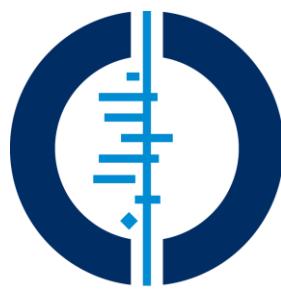


# **Annual report**

## **2017**

**Nordic Cochrane Centre**



**Cochrane  
Nordic**

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# Introduction

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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 10,000 regularly updated systematic reviews of interventions in health care or protocols for such reviews.

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.

It is a fundamental right that information, which is important to citizens is transparent and available. Few things are more important for people than having access to reliable information about the benefits and harms of interventions for preventing and treating diseases. Everyone has free access to abstracts of Cochrane reviews and half of the world's population has free access to full Cochrane reviews. Our ultimate aim is to provide free access to Cochrane reviews for everyone. Currently, our finances have allowed us to provide worldwide 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 2017 and the number of Cochrane reviews produced by the three review groups based in Denmark.

The [Strategic Plan 2016-20](#) 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. Our area of

responsibility include associate centres in [Finland](#), [Norway](#), [Poland](#), [Russia](#) and [Sweden](#), which perform similar work as our 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](#) (Denmark), 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. This funding also covers Copenhagen Trial Unit, which has the same leader as the Hepato-Biliary Group, Christian Gluud. Other funders are listed in our Annual Reports. 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

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

The Centre contributes substantially to the Cochrane Collaboration, particularly in research and dissemination of research results. Previously, we also contributed substantially to IT development.

Our main achievement in 2017 was the establishment of an associate [Swedish Cochrane Centre](#) in Lund, which was inaugurated in May 2017. Dr Matteo Bruschettini announced his interest in April 2016, in response to a paper we were involved with that was published two months earlier in Läkartidningen (Journal of the Swedish Medical Association).<sup>1</sup> Being the corresponding author of 14 Cochrane reviews, Bruschettini was an ideal candidate and he received wide support from important institutions, including Karolinska Institute in Stockholm and other universities. The centre is financially supported by Region Skåne and Lund's University.

Two other main achievements were when we, in collaboration with the Cochrane Editorial Unit in London, succeeded to establish new leaderships for the Colorectal Cancer Group and the Anaesthesia, Critical and Emergency Care Group, both based in Denmark. Jacob Rosenberg, previous editor of Ugeskrift for Læger (Journal of the Danish Medical Association) is the new co-ordinating editor of the Colorectal Cancer Group, and the latter group will be split into an Anaesthesia Group and a Critical and Emergency Care Group.

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<sup>1</sup> Johansson M, Marklund B. AllTrials-kampanjen och varför vi behöver Cochrane i Sverige. Läkartidningen 2016; 23 Feb. <http://www.lakartidningen.se/Opinion/Debatt/2016/02/AllTrials-kampanjen-och-varfor-vi-behoover-Cochrane-i-Sverige/>.

In 2017, the Nordic Cochrane Centre's director, Peter Gøtzsche, became an elected member of the Cochrane Governing Board, the uppermost decision-making body within the Cochrane Collaboration, with the most votes of the 11 candidates.

## Research

Randomised trials are the most reliable basis for clinical decisions, but many trials are biased by their design or analysis, or both, and selective reporting of outcomes or of whole trials is also common. The biases are so prevalent that almost half the trials included in recent Cochrane reviews were considered to be at high risk of bias.<sup>2</sup>

Furthermore, trials are often short-term, even for interventions that are used for decades, and important harms have often been omitted from publications. As an example, a review of 142 psychiatric drug trials found that half of the deaths and half of the suicides had been left out.<sup>3</sup>

Cochrane reviews are generally more thoroughly done and more reliable than other systematic reviews. However, users should be made aware of that many Cochrane reviews are too positive, on average, because of the pervasive flaws in reports of randomised trials, which can only partly be taken into account, as detailed information about trial conduct and most of the data are usually missing. Access to full trial protocols, anonymised raw data and case report forms is virtually non-existing.

