Annual Report 2022

Cochrane Denmark & Centre for Evidence-Based Medicine Odense

The following report describes the objective, organisation, and activities of Cochrane Denmark (CD) and Centre for Evidence-Based Medicine Odense (CEBMO), from January 1st, 2022 to December 31st 2022.

Introduction

Cochrane Denmark (CD) and Centre for Evidence-Based Medicine Odense (CEBMO) function as a merged 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). 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 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. 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".

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).

CD-CEBMO objectives

There is a considerable overlap in the objectives of Cochrane Denmark (CD) and Centre for Evidence-Based Medicine Odense (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 metaanalyses
- 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. <u>Organisation and governance</u>

CD-CEBMO is organised as a research centre at the Department of Clinical Research, University of Southern Denmark. The Head of CD-CEBMO will function both as leader of research and administration and refers to the Head of Department of Clinical Research, University of Southern Denmark. In matters relating to Cochrane, the Head of CD-CEBMO will operate in accordance with the collaboration agreement with Cochrane.

Staff
As of 31st of December 2022, the Centre had a staff of 16:

Title	Name	FTE ¹	
Head of Centre, professor	Asbjørn Hróbjartsson	1,0	
Professor	Karsten Juhl Jørgensen	1,0	
Associated Professor	Andreas Lundh	0,50	
Associated Professor	Jeppe B. Schroll	0,50	
Postdoc and Research Coordinator	Camilla Hansen Nejstgaard	1,0	
Postdoc	Helene Moustgaard	1.0	
PhD Fellow	Christoffer Bruun Korfitsen	1,0	
PhD Fellow	David Ruben Teindl Laursen	0,80	
PhD Fellow and Research Coordinator	Lasse Østengaard	1,00	
Research Assistant	Erlend Faltinsen	0,60	
Administrator	Frihild Askham	1,0	
Student Researcher	Daniel Malmsiø	Not applicable	
Student Researcher	Mette Bangshof Engmose	Not applicable	
Student Researcher	Mihaela Ivosevic	Not applicable	
Student Assistant	Lasse Adrup Benné Petersen	up Benné Petersen 0,13	
Student Assistant	Mia Elkjær	0,13	

¹Full time employment

In addition, the following researchers are associated with the Centre: Librarian Mette Brandt Eriksen (10% Associated Professor), An-Wen Chan from university of Toronto (Adjunct Professor), and Karsten Lauritsen (Consultant emeritus).

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 calls for a collaboration agreement between University of Southern Denmark and Odense University Hospital regarding CD-CEBMO, which was not finalised in 2022.

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 <u>strategic plan</u> for Cochrane is underway that will replace the current interim plan running from 2021-2023. The forthcoming adjusted structure of Cochrane will inform the CD-CEBMO's new activity plan relating to Cochrane activities.

Plans for research and activity

A research strategy and an activity strategy have been outlined but will await formal finalisation until the collaborative agreement between University of Southern Denmark and Odense University Hospital is finalised and the new strategy of Cochrane international is more elaborated. The intention is to have formalised research and activity strategies in place late 2023 or early 2024.

Advisory Board

As of 31st of December 2022, the Centre's advisory board included:

- 1. Lisa Bero (Professor of Medicine and Public Health, University of Colorado, US)
- Isabelle Boutron (Professor of epidemiology, Université de Paris and Director of Cochrane France, France)
- 3. Declan Devane (Professor of Nursing and Midwifery, National University of Ireland, and Scientific Director of Cochrane Ireland).
- 4. Lesley Stewart (Professor of Evidence Synthesis and Director of CDR, University of York, UK)
- 5. Kim Brixen (Medical Director, Odense University Hospital, Denmark)
- 6. Lone Kjeld Petersen (Professor of Gynaecology and Obstetrics, Odense University Hospital and Head of the Open Patient Data Explorative Network (OPEN), Odense, Denmark)
- 7. Kirsten Kyvik (Head of Department, University of Southern Denmark, Denmark)
- 8. Anders Perner (Professor of Intensive Care Medicine, University of Copenhagen, and Vice Chair of the Organization of Danish Medical Societies, Denmark)
- 9. Klaus Lunding (Chairman, Danish Patients, Denmark)
- 10. Ole Jakob Storebø (Professor and Head of the Center for Evidence-Based Psychiatry, Psychiatric Research Unit, Region Zealand, Denmark)

