Self-evaluation report of

the Copenhagen Trial Unit, Centre for Clinical Intervention Research

and

the Cochrane Hepato-Biliary Group

By the staffs

2019

Copenhagen Trial Unit
Centre for Clinical Intervention Research

Cochrane
Hepato-Biliary

Contents

Summary

The vision of the Copenhagen Trial Unit, Centre for Clinical Intervention Research, is to strengthen Danish clinical research for the benefit of patients by improving the prognosis of patients and thereby contributing to a world with more high-certainty systematic reviews and randomised clinical trials and less clinical research waste. The Copenhagen Trial Unit is an academic research organisation and a contract research organisation. We work within all medical specialities of the health care sector.

Since the launch of the Copenhagen Trial Unit in 1995, we have obtained about DKK 175 million (Euro 23.3 million) in public support from Hovedstadens Sygehusfælleskab (H:S) and from the Danish state calculated in 2018 DKK. Moreover, we have obtained about DKK 50 million (Euro 6.7 million) from other funders, like private funds and EU funds. In return, we have launched 139 randomised clinical trials randomising about 126,000 participants as well as established the Cochrane Hepato-Biliary Group, as part of the international Cochrane Collaboration. We have published over 1600 peer reviewed publications, giving a total public funding investment of about DKK 110,000 (Euro 14,666) per publication or about a total funding of about DKK 141,000 (Euro 18,800) per publication. The publications include more than 1030 journal articles; 367 Cochrane protocols for systematic reviews; and 218 Cochrane systematic reviews. The Hirsch index is above 79.

Moreover, we have developed randomisation systems; data management systems; educational materials; Trial Sequential Analysis; published several articles systematising and recommending how to conduct and analyse trials and reviews; and published on transparency in clinical research as well as barriers for clinical research.

Lastly, we have participated in educational activities in Denmark and abroad, resulting in more than 50 Ph.D. and doctoral dissertations.

Abbreviations

AASLD	American Association for Study of the Liver
Biopeople	Danish National Innovation Network
BMJ	British Medical Journal
CHBG	The Cochrane Hepato-Biliary Group
CORBEL	Coordinated Research Infrastructures Building Enduring Life-science Services
CRIC	Centre for Research in Intensive Care
CG	Christian Gluud
CTU	The Copenhagen Trial Unit
DCRIN	Danish Clinical Research Infrastructures Network
Dept.	Department
DN	Dimitrinka Nikolova
DSKE	Danish Society for Clinical Nutrition
DTAR	Diagnostic test accuracy review
EASL	European Association for Study of the Liver
ECRAN	European Communication on Research Awareness Needs
eCRF	Electronic case report form
ECRIN	European Clinical Infrastructures Network
EQUATOR	Enhancing the Quality and Transparency Of health Research
FC	Formal Contract
FTE	Full time equivalent
GCP	Good Clinical Practice
H:S	Hovedstadens Sygehusfælleskab
ICMJE	International Committee of Medical Journal Editors
ISSN	International Standard Serial Number
IT	Information Technology
JAMA	Journal of the American Medical Association
JCJ	Janus Christian Jakobsen
JIF	Journal impact factor
NASTRA	National Strategy Committee for Health Science Research
NC	No contract
NTA	Nordic Trial Alliance
PICOT	Participants, intervention, control, outcomes, time points
PW	Per Winkel
SLK	Sarah Louise Klingenberg
SOPs	Standard Operating Procedures
TSA	Trial Sequential Analysis
WHO	World Health Organisation

1 Strategy, organisation, management and economy

1.1 History and governance structure

1.1.1 Overview of the history of the centre

- *Please give a brief overview of the history of the centre, including a description of when, how and why the centre was established and the most important changes in the organisational setup and basic funding since the establishment.*

Denmark has a long tradition within health science research, achieving a strong position within the clinical research field (1-3). In 1995, the National Strategy Committee for Health Science Research (NASTRA)-parliamentary report 'Proposal for a national strategy for health science' was published (4). The report recommended a strengthening of the Danish health science research by giving high priority to the areas where Danish research already had strong positions. One of the four areas recommended was clinical research with preventive, diagnostic, therapeutic, and nursing care objectives (4). The other three areas were genetic research, brain research, and preventive research (4).

Many applied interventions within all parts of the health care sector have not been subjected to adequate evaluation of benefits and harms and their socioeconomic impacts are unknown. Moreover, a constantly growing number of new interventions awaits to become independently assessed before being introduced into clinical practise. Therefore, it is important to support research that evaluates the effects of new interventions before their implementation as well as the already implemented interventions and of. The selection of appropriately designed studies - i.e. randomised clinical trials and systematic reviews of such trials - is pivotal (5).

Clinical researchers, like the ones behind the EQUATOR Network (6), The European Good Clinical Practice (GCP) guidelines, EU directives and regulations for clinical research, as well as other initiatives, have contributed to the rise of the quality and hence certainty of clinical research. However, these positive developments have also put a heavy workload on clinical researchers. Collaboration between the clinical researchers and clinical trial units, sharing the ambition of securing scientific quality in the conduct of trials, has become essential (5, 7).

Preceding the NASTRA-report (4), the Copenhagen Health Services considered the possibility of establishing a centre for clinical research within their primary and secondary health care sectors. A group was formed with the objective to examine these possibilities (7). During 1993, more than 40 research centres in Europe and North America were visited (7). Extensive interviews were conducted in these centres among their key researchers. Based on these investigations, a report was prepared. The report was then circulated internationally and nationally for comments. Clinicians, various research institutions, and the drug industry in Denmark and abroad, supported the proposal for establishing a centre for clinical research. Many national organisations and institutions believed the establishment of a clinical trial unit could contribute to strengthen the Danish clinical research. The final report formed the concrete basis for the Copenhagen City Council to establish the Copenhagen Trial Unit (CTU) in October 1994 (7).

On January 1, 1995, the Copenhagen Health Services were transformed into Hovedstadens Sygehusfællesskab (H:S) (the Hospital Association of the Capital) to run health care services in Copenhagen and Frederiksberg. Five large hospitals were associated in Hovedstadens Sygehusfællesskab (H:S). On June 1, 1995, Christian Gluud, was appointed Head of Department of the Copenhagen Trial Unit. On January 1, 1996, after a phase of planning and preparation, the Copenhagen Trial Unit was in function.

During 1995 to 1999, the Copenhagen Trial Unit was operated from the Kommunehospital, affiliated with the Institute of Preventive Medicine. From 2000, the Copenhagen Trial Unit was relocated to Rigshospitalet, the Copenhagen University Hospital. During the years at Rigshospitalet from 2000 to present, the Copenhagen Trial Unit has been operated from four different premises (premises of the Department of Infectious Diseases, Rigshospitalet (2000 to 2001); the Military Hospital Building, Rigshospitalet (2001 to 2006); the Panum Institute, Rigshospitalet (2006 to 2012); and Tagensvej 22, Rigshospitalet (2012 to present)). The frequent moving required substantial investments from the employees as well as investments in rebuilding the department including its IT infrastructures. These monetary investments have been taken out of the annual budget.

During 1995 to 2006, the Copenhagen Trial Unit was core funded by Hovedstadens Sygehusfællesskab (H:S). In 1996, the first year of full activity, the core funding was about DKK 2.5 million, equivalent to about DKK 6.85 million in 2018 DKK. After the structural reorganisation of the Danish infrastructure (communes; regions; etc.) in 2007, the Capital Region of Denmark took over the governance of the Copenhagen Trial Unit with funding provided by the Danish state (government grant). During 2018, core funding from the Danish State amounted to DKK 7.735 million.

The Copenhagen Trial Unit is collaborating with the international Cochrane Collaboration in preparing, maintaining, and disseminating systematic reviews of the effects of health care. The Editorial Team Office of the Cochrane Hepato-Biliary Group, part of the Cochrane Collaboration, is hosted within the Copenhagen Trial Unit. The Cochrane Hepato-Biliary Group grew in parallel with the Copenhagen Trial Unit. Sir Iain Chalmers invited Christian Gluud in June 1993 to form such a group as part of the Cochrane Collaboration. Christian Gluud participated in the establishment of the Cochrane Collaboration in October 1993. Several exploratory meetings were held during 1993 to 1996 on establishing the Cochrane Hepato-Biliary Group, which was formally launched in 1996. Ever since, it has functioned as an integrated part of the Copenhagen Trial Unit, providing expertise in systematic reviewing and searching the literature. Details of its history can be found on the website of the Copenhagen Trial Unit (8) and the website of the Cochrane Hepato-Biliary Group (9).

