Annual Report 2021

Cochrane Denmark & Centre for Evidence-Based Medicine Odense

The following report describes the joint objectives, organisation, and activities of Cochrane Denmark (CD) (previously named "The Nordic Cochrane Centre") and Centre for Evidence-Based Medicine Odense (CEBMO), from January 1st, 2021 to December 31st 2021.

Introduction

Cochrane Denmark (CD) and Centre for Evidence-Based Medicine Odense (CEBMO) function as a joint research centre (CD-CEBMO) at the Department of Clinical Research, University of Southern Denmark.

In June 2020, the Danish Ministry of Health decided that the Nordic Cochrane Centre, situated at Rigshospitalet in Copenhagen, be closely affiliated with Centre for Evidence-Based Medicine Odense (CEBMO). This decision was informed by a 2019 report on the activities of the Nordic Cochrane Centre by the Danish Centre for Social Science Research (VIVE), and subsequently endorsed by University of Southern Denmark and Cochrane. The Nordic Cochrane Centre then moved from Rigshospitalet to the University of Southern Denmark in Odense, and in the process, changed its name to Cochrane Denmark. Similarly, CEBMO moved its organizational setting from Odense University Hospital to University of Southern Denmark. The two centres were hereafter functionally merged into one larger centre, CD-CEBMO, effective of January 1st 2021.

Cochrane Denmark

Cochrane Denmark is funded by the Danish government as a national Cochrane centre. The activities of Cochrane Denmark are guided by Cochrane's general strategy and the Ministry of Health's note as of June 2020 (supplemented by recommendations from the VIVE report).

In summary, Cochrane Denmark's core activities are methods research, promoting Cochrane, and supporting Cochrane members in Denmark (e.g. offering training). The Ministry of Health's note on the matter specified that the "political level believes" the new organisational setup "may create a strong research centre …, and at the same time enhance close clinical collaboration with Odense University Hospital and contribute to a broader cooperation across the country".

CEBMO

The Centre for Evidence-Based Medicine Odense (CEBMO) is funded by Odense University Hospital and University of Southern Denmark as a regional research centre. The activities of CEBMO are guided by a term of reference (Appendix 1).

In summary, CEBMO's core activities are research in evidence-based medicine, methods support and guidance for authors of systematic reviews, and pre-graduate and post-graduate teaching.

CD-CEBMO objectives

There is a considerable overlap in the objectives of Cochrane Denmark and CEBMO, which was part of the Ministry's rationale for the functional merger. Overall, CD-CEBMO has four main objectives:

- To conduct research in evidence-based medicine, clinical research methodology, and other types of research relevant for evidence synthesis
- To promote Cochrane in Denmark and support Cochrane authors based in Denmark as well as Cochrane internationally

- To run a counselling and research methods guidance service for researchers at Odense University Hospital and at University of Southern Denmark with a focus on systematic reviews and meta-analyses
- To contribute to undergraduate teaching in evidence-based medicine at University of Southern Denmark and to PhD courses, for example in systematic reviews and meta-analysis

The disposition of this report broadly follows the four main objectives, preceded by a section on organisation and governance.

I. Organisation and governance

The following section presents the centre's general organisation, advisory board, staff, initiatives for a collaborative agreement between University of Southern Denmark and Odense University Hospital, relation between CD-CEBMO and Cochrane international, and the planning of activity and research strategy.

General organisation
CD-CEBMO is organised as a research centre under the Department of Clinical Research, University of Southern Denmark. The centre is led by a Head of Centre and is situated on the university's campus close to Odense University Hospital.

The first year of the merged centre, 2021, was characterised by considerable activities to support a smooth fusion process, create a common culture, and establish practical working routines. We held four workshops focusing on the challenges and possibilities of merging two research units and invited an external expert in mergers to give a talk and provide advice on this process.

The change of name from "The Nordic Cochrane Centre" to "Cochrane Denmark" was part of the new standard Cochrane nomenclature for geographical centres. The name signals Cochrane's wish for a national perspective and is in chord with the Danish government's funding framework.

The different funding sources for Cochrane Denmark and CEBMO, and the considerable disruption of routines associated with organising the functional merger, meant that the details of the financial framework for centre activities were clarified in late 2021.

Advisory Board
During 2021, a joint advisory board was established. It consists of the following international experts in evidence synthesis and Cochrane and national experts with extensive knowledge of the Danish clinical and health policy agendas:

Thomas Benfield - Professor at the Department of Clinical Medicine, University of Copenhagen and consultant at the Department of Infectious Diseases, Hvidovre Hospital, Denmark

Lisa Bero - Professor of Medicine and Public Health, Chief Scientist, Center for Bioethics and Humanities University of Colorado Anschutz Medical Campus, US, and Senior Editor for Research Integrity and Public Health and Health Systems, Cochrane

Isabelle Boutron - Professor of epidemiology at Université de Paris and Director of Cochrane France, France

