Annual report
2016

Nordic Cochrane Centre
Introduction

Updated systematic reviews of clinical research are essential for rational decision making in health care and for guiding the planning of new research. The Cochrane Collaboration is a registered charity, founded in 1993. Its major product, The Cochrane Library, contains more than 7,000 regularly updated systematic reviews of interventions in health care. Cochrane reviews are indexed in PubMed. The impact factor of the Cochrane Database of Systematic Reviews is about 6, which means that it is ranked 12th of the 152 journals in the Medicine, General & Internal category. The Cochrane Collaboration’s organisational structure is described at http://www.cochrane.org/.

It is a fundamental right that information that is important to the citizens is transparent and available. Few things are more important than having access to reliable information about the benefits and harms of interventions for preventing and treating diseases. Half of the world's population has free access to Cochrane reviews and the other half has free access to abstracts of Cochrane reviews. Our ultimate aim is to provide free access to Cochrane reviews for everyone; currently, our finances has allowed us to provide free access to all Cochrane reviews 12 months after they have been published or updated.

We report here the main achievements of the Nordic Cochrane Centre for 2015 and the three review groups based in Denmark in relation to our Strategic Plan 2016-20 (see http://nordic.cochrane.org/).

The strategic plan for the Nordic Cochrane Centre has a broad perspective. Its overall aim is to help citizens, patients, health care professionals and the payers of health care services to choose - or to avoid to use - interventions rationally, in an evidence-based fashion, and with a focus on benefits, harms and costs. Our strategic plan encompasses the goals of the Cochrane Collaboration internationally as outlined in its “Strategy to 2020” and other documents, but goes beyond these. The goals in “Strategy to 2020” are:

**Goal 1: Producing evidence**
To produce high-quality, relevant, up-to-date systematic reviews and other synthesised research evidence to inform health decision making.

**Goal 2: Making our evidence accessible**
To make Cochrane evidence accessible and useful to everybody, everywhere in the world.

**Goal 3: Advocating for evidence**
To make Cochrane the ‘home of evidence’ to inform health decision making, build greater recognition of our work, and become the leading advocate for evidence-informed health care.

**Goal 4: Building an effective & sustainable organisation**
To be a diverse, inclusive and transparent international organisation that effectively harnesses the enthusiasm and skills of our contributors, is guided by our principles, governed accountably, managed efficiently and makes optimal use of its resources.

The Nordic Cochrane Centre is located at Rigshospitalet in Copenhagen. It was established on 13 October 1993, the same month the Cochrane Collaboration was launched. There are associate
centres in Finland, Norway, Poland, Russia and Sweden (established in 2017), which perform similar work as the Centre but have less formal obligations.

Six Cochrane groups are based in the Nordic countries: the Hepato-Biliary Group (Denmark), the Colorectal Cancer Group (Denmark), the Anaesthesia, Critical and Emergency Care Group, the Work Group: Health & Safety at work (Finland), the Norwegian satellite of the Effective Practice and Organisation of Care Group (Norway), and the Cochrane Bias Methods Group (Denmark).

The Nordic Cochrane Centre and the three review groups based in Denmark are financed by the Danish Government. Other funders are listed in our Annual Reports (http://nordic.cochrane.org/). Like other Cochrane groups, we do not accept industry funding.

Citizens in Denmark, Iceland, Norway and Poland, and almost all physicians in Finland, have free Internet access to the Cochrane Library, which is often consulted in these countries.

**Selected main achievements**

The Nordic Cochrane Centre is internationally oriented. Over the years we have had employees from Armenia, Colombia, Denmark, the Faroe Islands, Finland, Germany, Iceland, India, Italy, Moldovia, Nigeria, Norway, Pakistan, Spain, Sweden, the UK, and the USA. In addition, unpaid volunteers have helped us from China, Egypt, France, Japan, Netherlands, Poland, Portugal, and Russia.

The Centre has contributed substantially to the Cochrane Collaboration, particularly in research and IT development, and dissemination of research results.

**Research**

Randomised trials are the most reliable basis for clinical decisions but many of them are biased by their design or analysis, and selective reporting of outcomes or of whole trials are also common. The biases are so prevalent that almost half the trials included in recent Cochrane reviews were considered to be at a high risk of bias. Furthermore, trials are often short-term, even for interventions that are used for decades, and important harms have often been left out, even when they were deadly.

Cochrane reviews are generally more thoroughly done and more reliable than other systematic reviews, but users of Cochrane reviews need to be aware that they are too positive, on average, because of the pervasive flaws in biomedical research and publication, which can only partly be known and taken into account.