II. Research

The research activity of the Centre is organised in four "clusters". Each cluster is led by a senior researcher:

- i. Bias in clinical research, led by Asbjørn Hróbjartsson
- ii. De-implementation and screening, led by Karsten J. Jørgensen
- iii. Conflicts of interest, led by Andreas Lundh
- iv. Medical devices (under development), led by Jeppe B. Schroll

Research publications: overview

In total, researchers at the Centre authored 51 scholarly publications in 2022: 28 articles in peer reviewed journals, one book (edited and co-authored), 17 book chapters, and five letters to the editor.

Of the 28 articles in peer reviewed journals, 11 articles (39%) were published in journals with a Web of Science Journal Impact Factor (IF) \geq 10, and 23 articles (82%) in journals with an IF \geq 5. There were 13 articles (46%) in core journals for evidence-based medicine and clinical research methodology: Cochrane Database of Systematic Reviews, Journal of Clinical Epidemiology, and Research Synthesis Methods. One article was published in a very high impact journal (Nature Medicine).

A total of 15 articles (52%) had main authors (first or last) from the Centre (underlined in the list below).

List of publications: Articles (full articles or editorials) in peer reviewed journals

1) Albarqouni L, Ringsten M, Montori V, <u>Jørgensen KJ</u>, Bulbeck H, Johansson M. Evaluation of evidence supporting NICE recommendations to change people's lifestyle in clinical practice: cross sectional survey. BMJ Medicine. 2022;1(1):e000130.

- 2) Boesen K, <u>Jørgensen KJ</u>, 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. 2022;143:242-253.
- 3) Boesen K, <u>Paludan-Müller AS</u>, Gøtzsche PC, <u>Jørgensen KJ</u>. Extended-release methylphenidate for attention deficit hyperactivity disorder (ADHD) in adults. Cochrane Database of Systematic Reviews. 2022(2):CD012857.
- 4) Davidson M, Menon S, Chaimani A, Evrenoglou T, Ghosn L, Graña C, Henschke N, Cogo E, Villanueva G, Ferrand G, Riveros C, Bonnet H, Kapp P, Moran C, Devane D, Meerpohl JJ, Rada G, <u>Hróbjartsson A</u>, Grasselli G, Tovey D, Ravaud P, Boutron I. Interleukin-1 blocking agents for treating COVID-19. Cochrane Database of Systematic Reviews. 2022;2022(1):CD015308.
- 5) <u>Fabbri A, Nejstgaard CH,</u> 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. 2022;37(2):290-297.
- 6) <u>Fabbri A</u>, Hone KR, <u>Hróbjartsson A</u>, <u>Lundh A</u>. Conflict of Interest Policies at Medical Schools and Teaching Hospitals: A Systematic Review of Cross-sectional Studies. International Journal of Health Policy and Management. 2022;11(8):1274-1285.
- 7) <u>Fabbri A</u>, Mulinari S, Johansson M, Ghaur W, Khalil AM, <u>Lundh A</u>. Content and strength of conflict of interest policies at Scandinavian medical schools: a cross sectional study. BMC Medical Education. 2022;22:812.
- 8) <u>Faltinsen E</u>, Todorovac A, Staxen Bruun L, <u>Hróbjartsson A</u>, Gluud C, Kongerslev MT, Simonsen E, Storebø OJ. Control interventions in randomised trials among people with mental health disorders. Cochrane Database of Systematic Reviews. 2022;2022(4):MR000050.
- 9) Frandsen TF, <u>Eriksen MB</u>. Anvendelse af søgefiltre i systematiske søgninger. Ugeskrift for Laeger. 2022;184(19):V12210901
- 10) Frandsen TF, Nielsen MFB, <u>Eriksen MB</u>. Avoiding searching for outcomes called for additional search strategies: A study of Cochrane review searches. Journal of Clinical Epidemiology. 2022;149:83-88.
- 11) <u>Frost AD, Hróbjartsson A, Nejstgaard CH</u>. Adherence to the PRISMA-P 2015 reporting guideline was inadequate in systematic review protocols. Journal of Clinical Epidemiology. 2022 okt.;150:179-187.
- 12) Graña C, Ghosn L, Evrenoglou T, Jarde A, Minozzi S, Bergman H, Buckley BS, Probyn K, Villanueva G, Henschke N, Bonnet H, Assi R, Menon S, Marti M, Devane D, Mallon P, Lelievre JD, Askie LM, Kredo T, Ferrand G, Davidson M, Riveros C, Tovey D, Meerpohl JJ, Grasselli G, Rada G, <u>Hróbjartsson A</u>, Ravaud P, Chaimani A, Boutron I. Efficacy and safety of COVID-19 vaccines. Cochrane Database of Systematic Reviews. 2022;2022(12):CD015477.
- 13) Hopewell S, Boutron I, Chan A-W, Collins GS, Beyer JAD, <u>Hróbjartsson A, Nejstgaard CH, Østengaard L</u>, Schulz KF, Tunn R, Moher D. An update to SPIRIT and CONSORT reporting guidelines to enhance transparency in randomized trials. Nature Medicine. 2022;28(9):1740-1743.