At the Nordic Cochrane Centre, we have always prioritised research that aims at elucidating sources of bias in clinical research. As a sign of this commitment, the Cochrane Bias Methods Group is co-ordinated from Denmark and has a previous chief physician from our Centre, Asbjørn Hróbjartsson, as one of its four convenors.

Our strong dedication to this type of research has resulted in the establishment of two unique, new professorships in Denmark, which in reality might be seen as Cochrane professorships. The Director of the Nordic Cochrane Centre, Peter Gøtzsche, became Professor of Clinical Research Design and Analysis in 2010 at the University of Copenhagen, and Asbjørn Hróbjartsson became professor of Evidence-based Medicine and Clinical Research Methods in 2015 at the University of Southern Denmark.

We regularly update 17 Cochrane reviews published through 11 different Cochrane review groups and also work on new reviews, including one of screening for melanomas.<sup>4</sup> These reviews span many different topics, including screening for diseases or risk factors, infectious diseases, cancer, asthma, enzyme deficiency, liver disease, rheumatology, psychiatry, bias related to conflicts of interest, and the placebo effect.

We continue to expand our research collaboration with colleagues internationally, primarily with researchers in Australia, Canada, France, Italy, Norway, Sweden, UK, and USA. Gøtzsche is co-author on guidelines on standards for good reporting of research: CONSORT for trials, STROBE

<sup>2</sup> Yordanov Y, Dechartres A, Porcher R, Boutron I, Altman DG, Ravaud P. Avoidable waste of research related to inadequate methods in clinical trials. *BMJ* 2015;350:h809.

<sup>3</sup> Hughes S, Cohen D, Jaggi R. Differences in reporting serious adverse events in industry sponsored clinical trial registries and journal articles on antidepressant and antipsychotic drugs: a cross-sectional study. *BMJ Open* 2014;4:e005535.

<sup>4</sup> Johansson M, Brodersen J, Gøtzsche PC, Jørgensen KJ. Screening for reducing morbidity and mortality in malignant melanoma. *Cochrane Database Syst Rev* 2016;9:CD012352.

for observational studies, PRISMA for systematic reviews and SPIRIT for protocols, which many top journals require authors to adhere to when they submit manuscripts.

Because published research is often unreliable, we will continue working on the part of our research that focuses on unpublished clinical study reports. In 2010, the Nordic Cochrane Centre set an important precedent when, after a complaint to 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).<sup>5</sup>

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 collaborate with the Commons Network (and other large consumer organisations), the International Society of Drug Bulletins, and politicians and lobbyists in the European and other parliaments, and Gøtzsche is a member of Council for Evidence-based Psychiatry (UK) and Critical Psychiatry Network (UK).

We are particularly aware of the set-backs that occurred when EMA - after our 2010 breakthrough – either denied access to study reports or redacted information of vital importance for proper, independent analysis of the trials. The drug industry is so powerful that the battle for access to vitally important data never ends.

Under the Dutch EU chairmanship, an international working group including patient representatives, industry leaders, academics, regulators, payers and government representatives was set up to explore potential solutions to the complex societal challenge of high drug prices and medical innovation. Gøtzsche participated and suggested a future scenario where there would be no patents and where drug research and development would be a public enterprise.<sup>6</sup> The chair of the working group found these ideas far-fetched and became very surprised when it turned out that 10 of the 30 invited people were willing to join Gøtzsche.<sup>7</sup>

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. The visible outcomes of these efforts are evidenced, for example, by our 30 publications during 2011-2016 in the big five general medical journals (BMJ, Lancet, JAMA, Annals of Internal Medicine and New England Journal of Medicine) and the many news stories our research has led to. 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 also to knowledge translation by providing information to the public in the media in a format that is easy to understand.

## **Areas we focus on in particular**

As just mentioned, we prefer to focus on areas that affect many people because this is where our research could be most valuable.

<sup>5</sup> Gøtzsche PC, Jørgensen AW. Opening up data at the European Medicines Agency. BMJ 2011;342:d2686.