Kim Brixen - Medical Director, University Hospital Odense, Denmark

Declan Devane - Professor of Nursing and Midwifery at the National University of Ireland, Galway, Director of Evidence Synthesis Ireland, Scientific Director of Cochrane Ireland and Scientific Director of the HRB-Trials Methodology Research Network, Ireland

Kirsten Kyvik - Head of Department, Professor at the Department of Clinical Research, University of Southern Denmark, Denmark

Anders Perner - Professor of Intensive Care Medicine and Vice Chair of the Organization of Danish Medical Societies, Denmark

Lone Kjeld Petersen - Professor at the Department of Gynaecology and Obstetrics, Odense University Hospital and Head of the Open Patient Data Explorative Network (OPEN), Odense, Denmark

Klaus Lunding - Chairman, Danish Patients, Denmark

Lesley Stewart - Professor of Evidence Synthesis and Director/Head of Department, Centre for Reviews and Dissemination, University of York, UK

Ole Jakob Storebø - Professor and Head of the Center for Evidence-Based Psychiatry, Psychiatric Research Unit, Region Zealand, Denmark

Staff
As of 1st January 2022, our Centre had a staff of 14:

Title	**Name**	**FTE[1]**
Head of Centre, professor	Asbjørn Hróbjartsson	1,0
Professor	Karsten Juhl Jørgensen	1,0
Associate Professor	Anders Huitfeldt	1,0
Associate Professor	Klaus Munkholm	1,0
Senior Researcher	Andreas Lundh	0,50
Postdoc and Research Coordinator	Camilla Hansen Nejstgaard	1,0
Postdoc	Asger Sand Paludan-Müller	1,0
PhD student	Christoffer Bruun Korfitsen	1,0
PhD Student	David Ruben Teindl Laursen	0,80
PhD Student	Lasse Østengaard[2]	0,50
Research Assistant	Erlend Faltinsen	0,60
Student Researcher	Daniel Malmsiø	1,0
Administrator	Frihild Askham	1,0
Administrator (communications)	Dina Muscat Meng	0,80

[1]Full time employment; [2]Works for the centre half time, but formally employed by SDUB, the University Library.

During the year, tentative plans were outlined for 4-6 new employees to be hired during 2022 and 2023.

Collaborative agreement between University of Southern Denmark and Odense University Hospital
CEBMO is funded largely by Odense University Hospital. While primarily being part of CD-CEBMO at University of Southern Denmark, CEBMO is administratively linked to the hospital's Open Patient Data Explorative Network (OPEN).

This construction implies a need for a collaboration agreement between University of Southern Denmark and Odense University Hospital regarding CD-CEBMO. In 2022, a working group with representatives from both institutions and CD-CEBMO has started working on the agreement.

CD-CEBMO and Cochrane international
In 2021 it became clear that Cochrane as an international organisation is changing, in part due to a different funding situation in UK and in part due to a commitment to open access publishing. A new strategic plan for Cochrane is underway that will replace the current interim plan running from 2021-2023. The forthcoming adjusted structure of Cochrane as an international organisation will inform the CD-CEBMO's new activity plan relating to Cochrane activities.

Plans for research strategy and activity strategy
Plans for a research strategy and for an activity strategy have been outlined, but it was considered prudent to wait with finalising formal strategies until the fusion process was more advanced, the details of the financial framework of the centre fully clarified, the collaborative agreement between University of Southern Denmark and Odense University Hospital finalised, and the new strategy of Cochrane international more elaborated.

The intention is to have formalised research and activity strategies in place during 2022 or 2023.

II. Research

The following section presents the centre's research organisation, an overview of publications, a list of different types of publications, an overview of selected large international projects, the centre's PhD projects, and a description of applications for external funding.

Research organisation
The research activity of the centre is organised in four "pillars". Each pillar is led by a senior researcher:

i. Bias in general, led by Asbjørn Hróbjartsson
ii. Reporting bias, led by Klaus Munkholm
iii. De-implementation and screening, led by Karsten J. Jørgensen
iv. Conflicts of interest, led by Andreas Lundh

There is an explicit ideal of cross-collaboration between the pillars, reinforced at research meetings twice a month also used as a forum for discussing progress of selected projects.

Research publications: overview
In total, researchers at the centre have authored 44 scholarly publications: 37 articles in peer reviewed journals, one book chapter, and six letters to the editor.

Of the 37 articles in peer reviewed journals, four articles (11%) were published in a top journal (BMJ and JAMA) and 25 articles (68%) were published in a high impact journal (Web of Science Journal Impact Factor > 5). The articles included three Cochrane Reviews and five protocols for Cochrane Reviews. A total of 13 articles (35%) had first or last author from the centre.

List of publications: Articles (full paper or editorials)

1) Boesen K, Jørgensen KJ, Gøtzsche PC. Clinical trials were missing from regulatory documents of extended-release methylphenidate for ADHD in adults: a case study of public documents. Journal of Clinical Epidemiology. 2021:S0895-4356(21)00351-6.

2) Boesen K, Simonsen AL, Jørgensen KJ, Gøtzsche PC. Cross-sectional study of medical advertisements in a national general medical journal: evidence, cost, and safe use of advertised versus comparative drugs. Research Integrity and Peer Review. 2021;6:8.