- 14) <u>Munkholm K, Jørgensen KJ, Paludan-Müller AS</u>. Electroconvulsive therapy for preventing relapse and recurrence in people with depression. Cochrane Database of Systematic Reviews. 2022;2022(1):CD015164.
- 15) ¹Nejstgaard CH, Lundh A, Abdi S, Clayton G, Gelle MHA, Laursen DRT, Olorisade BK, Savović J, <u>Hróbjartsson A</u>, COMFIT consortium. Combining meta-epidemiological study datasets on commercial funding of randomised clinical trials: database, methods, and descriptive results of the COMFIT study. Research Synthesis Methods. 2022;13(2):214-228.
- 16) Netra S, Sørensen P, <u>Hansen Nejstgaard C</u>. Does Public Managers' Type of Education Affect Performance in Public Organizations? A Systematic Review. Public Administration Review. 2022;82(6):1004-1023.
- 17) 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, <u>Hróbjartsson A</u>, 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. A declaração PRISMA 2020: diretriz atualizada para relatar revisões sistemáticas. Revista Panamericana de Salud Publica. 2022;46:e112.
- 18) 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, <u>Hróbjartsson A</u>, 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. A declaração PRISMA 2020: diretriz atualizada para relatar revisões sistemáticas. Epidemiologia e Serviços de Saúde_2022;31:2
- 19) <u>Paludan-Müller AS</u>, <u>Maclean-Nyegaard IR</u>, <u>Munkholm K</u>. Substantial delays in clinical data published by the European Medicines Agency a cross sectional study. Journal of Clinical Epidemiology. 2022;146:68-76.
- 20) Pizarro AB, Persad E, Durao S, Nussbaumer-Streit B, Engela-Volker JS, McElvenny D, Rhodes S, Stocking K, Fletcher T, Martin C, Noertjojo K, Sampson O, Verbeek JH, <u>Jørgensen KJ</u>, Bruschettini M. Workplace interventions to reduce the risk of SARS-CoV-2 infection outside of healthcare settings. Cochrane Database of Systematic Reviews. 2022;2022(5):CD015112.
- 21) Sandau N, Buxbom P, <u>Hróbjartsson A</u>, Harris IA, Brorson S. The methodological quality was low and conclusions discordant for meta-analyses comparing proximal humerus fracture treatments: a meta-epidemiological study. Journal of Clinical Epidemiology. 2022;142:100-109.
- 22) Smedemark SA, Llor C, Aabenhus R, Fournaise A, <u>Jørgensen KJ</u>, Olsen O. Biomarkers as point-of-care tests to guide prescription of antibiotics in people with acute respiratory infections in primary care. Cochrane Database of Systematic Reviews. 2022;2022(10):CD010130.
- 23) Sørensen A, <u>Juhl Jørgensen K</u>, <u>Munkholm K.</u> Clinical practice guideline recommendations on tapering and discontinuing antidepressants for depression: a systematic review. Therapeutic Advances in Psychopharmacology. 2022;12.

