereby to ensure that all clinical decisions in the treatment 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 2020 we published 45 peer reviewed articles in international medical journals, and we have brought external fundraising into a special focus of interest.

Bente Mertz Nørgård

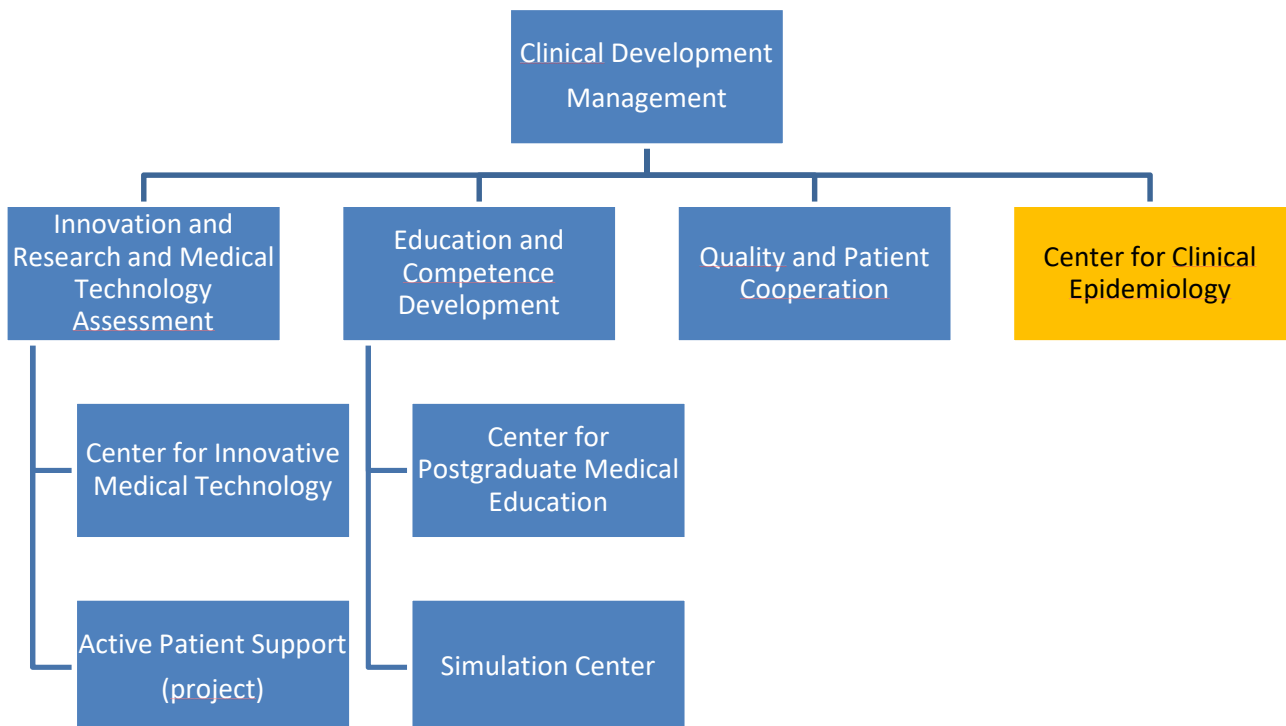
Professor and head of Center for Clinical Epidemiology and the Research Unit of Clinical Epidemiology

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: <http://www.ouh.dk/wm270762>

Clinical Development



WORKING RELATIONS

Activities within the following special projects and consultancy tasks in particular have occupied the center's resources in 2020 (the following is not a complete list of consultancy functions):

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 2021.

We have a consultancy agreement with Professor Carsten Bindslev-Jensen (Dermatology and Allergy, OUH). During the last years we have supported a clinical database (AC Basen, OUH) with academic data management (new data integrations, linkage of data, data extraction). The database is hosted at Odense Research Center for Anaphylaxis, Dermatology and Allergy, OUH.

A consultancy agreement with Professor 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.

Our collaboration with Head of research 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 2021.

We have had an advisory cooperation with Professor Berit Schiøttz-Christensen, Rygcenter Middelfart (Research Department Spine Centre of Southern Denmark,

Hospital Lillebaelt, Middelfart) on a number of projects with relation of patients with back pain. Such projects include a variety of analyses to determine important prognostic clinical outcomes. Based on the identified prognostic models algorithms are set up to develop individually adapted decision tools, and new projects within machine learning are in pipeline.