<sup>6</sup> Gøtzsche PC. Patients not patents: Drug research and development as a public enterprise. Eur J Clin Invest 2017;e12875.

<sup>7</sup> Gøtzsche PC. A totally new system is needed for drug research and development. Eur J Clin Invest 2018;e12883.

We continue our research on mammography screening, which started in 1999 and resulted in the Cochrane review on this issue, first published in 2001,<sup>8</sup> numerous other publications including a major one in 2017,<sup>9</sup> and a book.<sup>10</sup> Deputy director Karsten Juhl Jørgensen is responsible for this line of research.

Jørgensen has established an international working group whose main aim is to write guidelines about when screening for diseases or risk factors should stop. There are numerous guidelines about when to start screening or treatment with drugs, but no guidelines about when the evidence against screening is sufficiently strong to call for stopping screening, and virtually no guidelines about when to stop treatment with drugs and how to do it safely in order to reduce the risk of withdrawal symptoms.

We currently have 9 PhD students, 5 of whom work with psychiatry.

### Psychiatry

One of the most problematic areas in health care is psychiatry. It is the only specialty where the patients are quite often dissatisfied with the treatments they receive and where forced treatment with drugs is allowed. There is a growing recognition, not only among patients, their relatives and other non-professionals, but also among psychiatrists, that psychiatric drugs and electroshock are being used far too much and often in a non-evidence based fashion, although they have many harms, which include deaths, irreversible brain damage, and drug dependency.

To strengthen our research in this area, we employed DrMedSci, chief psychiatrist, Klaus Munkholm from Rigshospitalet part-time in 2017. Our general objective is to provide a more reliable evidence base for psychiatric treatments including guidance that may assist professionals to support their patients in the best possible way when helping them to taper off their drugs.

In recent years, we have published a number of important reviews, both of human and animal studies, several of which have been based exclusively on clinical study reports we have obtained from European drug regulators. This research has documented hitherto unrecognised harms of psychiatric drugs<sup>11 12 13</sup> (see also Publications by the end of this report and in earlier Annual Reports).

We currently have 5 PhD students working with psychiatry. Dr Kim Boesen works with ADHD and his work includes a Cochrane review on extended release methylphenidate for adult ADHD,<sup>14</sup> which is an elaboration on work performed for a national clinical guideline where Karsten Juhl

<sup>8</sup> Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Sys Rev 2013;(6):CD001877.

<sup>9</sup> Jørgensen KJ, Gøtzsche PC, Kalager M, Zahl PH. Breast Cancer Screening in Denmark: A Cohort Study of Tumor Size and Overdiagnosis. Ann Intern Med 2017;166:313-23.

<sup>10</sup> Gøtzsche PC. Mammography screening: truth, lies and controversy. London: Radcliffe Publishing; 2012.

<sup>11</sup> Maund E, Tendal B, Hróbjartsson A, Lundh A, Gøtzsche PC. Coding of adverse events of suicidality in clinical study reports of duloxetine for the treatment of major depressive disorder: descriptive study. BMJ 2014;348:g3555.

<sup>12</sup> Maund E, Tendal B, Hróbjartsson A, Jørgensen KJ, Lundh A, Schroll J, Gøtzsche PC. Benefits and harms in clinical trials of duloxetine for treatment of major depressive disorder: comparison of clinical study reports, trial registries, and publications. BMJ 2014;348:g3510.

<sup>13</sup> Maund E, Guski LS, Gøtzsche PC. Considering benefits and harms of duloxetine for treatment of stress urinary incontinence: a meta-analysis of clinical study reports. CMAJ 2017;189:E194-203.

<sup>14</sup> Boesen K, Danborg PB, Gøtzsche PC, Jørgensen KJ. Extended-release methylphenidate for attention deficit hyperactivity disorder (ADHD) in adults (Protocol). Cochrane Database Syst Rev 2017;11:CD012857.