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¹ Epub in 2021 in annual report 2021.

- 24) Sørensen A, <u>Jørgensen KJ</u>, <u>Munkholm K</u>. Description of antidepressant withdrawal symptoms in clinical practice guidelines on depression: A systematic review. Journal of Affective Disorders. 2022;316:177-186.
- 25) Sørensen A, Ruhé HG, <u>Munkholm K</u>. The relationship between dose and serotonin transporter occupancy of antidepressants—a systematic review. Molecular Psychiatry. 2022;27(1):192-201.
- 26) Stoffers-Winterling JM, Storebø OJ, Kongerslev MT, <u>Faltinsen E</u>, Todorovac A, Sedoc Jørgensen M, Sales CP, Edemann Callesen H, Pereira Ribeiro J, Völlm BA, Lieb K, Simonsen E. Psychotherapies for borderline personality disorder: A focused systematic review and meta-Analysis. British Journal of Psychiatry. 2022;221(3):538-552.
- 27) Winckelmann A, Fahnøe U, Bajpai PS, Dalegaard MI, <u>Lundh A</u>, Ryom L, Bukh J, Weis N. Novel hepatitis B virus reverse transcriptase mutations in patients with sustained viremia despite long-term tenofovir treatment. Journal of Clinical Virology. 2022;150-151:105159.
- 28) Ødegård ES, Langbråten LS, <u>Lundh A</u>, Linde DS. Two-way text message interventions and healthcare outcomes in Africa: Systematic review of randomized trials with meta-analyses on appointment attendance and medicine adherence. PLOS ONE. 2022;17(4):e0266717.

List of publications: Book (editors)

1) <u>Hróbjartsson A</u> (ed.), <u>Lundh A</u>, (ed.), Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022.

List of Publications: Book chapters

- 1) Brorson S, <u>Hróbjartsson A.</u> Teori, biologi, empiri. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 375-393
- 2) <u>Hansen Nejstgaard C, Laursen DRT, Østengaard L.</u> Critically Appraised Topic (CAT). In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022 Link: https://evidensbaseretmed.digi.munksgaard.dk/?id=437
- 3) <u>Hróbjartsson A.</u> Introduktion til evidensbaseret medicin og klinisk forskningsmetode. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 21-34
- 4) <u>Hróbjartsson A</u>. Raporteringsbias. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 433-453
- 5) <u>Hróbjartsson A</u>. Studier af andre studier: systematiske oversigter og metaanalyser. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 263-297
- 6) <u>Hróbjartsson A, Lundh A</u>. Forord. In Hróbjartsson A, Lundh A, (eds.), Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 15-19
- 7) Jørgensen AW, <u>Eriksen MB</u>. Identifikation af kliniske studier. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 73-88

- 8) <u>Jørgensen KJ</u>. Screening. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 475-490
- 9) <u>Jørgensen KJ</u>. Assessment of Cancer Screening (Foreword). Pamela M. Marcus, National Institutes of Health, Cancer Control and Population Sciences, Bethesda, MD, USA. Springer 2022. p. v-vi
- 10) <u>Laursen DRT, Hróbjartsson A</u>. Placebo. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 455-474
- 11) <u>Lundh A,</u> Dahl Steffensen K. Evidensbaseret klinisk beslutningstagning om behandling. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 299-311
- 12) <u>Lundh A</u>, <u>Huitfeldt A</u>. Generaliserbarhed af resultaterne fra et klinisk studie. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 57-72
- 13) <u>Lundh A, Wien C. Formidling af klinisk forskning. In Hróbjartsson A, Lundh A, (eds.)</u>. Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 507-520
- 14) <u>Lundh A</u>, Lindberg M. Interessekonflikter i klinisk forskning. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 413-431
- 15) <u>Lundh A, Jørgensen KJ</u>. Ukontrolleret erfaring og bias i klinisk forskning. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 35-56
- 16) <u>Munkholm K.</u> Studier af enighed: observatørvariation. In Hróbjartsson A, Lundh A, (eds.). Evidensbaseret medicin og klinisk forskningsmetode. Munksgaard. 2022. s. 223-241
- 17) Vedula SS, <u>Hróbjartsson A</u>, Page MJ. Reporting Biases. In Piantadosi S, Meinert CL, (eds.). Principles and Practice of Clinical Trials. Springer. 2022. s. 2045-2071