For these reasons, we continue to prioritise research that aims at elucidating sources of bias in clinical research and to focus on getting access to more reliable data than what has been published in journal articles.

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The part of our research that focuses on unpublished clinical study reports will continue. In 2010, the Nordic Cochrane Centre set an important precedent when, helped by the European Ombudsman, we succeeded to get access to unpublished clinical study reports and their corresponding protocols for two anti-obesity drugs at the European Medicines Agency (EMA). In 2016, we have continued our efforts to help ensure that all results of clinical research, the corresponding trial protocols and all separate agreements between researchers and sponsors, the raw anonymised patient level data, and animal toxicology studies become publicly available. We have done this, for example, by collaborating with the Commons Network and other large consumer organisations, the International Society of Drug Bulletins, Council for Evidence-based Psychiatry (UK), Critical Psychiatry Network (UK), politicians and lobbyists in the European and other parliaments. We are particularly aware of the set-backs that have occurred when the EMA denied access to study reports or redacted information of vital importance for the needs of independent researchers for no good reason.

In 2016, we complained to the European Ombudsman about the EMA’s handling of the suspected serious harms of the HPV vaccines, which we consider a case of maladministration. We started a research project based on the clinical study reports of the vaccines, which we had obtained from the EMA.

Also in 2016, we showed that the EMA’s idea of “adaptive pathways”, which would lower the regulatory barrier for approving new drugs, would have serious public health consequences. Under the Dutch EU chairmanship, we suggested a future scenario where there would be no patents and where drug research and development would be a public enterprise.

Our aspiration has always been to produce research of high quality that makes a difference for many people and to contribute to improving the methods for doing and reporting research. We believe we have succeeded quite well with this, as evidenced for example by our 30 publications during 2011-2016 in the big five general medical journals (BMJ, the Lancet, JAMA, Annals of Internal Medicine and New England Journal of Medicine) and the many news stories internationally our research has led to, also in 2016. Much of this research has a methodological component, which contributes to improving the quality and reliability of Cochrane reviews, randomised trials and other types of research and to knowledge translation, i.e. providing information to the public that is easy to understand.

Areas we focus on in particular

One of the most problematic areas in health care is psychiatry. Psychiatric drugs and electroshock are being used far too much and often in a non-evidence based fashion, although they have many

harmful effects, which include deaths, irreversible brain damage, and dependency. Our research in this area aims at providing a more reliable evidence base and at helping people who wish to come off the drugs. In 2016, we published several important reviews, both of human and animal studies, and we currently work on two Cochrane reviews in psychiatry, one on extended release methylphenidate for adult ADHD and one on safe withdrawal of antidepressant drugs. We have also started research on withdrawing patients from psychiatric drugs and we study court cases of forced medication to elucidate whether the patients’ rights are being respected. In 2016, Peter Gotzsche cofounded the International Institute for Psychiatric Drug Withdrawal, and in 2017, the first courses on drug withdrawal will he held in Göteborg and Copenhagen.

We regularly update 17 Cochrane reviews published in 11 different Cochrane review groups and publish new reviews, focusing primarily on issues of major importance for public health or for rational use of health care resources. These reviews span many different topics, including screening for diseases or risk factors, infectious diseases, cancer, asthma, enzyme deficiency, liver disease, rheumatology, psychiatry, and the placebo effect. Apart from our reviews of psychiatric drugs, we currently work on a new Cochrane review of screening for melanomas.

We currently have seven PhD students. They work with psychiatric drugs and other issues in psychiatry; the influence of industry sponsorship and other conflicts of interest on the outcomes and quality of systematic reviews; possible serious harms of the HPV vaccines; and on whether contemporary trials are both scientifically and ethically defensible given what was known or could have been known if a systematic review of previous trials had been carried out.

We continue to expand our research collaboration with colleagues internationally, primarily with researchers in Canada, France, Italy, Norway, Sweden, the UK, and the USA. We co-author guidelines on standards for good reporting of research: CONSORT for trials, STROBE for observational studies, PRISMA for systematic reviews and SPIRIT for protocols, which many top journals require authors to adhere to when they submit manuscripts.

**Value of the Centre for Denmark**

The Nordic Cochrane Centre and the three Cochrane review groups based in Denmark have been funded by the Danish government since 2001. This investment has paid off handsomely, which we shall illustrate by three reviews produced by the Nordic Cochrane Centre. Taken together, we estimate that the three reviews have saved over 500 mio Danish crowns annually, which is about 100 times our annual budget.