3) Clarke M, Born K, Johansson M, Jørgensen KJ, Levinson W, Madrid E, Meng DMM, Franco JVA. Making wise choices about low-value health care in the COVID-19 pandemic. Cochrane Database of Systematic Reviews. 2021:ED000153.

4) Fabbri A, Hone KR, Hróbjartsson A, Lundh A. Conflict of Interest Policies at Medical Schools and Teaching Hospitals: A Systematic Review of Cross-sectional Studies. International Journal of Health Policy and Management. 2021:10.34172/ijhpm.2021.12.

5) Fabbri A, Nejstgaard CH, Grundy Q, Bero L, Dunn AG, Mohammad A, Mintzes B. Association Between Conflicts of Interest and Authors' Positions on Harms of Varenicline: a Cross-Sectional Analysis. Journal of General Internal Medicine. 2021:10.1007/s11606-021-06915-1.

6) Ghosn L, Chaimani A, Evrenoglou T, Davidson M, Graña C, Schmucker C, Bollig C, Henschke N, Sguassero Y, Nejstgaard CH, Menon S, Nguyen TV, Ferrand G, Kapp P, Riveros C, Ávila C, Devane D, Meerpohl JJ, Rada G, Hróbjartsson A, Grasselli G, Tovey D, Ravaud P, Boutron I. Interleukin-6 blocking agents for treating COVID-19: a living systematic review. Cochrane Database of Systematic Reviews. 2021:CD013881.

7) Hansen MR, Hróbjartsson A, Pottegård A, Damkier P, Madsen KG, Pareek M, Olesen M, Hallas J. Postponement of cardiovascular outcomes by statin use: A systematic review and meta-analysis of randomized clinical trials. Basic and Clinical Pharmacology and Toxicology. 2021;128:286-96.

8) Israelsen SB, Ernst MT, Lundh A, Lundbo LF, Sandholdt H, Hallas J, Benfield T. Proton Pump Inhibitor Use Is Not Strongly Associated With SARS-CoV-2 Related Outcomes: A Nationwide Study and Meta-analysis. Clinical Gastroenterology and Hepatology. 2021;19:1845-54.

9) Johansson M, Borys F, Peterson H, Bilamour G, Bruschettini M, Jørgensen KJ. Addressing harms of screening – A review of outcomes in Cochrane reviews and suggestions for next steps. Journal of Clinical Epidemiology. 2021;129:68-73.

10) Jørgensen CK, Juul S, Siddiqui F, Barbateskovic M, Munkholm K, Hengartner MP, Kirsch I, Gluud C, Jakobsen JC. Tricyclic antidepressants versus 'active placebo', placebo or no intervention for adults with major depressive disorder: a protocol for a systematic review with meta-analysis and Trial Sequential Analysis. Systematic Reviews. 2021;10:227.

11) Jukema M, Borys F, Sibrecht G, Jørgensen KJ, Bruschettini M. Antileukotrienes for the prevention and treatment of chronic lung disease in very preterm newborns: a systematic review. Respiratory Research. 2021;22(1):208.

12) Karanges EA, Nangla C, Parker L, Fabbri A, Farquhar C, Bero L. Pharmaceutical industry payments and assisted reproduction in Australia: A retrospective observational study. BMJ Open. 2021;11:e049710.

13) Larsen CM, Juul-Kristensen B, Kasch H, Hartvigsen J, Frich LH, Boyle E, Østengaard L, Biering-Sørensen F. The Danish Spinal Cord Injury Shoulder (DanSCIS) cohort: methodology and primary results. Spinal Cord. 2021;59:821-31.

14) Munkholm K, Jørgensen KJ, Paludan-Müller AS. Adverse effects of electroconvulsive therapy Cochrane Database of Systematic Reviews (Protocol). 2021:CD014995.

15) Munkholm K, Jørgensen KJ, Paludan-Müller AS. Electroconvulsive therapy for preventing relapse and recurrence in bipolar disorder. Cochrane Database of Systematic Reviews (Protocol). 2021:CD015172.

16) Munkholm K, Jørgensen KJ, Paludan-Müller AS. Electroconvulsive therapy for acute affective episodes in people with bipolar disorder. Cochrane Database of Systematic Reviews (Protocol). 2021:CD014996.

17) Munkholm K, Jørgensen KJ, Paludan-Müller AS. Electroconvulsive therapy for depression. Cochrane Database of Systematic Reviews (Protocol). 2021:CD013843.

18) Nejstgaard CH, Lundh A, Abdi S, Clayton G, Gelle MHA, Laursen DRT, Olorisade BK, Savovic J, Hróbjartsson A. Combining meta-epidemiological study datasets on commercial funding of randomised clinical trials: database, methods, and descriptive results of the COMFIT study. Research Synthesis Methods. 2021:10.1002/jrsm.1527.