Jørgensen served as methods consultant for the Danish National Board of Health.<sup>15</sup> Boesen was also involved in the retraction of a Cochrane review on immediate-release methylphenidate for adult ADHD that had not considered many serious flaws and other shortcomings of the included trials.<sup>16</sup>

Psychologist Anders Sørensen works on a Cochrane review on safe withdrawal of depression drugs.<sup>17</sup> He also studies whether the patients' rights are being respected and the scientific arguments for using forced treatment are valid in a cohort of cases we have received access to in Det Psykiatriske Ankenævn (the Psychiatric Appeals Committee).

Biologist Pia Danborg performs systematic reviews of animal research, studies long-term harms of psychiatric drugs in patients, and has finished a systematic review of neuroleptics in drug-naïve patients with psychosis for which she did not find a single trial apart from one that reported results that cannot possibly be correct (submitted for publication).

Psychologist Marie Bohlbro does systematic reviews of drugs and psychotherapy and studies biases in psychiatric trials.

MSc Tarang Sharma will defend her PhD on depression pills in 2018, which builds entirely on clinical study reports we have obtained from European drug regulators.<sup>18</sup> One of her unique results is that depression drugs double the occurrence of aggression in children and adolescents, which may help explain why these drugs have often been implicated in school shootings in USA. Another unique result is that more patients drop out of the trials when they are on a drug than when they are on placebo, which means that placebo provides a better balance between benefits and harms than drugs do (submitted for publication).

We have shown in our research that depression drugs increase the risk of suicide and violence, with no upper age limit.<sup>19 20 21</sup> In contrast, we showed in a systematic review that cognitive behavioural therapy halves suicide attempts in people who have been admitted to hospital after a suicide attempt.<sup>22</sup> These findings - considering also that the effect of depression drugs on the depression is of doubtful clinical relevance<sup>23</sup> - are very important, as they suggest that people with depression should not be treated with drugs, but with psychotherapy, in stark contrast with current practice.

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<sup>15</sup> <https://www.sst.dk/da/nyheder/2015/~/media/91742BB2537F480E9481E415144C3687.ashx>.

<sup>16</sup> Boesen K, Saiz LC, Erviti J, Storebø OJ, Gluud C, Gøtzsche PC, et al. The Cochrane Collaboration withdraws a review on methylphenidate for adults with attention deficit hyperactivity disorder. Evid Based Med 2017;22:143-7.

<sup>17</sup> Sørensen A, Gøtzsche PC. Withdrawal of antidepressants [Protocol]. Cochrane Database Syst Rev 2017 (submitted).

<sup>18</sup> Sharma T, Guski LS, Freund N, Gøtzsche PC. Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. BMJ 2016;352:i65.

<sup>19</sup> Gøtzsche PC. Deadly psychiatry and organised denial. Copenhagen: People's Press; 2015.

<sup>20</sup> Bielefeldt AØ, Danborg PB, Gøtzsche PC. Precursors to suicidality and violence on antidepressants: systematic review of trials in adult healthy volunteers. J R Soc Med 2016;109:381-92.

<sup>21</sup> Maund E, Guski LS, Gøtzsche PC. Considering benefits and harms of duloxetine for treatment of stress urinary incontinence: a meta-analysis of clinical study reports. CMAJ 2017;189:E194-203.

<sup>22</sup> Gøtzsche PC, Gøtzsche PK. Cognitive behavioural therapy halves the risk of repeated suicide attempts: systematic review. J R Soc Med 2017;110:404-10.

<sup>23</sup> Jakobsen JC, Katakam KK, Schou A, et al. Selective serotonin reuptake inhibitors versus placebo in patients with major depressive disorder. A systematic review with meta-analysis and Trial Sequential Analysis. BMC Psychiatry 2017;17:58.

In 2017, psychiatrist Joakim Börjesson from Sweden visited our centre and we did a meta-analysis of the effect of lithium in drug-naïve patients on mortality and suicide (submitted for publication).

In 2016, Peter Gøtzsche cofounded the International Institute for Psychiatric Drug Withdrawal, a charity based in Göteborg, and in 2017, we held the first courses on drug withdrawal in Göteborg and Copenhagen.