List of Publications: Letters to the editor

- 1) Boesen K, <u>Jørgensen KJ</u>, 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. 2022 maj;145:183-184.
- 2) Horowitz MA, <u>Munkholm K</u>, Moncrieff J. Unbalanced appraisal of psychosocial versus antipsychotic literature. The Lancet Psychiatry. 2022 jul.;9(7):540-541.
- 3) <u>Munkholm K, Paludan-Müller AS</u>. Combination Antidepressant Therapy vs Monotherapy Further Considerations. JAMA Psychiatry. 2022 aug. 1;79(8):831.
- 4) <u>Munkholm K</u>, Horowitz MA, Moncrieff J. Maintenance antipsychotic trials and the effect of withdrawal. The Lancet. 2022 sep. 24;400(10357):995.
- 5) Zahl PH, <u>Jørgensen KJ</u>. To the editor: Comment on "Estimation of Breast Cancer Overdiagnosis in a U.S. Breast Screening Cohort". Annals of Internal Medicine. 2022 okt.;175(10):W114-W115.

Overview of selected large international projects

The following section presents main international projects that the Centre was engaged in during 2022.

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. See the TACIT website. The project is colled by Andreas Lundh and Asbjørn Hróbjartsson. The main publication is expected in 2024.

COMFIT – Commercial Funding in Trials. 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 is co-led by Asbjørn Hróbjartsson, Andreas Lundh, and Camilla Hansen Nejstgaard. The main publication is expected in 2023.

PRISMA-P 2025 – An updated reporting guideline for systematic review protocols. In late 2022, planning started for updating the PRISMA-P reporting guideline, originally published in 2015: PRISMA-P 2025. The leading researchers behind the original PRISMA-P initiative were contacted and a collaboration was agreed on. The project is co-led by Asbjørn Hróbjartsson and Professor Lesley Stewart from University of York. Initial starting date is August 2023 and main publication is expected in 2025.

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 public. 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. The project is led by Karsten Juhl Jørgensen.

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 Denmark, Cochrane Germany, Cochrane Ireland, Cochrane Chile, Cochrane South Africa, and others, including the Cochrane Bias Methods Group. Find more information about this project on the COVID-NMA website.

SPIRIT-CONSORT — Reporting guidelines for protocol and final report of randomised clinical trials. Our Centre was represented in the Executive Group for the update of the SPIRIT 2013 and CONSORT 2010 statements. The Centre initiated the development of a supportive database of relevant literature and published a scoping review in Journal of Clinical Epidemiology in 2022 of comments and suggestions for adjustments to SPIRIT 2013 and CONSORT 2010. A summary of the project was published in Nature Medicine in 2022. The main publication is expected in 2023.

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. The main publication is expected in 2023.

PhD projects

In 2022, there were three PhD Fellows at CD-CEBMO: David Ruben Teindl Laursen, Lasse Østengaard, and Christoffer Bruun Korfitsen.

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. Asbjørn Hróbjartsson is primary supervisor.

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 PhD study. Asbjørn Hróbjartsson is primary supervisor.

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. Andreas Lundh is primary supervisor.

Project supervision

Senior researchers at the Centre have also acted as project supervisor for four other PhD Fellows, who have primarily been affiliated with other centres: Anders Sørensen supervised by Karsten J. Jørgensen, Cille Bülow supervised by Andreas Lundh, and Nicolai Sandau and Lars Bastholt, supervised by Asbjørn Hróbjartsson.