19) Nguyen VT, Rivière P, Ripoll P, Barnier J, Vuillemot R, Ferrand G, Cohen-Boulakia S, Ravaud P, Boutron I; COVID-NMA Consortium Team (Alawadhi S, Amer-Yahia S, Ávila C, Bafeta A, Baudry J, Bollig C, Bonnet H, Boutron I, Bouet GC, Chaimani A, Chavalarias D, Chen Y, Chevance A, Cohen-Boulakia S, Coquery E, Conil F, Davidson M, De Nale L, Devane D, Diard E, Doreau B, Evrenoglou T, Fabri A, Feron G, Ferrand G, Fezeu L, Fouet M, Ghosn L, Graña C, Grasselli G, Grolleau F, Hacid MS, Haddy L, Hansen C, Hohlfeld A, Hróbjartsson A, Julia C, Mavridis D, Meerpohl JJ, Meyer B, Naidoo N, Thu VN, Oikonomidi T, Pienaar E, Quirke F, Rada G, Ravaud P, Ripoll P, Riveros C, Rivière P, Sauvant M, Schmucker C, Toumani F, Tovey D, Vuillemot R, Xia J, Yu X, Zoletic E, Zweigenbaum P). Research response to coronavirus disease 2019 needed better coordination and collaboration: a living mapping of registered trials. Journal of Clinical Epidemiology. 2021;130:107-16.

20) Orkin AM, Gill PJ, Ghersi D, Campbell L, Sugarman J, Emsley R, Steg GP, Weijer C, Simes J, Rombey T, Williams HC, Wittes J, Moher D, Richards DP, Kasamon Y, Getz K, Hopewell S, Dickersen K, Wu T, Ayala AP, Schulz KF, Calleja S, Boutron I, Ross JS, Golub RM, Khan KM, Mulrow C, Siegfried N, Heber J, Lee N, Kearney PR, Wanyenze K, Hróbjartsson A, Williams R, Bhandari N, Juni P, Chan A. Guidelines for Reporting Trial Protocols and Completed Trials Modified Due to the COVID-19 Pandemic and Other Extenuating Circumstances: The CONSERVE 2021 Statement. JAMA. 2021;326:257-65.

21) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Journal of Clinical Epidemiology. 2021;134:178-89.

22) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. International Journal of Surgery. 2021;88:105906.

23) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Systematic Reviews. 2021;10:89.

24) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. PLoS Medicine. 2021;18:e1003583.

25) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.

26) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. Pravila prisma 2020. ažurirane smjernice za izvještavanje u sustavnim pregledima. Medicina Fluminensis. 2021;57:444-65.

27) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer, L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Tianjing L, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. Declaración PRISMA 2020: una guía actualizada para la publicación de revisiones sistemáticas. Revista Española de Cardiología. 2021;74:790-9

28) Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, McKenzie JE. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.

29) Paludan-Müller AS, Créquit P, Boutron I. Reporting of harms in oncological clinical study reports submitted to the European Medicines Agency compared to trial registries and publications-a methodological review. BMC Medicine. 2021;19:88.

30) Paludan-Müller AS, Lundh A, Page MJ, Munkholm K. Protocol: Benefits and harms of remdesivir for COVID-19 in adults: A systematic review with meta-analysis. PLoS ONE. 2021;16:e0260544.

31) Paludan-Müller AS, Ogden MC, Marquardsen M, Jørgensen KJ, Gøtzsche PC. Are investigators' access to trial data and rights to publish restricted and are potential trial participants informed about this? A comparison of trial protocols and informed consent materials. BMC Medical Ethics. 2021;22:115.

32) Parker L, Bennett A, Mintzes B, Grundy Q, Fabbri A, Karanges EA, Bero L. "There are ways … drug companies will get into DTC decisions": How Australian drug and therapeutics committees address pharmaceutical industry influence. British Journal of Clinical Pharmacology. 2021;87:2341-53.

33) Pizarro AB, Persad E, Durao S, Nussbaumer-Streit B, Garritty C, Engela-Volker JS, McElvenny D, Rhodes S, Stocking K, Fletcher T, Van Tongeren M, Martin C, Noertjojo K, Sampson O, Jørgensen KJ, Bruschettini M. Workplace interventions to reduce the risk of SARS-CoV-2 infection outside of healthcare settings (Protocol). Cochrane Database of Systematic Reviews. 2021:CD015112.

34) Ropers FG, Barratt A, Wilt TJ, Nicholls SG, Taylor-Phillips S, Kramer BS, Esserman LJ, Norris SL, Gibson LM, Harris RP, Carter SM, Jacklyn G, Jørgensen KJ. Health screening needs independent regular re-evaluation. BMJ. 2021;374:n2049.

35) Sethi NJ, Safi S, Korang SK, Hróbjartsson A, Skoog M, Gluud C, Jakobsen JC. Antibiotics for secondary prevention of coronary heart disease. Cochrane Database of Systematic Reviews. 2021:CD003610.

36) Siddiqui F, Barbateskovic M, Juul S, Katakam KK, Munkholm K, Gluud C, Jakobsen JC. Duloxetine versus 'active' placebo, placebo or no intervention for major depressive disorder; a protocol for a systematic review of randomised clinical trials with meta-analysis and trial sequential analysis. Systematic Reviews. 2021;10:171.