### Other PhD projects

MSc Asger Paludan-Müller studies 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 when the protocol was written. Based on the cohort of protocols we are currently analysing, we published a study in January 2018 showing that - when independent researchers ask for access via research ethics committees - industry sponsors redact their protocols particularly in those sections where there is empirical evidence of substantial problems with the trustworthiness of published drug trials.<sup>24</sup>

Dr Kristine Rasmussen will defend her PhD in 2018 about the influence of industry sponsorship and other conflicts of interest on the outcomes and quality of systematic reviews.

MSc Camilla Hansen also studies bias related to conflicts of interest in clinical research, in collaboration with Professor Asbjørn Hróbjartsson at the University of Southern Denmark.

Dr Lars Jørgensen studies serious harms of the HPV vaccines, see next section.

### HPV vaccines

In May 2016, we complained to the European Ombudsman about EMA's handling of the suspected serious neurological harms of the HPV vaccines, which we consider a case of scientific maladministration.<sup>25</sup> In her decision in October 2017, the Ombudsman noted that it is not her task to take a view on the science, but she criticised EMA for other issues we had raised. She recommended that EMA's appointed experts should be allowed to participate freely in the public debate and suggested that EMA considers adapting its standard confidentiality clause. She also suggested that EMA continues to explore ways to explain to the public in more detail how its scientific committees arrive at scientific conclusions, and how differences in views that arise during the assessment are addressed. Finally, she suggested that EMA considers making publicly available lists of all relevant documents in its possession related to a specific referral procedure but noted that, "Unfortunately, EMA did not address this suggestion." The Ombudsman therefore repeated her suggestion in her decision closing her inquiry.

We are carrying out a research project based on the clinical study reports of the HPV vaccines we have obtained from EMA. For this work, we employed Dr Lars Jørgensen as a PhD student and, in a part-time position, Dr Tom Jefferson from the Oxford Centre for Evidence-based Medicine.

<sup>24</sup> Marquardsen M1, Ogden M1, Gøtzsche PC. Redactions in protocols for drug trials: what industry sponsors concealed. *J R Soc Med* 2018 Jan 1:141076817750554. doi: 10.1177/0141076817750554. [Epub ahead of print]

<sup>25</sup> Our Assessment of the European Ombudsman's decision. 2 Nov 2017. <http://nordic.cochrane.org/news/complaint-filed-european-medicines-agency-over-maladministration-related-safety-hpv-vaccines>.

Jefferson's outstanding work with clinical study reports of oseltamivir (Tamiflu) has taught us that our governments have wasted billions of Euros on a treatment for influenza that seems to have no important effects.<sup>26</sup> In May 2014, we requested the study programmes' corresponding clinical study reports from EMA, but the release rate from EMA was too slow to provide us with all eligible trials' clinical study reports before our data lock date three years later.<sup>27</sup> Thus, the new openness policy, which was enforced upon EMA by the Ombudsman in 2010, has been stalled. The results from this research project will be published in due course.

### Statins

Another controversial area is the use of cholesterol lowering drugs for primary prevention of heart disease. According to the clinical trials and systematic reviews of the trials, muscular harms of statins are rare, but in clinical practice, many patients complain of pronounced muscular problems that disappear when they stop taking their statin. We focus on clinical study reports, which we are currently receiving from EMA, and collaborate with Jefferson on this.

### Administrative support

In all this work, we are well supported by our two administrators/secretaries Jannie Hedegaard and Frihild Askham who have worked with us for a total of 30 years.

## **Value of the Centre for Denmark**

The Nordic Cochrane Centre, the three Cochrane review groups based in Denmark, and Copenhagen Trial Unit have been funded by the Danish government since 2001. This investment has paid off. Just three reviews produced by the Nordic Cochrane Centre have saved over 500 mio. Danish crowns annually, which is about 100 times our Centre's 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 and 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 had 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. We have published many papers on mammography screening and have explained why we conclude that it does more harm than good: Screening does not reduce the incidence of advanced cancers; it does not reduce mortality; whereas it causes substantial overdiagnosis and also leads to many false positive findings that result in psychological harm. Based on official estimates of the cost, in all those 17 years where we only had screening in 20% of the country,

<sup>26</sup> Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, Spencer EA, Onakpoya IJ, Mahtani KR, Nunan D, Howick J, Heneghan CJ. Neuraminidase inhibitors for preventing and treating influenza in adults and children. Cochrane Database Syst Rev 2014;4:CD008965.