Applications for external research funds

During 2022, members of staff have applied for external funding, or received feedback, from the following sources:

Applied to	Type of funding & amount in DKKR	Project	Status
Independent Research Fund, Denmark	5.898.820	The ProEPI study	Rejected
Independent Research Fund, Denmark	1.600.000	Reporting Guideline for Disease Awareness Campaigns.	Rejected
Independent Research Fund, Denmark	927.360	Conflicts of interest in research and professional practice across scientific disciplines and professions	Pending
The Danish Cancer Society	60.000	'Exploration of reasons for variation in adequacy of reporting of randomised trial protocols and publications: systematic review of studies on adherence to the SPIRIT 2013 and CONSORT 2010 reporting guidelines'	Rejected

III. <u>Promotion of Cochrane in Denmark and support to Cochrane authors based in Denmark as well as Cochrane internationally</u>

Supporting national collaboration within Cochrane and evidence-based medicine
The heads of the three Cochrane Review Group based in Denmark and Asbjørn Hróbjartsson have established routine video meetings approximately every two months. The meetings provide a forum for discussing recent Cochrane developments.

Furthermore, on the 3rd May 2022, the Centre initiated a half day seminar on evidence-based medicine. The seminar was well attended, and participants explored the possibility of setting up a more formal Collaborative Network and discussing recent developments within Cochrane. After the meeting, the Danish EBM Network was established. The Network aims to foster collaboration between persons interested in evidence-based medicine and Cochrane activities in Denmark. There are now 46 persons on the mailing list. Lasse Østengaard is daily coordinator.

We provided a tailored course for training new staff at the Danish Medicines Council, and we will continue that collaboration.

Talks and teaching sessions on Cochrane methods and review methodology

Staff gave talks on Cochrane Denmark for the Research Council at Odense University Hospital, and for newly appointed professors; on Cochrane methods and evidence-based medicine for REHPA Nyborg; and on Cochrane Review methodology at Department of Clinical Biochemistry at Odense University Hospital, and on systematic review methods at Department of Otorhinolaryngology at Odense University Hospital x

2. Also, a staff member gave a talk a Cochrane review on control interventions in psychiatry trials. Research staff from our centre also contributed to PhD courses at Lund University and the University in Bergen.

Finally, the Centre arranged and ran a half day special course on risk of bias assessment and GRADE methods for new staff at Danish Medicines Council (Medicinrådet), which provides guidance about new medicines for use in the Danish hospital sector. The Centre also gave two talks at the Danish Health Technology Council (Behandlingsrådet) on ROBINS-I and on Prioritization in healthcare.

Training Cochrane authors

See below under 'Course activity on Cochrane methodology and systematic reviews'

Media contact

During the year, Centre staff had 21 media contacts, or the Centre was otherwise mentioned in the following media: Tv2, Radio4 (x2), DR P1, Tv2, Berlingske Tidende, Dagens Medicin (x2), BT, Ekstra Bladet, Journalisten, Videnskab.dk (x4), Femina, Ugeskr. Laeger, deuafhængige.dk, NetavisenPio, Jyske Vestkysten, Podcast on opioid crisis for Ciencia Suja (Brazil).

International Cochrane activities

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 Matt Page, Cochrane Australia; Professor Isabelle Boutron, Cochrane France; and Professor Julian Higgins, University of Bristol, UK. The group's research coordinator is Camilla Hansen Nejstgaard.

In 2022, the focus for the group has been on implementing training for the revised tool to assess risk of bias in randomised trials (RoB2). 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 exposures (ROBINS-E).

Members of staff served on Cochrane's scientific advisory board (Cochrane Scientific Committee), on the Advisory Board for Cochrane Sweden, and Cochrane Sustainable Healthcare.

IV. Research training and methods guidance

Throughout 2022, 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 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 up to 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 up to 10-hours support. It is available to PhD Fellows 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 25 projects in pipeline for long term guidance.