In general, for several of our partners within consultancy activities we experience an increasing interest regarding machine learning and artificial intelligence. Therefore, we have increased our general activities within this area and expanded our competences within the overall area related to big data, machine learning and artificial intelligence.

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. 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 affiliated Pedro Manuel Sarmiento 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.

The Research Unit of Clinical Epidemiology has 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 biostatistical 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'):

- Machine learning and artificial intelligence
- 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/wm276682>

PHD-STUDENTS

Phd-students supervised by Center for Clinical Epidemiology staff members, 2020

- Ken Lund: Disease control in pediatric and adolescent patients with inflammatory bowel disease: aspects of Anti-TNF- α and physical activity. 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.
- Karen Husby. Tentative title: "Pelvic organ prolapse surgery and risk of gynecological cancer".
- Alice Markussen, "Real-world treatment patterns and outcomes in patients with biliary tract cancer: Danish nationwide population-based analysis". Ongoing.

Future PhD-students at the center:

- 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 2020 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
- associate editor for the journal "Inflammatory Bowel Diseases"
- participated in scientific congresses nationally and internationally (virtually, due to the corona pandemic)
- given scientific oral presentations (virtually, due to the corona pandemic)
- 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)
- board membership of the Danish Association of Occupational Medicine (DAMO)
- co-organizer of a conference/seminar within occupational medicine

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:

OUH Innovationspulje: Machine Learning og tidlig prædiktion af cancer

Helsefonden: Use and cessation of opioids in patients with chronic pain

Beckett Fonden: COVID-19 infection, patients with autoimmune and chronic inflammatory diseases in medical treatment and clinical outcomes (udvidet protokol)

Beckett Fonden: The risk of non-malignant diseases in a nationwide cohort of patients with pediatric-onset of ulcerative colitis and Crohn's disease

OUH (Odense University Hospital) free funds: The risk of non-malignant diseases in a nationwide cohort of patients with pediatric-onset of ulcerative colitis and Crohn's disease (Bente)

Pfizer: COVID-19 infection, patients with autoimmune and chronic inflammatory diseases in medical treatment and clinical outcomes (udvidet protokol)

Pfizer: The IBD-FITT study

Janssen: Biologic therapies and short-term outcomes

Jasha Fonden: Adverse pregnancy and birth outcomes in women with multiple sclerosis – nationwide clinical epidemiological studies

[Region Syddanmark](#): "Diagnose, behandling og overlevelse efter galdekræft i Danmark"

PUBLICATIONS

Scientific publications

In 2020, 45 papers were published in peer-reviewed journals (extracted date: 11 December 2020). 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. Rare cancers of unknown etiology: lessons learned from a European multi-center case-control study. Lynge, E., Kaerlev, L., Olsen, J., Sabroe, S., Afonso, N., Ahrens, W., Eriksson, M., Merletti, F., Morales-Suarez-Varelas, M., Stengrevics, A. & Guénel, P., 17. jul. 2020, I European Journal of Epidemiology
2. Turning the tide: reducing mortality among Danish merchant seafarers. Ugelvig Petersen, K., Lyngbeck Hansen, H., Kaerlev, L. & Hansen, J., 8. jul. 2020, I : Occupational and Environmental Medicine
3. A way towards ventilator-associated lower respiratory tract infection research. Martin-Loeches, I., Póvoa, P. & Nseir, S., jul. 2020, I : Intensive Care Medicine. 46, 7, s. 1504-1505
4. Association between head and neck cancer and sexually transmitted diseases: a Danish nationwide, case-control study. Grønhøj, C., Jakobsen, K. K., Wingstrand, V. L., Jensen, D., Iachina, M., Egeberg, A., Thyssen, J. P. & von Buchwald, C., jul. 2020, I : Acta Oto-Laryngologica. 140, 7, s. 615-619
5. The longitudinal association between shift work and headache: results from the Danish PRISME cohort. Appel, A. M., Török, E., Jensen, M. A., Garde, A. H., Hansen, Å. M., Kaerlev, L., Grynderup, M. B. & Nabe-Nielsen, K., jul. 2020, I : International Archives of Occupational and Environmental Health. 93, 5, s. 601-610
6. Live-born children after assisted reproduction in women with type 1 diabetes and type 2 diabetes: a nationwide cohort study. Larsen, M. D., Jensen, D. M., Fedder, J., Jølvig, L. R. & Nørgård, B. M., 16. jun. 2020, I : Diabetologia
7. Biomarkers in the ICU: less is more? Not sure. Póvoa, P., Salluh, J. I. F. & Lisboa, T., 3. jun. 2020, (Accepteret/In press) I : Intensive Care Medicine
8. A simulation-based comparison of two methods for determining the treatment effect in children diagnosed with hyperkinetic disorder. Iachina, M. & Morling, P., 2. jun.