<sup>27</sup> Jørgensen L, Gøtzsche PC, Jefferson T. Index of the human papillomavirus (HPV) vaccine industry clinical study programmes and non-industry funded studies: a necessary basis to address reporting bias in a systematic review. Syst Rev. 2018;18:7:8.

Danish taxpayers saved more than 200 mio. Danish crowns every year.

Our Cochrane review on mammography screening,<sup>28</sup> which was first published in 2001, is often in the top ten for worldwide downloads of Cochrane reviews and is still the basis for official re-assessments of breast screening, e.g. in the UK, France and Switzerland.

In 2008, a majority in Parliament wanted to reimburse alpha-1 antitrypsin for treatment of patients with lung disease and this enzyme deficiency. However, the Health Committee asked Gøtzsche to assess the trials. He concluded 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 such as 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 published a Cochrane review of this treatment, which we have updated.<sup>29</sup> Based on the initial report, reimbursement of the drug was declined, which, based on cost estimates published by the Danish drug agency, has saved at least 100 mio. Danish crowns annually.

General health checks are popular, but we decided to do a Cochrane review<sup>30</sup> 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 them, as our results were very convincing. 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. In 2014, a large Danish trial was published, which added 3,163 deaths to our Cochrane review.<sup>31</sup> The relative risk for death remained the same; 0.99 (95% confidence interval 0.95 to 1.03) in our Cochrane review, and 0.99 (0.95 to 1.02) with the Danish data added. Our review has saved over 200 mio. Danish crowns annually, based on officially available cost estimates, and it is currently being updated.

## Dissemination and usage of research results

Dissemination of research results to a broader audience is as important as producing them. This work should not be undertaken lightly, and it requires considerable quality control because so many original research results, and therefore also systematic reviews of such results, exaggerate the benefits of interventions and underestimate their harms.

“Advocating for evidence” is a core goal for the Cochrane strategy to 2020, and part of this is knowledge translation, which means providing information in a more easily understandable format than reviews. We contribute substantially to this. We proactively disseminate our research findings to various media outlets, both Danish and international, with the aim of communicating to a broad audience. Our active approach is aimed at contributing to improve practice and knowledge in health care settings and enabling people to make informed decisions based on robust evidence.

<sup>28</sup> Gøtzsche PC, Jørgensen KJ. Screening for breast cancer with mammography. Cochrane Database Sys Rev 2013;(6):CD001877.

<sup>29</sup> Gøtzsche PC, Johansen HK. Intravenous alpha-1 antitrypsin augmentation therapy for treating patients with alpha-1 antitrypsin deficiency and lung disease. Cochrane Database Sys Rev 2016;(9):CD007851.

<sup>30</sup> Krogsbøll LT, Jørgensen KJ, Grønhøj Larsen C, Gøtzsche PC. General health checks in adults for reducing morbidity and mortality from disease. Cochrane Database Sys Rev 2012;(10):CD009009.

<sup>31</sup> Jørgensen T, Jacobsen RK, Toft U, et al. Effect of screening and lifestyle counselling on incidence of ischaemic heart disease in general population: Inter99 randomised trial. BMJ 2014;348:g3617.

We are contacted daily by journalists from countries all over the world. They contact us because of our broad knowledge of many health care topics and because it is difficult to find experts in health care who do not have financial or other conflicts of interest. We help the journalists get the evidence right in their stories, often alerting them to relevant Cochrane reviews. In 2017, our research received detailed coverage in New York Times, Washington Post, Time Magazine, Forbes, and in many other international news sources.

By the end of 2016, we employed a communication consultant, Dina Meng, to help us with our knowledge translation work and external communication activities.