1.1.2 The overall governance setup of the centre

- *Please describe which authority holds the contract for the centre and the centre's contractual relationship with this authority*

During the period 1995 to 2000, the Copenhagen Trial Unit was situated at the Kommunehospital (the City Hospital) as an independent centre affiliated with the Institute of Preventive Medicine. From 2000, the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group moved as an independent centre to Rigshospitalet,

the Copenhagen University Hospital. Here, we refer to the Vice President of Rigshospitalet with delegated services from the Human Resource Department regarding hiring and firing of staff, and placement of salaries and pension. Regarding approval of expenses for the Head of Department and expenses over DKK 50,000.00, this task was delegated to the Nordic Cochrane Centre. Otherwise, the Copenhagen Trial Unit and the Nordic Cochrane Centre have had no collaboration regarding non-Cochrane matters. The Cochrane Hepato-Biliary Group referred to the Nordic Cochrane Centre regarding general Cochrane matters and to the Central Editorial Unit in London regarding Cochrane systematic review-related matters.

1.1.3 How does the centre seek advice and support about its vision/mission and strategy?

The visions, missions, and strategies (see below) have been stable during the years and proven sustainable. The interest in having decisions based on evidence have increasingly become main stream within more and more parts of the health care system as well as within other fields of society.

Using our collaborative capacities with national and international collaborators (see Section 4); we have built an extended network of people to attain our visions, missions, and strategies. They are ad hoc supplemented with advice from Danish and international organisations on regulatory affairs; data laws; ethics; trial conduct (European Clinical Research Infrastructure (ECRIN); Nordic Trial Alliance; Cochrane); etc.

The employees at the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group strive to be aware on laws, regulations, and guidelines for clinical trials and systematic reviews. The standard operating procedures (SOPs) of the Copenhagen Trial Unit are revised regularly to obtain the newest and best information regarding laws, regulations, and guidelines for clinical trials and good clinical practice (10).

1.1.4 Does the centre have and use a board?

- *If the centre has a board or similar structure, please provide information about:*
  a) The role of the board
  b) The election of members, their obligations, their compensation
  c) How and how often the board is involved in the centre's activities (i.e. through regular meetings, ad-hoc consultations etc.)
  d) One or more example(s) illustrating the role of the board for the centre.
  If the centre does not have a board, please provide reflections upon this choice.

The Copenhagen Trial Unit does not have a board. The reasons for this are historic, organisational, and practical. Staff members at the Copenhagen Trial Unit have been, and are, active members of several steering committees and research groups nationally and internationally, so we are in constant dialog with researchers throughout the World. However, as our visions and missions agree with what clinical researchers want to obtain, we see the potential advantages of having a board to be superseded by the costs and complexities such a board would create. During the formation of the Copenhagen Trial Unit, a board was discussed and decided against.

Moreover, most strategic and tactical decisions in the activities within the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group must be taken with a deep understanding of the topic at hand and relate to the protocol for the individual project, the researchers involved as well as the economic constraints of the individual projects. Accordingly, a board member would not normally have the necessary detailed information at hand to be able to give cost-effective recommendations. The tasks must be solved by the member of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group staff responsible for the project. This person needs to get strategic or tactical advice from either a more senior person at the Copenhagen Trial Unit or the steering group of the individual project, according to the type of task.

Furthermore, most trial service units do not have boards. If they refer to anything, it is more often to an advisory board.

1.1.5 Does the centre have and use an advisory board?

- *If the centre has an advisory board or similar structure, please provide information about:*
  a) The role of the advisory board
  b) The election of members, their obligations, compensation
  c) How and how often the advisory board is involved in the centre's activities (i.e. through regular meetings, ad-hoc consultations etc.)
  d) One or more example(s) illustrating the role of the advisory board for the centre.

  If the centre does not have an advisory board, please provide reflections upon this choice

The Copenhagen Trial Unit invited members to our advisory board during 1995 and 1996. During the first years of existence, from 1996 to 2002, we conducted detailed annual reports of activities in the Copenhagen Trial Unit (11). We also arranged annual meetings with the advisory board during the 1996 to 2006 period. The members of the advisory board provided several good pieces of advice and recommendations, especially regarding strategic and tactical matters. As the years went by, the visions, missions, and strategies of the Copenhagen Trial Unit were getting clearer and the experience with the tasks more extensive, and the advice offered by the advisory board was not necessarily timely. Therefore, we chose to approach the members of the advisory board ad-hoc. Gradually, this approach made the annual meetings less necessary after 2006.

The members of the advisory board were elected among the researchers of Hovedstadens Sygehusfællesskab (H:S) with the largest experience in conducting randomised clinical trials. Their tasks were to provide advice. Apart from information on the activities within the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group as well as a dinner, the members of the advisory group did not receive any compensation.

During the 2000s, the Copenhagen Trial Unit condensed the annual reports to a report of scientific publications and the journal impact factors achieved. Moreover, protocols for both systematic reviews and randomised clinical trials became more often published or publicly available via trial registries. Accordingly, the demand for

full transparency on all major activities (protocols; data management plans; statistical analysis plans; interim analyses; etc.) made detailed annual reports increasingly redundant.

Should we point to a negative aspect of not issuing detailed annual reports, then we should refer to those of our projects and related activities that fail during their development and, therefore never reach the public via registers or publications. During the years of existence, the Copenhagen Trial Unit has been involved in more than 500 development plans for randomised clinical trials. Only 139 (about 28%) have been launched with the Copenhagen Trial Unit as a partner. There are many reasons for a number of these trials not being launched, including industry involvement not wanting to comply with the transparency we request; lack of understanding of the importance of systematic reviews before trials are launched; and lack of ability to raise the needed monetary support to conduct the trials; etc. Within the Cochrane Hepato-Biliary Group, comparable experiences exist. More than 569 titles for systematic reviews have been registered; but only 367 protocols for systematic reviews have been published; and only 218 systematic reviews have been published until now. Although detailed reports on such 'failed' trials and reviews can show what the staff of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group has been engaged in, it is usually limited what can be deducted from such failed projects.

A negative aspect of not having a functioning advisory board is that it could leave one with the impression that the Copenhagen Trial Unit has been sailing through the years without external input and influence. However, this has not raised concern as all activities within the Copenhagen Trial Unit have been well thought activities and are conducted in close collaboration with external partners. Staff members at the Copenhagen Trial Unit have been, and are, active members of several steering committees and research groups nationally and internationally, so we are in constant dialog with researchers throughout the World. Hence; Copenhagen Trial Unit staff members are regularly informed about relevant developments in the health-care and university sectors of Denmark, as well as abroad; and how the external partners perceive the activities within the Copenhagen Trial Unit as well as the Cochrane Hepato-Biliary Group.

1.1.6 The governance structure's ability to hold the management of the centre accountable

- *Please elaborate on the ways in which the described governance structure enables accountability.*

In terms of trying to fulfil the visions; missions; and strategies of the Copenhagen Trial Unit (see below), all our products are at open display through our protocols for randomised clinical trials, systematic reviews, and other research activities, and the results of these research projects, through the published articles on results. These activities are registered at our home page www.ctu.dk and in international registers.

In terms of quality and adequacy of protocols for randomised clinical trials, they must all be approved by regional ethics committees; the Danish Data Protection Agency; and if relevant the Danish Medicines Agency before launch. In terms of quality and adequacy of manuscripts describing results of randomised clinical trials, they all

undergo extensive peer review and editorial handling before being accepted for publication in medical journals.

In terms of production of journal articles, the Copenhagen Trial Unit is a part of Rigshospitalet, the Copenhagen University Hospital, and therefore every year we are held accountable for the number of articles produced according to the software program PURE, which is used within the entire Capital Region of Denmark.

In terms of quality and adequacy of Cochrane protocols and systematic reviews, they all undergo extensive external peer review and internal editorial processing before being published. In addition, all protocols and systematic reviews are subjected to further independent quality checks and assessment of their adequacy; this has been performed by the earlier Cochrane Central Editorial Unit (the current Cochrane Editorial and Methods Department) and after the implementation of the new Cochrane structure towards the end of 2018, by any of the three of our Network editors. Thus, at least six different editorial Network and Group staff members provide comments on a protocol or a review before their publication. Once a year, we receive from Cochrane an evaluation of the number of protocols and systematic reviews produced; how often they are downloaded; accessed through various social media, podcasts produced, impact factor, and alike.

We do not have regular (annual) meetings with Cochrane or with the Rigshospitalet, at which our scientific production in relation to our missions; visions; or strategies is assessed retrospectively. However, The Cochrane Hepato-Biliary Group has signed in June 2018 a five-year collaboration agreement with the Cochrane Collaboration which defines the goals including our responsibilities (our commitment to produce evidence), requirements to adhere to Cochrane policies and standards for reviews, ensuring that our products are accessible, and how to achieve sustainability. In 2021, The Cochrane Hepato-Biliary Group's work will be assessed in detail based on the Agreement.

In terms of economy, the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group are subject to the accounting of the Capital Region of Denmark, and therefore, subject to strict regulations for the use of both the Government grant and other revenue-based research grants from both domestic and foreign investigators, including EU grants.

- *Please reflect: Which opportunities for improvement do you see?*

The premises that we presently have are considered acceptable and have shown sufficiently flexible to accommodate our requirements for extra space with access to extra office space on the third floor. Having been moved around extensively during the past sends few promising thoughts through the minds of the staff at the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group when discussing eventual relocation.