- 2020, I Communications in Statistics: Simulation and Computation. 49, 6, s. 1385-1396
9. Contributing factors to the plasma albumin level at diagnosis of hematological malignancy. Gradel, K. O., Engberg, H., Zampieri, F. G., Póvoa, P., Simonsen, S. F., Vinholt, P. J., Garvik, O. S., Ljungdahl, P. S. & Frederiksen, H., 2. jun. 2020, I : Hospital practice (1995). 7 s.
 10. Comparison of Time to Pregnancy in Women With and Without Inflammatory Bowel Diseases. Friedman, S., Nielsen, J., Nøhr, E. A., Jølvig, L. R. & Nørgård, B. M., jun. 2020, I : Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association. 18, 7, s. 1537-1544.e1
 11. C-reactive protein and albumin kinetics after antibiotic therapy in community-acquired bloodstream infection. Póvoa, P., Garvik, O. S., Vinholt, P. J., Pedersen, C., Jensen, T. G., Kolmos, H. J., Lassen, A. T. & Gradel, K. O., jun. 2020, I : International Journal of Infectious Diseases. 95, s. 50-58
 12. Author response: Use of β 2-adrenoreceptor agonist and antagonist drugs and risk of Parkinson disease. Pottegård, A., Hopfner, F., Wod, M., Höglinger, G. U., Blaabjerg, M., Rösler, T. W., Kuhlenbäumer, G., Christensen, K. & Deuschl, G., 19. maj 2020, I Neurology. 94, 20, 899
 13. Sepsis Associated Delirium. Atterton, B., Paulino, M. C., Póvoa, P. & Martin-Loeches, I., 18. maj 2020, I : Medicina. 56, 5, 10 s., 240
 14. Incidence of community-onset extended-spectrum β -lactamase-producing Escherichia coli and Klebsiella pneumoniae infections: an 11-year population-based study in Denmark. Richelsen, R., Smit, J., Anru, P. L., Schønheyder, H. C. & Nielsen, H., 13. maj 2020, I Infectious Diseases. 52, 8, s. 547-556
 15. New biomarkers for respiratory infections. Póvoa, P., Coelho, L. & Bos, L. D. J., 1. maj 2020, I : Current Opinion in Pulmonary Medicine. 26, 3, s. 232-240
 16. Live birth in women with multiple sclerosis receiving assisted reproduction. Jølvig, L. R., Larsen, M. D., Fedder, J. & Nørgård, B. M., maj 2020, I : Reproductive BioMedicine Online. 40, 5, s. 711-718
 17. Antifungal use in the surgical ICU patient. Póvoa, P., Coelho, L., Nora, D. & Martin-Loeches, I., apr. 2020, I : Current Opinion in Anaesthesiology. 33, 2, s. 131-138
 18. Focus on infection. Martin-Loeches, I., Póvoa, P. & Poulakou, G., apr. 2020, I : Intensive Care Medicine. 46, 4, s. 787-789
 19. Longitudinal trajectory patterns of plasma albumin and C-reactive protein levels around diagnosis, relapse, bacteraemia, and death of acute myeloid leukaemia patients. Gradel, K. O., Póvoa, P., Garvik, O. S., Vinholt, P. J., Nielsen, S. L., Jensen, T. G., Chen, M., Dessau, R.