Mammography screening was carried out in Denmark in the 1990s in a limited geographical area, corresponding to 20% of the population in the relevant age group. In 1997, a report from the National Board of Health recommended it be introduced in the rest of the country, but the Danish Medical Association had doubts about its effects. We were asked to assess the trials in 1999. Our conclusion was that we could not exclude the possibility that screening did more harm than good. Next, the National Board of Health funded a Cochrane review, which we published in 2001, with similar reservations. Mainly because of our research, the Danish regions decided to postpone the introduction of screening in the remaining 80% of the country, but were ultimately required to introduce it by the government. From late 2007, the remaining regions gradually introduced screening although coverage was not complete even as late as in 2014 due to lack of staff. We have published many papers on mammography screening, a doctoral thesis, and a 388-page...
book and have explained why we are convinced that it does more harm than good and should be stopped. In all those years where we only had screening in 20% of the country, Danish taxpayers saved more than 200 mio Danish crowns every year. Our Cochrane review on mammography screening is often in the top ten for world-wide downloads of Cochrane reviews.

In 2008, a majority in Parliament wanted to reimburse alpha-1 antitrypsin for treatment of patients with lung disease who had this enzyme deficiency. However, the Health Committee asked the Nordic Cochrane Centre’s director to assess the trials, and he delivered a report after four weeks. His conclusion was that there was no good reason to use the treatment, as there was no conclusive effect on lung function and a lack of data on patient relevant outcomes, e.g. symptoms, quality of life, acute exacerbations, infections and survival. Two years earlier, the Danish Drug Agency had claimed that treatment with alpha-1-antitrypsin could reduce the loss of lung function and reduce mortality, but there was no reliable evidence for these claims, and the drug agency did not respond to our request for documentation for these effects. We later published a Cochrane review of this treatment. Based on the initial report, reimbursement of the drug was declined, which has saved at least 100 mio Danish crowns annually.

General health checks are popular but we decided to do a Cochrane review to find out whether they worked. When we saw the results in 2011, we asked for a meeting with the Minister of Health and she abandoned the government’s plans of introducing it, as the results were very convincing and were supported by preliminary results from a large Danish randomised trial performed by the Centre for Health and Prevention, which had not yet been published. There were almost 12,000 deaths in the trials but no effect on mortality whereas health checks led to more diagnoses, which increase drug usage. It is therefore likely that health checks do more harm than good. Our review has saved over 200 mio Danish crowns annually.

**Dissemination and usage of research results**

Dissemination of research results is as important as producing them because pivotal results are often unknown to clinicians and policy-makers. This work should not be undertaken lightly and it requires some degree of quality control, since so many original research results and therefore also systematic reviews of such results exaggerate the benefits of interventions and underestimate their harms.

Cochrane reviews are being widely used in the Nordic area. Norway and Denmark have national subscriptions to the Cochrane Library, which is likely one of the reasons that there are more full-text downloads in these countries than in Sweden and Finland. Downloads per million inhabitants:

- Norway: 26.115
- Denmark: 18.258
- Sweden: 11.558
- Finland: 7.530

Knowledge translation, which means providing information in a more easily understandable format than reviews, is an important activity in the Cochrane Collaboration. We contribute substantially to this. In 2016, we were contacted by over 100 different journalists who came to us because it is difficult to find experts in health care who do not have financial conflicts of interest or are biased in other ways.
In the Danish Infomedia database, “Cochrane” appeared 511 times in 2016, of which 35 were in national newspapers. This list is not complete. For example, there were 14 listed appearances in national radio or TV, which is far below the number of times researchers at the Centre actually appeared on national radio or TV. In addition to the national appearances, we give many interviews to electronic and printed media in other countries. We also write many newspaper articles, letters to the editors, blogs and twitter messages, and upload comments on PubMed abstracts when we find that published research is misleading.

Peter Gøtzsche’s two evidence-based books from 2013 and 2015 about drugs are important contributions to the goals of the Cochrane Collaboration, as they help the citizens to make more informed decisions about the drugs they are being offered.⁷ ⁸ Doctors rarely know much about drugs that goes beyond what the drug industry has told them, which is an important reason why our prescription drugs are the third leading cause of death after heart disease and cancer. These book have been translated into many languages and continue to create a lot of attention, also among journalists.