37) Sørensen A, Ruhé HG, Munkholm K. The relationship between dose and serotonin transporter occupancy of antidepressants-a systematic review. Molecular Psychiatry. 2021:10.1038/s41380-021-01285-w.

List of Publications: Book chapters

38) Boutron I, Page MJ, Higgins JPT, Altman DG, Lundh A, Hróbjartsson A. Chapter 7: Considering bias and conflicts of interest among the included studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021.

List of Publications: Letters to the editor

39) Lundh A. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. New England Journal of Medicine. 2021;384:1473.

40) Hone KR, Lundh A. Review articles with conflicts of interest. Ugeskrift for Laeger. 2021;183:92.

41) Munkholm K, Paludan-Müller AS. Caution is advised when interpreting subgroup analyses. Neuropsychopharmacology. 2021;46:1551.

42) Munkholm K. Long-acting injectable versus oral antipsychotics for schizophrenia. The Lancet Psychiatry. 2021;8:566-7.

43) Munkholm K. Unconvincing evidence for peripheral biomarkers in major mental disorders. Translational Psychiatry. 2021;11:237.

44) Boesen K, Jørgensen KJ, Gøtzsche PC. Clinical trials were missing from regulatory documents of extended-release methylphenidate for ADHD in adults: a case study of public documents: author's reply. Journal of Clinical Epidemiology. 2021:S0895-4356(21)00425-X.

Main international projects
The following section presents main international projects that the centre was engaged in during 2021.

COMFIT – Commercial Funding in Trials: The COMFIT study
Our Centre led the work on constructing a database, combining unpublished data from multiple methods studies to investigate the impact of commercial funding on estimated intervention effects in randomized clinical trials. The COMFIT study is based on a consortium of researchers who agreed to share unpublished data. The project will provide an unprecedented opportunity to investigate the impact of commercial funding.

TACIT – Tool for Addressing Conflicts of Interests in Trials
Our centre led the development of a tool for addressing conflicts of interests in randomized trials included in systematic reviews. The project is supported by an international working group and a steering group. Two supportive preliminary projects have been published in the BMJ and Journal of Clinical Epidemiology, and the tool is expected to be pilot tested during 2022. Find more information about TACIT on the TACIT website.

Re-evaluation of screening interventions directed at the general public
Our centre led a group of international screening experts, outlining the principles for a framework for regular re-evaluation of existing screening interventions directed at the general public, published in BMJ in 2021. A series of papers has been planned, e.g. a paper exploring screening recommendation from major guideline issuing authorities (US Preventive Services Task Force; UK National Screening Committee; Canadian Task Force on Preventive Health Care), how they differ, and why they do that. This series can be viewed as contributing to a stronger emphasis on evidence-informed prioritization and de-implementation in healthcare.

Reporting bias and clinical study reports
Our centre led a project on reporting bias and the use of clinical study reports (CSRs) in systematic reviews. CSRs are comprehensive reports describing methodology and presenting results of clinical trials conducted by pharmaceutical companies. The primary mode of access to CSRs is Freedom of Information requests to regulatory authorities, to whom the CSRs are submitted as part of applications for marketing authorization. The core idea of the project is to explore and analyse to which degree access to such documents makes a difference to results and conclusions in meta-analyses.

COVID-NMA – A COVID-19 living evidence project
Our Centre was represented in the Steering Group of the COVID-NMA project. The project involves an international team of researchers from the Cochrane collaboration who have compiled living evidence related to COVID-19. The initiative is led by Cochrane France in collaboration with Cochrane Germany, Cochrane Ireland, Cochrane Chile, Cochrane South Africa, and others, including the Cochrane Bias Methods Group. The COVID-NMA project team brings together the latest evidence related to COVID-19, presenting data on trials registered all over the world, as well as living evidence synthesis (including network meta-analyses) of results from these trials. Find more information about this project on the COVID-NMA website.

SPIRIT-CONSORT – Reporting guidelines for protocol and final paper on randomised clinical trials

Our Centre was represented in the Executive Group for the update of the SPIRIT and CONSORT statements. The SPIRIT guideline focuses on reporting of protocols to randomised clinical trials and was published in 2013. The SPIRIT and CONSORT Executive Group are planning a programme of work to update the SPIRIT 2013 and CONSORT 2010 guidelines concurrently and to provide a uniform template that will incorporate and align both checklists within the same document. The centre participates in the Executive Group, led the development of a database of relevant literature and a review of comments and published suggestions for adjustments to SPIRIT 2013 and CONSORT 2010.

ROB-ME – Risk of bias due to missing evidence in meta-analyses
Our Centre contributed to the ROB-ME tool, which is intended for authors of systematic reviews to assess risk of bias due to missing evidence (e.g. unpublished trials or unreported trial results) in meta-analyses of the effects of interventions. ROB-ME operates in the same manner as the RoB 2 and ROBINS-I tools, whereby responses to signalling questions provide the basis for a judgement about the risk of bias in the specific synthesized result being assessed.