- B., Møller, J. K., Coia, J. E., Ljungdahl, P. S., Lassen, A. T. & Frederiksen, H., 24. mar. 2020, I : BMC Cancer. 20, 13 s., 249
20. Corticosteroids prior to embryo transfer in assisted reproduction in women with Crohn's disease and ulcerative colitis – a nationwide cohort study. Nørgård, B. M., Larsen, M. D., Friedman, S. & Fedder, J., mar. 2020, I : Clinical Epidemiology. 12, s. 317-326
21. O que todo intensivista precisa saber sobre delirium subsindrômico na unidade de terapia intensiva. Serafim, R. B., Paulino, M. C. & Póvoa, P., mar. 2020, I : Revista Brasileira de Terapia Intensiva. 32, 1, s. 14-16
22. Sexual health in women with inflammatory bowel disease in the Danish National Birth Cohort. Nohr, E. A., Nielsen, J., Nørgård, B. M. & Friedman, S., 27. feb. 2020, I : Journal of Crohn's and Colitis
23. Respiratory viruses in mechanically ventilated patients: a pilot study. Nazareth, R., Chasqueira, M. J., Rodrigues, M. L., Paulino, C., Conceição, C., Lêdo, L., Segura, Ú., Santos, M., Messias, A., Póvoa, P. & Paixão, P., 13. feb. 2020, I : BMC Pulmonary Medicine. 20, 6 s., 39
24. Regional and socio-economic variation in survival after a pancreatic cancer diagnosis in Denmark. Engberg, H., Steding-Jessen, M., Øster, I., Jensen, J. W., Frstrup, C. W. & Møller, H., 1. feb. 2020, I : Danish Medical Journal. 67, 2, 7 s., A08190438
25. The role of steroids in severe CAP. Nora, D., Nedel, W., Lisboa, T., Salluh, J. & Póvoa, P., 1. feb. 2020, I : Hospital Practice. 48, 1, s. 12-22
26. A nationwide cohort study of hospital contacts after surgical treatment for urinary incontinence. Foss Hansen, M., Bóel Sigurdardóttir, H., Gradel, K.O., Schiøler Kesmodel, U. & Lose, G., feb. 2020, I : Neurourology and Urodynamics. 39, 2, s. 665-673
27. Cardiovascular Events After Community-Acquired Pneumonia: A Global Perspective with Systematic Review and Meta-Analysis of Observational Studies. Tralhão, A. & Póvoa, P., feb. 2020, I : Journal of Clinical Medicine. 9, 2, 23 s., 414
28. Ventilator-associated pneumonia diagnosis: a prioritization exercise based on multi-criteria decision analysis. Ferreira-Coimbra, J., Ardanuy, C., Diaz, E., Leone, M., De Pascale, G., Póvoa, P., Prat-Aymerich, C., Serrano-Garcia, R., Solé-Violan, J., Zaragoza, R. & Rello, J., feb. 2020, I : European Journal of Clinical Microbiology and Infectious Diseases. 39, 2, s. 281-286
29. C-reactive protein and albumin kinetics before community-acquired bloodstream infections- A Danish population-based cohort study. Garvik, O. S., Póvoa, P., Magnussen, B., Vinholt, P. J., Pedersen, C., Jensen, T. G., Kolmos, H. J., Lassen, A. T. & Gradel, K. O., 1.