In 2022, we held ten methods clinics. We provided short term advice to 32 projects (at individual meetings or at workshops), and also long-term advice to 32 consultancy projects, including three Cochrane reviews. We will continue to provide guidance in 2023 for 23 of these projects.

Course activity on Cochrane methodology and systematic reviews

We have a portfolio of courses on Cochrane methodology on how to conduct a systematic review or evidence synthesis. The courses are aimed at Cochrane authors from Denmark broadly and for researchers at 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. Both courses were held once in 2022 and were well attended.

V. <u>Teaching Evidence-Based Medicine at University of Southern Denmark</u>

Our Centre led the course in evidence-based medicine for medical students at the University of Southern Denmark. We organised the course, taught, and examined approximately 30 medical students. 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 Fellows contribute with 18 hours of case-work instructions and 330 hours of instructions and feedback to written assignments of a critically appraised topic (CAT). We planned a revision of the course, which will be implemented in autumn 2023.

Senior researchers at the Centre edited and co-wrote a textbook in evidence-based medicine which was published by Munksgaard in 2022. It is aimed to serve both as a textbook for the course and as a general introduction to the field for readers with an interest in evidence-based health care and clinical research methodology.

Two members of our team also 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) had status as PhD courses.

Members of staff also taught at 'Introduction to new PhD Fellows' at the Faculty of Health Sciences.

VI. Other activities

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 contributed 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.

Board and committee membership (non-Cochrane)

Members of staff served as member of the Scientific Committee of Preventing Overdiagnosis, Vice-chair of Doctors without Sponsor, Advisory Board member for the Danish healthcare think tank SundFornuft, member of the Working Group for the re-assessment of the Danish breast screening programme (Danish Health Authority), Vice-chair of Doctors without Sponsor, and Advisory Board member for the Danish healthcare think tank SundFornuft. Treasurer for Danish Society for Medical Philosophy, Ethics and Methods, and Treasurer at Danish Society for Tropical Medicine and International Health, advisory board member for Centre for Evidence-Based Psychiatry, and Board Member of the PhD Association at the University of Southern Denmark. Members of staff also headed the group facilitating the implementation of Odense University Hospital research strategy: evidence-based medicine, contributed to Odense University Hospital.

Talks (non-Cochrane)

Staff from the Centre gave talks on teaching Evidence-Based Medicine for a group of curriculum planners at University of Copenhagen; on Rational Clinical Decision Making and on Rational Pharmacotherapy at the Danish Health Authority; on regression by composition at the Berlin Epidemiology Methods Colloquium; and on conflicts of interest in peer review at Research Unit for Musculoskeletal Function and Physiotherapy at University of Southern Denmark.

Specialist training

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.

Assessments of academic theses or positions

Members of staff contributed to the assessment of two PhD theses for University of Copenhagen and served as head of committee for one assessment of a PhD thesis for University of Southern Denmark.

Members of staff also assessed applications for a professorship, an associated professorship, an assistant professorship, and a senior researcher.

VII. Overview of main developments and changes from 2021

2022 was the second year following the functional merger of Cochrane Denmark and Centre for Evidence-Based Medicine Odense. A natural feature of 2021 was an initial uncertainty relating to the relocation of Cochrane Denmark to Odense and the disruption of previous routines. In 2022 new routines were consolidated, some individuals left the Centre and new staff arrived, and a unified working culture was more clearly emerging.

In 2022 researchers at the Centre published a robust number of articles in journals with high impact factors and central to clinical research methodology, often involving international collaboration and with first/last author from the Centre. Staff at the Centre were responsible for editing and writing a textbook in Evidence-based Medicine and Clinical Research Methods. Thus, the expected reduction in research output due to the organizational challenges of the merger did not occur in 2022.

The year also involved establishing a more ambitious methods consultancy activity, running successful PhD courses and a course tailored for new staff at Danish Medicines Council (Medicinrådet), establishing a national Danish EBM Network, and planning a revised pre-graduate course in Evidence-based Medicine at the University of Southern Denmark.

Odense, 09.03.2023

Asbjørn Hróbjartsson Professor, Head of Centre

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