PRISMA – Preferred Reporting Items of Systematic reviews and Meta-Analyses statement
Our Centre contributed to the update of the PRISMA statement, an evidence-based guideline with a minimum set of items for reporting in systematic reviews and meta-analyses. Its two main papers were published in the BMJ in 2021. The statement was designed to help systematic reviewers transparently report why the review was done, what the authors did, and what they found. A global team of methodologists, search specialists, biostatisticians and systematic reviewers have spent the last few years updating the PRISMA statement. Find more information about PRISMA on the PRISMA website.

PhD projects
In 2021, there were five PhD students at CD-CEBMO: Asger Sand Paludan-Müller, Camilla Hansen Nejstgaard, David Ruben Teindl Laursen, Lasse Østengaard, and Christoffer Bruun Korfitsen.

Two of the students have successfully defended their thesis:
Asger Sand Paludan-Müller. When is a randomised trial justified? PhD thesis defended March 2021 (University of Southern Denmark).

Camilla Hansen Nejstgaard. Conflicts of interest in clinical research. PhD thesis defended November 2021 (University of Southern Denmark).

The remaining three PhD students at the Centre have worked on the following projects during the year:
David Laursen: Active placebo as control intervention in pre-clinical and clinical randomised trials. The first two sub-projects investigated the impact of using active placebo controls (rather than standard non-active placebos) on estimated drug effect, and the last project is planned to investigate the rationale for using active placebo controls. The current submission deadline is September 2022.

Lasse Østengaard: Citation principles in clinical research.
The objective of Lasse's PhD project is to characterise and analyse the content and variability of principles for citations in clinical research. The study will provide an empirical basis for reflections on adequacy of citations and serve as the evidence foundation for the development of a citation guideline which is a planned extension of the present PhD study. The current submission deadline is set for 2024.

Christoffer Bruun Korfitsen: Conflicts of interest in peer review of biomedical research.
Christoffer's PhD project aims to investigate conflicts of interest in peer review of biomedical research. The subprojects will investigate the prevalence of peer reviewers' conflicts of interest in biomedical research, journal editors' experiences with peer reviewers' conflicts of interest, journal policies for peer reviewers' conflicts of interest, and the association between peer reviewer conflicts of interest and review recommendations. The current submission deadline is set for 2025.

Project supervision
Senior researchers at the centre have also acted as project supervisor for five other PhD students, who have primarily been affiliated with other centres: Anders Klokmose and Kim Boesen (supervised by Karsten J. Jørgensen), Cille Bülow supervised by Andreas Lundh), and Nicolai Sandau and Lars Bastholt (supervised by Asbjørn Hróbjartsson).

One such student, Kim Boesen, successfully defended his thesis: Methodological limitations of psychiatric drug trials with a focus on extended-release methylphenidate for adults with ADHD (University of Copenhagen).

Applications for external research funds
During 2021, we have received external funding from the following sources:

Applied to	Type of funding & amount in DKK	Project	Comment
Independent Research Fund, Denmark	Research grant, 2.872.440 (until October 2024)	Conflicts of interest in peer review of biomedical research	Christoffer Korfitsen's PhD
SDUB*	Agreement, equivalent to grant of 275.000 (no finishing date)	Citation principles in clinical research	50% PhD position for Lasse Østengaard
The Danish Cancer Society	Scholarship, 100.000 (until January 2022)	Scoping review: Protocol content guides for cohort and case-control studies	Student researcher Daniel Malmsiø

*Work for the centre half time, but formally employed by SDUB, the University Library.

During 2021, we have applied for external funding from the following sources:

Applied to	Type of funding & amount in DKKR	Project	Status
Independent Research Fund, Denmark	5.898.820	The ProEPI study	Pending
Independent Research Fund, Denmark	650.000	The UnBlinding project	Rejected

III. Promotion of Cochrane in Denmark and support to Cochrane authors based in Denmark as well as Cochrane internationally

Below follows the centre's activity relating to supporting collaboration within Cochrane and evidence-based medicine, provision of teaching unrelated to University of Southern Denmark, talks, media contact, other communication activities and knowledge translation, and training of Cochrane authors.

Supporting national collaboration within Cochrane and evidence-based medicine
All Cochrane Review Group based in Denmark were contacted during the year and consulted to explore options for closer collaboration.

On that basis, the centre planned and hosted a first national meeting on the 30th November for researchers and others with an interest in Cochrane and Evidence-Based Medicine in Denmark. All Cochrane Review Groups, and evidence-based centres, participated. The intention was to have an in-person meeting but due

to the COVID-19 situation in Denmark at the time, we reorganised the meeting into a virtual meeting instead for safety precautions, and 30 people attended this event via Zoom.

We have had a positive response from attendants and have decided to have a follow-up meeting in-person on the 3rd May 2022 to further discuss how to develop our network and facilitate collaboration.