### Evidence-based books

Our evidence-based books and book chapters contribute importantly to knowledge translation and thereby also to the goals of the Cochrane Collaboration, as they help citizens make more informed decisions about the interventions they are being offered. Our Cochrane review on mammography screening is the central theme in a book about mammography screening,<sup>32</sup> which also draws attention to an evidence-based leaflet about screening that we first published in the BMJ, and which is available on our [website](#) in 17 languages.

Two of the evidence-based books are about drugs in general and psychiatric drugs in particular and have 31 and 35 references to Cochrane reviews, respectively.<sup>33 34</sup> Doctors know little about drugs that go 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 and why these books have been translated into many languages. We have also contributed chapters to textbooks.<sup>35 36 37</sup>

A new book to appear in 2018 has 55 references to Cochrane reviews.<sup>38</sup> This book is intended to be a self-help guide to finding the most reliable evidence about diagnostic methods and treatments in health care. With numerous examples, it aims at giving people confidence that they can look up answers themselves to the questions they have. This could empower patients in discussions with their doctor and other health care professionals and could help them reject some of the diagnostic methods and treatments suggested to them, e.g. when they have concluded that they likely don't work, are too dangerous, or both.

We have also translated "Testing Treatments" into Danish, a book written by the founder of the Cochrane Collaboration, Sir Iain Chalmers with three others. It explains very well why randomised trials are so essential.<sup>39</sup> We will upload it on our website in 2018 and make it freely available, as it is in other languages, e.g. through [www.cochrane.org](http://www.cochrane.org).

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<sup>32</sup> Gøtzsche PC. Mammography screening: truth, lies and controversy. London: Radcliffe Publishing; 2012.

<sup>33</sup> Gøtzsche PC. Deadly medicines and organised crime: How big pharma has corrupted health care. London: Radcliffe; 2013.

<sup>34</sup> Gøtzsche PC. Deadly psychiatry and organised denial. Copenhagen: People's Press; 2015.

<sup>35</sup> Peter C. Gøtzsche. Overdiagnostik og overbehandling i psykiatrien. I: Brinkmann S, Petersen A, red. Diagnoser, Perspektiver, Kritik og Diskussion; 2015: 155-82.

<sup>36</sup> Karsten Juhl Jørgensen. A critical overview of screening for cancer. In: Poston G, Wyld L, Audisio RA, eds. Surgical Oncology: Theory and Multidisciplinary Practice. 2 ed. UK: CRC Press (Taylor and Francis Group); 2016: 33-42.

<sup>37</sup> Peter C. Gøtzsche. Psychopharmacology is not evidence-based medicine. In: Davies J, ed. The Sedated Society. London: Palgrave Macmillan; 2017: 23-50.

<sup>38</sup> Gøtzsche PC. How to survive in an overmedicated world: look up the evidence yourself. 2018 (in press in several languages).

<sup>39</sup> Evans I, Thornton H, Chalmers I, Glasziou P. Testing treatments. London: Pinter & Martin; 2011.

## TV news, documentaries and radio shows

The Centre's director and deputy director have participated in numerous news broadcasts, TV and movie documentaries and radio shows in more than 15 countries about issues related to our research or to Cochrane reviews produced by others. We prioritise knowledge translation via the media, particularly in documentaries, as the message reaches many people, which can be a highly effective way of reducing the harms and costs in health care.

In October 2017, a movie documentary about Peter Gøtzsche's work with reforming psychiatry, "Diagnosing Psychiatry," had world premiere in Copenhagen. In 2018, Danish national TV will run a series of documentaries about psychiatry where Gøtzsche will participate as an evidence expert.

## **Partnerships**

In Denmark, it has always been respected and highly valued that the Nordic Cochrane Centre is completely independent of political interests and institutions and has full academic freedom to criticise anything we feel merits critique, even procedures at Rigshospitalet that hosts the Centre.

We prefer informal strategic partnerships with other organisations and have established many of these. Formalised collaboration can sometimes turn out to be counter-productive and it inevitably leads to increased bureaucracy. Furthermore, it can be a threat to academic freedom, also when public institutions are involved, and we give some examples of this in our [Strategic Plan 2016-20](#).