Being a part of Rigshospitalet, Copenhagen University Hospital, the Capital Region is also seen as an advantage. A major part of our collaborators come from Rigshospitalet or from other hospitals within the Capital Region. This eases dialogue in common projects and lifts off charging of overhead.

Due to a large number of Ph.D.s and other students affiliated to the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group, we need a stronger affiliation with the Copenhagen University, Faculty of Health Sciences and other universities. Presently, we use connections with professors at the Copenhagen University or other universities, but a direct access to function ourselves as thesis supervisors and teachers would be an important strength.

The Copenhagen Trial Unit needs more expertise regarding statistical issues. We have developed an excellent collaboration with the Section of Biostatistics, University of Copenhagen, but it would be an asset to have one or two statisticians working in house. Up until now it has for monetary reasons not been possible to hire such expertise. Moreover, the Danish drug and device industry is able of paying much larger salaries than we are as part of a public institution.

The Cochrane Hepato-Biliary Group also needs extra support for the Managing Editor and the Information Specialist, including general editorial support.

Although collaboration between the Nordic Cochrane Centre and the Copenhagen Trial Unit has been excellent during the years, even the small connection between the two institutions has historically also been a weakness. Several potential collaborators may not have requested the collaboration with the Copenhagen Trial Unit due to their conflicts with the Nordic Cochrane Centre. Several collaborators only choose to work with the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group after being assured that no formal connection is present between the Nordic Cochrane Centre and the Copenhagen Trial Unit. Therefore, in the future, no connection between the two institutions should be in operation, apart from the connections naturally occurring within the Cochrane Collaboration. Technically, this can be achieved by the financial administration at Rigshospitalet taking over the approval of extraordinary costs.

During the years, we have considered to relaunch the advisory board by asking Rigshospitalet (e.g. two members) and the medical faculties of the Danish universities (e.g. one member from each of four universities) to appoint members of the advisory board and revoke the annual meetings, e.g. as teleconferences. This would have the advantage of connecting the Copenhagen Trial Unit more to research activities outside the Capital Region of Denmark.

1.1.7 Relevant documents and additional information

- *Please provide documents and information that you consider relevant for the evaluation of the centre's governance structure.*

Please see organisation diagrams in Figure 1-1 and Figure 1-2 for Rigshospitalet, the Copenhagen University Hospital and the Copenhagen Trial Unit, including the Cochrane Hepato-Biliary Group.

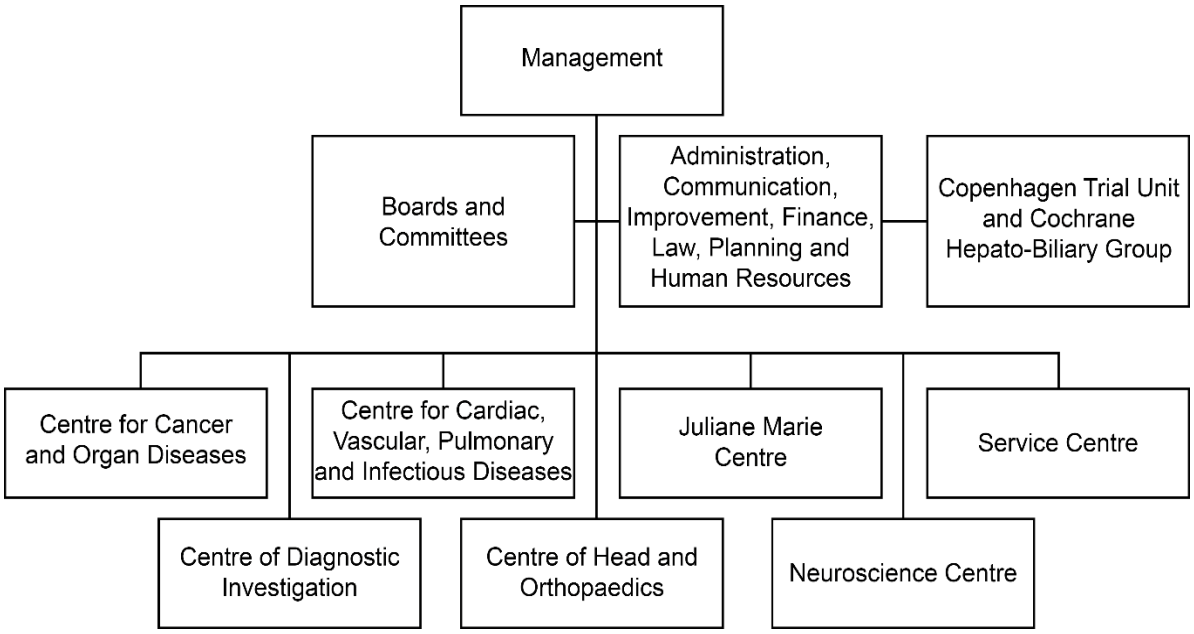

Figure 1-1 Rigshospitalet, the Copenhagen University Hospital organisation diagram.

Rigshospitalet, the Copenhagen University Hospital consists of seven centres, a hospital management and a central administration. In addition, the Administration also includes the Copenhagen Trial Unit, the Nordic Cochrane Centre, and the USCF, The University Hospitals Centre for Health Research.

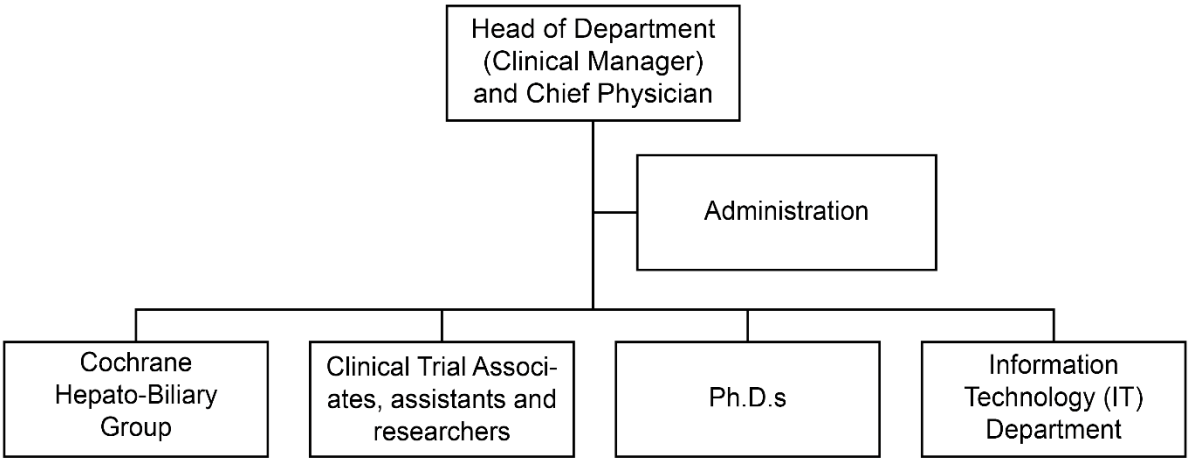

Figure 1-2 Copenhagen Trial Unit organisation diagram.

For more details, please see the website of the Copenhagen Trial Unit (http://ctu.dk/) and the publication overview of the last five years:

- 2014: http://ctu.dk/media/11564/2014_RH_PublicationList.pdf
- 2015: http://ctu.dk/media/12652/2015_Forskningsevaluering.pdf
- 2016: http://ctu.dk/media/12621/Publications-1995-2016.pdf
- 2017: http://ctu.dk/media/13628/Pure-research-outputs-2017.pdf
- 2018: http://ctu.dk/media/13631/Pure-research-outputs-2018.pdf

1.2 Management and organisation

1.2.1 Describe the centre's organisational and economic relationship to each of the following organisations

a) Relationship to Rigshospitalet, the Copenhagen University Hospital

Rigshospitalet, the Copenhagen University Hospital, is the hosting organisation of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group. The Head of Department reference is the Vice President of Rigshospitalet.

The economic relationship to Rigshospitalet is headed by the Chief Financial Department at the Capital Region of Denmark and the rules and regulations of this department. The Capital Region has strict and specific procedures for using grants of the Capital Region of Denmark from which the Danish state grant to the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group, and other revenue-based research grants from both domestic and foreign investigators, including EU grants, are controlled.

The Human Resource Department of Rigshospitalet participates in all hiring and firing activities of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group.