Teaching unrelated to University of Southern Denmark
Research staff from our centre have contributed to a PhD course (Introduction to Cochrane Methodology, Cochrane Sweden, Lund University), and to a Master's course (Introduction to the Cochrane collaboration and systematic reviews, the Faculty of Health and Sciences, University of Copenhagen).

Also, senior staff have contributed to specialist training for clinicians in Denmark (research training programme for internal medicine and for oncology) and across clinical specialties on implementation of clinical research.

Research dissemination: talks
Staff from the centre gave 17 talks:
India Breast cancer screening (at Breast Global Conference); Conflicts of Interest in clinical research and Financial conflicts of interest and physician behaviour (at Doctors without Sponsors); Influence and management of conflicts of interest in randomised clinical trials (at Webinar for the HRB-Trials Methology Research Network, Ireland); Presentation on the Cochrane Collaboration (at The junior researcher's network for Herlev and Gentofte Hospital's research seminar); Association between conflicts of interest and favourable recommendations in clinical guidelines, advisory committee reports, opinion pieces, and narrative reviews: systematic review (at Department of Clinical Pharmacology, Bispebjerg Hospital); Presentation on the Cochrane Collaboration and how to use Cochrane databases (at the Insurance Medicine's Association research meeting; Placebo, usual care and wait-list interventions for all mental health disorders (at Centre for Evidence-Based Psychiatry Psychiatry, Region Zealand); Active placebo versus standard placebo control interventions in pharmacological randomised trials) (at Centre for Evidence-Based Psychiatry Psychiatry, Region Zealand; The Value of Cochrane Evidence: A Global Experience, and Cochrane Sustainable Healthcare - a collaboration to tackle medical excess (at 3rd International Cochrane Workshop. Russian Medical Academy of Continuous Professional Education (RMANPO) and Cochrane); Cochrane and research waste (at the Health Technology Council at Odense University Hospital); New trends in evidence-based medicine (at the Danish Medicines Council); Systematic reviews of prevalence studies (at Department of Psychology at University of Southern Denmark; Non-inferiority trials (at Odense University Hospital's Health Technology Council); Cochrane Denmark and SIF (at National Institute of Public health); Evidence and Cochrane (at Department of Oncology at Odense University Hospital); Cochrane Denmark and CEBMO (at The Danish Medicines Council); Cochrane Denmark (at The Danish Health Authority).

Research dissemination: media contact
During the year, centre staff had 29 contacts with journalists, or the centre was otherwise mentioned in the following media: videnskab.dk (x8), Dagens Medicin (x2), Politiken (x2), avisendanmark, Sundhedspolitisk Tidsskrift, sundfornuft (x2), Fyns Stiftstidende, Sjællandske, Nordjyske Stiftstidende, Børsen, Fyns Amtsavis, Ritzau, Dagbladet Ringsted, New York Times (x2), CBSNews Canada, inewspaper, and Stats News.

Research dissemination: other communication activities and knowledge translation
We maintain and develop our websites and translate relevant content to Danish on the Cochrane Denmark website.

We also engage with audiences through Twitter and disseminate Cochrane research and activities through several communication channels including the Cochrane.dk website and Twitter platform @CochraneDK in English and Danish, and in collaboration with the Cochrane Knowledge Translation team. As part of the

establishment of CD-CEBMO, a new website was developed on the University of Sothern Denmark website platform to create a 'go-to' place for both units and enhance better visibility and awareness of our new organisational setup. This website will in collaboration with the Cochrane.dk website be utilised to promote our work and future training activities.

In 2019, the Cochrane Knowledge Translation team developed the Dissemination Checklist - a user-tested, evidence-informed resource to improve the quality of dissemination products from Cochrane Reviews. In 2021, a member of staff was part of this project group who helped develop online resources.

The centre has also contributed to the establishment of a Special Collection of Cochrane Reviews focusing on de-implementation of low-value health care.

Training for Cochrane authors
See below.

Bias Methods Group
The centre hosts the secretariat for the Cochrane Bias Methods Group. The group is responsible for methods guidance to Cochrane, contributing to the Cochrane Handbook, developing the Cochrane Risk of Bias Tool, and coordinating methods research on bias.

Asbjørn Hróbjartsson is co-convenor with Senior Research Fellow Page, Cochrane Australia, Professor Isabelle Boutron, Cochrane France and Professor Julian Higgins, University of Bristol, UK. The group's research coordinator is Camilla Hansen.

In 2021, the focus for the group has been on implementing training for the revised tool to assess risk of bias in randomised trials (RoB2), published in the BMJ 2019. The group have also been working on three methods tools. The first tool assesses risk of bias due to missing evidence in meta-analyses (ROB-ME, see above). The second tool addresses conflicts of interest in randomised trials (TACIT, see above). The third tool assesses risk of bias in non-randomised studies of exposure (ROBINS-e).

Involvement in International Cochrane boards and committees
Members of staff served on Cochrane's Governing Board, on the scientific advisory board for Cochrane (Cochrane Scientific Committee), and on the Advisory Board for Cochrane Sweden.