The two books have been very helpful for our dissemination activities more generally, also for dissemination of results from Cochrane reviews, both directly (they have 31 and 35 references to Cochrane reviews, respectively) and indirectly. The Centre’s director has been contacted by over 50 TV crews and filmmakers and has participated in over 20 radio shows and numerous news broadcasts in more than 15 countries about issues described in the books. Our contribution to reforming the way we look at drugs has been much appreciated by patients and healthcare professionals worldwide and has led to several awards and other honours, e.g. Winner of the British Medical Association’s Annual Book Award in the category Basis of Medicine (2014), Award from the International Society of Ethical Psychology and Psychiatry (2014), Honourable Award, Consul General Ernst Carlsen’s Foundation (2015), Book of the Year, US Tributaries Radio (2015), and HealthWatch Award, London (2016). In 2015, the Centre’s director was a top ten finalist for the award “Dane of the year” nominated by psychiatric patients and in 2016, he became Protector for the Hearing Voices Network in Denmark.

The Centre’s deputy director is also very often in the media. Dissemination via the media, particularly in TV documentaries, can be highly effective as it reaches so many people. We will therefore consider, also in future, writing books or booklets about health care interventions.

We are currently translating “Testing Treatments” into Danish, a book written by the founder of the Cochrane Collaboration, Sir Iain Chalmers and others. It explains very well why randomised trials are so essential.⁹ We will upload it on our website and make it freely available, as it is in other countries.

Our approach to dissemination has previously mostly been reactive, but we are gradually becoming more proactive in order to disseminate important research information more effectively to the public. By the end of 2016, we employed a communication consultant to help us with this work.

Partnerships with other organisations

In Denmark, it has always been respected and highly valued that the Nordic Cochrane Centre is completely independent of any political interests and institutions, and has full academic freedom to criticise anything we feel merits critique, even procedures at the hospital that hosts the Centre. We prefer informal strategic partnerships with other organisations and are involved in many of these. If partnerships are being formalised, they can sometimes turn out be counter-productive. Formalised collaboration inevitably leads to increased bureaucracy and can be a threat to academic freedom, also when public institutions are involved, and we give some examples of this in our Strategic Plan 2016-2020.

We had a fruitful partnership with the National Board of Health until mid-2016 when the funding ended. The deputy director of our Centre was employed one day a week as a methods consultant on the development of national clinical guidelines based on Cochrane methodology and grading the quality and certainty of the evidence and the strength of recommendations with the GRADE tool.

Cochrane workshops

For many years, we have offered four Cochrane workshops annually, two for protocols and two for review completion. We also offer people to get advice over the phone, in writing or at one-to-one meetings, and we hold workshops in other countries if there are a sufficient number of people with registered review titles or with data for a review. In 2016, we held Cochrane workshops for our associate centre in Russia, which was established in 2015 with our support.

Review Groups in the Nordic region

Cochrane Hepato-Biliary Group

The group was registered on 29 March 1996 and is based in Copenhagen. In March 2017, the Cochrane Library contained 190 reviews and 141 protocols. For further information, see the Cochrane Library or [http://hbg.cochrane.org/](http://hbg.cochrane.org/).

Cochrane Colorectal Cancer Group

The group was registered on 27 January 1998 and is based in Copenhagen. In March 2017, the Cochrane Library contained 106 reviews and 79 protocols. For further information, see the Cochrane Library or [http://cc.cochrane.org/](http://cc.cochrane.org/).

Cochrane Anaesthesia, Critical and Emergency Care Group

The Anaesthesia Group (CARG) was registered in February 2000 and is based in Copenhagen. In March 2017, the Cochrane Library contained 197 reviews and 71 protocols. For further information, see the Cochrane Library or [http://ace.cochrane.org/](http://ace.cochrane.org/).
Cochrane Work Group: Health & Safety at work

The Work Group was registered in July 2010 and is based in Kuopio. In March 2017, the Cochrane Library contained 29 reviews and 22 protocols. For further information, see the Cochrane Library or http://work.cochrane.org/.

Norwegian Satellite of the Cochrane Effective Practice and Organisation of Care (EPOC) Group

The Norwegian EPOC Satellite was launched in Oslo in November 2006. The aim of the satellite is to support review authors in low- and middle-income countries and reviews relevant to such countries, as well as supporting EPOC review authors in the Nordic area. For further information, see The Cochrane Library or http://epoc.cochrane.org/.

Cochrane Bias Methods Group

The Bias Methods Group moved its secretarial base from Ottawa in Canada to Odense in Denmark on 1 January 2016. It is headed by Professor Asbjørn Hrobjartsson, former chief physician at the Nordic Cochrane Centre. The group’s main aims are to undertake methodological research on how to identify and address potential biases in systematic reviews and meta-analyses; help to complete and co-ordinate systematic reviews of methods; to provide guidance to Cochrane groups; and to update relevant sections of the Cochrane Handbook. For further information, see The Cochrane Library or http://methods.cochrane.org/bias/.