Moreover, the Legal Department of Rigshospitalet is responsible for all legal matters that the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group becomes involved in, including development of contracts.

b) Relationship to the Nordic Cochrane Centre

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group were invited by Peter Gøtzsche, the Nordic Cochrane Centre, to become part of Rigshospitalet in 1999. The move was sanctioned by the leaders of the hospitals as well as the director of Hovedstadens Sygehusfællesskab (H:S). As stated above, there have been only few formal connections between the two centres, i.e. the Nordic Cochrane Centre approved expenses for the Head of Department (representation; travel) and expenses over DKK 50,000.00 (e.g. IT equipment) and the connections that arose ad hoc between the Cochrane Hepato-Biliary Group and its regional Cochrane centre. As part of the latter connections, we were regularly invited to the monthly scientific meetings at the Nordic Cochrane Centre. Furthermore, the Nordic Cochrane Centre invited leaders from the three Danish Cochrane Review Groups to an annual business lunch where common problems were discussed. That activity ceased in 2013. Moreover, staff from the Nordic Cochrane Centre has served as tutors for Ph.D. students at the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group and staff from the Copenhagen Trial Unit has served as tutors for Ph.D. students at the Nordic Cochrane Centre. Apart from these connections, the research collaboration has been occasional and limited. The Nordic Cochrane Centre was not involved in management of staff or scientific projects of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group, or vice versa.

c) Relationship to the two other Danish Cochrane Review Groups

As stated above, the three Danish Cochrane Review Groups met annually at the Nordic Cochrane Centre for two to three hours to discuss common problems. That activity ceased in 2013. The Cochrane Hepato-Biliary Group has had occasional meetings and discussions with the two other Cochrane Review Groups with an editorial office in Denmark and has provided occasional educational activities, editorial consulting, and peer review tasks to the other two groups.

d) Relationship to the Cochrane organisation

The Cochrane Hepato-Biliary Group collaborates with members of the Cochrane organisation, including members of the Bias Methods Group; the Statistical Methods Group; and of course, the Central Editorial Unit (now the Cochrane Editorial and Methods Department). Moreover, we have been participating in most of the coordinating editors' annual meetings as well as most of the Cochrane Colloquia. Furthermore, we regularly participate in telephone conferences and other meetings for IT Specialists; Managing Editors, and Editors.

1.2.2 Which managerial positions exist at the centre and what are their tasks and responsibilities?

- *Please provide a description of all managerial positions of the centre, including the following topics*

a) Title and managerial position

Head of Department.

b) Primary tasks

The Head of Department handles the daily management of the clinic. Furthermore, the Head of Department:

- has the responsibility for overall staff and operating budget;
- has the responsibility for rational, efficient organisation, follow-up, and development of the tasks of the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group;
- ensures that the staff is constantly evolving so that they can continuously meet the professional requirements and needs;
- creates a framework that meets the staff's opportunities or the need for professional and personal development;
- secures that the visions, missions, and strategies are implemented in the handling of tasks.

c) Staff responsibilities (yes/no). If yes: number of staff members

Yes. Copenhagen Trial Unit has by the end of 2018, 22 staff members. Their positions are shown in Table 1-1.

Table 1-1 Full list of employees at the Copenhagen Trial Unit

Number	Title	Category
1	Head of Department	Researchers
2	Chief Physician	
3	Clinical Research Consultant	
4	Senior Registrar	
5	Senior Researcher	
6	Clinical Research Consultant	
7	Clinical Research Associate	
8	Clinical Research Consultant / Regulatory Affairs Associate	
9	Managing Editor	CHBG Researchers
10	Information Specialist	
11	Secretary	Administration and IT
12	Data Manager, Web administrator	
13	Data Manager, Software Developer, IT person	
14	Ph.D. student	Ph.D. students
15	Ph.D. student	
16	Student research assistant	Training
17	Student research assistant	Training
18	Student assistant	Student assistants
19	Student assistant	
20	Student assistant	
21	Student assistant	
22	Student assistant	

1.2.3 How is the centre organised?

The Copenhagen Trial Unit is organised by Rigshospitalet, Copenhagen University Hospital, The Danish Capital Region, the Administration being the superior department. The organisational structure is shown in the diagrams in Figure 1-1 and Figure 1-2.

1.2.4 How does the centre provide organisational support for its researchers?

- *Please describe the support functions for researchers available within the organisation.*
- *Please describe the support functions for researchers made available by the centre outside of the organisation.*

The Copenhagen Trial Unit has access to expertise in house regarding literature searching, systematic reviewing; protocol development; information technology; and statistical analyses. Three members of the staff, chief physician Jørn Wetterslev; senior registrar Janus C Jakobsen (working part time at the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group); and doctor Per Winkel (part time consultant at the Copenhagen Trial Unit) all have a broad interest and expertise in statistical analyses.

All the different sections of the Copenhagen Trial Unit (administration; Cochrane Hepato-Biliary Group; IT; and trial support) assist individual researchers as well as

each other. If external expertise is needed (Danish Medicines Agency; Ethics Committees; legal matters; data protection matters; etc.), such expertise is requested.

The staff at the Copenhagen Trial Unit is a highly professional staff, seeking advice among the above mentioned, or the staff seek necessary support functions online for outside support functions if needed.

1.3 Vision and strategy

1.3.1 What is the centre's vision, mission and/or goals?

- *Please describe the centre's vision, mission and/or goals of the centre*

The visions of the Copenhagen Trial Unit are to strengthen the Danish clinical research in order to improve the prognosis of patients and to contribute to a world with more high-certainty findings in systematic reviews and randomised clinical trials, and less clinical research waste (12-24).

The missions of the Copenhagen Trial Unit are to:

- support, coordinate, and conduct randomised clinical trials in the primary and secondary health-care sectors. The trials may have preventive, diagnostic, therapeutic, or care objectives;
- support, coordinate, and conduct systematic reviews of the literature based on meta-analyses, and participate in the international Cochrane Collaboration;
- participate in the development of methods for randomised clinical trials and meta-analyses;
- educate students, candidates, and researchers in evidence-based medicine, randomised clinical trials, meta-analyses, and trial sequential analysis.

The Copenhagen Trial Unit's scientific social responsibility is that clinical researchers, investigators, and assisting staffs, from all sectors of the health-care system, working at the Copenhagen Trial Unit or together with the Copenhagen Trial Unit position and define their research activities in a context where they are able to contribute to the betterment of our societies and to help meet the challenges of our time.

The Cochrane Hepato-Biliary Group follows Cochrane's vision, missions, and goals (25).

1.3.2 What is the centre's strategy?

- *Please describe the centre's strategy, as well as the development process resulting in the formulation of the centre's strategy and the time period of the strategic plans and how frequently are they assessed*

The randomised clinical trial and systematic reviews of such trials are the cornerstones in evaluating the benefits and harms of interventions (21-24). Systematic reviews with meta-analyses of randomised clinical trials have been acknowledged as essential tools in the evaluation of already implemented interventions, when implementation of new interventions is considered, and in the planning of randomised clinical trials.

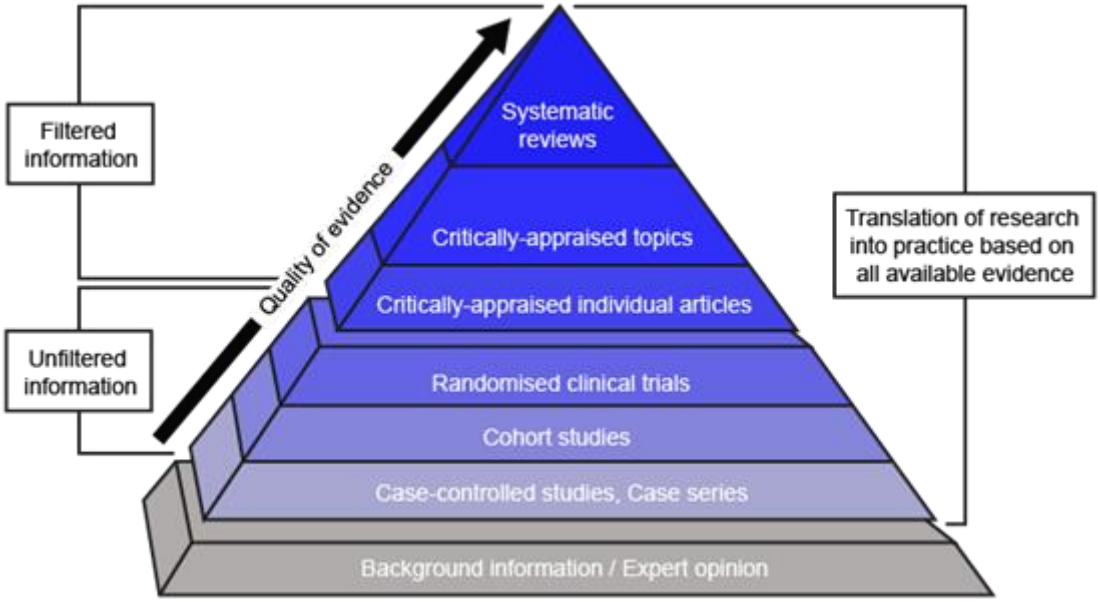

Figure 1-3 The evidence triangle.

The Copenhagen Trial Unit is a non-specialty oriented clinical intervention research unit. We offer flexible collaboration at all stages of clinical research as well as education in clinical trials. Trial methodology development is an indelible part of our services as it is recognised as an important tool for the quality of the clinical trial.