We had a fruitful partnership with the Danish National Board of Health until mid-2016 when the funding for the national clinical guidelines project ended. The deputy director of our Centre, Karsten Juhl Jørgensen, was employed one day a week as a methods consultant on the development of 6 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 give people 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.

We also contribute to courses and workshops arranged by Cochrane Sweden:

- June 2017, Lund University Library, Karsten Juhl Jørgensen was the main tutor.
- September 2017, Cochrane review preparation in Lund. Two new Cochrane reviews have been registered thanks to this event, Jørgensen was the main tutor.
- October 2017, sharing advice about Bruschettini's participation as a tutor at the Cochrane Russia workshop in Kazan.

- Application to Lund University for funding for a PhD course. The application was granted in November 2017 and courses are scheduled in April and September 2018. Part of the course will use the Cochrane Interactive Learning; Jørgensen will be the main tutor.
- Planning a Cochrane workshop in Uppsala in March 2018; 40 registered participants. Jørgensen will be the main tutor.
- Planning a Cochrane workshop at Karolinska Institute in April 2018; 60 registered participants. Jørgensen will be the main tutor.

## **Review Groups in the Nordic region**

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### **Cochrane Hepato-Biliary Group**

The group was registered on 29 March 1996 and is based in Copenhagen. In March 2017, the Cochrane Library contained 207 reviews and 135 protocols.

### **Cochrane Colorectal Cancer Group**

The group was registered on 27 January 1998 and is based in Copenhagen. In March 2017, the Cochrane Library contained 114 reviews and 75 protocols.

### **Cochrane Anaesthesia, Critical and Emergency Care Group**

The group was registered in February 2000 and is based in Copenhagen. In March 2017, the Cochrane Library contained 211 reviews and 66 protocols.

### **Cochrane Work Group: Health & Safety at work**

The group was registered in July 2010 and is based in Kuopio. In March 2017, the Cochrane Library contained 33 reviews and 22 protocols.

### **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.

### **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 Hróbjartsson, 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.

## Nordic Cochrane reviews

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A detailed survey we performed in 2011 showed that review production in the Nordic countries is very high, apart from Sweden<sup>40</sup> Measured as number of reviews per 1 million inhabitants, Denmark was ranked 6, Norway 10 and Finland 11.

In issue 2, 2018 of The Cochrane Library, 214 reviews and 87 protocols were listed with a Nordic contact address:

| Country      | Reviews    | Protocols |
|--------------|------------|-----------|
| Denmark      | 108        | 51        |
| Norway       | 46         | 13        |
| Finland      | 29         | 5         |
| Iceland      | 3          | 1         |
| Sweden       | 19         | 8         |
| Poland       | 5          | 8         |
| Russia       | 4          | 1         |
| <b>Total</b> | <b>214</b> | <b>87</b> |

From 2015 to 2016, number of reviews and protocols in Sweden went up from 11 and 9, respectively, to 20 and 8, which was because a very active producer of Cochrane reviews, Matteo Bruschettini, now Director of the newly established Cochrane Sweden, moved from Italy to Sweden.

## Advisory Board for the Nordic Cochrane Centre

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The Advisory Board for the Nordic Cochrane Centre provides advice and support about the strategic direction for activities within the Centre. We previously held annual advisory board meetings but, similar to some other Cochrane centres, we now consult members ad hoc, usually over the phone, as we have found this to be more productive. It is not obligatory to have an advisory board and some Cochrane centres do not have one. In 2017, 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

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<sup>40</sup> Gøtzsche PC, Tendal B, Clarke M. Review production in The Cochrane Collaboration – where is it happening and why? Cochrane Methods. Cochrane DB Syst Rev 2011 Suppl 1:16-9.

## Acknowledgements

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

## Awards

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None in 2017.

## Publications by staff at the Nordic Cochrane Centre

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### *PhD dissertations*

None in 2017.

### *Books and book chapters*

Gøtzsche PC. Psychopharmacology is not evidence-based medicine. In: Davies J, ed. The Sedated Society: The Causes and Harms of our Psychiatric Drug Epidemic. London: Palgrave Macmillan; 2017:23-50.

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