Nordic Cochrane reviews

Review production in the Nordic countries is very high, apart from Sweden10 Measured as number of reviews per 1 million inhabitants, Denmark was ranked 6, Norway 10 and Finland 11.

In issue 3, 2017 of The Cochrane Library, 198 reviews and 90 protocols were listed with a Nordic contact address:

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<thead>
<tr>
<th>Country</th>
<th>Reviews</th>
<th>Protocols</th>
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<tbody>
<tr>
<td>DENMARK</td>
<td>96</td>
<td>54</td>
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<tr>
<td>NORWAY</td>
<td>43</td>
<td>15</td>
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<tr>
<td>FINLAND</td>
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<td>6</td>
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<tr>
<td>SWEDEN</td>
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<td>8</td>
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<td>POLAND</td>
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<td>7</td>
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<td>RUSSIA</td>
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<tr>
<td>Total</td>
<td>198</td>
<td>90</td>
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Number of reviews and protocols in Sweden went up from 11 and 9, respectively, to 20 and 8, from 2015 to 2016, which was because a very active contributor to Cochrane reviews, Matteo Bruchettini, moved from Italy to Sweden.

In May 2017, Bruchettini became the director of the newly opened Swedish Associate Cochrane Centre in Lund, after a process we facilitated.

**Advisory Board for the Nordic Cochrane Centre**

The Advisory Board for the Nordic Cochrane Centre provides advice and support about the strategic direction for activities within the Centre. In 2016, the members were:

- Douglas Altman, Professor of Statistics in Medicine, Oxford, UK
- Gerd Antes, Director, German Cochrane Centre
- Mike Clarke, former Director, UK Cochrane Centre
- Sine Jensen, Senior Health Adviser, Danish Consumer Council
- Cindy Mulrow, Editor, Annals of Internal Medicine
- Maryann Napoli, Associate Director, Center for Medical Consumers, USA
- Drummond Rennie, Editor, JAMA
- David Tovey, Editor-in-Chief, The Cochrane Collaboration
- Erick Turner, Department of Psychiatry, Oregon Health & Science University

**Acknowledgements**

The Cochrane Collaboration is registered as a charity and it is the responsibility of all contributors and groups to secure their own funding. The staff at the Nordic Cochrane Centre are grateful for the financial support received from our funders and the voluntary help received from many people and institutions since the Centre was founded in 1993 (see previous Annual Reports and Strategic Plans on [http://nordic.cochrane.org/](http://nordic.cochrane.org/)). Currently, the funders for the Centre or its projects are:

- Danish Government
- Helsefonden
- Laura and John Arnold Foundation, Texas
- University of Copenhagen

**Awards**

Peter C Gøtzsche: HealthWatch Award, London.

**Publications by staff at the Nordic Cochrane Centre**

*PhD dissertations*
Maund E. The effect of selective serotonin reuptake inhibitors (SSRIs) on suicidality and violent behaviour (PhD thesis). Defended at the University of Copenhagen 15 February 2016.

**Books and book chapters**


**New or updated Cochrane reviews and protocols**


**Journal articles and reports**


Kolthoff SK, Hestbech MS, Jørgensen KJ, Brodersen J. Do invitations for cervical screening provide sufficient information to enable informed choice?: A cross-sectional study of invitations for publicly funded cervical screening. JRSM 2016;109:274-81.


Other


Gøtzsche PC. Antidepressants are addictive and increase the risk of relapse. BMJ 2016;352:i574.


Gøtzsche PC. Author’s reply to Dubicka and colleagues and Stone. BMJ 2016;352:i915.


Gøtzsche PC. Forced admission and treatment in psychiatry are violations of basic human rights and must be abolished. Lecture in Anchorage 2 june 2016.


Gøtzsche PC. Seks ting der er værd at vide om massenskyderier. Videnskab.dk 2016;jun1.

Gøtzsche PC. Tvangsovene i psykiatrien skal afskaffes. Psykologernes Fagmagasin 2016;mar17.


Gøtzsche PC. Unblinding in SSRI trials due to side effects is an important source of bias. Br J Psychiatry 2016;208.


Johansson M, Juhl Jørgensen K, Marklund B, Hansson A, Brodersen J. Kräfttag krävs mot intellektuell bias: En högre vetenskaplig nivå samt krafttag mot intellektuell bias i expertgrupper är nödvändigt för att upprätthålla förtroendet för Socialstyrelsens rekommendationer. Läkartidningen 2016;113:EACF.

Johansson M, Juhl Jørgensen K, Marklund B, Hansson A, John B. Slutreplik: Oroväckande inställning från Socialstyrelsen och SBU. Lakartidningen 2016;113:ECRE.