The core staff of the Copenhagen Trial Unit consists of experienced methodologist, trialists, systematic reviewers, clinicians, epidemiologists, information-technology engineers, and data managers information specialists.

The Copenhagen Trial Unit collaborates with academy and industry to constantly improve the methods of the randomised clinical trials, herewith decreasing the risks of systematic errors (bias) and the risks of random errors (play of chance). In collaboration with universities and other research institutes, the Copenhagen Trial Unit is running courses dealing with the various aspects of randomised clinical trial methodology and design, systematic reviews, meta-analyses, and trial sequential analyses.

The Copenhagen Trial Unit's strategy is primarily based on the following activities directed at:

a) reducing the risk of testing the wrong questions in randomised clinical trials by conducting systematic reviews;
b) reducing the risk of systematic error (bias) by conducting trials at low risks of bias;
c) reducing the risk of random error (play of chance) by conducting trials sufficiently large to answer the posed questions;
d) reducing the risks of other design errors or other errors in research by employing proper PICOT (participants; intervention; control; outcomes; time points); IT infrastructure; SOPs for clinical trials and systematic reviews; detailed statistical analysis plans; data management plans; and transparency regarding plans and data;
e) increasing the knowledge and understanding about systematic reviews and randomised clinical trials.

a) Reducing the risk of testing the wrong questions in randomised clinical trials by conducting systematic reviews

When clinical researchers seek advice or collaboration with the Copenhagen Trial Unit, one of our first request is to search for all updated systematic reviews of the interventions they intend to address (experimental intervention; control intervention, and cointerventions offered to the patient group in question as part of the standard treatment). If such updated systematic reviews have not been conducted, then the clinical researchers need to do the job (with or without the assistance of the Copenhagen Trial Unit). Identification of the existing evidence safeguards against conducting research on clinical questions that have already been adequately addressed. Moreover, such systematic reviews give essential information on the design and dimensioning of new randomised clinical trials, including setting up the most relevant PICOT.

b) Reducing the risk of systematic error (bias) by conducting trials at low risks of bias

Many potential sources of risk of bias may raise concern in randomised clinical trials, namely generation of allocation sequence; allocation concealment; blinding of patients and treatment providers, blinding of outcome assessors; incomplete outcome data; selective outcome reporting; for profit bias; and other bias domains. Whenever the Copenhagen Trial Unit embarks on a new trial topic, we work on getting the design to be as bias-free as possible, including central randomisation; blinding; secure IT infrastructure; etc.

c) Reducing the risk of random error (play of chance) by conducting trials sufficiently large to answer the posed questions

Most randomised clinical trials and most systematic reviews of randomised clinical trials are underpowered. To attain a more precise estimation of the intervention effects, we aim to use plausible intervention effects often based on the relevant systematic review meta-analysis; adjust the level of alpha for risks of multiplicity; and rather use a beta of 10% than the too high 20%. When we conduct systematic reviews, we make thorough searches of the literature, including the grey literature, so that we identify as many eligible trials for inclusion as possible. We have published several articles on statistical aspects of trials and systematic reviews (21, 26-29).

d) Reducing the risks of other errors in research by employing proper PICOT; IT infrastructure; standard operating procedures for clinical trials and systematic reviews (SOPs); data management plans; detailed statistical analysis plans; and transparency regarding plans and data

If trials are run in outdated systems, e.g. using paper patient record forms, risks of errors, and risks of missing data or data being misread increases. Therefore, data capture at the source with direct data entry via the Internet secures more valid and full data. Clear and updated SOPs secure that trials are run according to national and international regulations, forming a solid foundation for The Copenhagen Trial Unit's employees and partners. All trials need to have data management plans that are adequately described in their protocols. All trials need to have detailed statistical analysis plans published before data are collected and analysed. The Copenhagen

Trial Unit works for full transparency regarding protocols; statistical analysis plans; and depersonalised or anonymised patient data.

e) Increasing the knowledge and understanding about systematic reviews and randomised clinical trials.

In order to improve the understanding of the necessity of randomised clinical trials, the Copenhagen Trial Unit became involved in several projects at the national, Nordic, and international level.

To improve the understanding of the public, the Copenhagen Trial Unit participated in the ECRAN (European Communication on Research Awareness Needs) project (30). We wrote an open letter to all ministers of education inviting them to put evidence-based medicine on the school curriculum.

To improve the understanding of the public and the professionals, the Copenhagen Trial Unit has been organising each year since 2006 the ECRIN's (European Clinical Research Infrastructures Network) celebration of the International Clinical Trials' Day (31). Christian Gluud proposed the celebration of the International Clinical Trials' Day in 2005 (32). Since then, the International Clinical Trials' Day is celebrated at or around the 20th May, on which day back in 1747, James Lind started the first known controlled trial comparing different interventions for scurvy. A Google search in March 2019 retrieved more than 150 million hits on 'International Clinical Trials' Day'. In comparison, 'Cochrane Collaboration' got 45.6 million hits.

The Copenhagen Trial Unit has been working for getting more transparency into clinical research (33, 34).

Moreover, staff at the Copenhagen Trial Unit participates in pre graduate and postgraduate educational activities; bachelor, Ph.D., and doctoral dissertations. The educational activities can be one to one; small groups; or larger groups with lectures.

The Copenhagen Trial Unit has been involved in the conduct of about 500 protocols for systematic reviews, which has materialised in the publication of about 300 systematic reviews published within and outside The Cochrane Collaboration. The Copenhagen Trial Unit has developed methodology and software for conducting Trial Sequential Analysis (TSA) (29). The Cochrane Hepato-Biliary Group Editorial Team office is also viewed as a large teaching and training unit as its core staff has not changed, and they have been developing their knowledge and understanding of systematic reviews since 1996. Both the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group provide advice to and support review authors and collaborate with all involved parties during the protocol and systematic review preparation. We offer expertise in search strategy design and conduct literature searches for systematic reviews, check or perform data extraction, and offer help with or conduct of meta-analyses.

The strategies are under constant surveillance and are updated when needed.

1.3.3 How are the vision and strategy anchored in the centre's activities?

- *Please describe the organisational activities specifically conducted to reflect upon, develop or adjust the centre's achievements of goals and strategy*

The Copenhagen Trial Unit's main activities are anchored in the individual steering committees for the randomised clinical trials or the author teams for the individual systematic reviews. These core products undergo continuous and systematic quality improvement according to the pertinent SOPs and relevant strategies. Projects as well as other work issues are discussed at the once-a week staff meetings of the Copenhagen Trial Unit and The Cochrane Hepato-Biliary Group. The usual topics for discussion encompass: randomised clinical trials: systematic reviews; IT; and any other business.

Support activities are organised in Copenhagen Trial Unit's staff units (Administration; Trial Support; Editorial Team Office of the Cochrane Hepato-Biliary Group; IT).

The structure creates coherence between responsibility and authority, so that the management processes are clear and consistent. Copenhagen Trial Unit's advisory, collaboration and communication systems ensure quality and involvement in the decisions.

As a constant quality check, we receive (and give) peer reviewer comments and editorial comments on all publications. This helps us in being well-informed about new trends and may define new research targets, such as better understanding of multiplicity issues; estimating the minimally required sample sizes; patient-relevant outcomes; etc.

The Copenhagen Trial Unit is managed as a line/staff organisation with an unbroken chain of command and in which managers have personal management responsibility for each scientific project, either as advisor to or a member of a steering committee for a randomised clinical trial, or as an author in a systematic review author team. This means that the single point of responsibility principle applies throughout the organisation, and that all staff have an immediate superior. Furthermore, the Copenhagen Trial Unit is being managed like a university department throughout the organisation. This gives freedom to act based on a dialogue and an extensive delegation of management competences. This is of course linked to full responsibility for completion of the assignment based on culture-borne common sense and consideration at all levels. This also entails a corporate culture that prefers and makes room for considered management decisions, rather than a rigid and detailed management by rules.

If projects are not developing, we try to identify reasons for that and decide about supporting or amending actions.

1.3.4 Relevant documents and additional information

- https://nta.nordforsk.org/
- https://www.ecrin.org/
- http://www.cric.nu/
- https://www.cochranelibrary.com/
- https://www.cochrane.org/
- http://www.equator-network.org/
- http://www.ctu.dk/

- https://hbg.cochrane.org/
- http://www.ctu.dk/about-the-ctu/the-cochrane-hepato-biliary-group.aspx
- https://www.ich.org/products/guidelines/efficacy/efficacy-single/article/integrated-addendum-good-clinical-practice.html

1.4 Economy and budget

1.4.1 How is the centre funded?

- *Please provide information about funding sources for the last five years, including both government funding and other sources.*
- *Please report in million DKK in 2018-prices with two decimals. Use figures from final accounts if available. For years, where final accounts are not available, use budgets and mark the year with a 'B'.*
    - *In the first table, please exclude any funds for Danish Cochrane Review Groups affiliated with the centre*

Table 1-2 The Copenhagen Trial Unit, Centre for Clinical Intervention Research's revenues 2014-2018 (excluding the Cochrane Hepato-Biliary Group affiliated with the centre).