jan. 2020, 1 : Epidemiology and Infection. 148, 6 s., e38

30. Incidence of ankylosing spondylitis and spondyloarthritis in 2000–2013: a nationwide Danish cohort study. Nygaard, A., Møller Ljungdalh, P., Iachina, M., Nikolov, T. N. & Schiøttz-Christensen, B., jan. 2020, 1 : Scandinavian Journal of Rheumatology. 49, 1, s. 21-27
31. In utero exposure to thiopurines/anti-TNF agents and long-term health outcomes during childhood and adolescence in Denmark. Nørgård, B. M., Nielsen, J. & Friedman, S., 2020, 1 Alimentary Pharmacology and Therapeutics 2020; 52: 829-842
32. Risk factors of community-onset extended-spectrum β -lactamase Escherichia coli and Klebsiella pneumoniae bacteremia: An 11-year population-based case-control study in Denmark. Richelsen R, Smit J, Anru PL, Schønheyder H & Nielsen H. Clinical Microbiology and Infection, 2020, S1198-743X(20)30481-X
33. Body mass index influences the risk of reoperation after first-time surgery for pelvic organ prolapse. A Danish cohort study, 2010-2016. Weltz, V., Guldborg, R., Larsen, M.D., Lose, G. International Urogynecology Journal August 2020
34. The effect of psychosocial work factors on headache: Results from the PRISME cohort study Kaerlev, L. et al. JOEM 2020; 62: e636-e643 (Manuscript #JOEM-20-8280R1)
35. All-cause mortality due to bacteraemia during a 60-day non-physician healthcare worker strike. Jansåker, F., Holm, M.K.A., Gradel, K.O., Knudsen, J.D., Boel, J.B. (2020): *Clinical Infectious Diseases* September 2020
36. Infliximab, immunomodulators and treatment failures in pediatric and adolescent patients with Crohn's disease – a nationwide cohort study. Lund, K., Larsen, M.D., Knudsen, T., Kjeldsen, J., Nielsen, R.G., Nørgård, B.M. *Journal of Crohn's and Colitis*, jjaa188, <https://doi.org/10.1093/ecco-jcc/jjaa188>
37. Long-term motor and cognitive function in the children of women with inflammatory bowel disease. Friedman, S., Nielsen, J., Jølvig, L.R., Nohr, E.A., Nørgård, B.M. PMID: 32497181 DOI: 10.1093/ecco-jcc/jjaa106
38. Outcome of community-onset extended-spectrum β -lactamase-producing Escherichia coli and Klebsiella pneumoniae bacteraemia and urinary tract infection: A population-based cohort study in Denmark. Richelsen RKB, Smit J, Schønheyder H, Anru PL, Gutiérrez-Gutiérrez B, Rodríguez-Baño J, Nielsen H. *Journal of Antimicrobial Chemotherapy*, 2020, 75 (12), 3656-3664.

39. Labour market affiliation among non-bullied colleagues at work units with reported bullying. Hansen, Å.M., Grynderup, M.B., Clausen, T., Bonde, J.P., Garde, A.H., Kærlev, L., Kolstad, H.A., Høgh, A. IAOE 2020 Int Arch Occup Environ Health, DOI 10.1007/s00420-020-01604-8
40. All-cause mortality due to bacteremia during a 60-day non-physician healthcare worker strike. Jansåker, F., Holm, M.K.A., Gradel, K.O., Knudsen, J.D., Boel, J.B. for the DACOBAN. Clinical Infectious Diseases September 2020
41. Clinical characteristics and outcomes among 2347 patients ≥ 85 years with major lymphoma subtypes: a Nordic Lymphoma Group study. Wasterlid, T., Gradel, K.O., Eloranta, S., Glimelius, I., El-Galaly, T.C., Frederiksen, H., Smedby, K.E. British Journal of Hematology November 2020
42. The efficacy of assisted reproductive treatment in women with epilepsy. Larsen, M.D., Jølving, L.R., Fedder, J., Nørgård, B.M. Reproductive BioMedicine Online 2020; 41 (6): 1015-1022
43. Hospitalization for COVID-19 in patients treated with selected immunosuppressant and immunomodulating agents, compared to the general population: A Danish cohort study. Nørgård, B.M., Nielsen, J., Knudsen, T., Nielsen, R.G., Larsen, M.D., Jølving, L.R., Kjeldsen, J. 2020. British journal of clinical pharmacology 2020
44. Activities of daily living at hospital admission and estimated survival time of older patients. Ryg, J., Engberg, H., Anru, P.L., Pedersen, S.G.H., Jørgensen, M.G., Vinding, K.L., Masud, T., Andersen-Ranberg, K. Age and Ageing November 2020
45. Relation between Accumulated Air Pollution Exposure and Sub-Clinical Cardiovascular Disease in 33,723 Danish 60-74-Year-Old Males from the Background Population (AIR-CARD): A Method Article. Lambrechtsen, J., Mayntz, S.K., Engdam, K.B., Egstrup, K., Nielsen, J., Steffensen, F.H., Frohn, L.M., Brandt, J., Ketznel, M., Diederichsen, A.C.P., Lindholt, J.S. Cardiology 2020; 1-8