IV. Research training and methods guidance

Throughout 2021, our team supported research training activities and methods guidance aimed at Cochrane authors in Denmark, and university students, healthcare researchers, guideline developers and health professionals at University of Southern Denmark and Odense University Hospital.

Research methods guidance
The Centre offers guidance for students and researchers to support them when conducting a systematic review. In special cases, the Centre offers guidance for preparing other types of research. We offer walk-in methods clinics, and short-term and long-term guidance.

The initial walk-in methods clinic was held in November 2021. The two-hour clinics are open to interested researchers and are held once every month (except January and July). They are open to researchers at the Department of Clinical Research at University of Southern Denmark, and Odense University Hospital.

The short-term service consists of a 1-hour guidance in systematic reviews and is open to researchers at the Department of Clinical Research at University of Southern Denmark and Odense University Hospital.

The long-term guidance consists of a total of 10-hours support. It is available to PhD students and other researchers from the Department of Clinical Research, University of Southern Denmark, specifically Cochrane review authors. Due to resource restrictions, we have specified a maximal number of 15 projects in pipeline for long term guidance. This number will increase to 25 in 2022 because of additional hospital funding. Evidence-based medicine is a priority for the 2021-2025 research strategy for Odense University Hospital and the Department of Clinical Research at the University of Southern Denmark (see below).

In 2021, we held two methods clinics, provided long term advise (up to 10 hours) to 17 consultancy projects, including one Cochrane review; and provided short term advice (< 1 hour) to 12 projects.

Course activity on Cochrane methodology and systematic reviews
In 2021, we planned a portfolio of courses of Cochrane methodology how to conduct a systematic review or evidence synthesis. The courses are aimed at Cochrane authors from Denmark broadly and for researchers from Odense University Hospital and Department of Clinical Research at the University of Southern Denmark.

The portfolio of courses consists of 1) free access to Cochrane Online Learning Modules; 2) a one-day introductory course on systematic reviews, and 3) a four-day advanced course on systematic reviews.

V. Teaching Evidence-Based Medicine at University of Southern Denmark

Below follows the centre's activities in relation to teaching evidence-based medicine courses for medical students and pharmacy students and PhD courses at University of Southern Denmark.

Evidence-based medicine course for medical students
Our Centre led the course in evidence-based medicine (EBM) for medical students at the University of Southern Denmark.

We organised the course, taught, and examined approximately 300 medical students per year. The course runs each semester and lasts a total of five weeks (8 ETCS). It aims to provide students with skills that allow them to frame a structured clinical question, identify the relevant scientific literature, and critically appraise the identified clinical studies. Each year, professors and associate professors from our Centre contribute with 32 hours of lectures, and postdocs and PhD students contribute with 18 hours of case-work instructions and 330 hours of instructions and feedback to written assignments of a critically appraised topic (CAT).

Senior researchers at the centre have edited and co-written a textbook in evidence-based medicine which will be published by Munksgaard in 2022. The book is approximately 360 pages and consists of 26 chapters. It is aimed to serve both as a textbook for the EBM course and as a general introduction to the field for readers with an interest in evidence-based health care and clinical research methodology.

Introduction to Evidence-Based Medicine and systematic literature reviews, Faculty of Health Sciences
Two members of our team gave two double-lectures as part of the MSc programme in Pharmacy at the Faculty of Health Sciences at University of Southern Denmark.

PhD courses
The two courses (1-day and 4-day course) described above (Course activity for Cochrane authors and for researchers wanting to do systematic reviews) will also have a PhD course level status
Other activities

Below follows a summary of the centre's activities relating to the research strategy of Odense University Hospital and the Department of Clinical Research at the University of Southern Denmark, board and committee membership, and assessments of PhD theses.

Evidence-based medicine and the hospital's research strategy
In 2021, Odense University Hospital and the Department of Clinical Research at the University of Southern Denmark published a joint research strategy for the years 2021-5. The strategy specifies evidence-based medicine as one of five central dimensions.

CD-CEBMO contributes to the strategy by expanding the research methods guidance service, leading the group responsible for implementation of that dimension of the strategy, and giving talks to clinical departments.

Also, as part of a strategy for better integration between clinical practice and evidence-based medicine, CD-CEBMO has planned to establish a senior researcher position jointly with the Department of Gynaecology.

Board and committee membership (non-Cochrane)
Members of staff served as Deputy Chair of the Scientific Committee of Preventing Overdiagnosis and Vice-chair of Doctors without Sponsor. Also, members of staff served as Advisory Board Member for the Danish healthcare think tank SundFornuft, Danish Society for Medical Philosophy, Ethics and Methods, Centre for Evidence-Based Psychiatry, and Danish Medical Association's Committee of drugs and devices ("lægemiddel og medikoudvalget").

Assessments of academic theses
Members of staff also contributed to the assessment a PhD thesis for University of Copenhagen and another for University of Southern Denmark, an assessment of a PhD application for University of Southern Denmark, and an assessment of a MSc Thesis for Humboldt University Berlin.

Odense, 24/3 2022

Asbjørn Hróbjartsson
Professor, Head of Centre