Million DKK 2018 prices per year	2014	2015	2016	2017	2018
Government grant (National Finance Act)[1]	6.034	5.987	6.040	6.177	6.188
Research councils and research funds	1.095	1.772	2.077	2.890	360
EU	655	96	1.002	319	0
The Copenhagen University Hospital ('Rigshospitalet')	0	0	0	0	0
Other revenues (including reimbursement of wage expenses by external collaboration partners)	28	2	12	545	844
Total revenues	**7813**	**7857**	**9131**	**9931**	**7392**
[1]The Cochrane Hepato-Biliary Group revenues are not registered separately in the accounting. Therefore, these are based on an estimated fixed rate of 20% of government grant (please see below).					

- *Please describe the source of the most important 'other revenue' sources.*

The source of the most important 'other revenue' sources is most likely to be the grant received from the Innovation Fund, Denmark, to the Intensive Care Unit, Copenhagen University Hospital, named CRIC – Centre for Research in Intensive Care and the grants from 7th Framework Programme for Research and Technological Development, European Commission, EU, Research and Innovation.

- *Please provide the same information for the Cochrane Hepato-Biliary Group affiliated with the centre*

Table 1-3 Revenues for the Cochrane Hepato-Biliary Group affiliated with the Copenhagen Trial Unit, Centre for Clinical Intervention Research.

Million DKK 2018 prices per year	2014	2015	2016	2017	2018
Government grant (National Finance Act)[1]	1.508	1.497	1.510	1.544	1.547
Research councils and research funds	0	0	0	0	0
EU	0	0	0	0	0
The Copenhagen University Hospital ('Rigshospitalet')	0	0	0	0	0
Other revenues (including reimbursement of wage expenses by external collaboration partners)	0	0	0	0	0
Total revenues	**1.508**	**1.497**	**1.510**	**1.544**	**1.547**

[1]The Cochrane Hepato-Biliary Group revenues are not registered separately in the accounting. Therefore, these are based on an estimated fixed rate of 20% of government grant.

The income from the Danish State during the 2014 to 2018 period amounts to DKK 38 million (Euro 5.1 million). During the same period, the Copenhagen Trial Unit has received funding from EU; other research funds; and other internal partners for about DKK 11 million (Euro 1.5 million). The Cochrane Hepato-Biliary Group received no extra funds. Based on experience during the 2000s, it was difficult to raise extra money for running the editorial team office.

During the whole period of existence of the Copenhagen Trial Unit, the public investment amounts to about DKK 175 million (Euro 23.3 million) and investments from private or public funding sources amounts to another DKK 50 million (Euro 6.7 million).

- *Please provide information about the distribution of expenditures for the last five years, including both wage costs and other operating costs.*
- *Please report in million DKK in 2018-prices with two decimals. Use figures from final accounts if available. For years where final accounts are not available use budgets and mark the year with a 'B'.*
    - *In the first table, please exclude expenditures for Danish Cochrane Review Groups affiliated with the centre*

Table 1-4 The Copenhagen Trial Unit, Centre for clinical Intervention Research's expenditures 2014-2018 (excluding the Cochrane Hepato-Biliary Group (CHBG) affiliated with the centre).

Million DKK 2018 prices per year	2014	2015	2016	2017	2018
Wage expenses					
Researchers, including management (excluding Ph.D.s)	3.799	3.499	3.475	3.878	3.928
Ph.D.s	647	722	492	650	710
Administrative functions	2.029	2.092	2.115	2.227	2.182
Other employees	330	313	180	192	360
Reimbursement for employees on sickness leave or maternity/parental leave (revenue)	-107	-308	-214	-776	-737
Total wage expenses	**6.698**	**6.318**	**6.048**	**6.171**	**6.443**
Operating expenses					
Premises (rent, utility expenses for water, heating etc.)	1.309	1.304	1.306	1.430	1.410
Office expenses (IT equipment, printers, paper etc.)	210	0	198	230	178
Conferences and other academic activities	643	0	278	156	166
Other operating expenses	202	-116[1]	878	715	521
Total operating expenses[2]	**2.107**	**921**	**1.958**	**1.893**	**1.640**
Total expenditures (wages and operating expenses)	**8.805**	**7.239**	**8.006**	**8.064**	**8.083**

[1]The positive costs in other operating expenses for 2015 is due to an accounting error made in 2014, which was corrected in 2015 after the closing of the accounting of the year 2014.
[2]The salaries for two part time researchers have been deducted from total operating expenses since these are registered under CTU and CHBG researchers.

Table 1-5 The Cochrane Hepato-Biliary Group expenditures 2014-2018.

Million DKK 2018 prices per year	2014	2015	2016	2017	2018
Wage expenses					
Researchers, including management (excluding Ph.D.s)[1]	1.811	1.756	1.708	1.705	1.711
Ph.D.s	0	0	0	0	0
Administrative functions	0	0	0	0	0
Other employees	0	0	0	0	0
Reimbursement for employees on sickness leave or maternity/parental leave (revenue)	0	0	0	0	0
Total wage expenses	**1.811**	**1.756**	**1.708**	**1.705**	**1.711**

Operating expenses					
Premises (rent, utility expenses for water, heating etc.)	327	326	327	358	353
Office expenses (IT equipment, printers, paper etc.)	53	0	49	57	44
Conferences and other academic activities	161	0	70	39	41
Other operating expenses	50	0	219	179	130
Total operating expenses[2]	**591**	**326**	**665**	**633**	**568**
Total expenditures (wages and operating expenses)	**2.402**	**2.082**	**2.373**	**2.338**	**2.279**

[1] The accounting of Cochrane Hepato-Biliary Group salaries is a calculation of two full time researchers and two part time researchers of respectively 30% and 40%.
[2] The Cochrane Hepato-Biliary Group expenses are not registered separately in the accounting. Therefore, these are based on a fixed rate of 20% of all expenses.

- *Please report the number of employees (Full Time Equivalents/FTE) at the centre for the last five years.*
    - *In the first table, please exclude employees at Danish Cochrane Review Groups affiliated with the centre*

Table 1-6 Employees (FTE) at the Copenhagen Trial Unit, Centre for Clinical Intervention Research (excluding employees at the Cochrane Hepato-Biliary Group affiliated with the centre).

Full time equivalent (FTE) per year	2014	2015	2016	2017	2018
Researchers, including management (excluding Ph.D.s)	5.43	5.38	5.69	5.91	7.10
Ph.D.s	1.0	1.23	1.0	1.0	1.17
Administrative functions	4	4	4	4	4
Other employees	0.97	0.54	0.28	0.51	1.0
Total number of employees (FTE) excluding the Cochrane Hepato-Biliary Group	**11.4**	**11.15**	**10.97**	**11.42**	**13.27**

Table 1-7 Employees (FTE) at the Cochrane Hepato-Biliary Group affiliated with the centre.

Full time equivalent (FTE) per year	2014	2015	2016	2017	2018
Researchers, including management (excluding Ph.D.s)	2.61	2.61	2.52	2.52	2.52
Ph.D.s	0	0	0	0	0
Administrative functions	0	0	0	0	0
Other employees	0	0	0	0	0
Total number of employees (FTE) at the Cochrane Hepato-Biliary Group	**2.61**	**2.61**	**2.52**	**2.52**	**2.52**

1.4.2 How successful is the centre in attracting funds?

- *Please provide a list of fund applications from the last five years, including the name of the fund/organisation, the applied for amount, status (rejected/granted), and if relevant, the amount granted.*

The Copenhagen Trial Unit attracts funds in a variety of ways. For most projects involving trials and systematic reviews, it is mainly the principal or coordinating investigator's task to provide funding for the project. When the Copenhagen Trial Unit is involved as a collaborator, the Copenhagen Trial Unit participates along the project Steering Committee in funding applications. This has proved a very time-consuming and difficult task, as possible sources for funding for clinical research has diminished during recent years and competition for available funds are increasing.

Table 1-8 shows some of the funding applications for some of the Copenhagen Trial Unit's development plans from 2014 until now. The list is incomplete, as investigators often apply for funding before contacting Copenhagen Trial Unit and several projects have been omitted. For funding granted, the amount (unless otherwise stated) is funding for the project, not for Copenhagen Trial Unit exclusively.

Table 1-8 Funding applications.

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
DanPaCT	2014	Kræftens Bekæmpelse Fond*	DKK 865,000	Granted	DKK 300,000
CopenHeart-RFA	2017	Åse og Ejner Danielsens Fond	DKK 100,000	Granted	DKK 100,000
CopenHeart-RFA	2015	Helsefonden	DKK 250,000	Granted	DKK 250,000
CopenHeart-RFA	2016	Hjerteforeningens Fond	DKK 205,000	Granted	DKK 205,000
CopenHeart-RFA	2014	Lundbeck Foundation	DKK 250,000	Granted	DKK 250,000
CopenHeart-IE	2017	Danish Agency for Science and Higher Education	DKK 310,000	Granted	DKK 310,000
CopenHeart-IE	2016	Heart Centre, internal funding, Rigshospitalet	DKK 65,000	Granted	DKK 65,000
CopenHeart-IE	2016	Hjerteforeningen	DKK 420,000	Granted	DKK 200,000
CopenHeart-IE	2017	Hjerteforeningen	DKK 350,000	Rejected	-
CopenHeart-IE	2016	Lundbeck Foundation	DKK 300,000	Rejected	-
CopenHeart-IE	2016	Novo Nordic Foundation	DKK 1,000,000	Rejected	-

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
CopenHeart-IE	2014	Rigshospitalets Forskningspulje	DKK 570,000	Granted	DKK 570,000
CopenHeart-IE	2016	Videnscenter for rehabilitering og palliation (REHPA)	DKK 220,000	Granted	DKK 220,000
D-Vine trial	2014	Danish Stratigic Research Council	DKK 10,400,000	Rejected	-
D-Vine trial	2014	DSM Nutritional Products, The Netherlands	Free delivery of oral supplementary vitamin D3 and matching placebo for about 22,000 participants	Granted	Estimated DKK 8,000,000 (never materialised)
D-Vine trial	2014	EU Horizon 2020	DKK 59,627,250	Rejected	-
CopenHeart-SF	2017	Hjertecentrets forskningsfond, Rigshospitalet	DKK 460,000	Granted	DKK 460,000
CopenHeart-SF	2014	Lundbeck Foundation	DKK 215,000	Granted	DKK 215,000
NICO trial and systematic review	2014	Danish Stratigic Research Council	DKK 15,800,000	Rejected	-
NEO trials and reviews	2014	Augustinus-fonden	DKK 500,000	Granted	DKK 500,000
TV Trial	2014	DASAIMs Forskningsinitiativ	DKK 25,000	Rejected	-
TV Trial	2017	Den lokale fond Næstved-Slagelse-Ringsted Sygehuse	DKK 682,794	Granted	DKK 682,794
TV Trial	2014	Den lokale forskningsfond Næstved, Region Sjælland	DKK 252,500	Granted	DKK 142,500
TV Trial	2014	Fonden for læge-videnskabens fremme	DKK 94,500	Rejected	-
TV Trial	2017	Fonden for læge-videnskabens fremme	DKK 100,000	Rejected	-

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
TV Trial	2017	Hjerteforeningen	DKK 507,000	Rejected	-
TV Trial	2014	Holger og Ruth Hesses mindefond	DKK 49,500	Rejected	-
TV Trial	2014	Læge Fritz Karners og hustru Edith Karners fond	DKK 30,000	Rejected	-
TV Trial	2014	Lippmannfonden	DKK 45,000	Rejected	-
TV Trial	2017	Produktion, Forskning og Innovation (PFI), Region Sjælland	DKK 507,000	Granted	DKK 507,000
TV Trial	2014	Prof., ovl. Sophus H. Johansens Fond af 23. august 1981	DKK 30,000	Rejected	-
TV Trial	2014	Professor, dr.med. Bjørn Ibsens Fond	DKK 25,000	Rejected	-
TV Trial	2015	Region Sjællands Sundheds-videnskabelige Forskningsfond	DKK 212,938	Granted	DKK 68,750
TV Trial	2015	Trygfonden	DKK 308,138	Rejected	-
PERISAFE	2014	Danish Research Council	Part of a larger application for DKK 40 million in total, DKK 3.5 million for CTU	Rejected	-
PANSAID	2014	Danish Research Council	Part of a larger application for DKK 40 million in total, DKK 3.5 million for CTU	Rejected	-
RECIPE	2014	Danish Research Council	Part of a larger application for DKK 40 million in	Rejected	-

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
			total, DKK 3.5 million for CTU		
PAPRICA	2014	Danish Stratigic Research Council	DKK 13,195,789	Rejected	-
PAPRICA	2015	Innovation Fund Denmark	DKK 20,487,500	Rejected	-
SUP-ICU (CRIC)	2014	Innovation Fund Denmark	Part of a larger application for Center for Research in Intensive Care (CRIC) for a total of DKK 50 million	Granted	DKK 36 million in total, DKK 3,651,000 for CTU
SUP-ICU (CRIC)	2016	Medicinpuljen	DKK 1,777,615	Granted	DKK 1,675,000
SUP-ICU (CRIC)	2016	Region Hovedstadens Forskningsfond	DKK 1,500,000	Granted	DKK 1,168,870
SUP-ICU (CRIC)	2015	Rigshospitalets forskningspulje	DKK 902,250	Granted	DKK 902,250
BUS (incitamenter)		Hjerteforeningen	DKK 795.000 for CTU	Rejected	-
FOCUS	2017	Muusfeldts Fond	DKK 250,000	Granted	DKK 250.000
FOCUS	2014	The Danish Council for Independent Research - Medical Sciences	DKK 1,855,629	Granted	DKK 1,855,629
FOCUS	2014	TrygFonden	DKK 3,570,000	Granted	DKK 3,570,000
SafeBoosC-III	2018	Alfred Benzon	DKK 3,000,000	Rejected	-
SafeBoosC-III	2018	Elsass Foundation	DKK 9,500,000	Granted	DKK 2,700,000
SafeBoosC-III	2020	Horizon 2020	DKK 45,000,000	Rejected	-
SafeBoosC-III	2017	Irish Health Research Board	DKK 7,500,000	Rejected	-
SafeBoosC-III	2018	Medtronic External	DKK 2,130,000	Rejected	-

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
		Research Program			
SafeBoosC-III	2017	Novo Nordic Foundation	DKK 18,000,000	Rejected	-
SafeBoosC-III	2018	Novo Nordic Foundation	DKK 6,500,000	Rejected	-
SafeBoosC-III	2017	Svend Andersen Fonden	DKK 1,000,000	Rejected	-
SMART trial and systematic review	2014	Axel og Martha Thomsens Fond	DKK 70,000	Granted	DKK 70,000
SMART trial and systematic review	2014	Region Hovedstadens Psykiatrifond	DKK 2,145,000	Granted	DKK 2,145,000
SIUTIT	2017	Naturinstituttet I Nuuk, Grønland	DKK 1,800,000	Granted	DKK 1,800,000
HOT	2017	Innovation Fund Denmark	DKK 12,106,987	Rejected	-
HOT	2018	Tandem-programme (Novo Nordisk Fonden)	DKK 14,996,354	Rejected	-
HOT	2017	TrygFonden	DKK 17,521,040	Rejected	-
TECTO trial	2019	Boserups Legat	DKK 300,000	Pending	
TECTO trial	2017	Brødrene Hartmanns Fond	DKK 200,000	Rejected	-
TECTO trial	2014	Gangstedfonden	DKK 216,000	Granted	DKK 216,000
TECTO trial	2018	Holms Mindelegat	DKK 1,575,000	No reply	-
TECTO trial	2018	Lægefonden AP Møller	DKK 100,000	Rejected	-
TECTO trial	2014	Lundbeck Foundation	DKK 390,000	Granted	DKK 390,000
TECTO trial	2014	Lundbeck Foundation	DKK 1,770,000	Granted	DKK 1,575,000
TECTO trial	2018	Lundbeck Foundation	DKK 500,000	Rejected	-

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
TECTO trial	2018	Lundbeck Foundation	DKK 1,575,000	Rejected	-
TECTO trial	2018	Netværk for Forskning og Kvalitetssikring i Psykoterapi	DKK 7,300	Granted	DKK 5,000
TECTO trial	2018	Netværk for Forskning og Kvalitetssikring i Psykoterapi	DKK 9,432	Granted	DKK 5,000
TECTO trial	2018	Novo Nordisk Foundation	DKK 1,976,148	Rejected	-
TECTO trial	2018	Novo Nordisk Foundation	DKK 19,984,856	Rejected	-
TECTO trial	2014	Psykiatrisk Forskningsfond af 1967	DKK 50,000	Granted	DKK 50,000
TECTO trial	2014	Region Hovedstadens Forskningsfond	DKK 1,659,000	Granted	DKK 1,475,000
TECTO trial	2014	Region Hovedstadens Forskningspulje	DKK 1,659,000	Granted	DKK 1,659,000
TECTO trial	2018	RH's Forskningsfond	DKK 4,960,000	Rejected	-
TECTO trial	2017	RHP's forskningspulje	DKK 1,965,000	Rejected	-
TECTO trial	2017	Trepilefonden (Glashof Legatet)	DKK 142,202	No reply	-
TECTO trial	2017	TrygFonden	DKK 3,840,000	Rejected	-
TECTO trial	2017	TrygFonden	DKK 3,971,721	Rejected	-
TECTO trial	2019	TrygFonden	DKK 12,643,345	Pending	
TECTO trial	2018	TrygFonden	DKK 21,494,984	Rejected	-
PATCH-it 2015 (TICH-2)	2015	Bispebjerg Hospitals Forskningsmidler	DKK 220,000	Granted	DKK 220,000
PATCH-it 2015 (TICH-2)	2016	Misc. small foundations	DKK 200,000	Granted	DKK 200,000

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
PATCH-it 2015 (TICH-2)	2015	Velux Foundation	DKK 1,600,000	Granted	DKK 1,600,000
AID-ICU-cohorte (CRIC)	2014	Innovation Fund Denmark	Part of a larger application for Center for Research in Intensive Care (CRIC) for a total of DKK 50 million	Granted	DKK 36 million in total, DKK 3,651,000 for CTU
ALUM	2017	Crowdfunding, Boomerang 2017	DKK 3,217,700	Partly granted	DKK 200,000 - but no funding for CTU
ALUM	2016	Innovation Fund Denmark	DKK 3,217,700	Rejected	-
ALUM	2017	PFA	DKK 50,000	Granted	DKK 50,000
ALUM	2016	NIHR Cochrane Review Incentive Scheme 2016	DKK 3,217,700	Rejected	-
HOT-ICU (CRIC)	2014	Innovation Fund Denmark	Part of a larger application for Center for Research in Intensive Care (CRIC) for a total of DKK 50 million	Granted	DKK 36 million in total, DKK 3,651,000 for CTU
CLASSIC-2	2017	Novo Nordic Foundation	DKK 10,400,880	Granted	DKK 10,400,880 granted for the project, DKK 450,000 for CTU
TREATRIA	2017	Several meetings with Bayer Pharmaceuticals to discuss possible collaboration	Supply of trial intervention placebo, approximately DKK 20,000,000	Pending	

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
Heart and Mind	2019	Helsefonden	DKK 650,000	Pending	
Heart and Mind	2019	Hjerteforeningen	DKK 2,000,000	Pending	
Heart and Mind	2016	Novo Nordic Foundation	DKK 7,500,000	Rejected	-
Heart and Mind	2018	Novo Nordic Foundation	DKK 7,500,000	Granted	DKK 7,500,000
Heart and Mind	2018	Region Hovedstaden	DKK 1,000,000	Granted	DKK 1,000,000
Heart and Mind	2019	Rigshospitalets Forskningspulje	DKK 500,000	Pending	
Heart and Mind	2017	TrygFonden	DKK 1,000,000	Rejected	-
AID-ICU (CRIC)	2014	Innovation Fund Denmark	Part of a larger application for Center for Research in Intensive Care (CRIC) for a total of DKK 50 million	Granted	DKK 36 million in total, DKK 3,651,000 for CTU
HOT FUT	2017	Novo Nordic Foundation	DKK 19,000,000	Rejected	-
TTM2	2016	Gorthon Foundation	SEK 1,000,000	Granted	SEK 1,000,000 - but no funding for CTU
TTM2	2016	Knutsson Foundation	SEK 1,000,000	Granted	SEK 1,000,000 - but no funding for CTU
TTM2	2016	Swedish Heart and Lung Foundation	SEK 3,000,000	Granted	SEK 3,000,000 - but no funding for CTU
TTM2	2016	Swedish Research Council	SEK 26,200,000	Granted	SEK 26,200,000 - but no funding for CTU

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
MBT Trial	2017	TrygFonden	DKK 2,600,000	Granted	DKK 2,600,000
COMPEX	2019	Lundbeck Foundation	DKK 5,600,000	Pending	
COMPEX	2019	TrygFonden	DKK 5,600,000	Pending	
COMPEX	2019	Velux Foundation	DKK 5,600,000	Pending	
SheppHeart-CABG trials	2014	Aase og Einar Danielsens Fond	DKK 75,000	Granted	DKK 75,000
SheppHeart-CABG trials	2015	Dansk Sygeplejerådsfond Sygeplejefaglige Forskningsfond	DKK 125,000	Rejected	-
SheppHeart-CABG trials	2015	Foreningen Østifterne	DKK 150,000	Granted	DKK 150,000
SheppHeart-CABG trials	2016	Foreningen Østifterne	DKK 75,000	Granted	DKK 75,000
SheppHeart-CABG trials	2015	Forskningspuljen mellem Odense Universitetshospital og Rigshospitalet	DKK 400,000	Granted	DKK 400,000
SheppHeart-CABG trials	2014	Helsefonden	DKK 200,000	Rejected	-
SheppHeart-CABG trials	2014	Hjerteforeningen	DKK 150,000	Rejected	-
SheppHeart-CABG trials	2015	Hjerteforeningen	DKK 100,000	Rejected	-
SheppHeart-CABG trials	2017	Kongres-ansøgning Hjerteforeningen	DKK 4,880	Granted	DKK 4,880
SheppHeart-CABG trials	2015	Lundbeck Foundation	DKK 300,000	Rejected	-
SheppHeart-CABG trials	2014	Lundbeck Foundation	DKK 100,000	Granted	DKK 100,000
SheppHeart-CABG trials	2015	Novo Nordisk Foundation	DKK 150,000	Rejected	-
SheppHeart-CABG trials	2014	Professions-højskolen Metropol	DKK 400,000	Granted	DKK 400,000
SheppHeart-CABG trials	2015	Rigshospitalets Forskningspulje	DKK 617,000	Granted	DKK 617,000

Project name	Year	Name of foundation	The applied for amount	Rejected or granted	If granted - the amount
SheppHeart-CABG trials	2015	Thoraxkirurgisk Kliniks Forskningsfond, Rigshospitalet	DKK 260,000	Granted	DKK 260,000
SheppHeart-CABG trials	2015	TrygFonden	DKK 150,000	Rejected	-
RoomLight trials	2018	Elforsk	DKK 2,000,000	Granted	DKK 2,000,000
RoomLight trials	2016	Grosserer L.F. Foghts fond	DKK 87,000	Granted	DKK 87,000
RoomLight trials	2017	Hans og Nora Buchards fond	DKK 173,000	Rejected	DKK 173,000
RoomLight trials	2015	Innovation Fund Denmark	DKK 12,400,000	Rejected	-
RoomLight trials	2016	Olga og Hans Svenningsens fond	DKK 410,000	Rejected	-
RoomLight trials	2016	Region Hovedstadens forskningsfond	DKK 750,000	Granted	DKK 750,000
RoomLight trials	2017	Slagtermester Wørzners mindelegat	DKK 29,000	Rejected	-
RoomLight trials	2017	Toyota Fonden	DKK 200,000	Granted	DKK 200,000
RoomLight trials	2019	TrygFonden	DKK 2,600,000	Pending	

* Fond or fonden in Danish means foundation in English.

1.4.3 How is the use of resources linked to the centre's vision/strategy?

- *Please describe how the centre allocates resources. Include a description of how it is prioritized which clinical fields are to be the subject of reviews to be conducted in the coming year(s). If relevant, describe how the resource allocation is related to the centre's goals and to the dimensioning of workload (Full Time Equivalent/FTE).*

Copenhagen Trial Unit is an integrated part of the Danish research environment, and as such, we have been approached by several collaborators throughout the years, and we offer our expertise to these collaborators or partners. As such, we function as a demand-driven academic research organisation. The clinical relevance of the proposed projects is examined through conduct of systematic reviews of the experimental intervention as well as of control interventions and any cointerventions. If the systematic review shows lack of evidence or uncertainty of the evidence, then we find it reasonable to collaborate. The decision to collaborate is not driven by specialty; type of patients, type of interventions. Rather, we prefer projects that

assess patient-relevant outcomes than unvalidated surrogate outcomes. Copenhagen Trial Unit staff is trying to obtain grants together with, or from the respective collaborators, for the rendered services.

An investigator's wish to launch a randomised clinical trial assessing X versus Y dictates the necessary updated systematic reviews going to be present before the final design of the trial. Often, systematic reviews assessing the experimental intervention; the control intervention, as well as any co-interventions are needed.

Resource allocation is delivered to investigators to sharpen their ideas for randomised clinical trials. The Copenhagen Trial Unit has participated in over 500 development plans, of which 139 have materialised into launched randomised clinical trials. This means that a lot of meetings were held without a specific trial protocol was formulated. The reasons can be various, but the long-term commitment, and strenuous efforts coupled with good knowledge and insufficient funding, are playing a role in the success of trial in terms of patient-relevant outcomes. And more often, it is difficult or impossible to raise the necessary funding, even if protocols were finalised.

When an investigator and her/his team have had several meetings with the Copenhagen Trial Unit and the project starts to take shape, we usually develop a contract with shared responsibilities. Based on that, we develop a budget which is mutually accepted. Then, the tasks of raising the money starts.

1.4.4 How is the financial management of the centre organised and linked to the centre's vision/strategy?

- *Please describe how the financial management of the centre is organised. If relevant, describe how the resource allocation and financial management is related to the centre's goals and to the dimensioning of workload (Full Time Equivalent/FTE).*

The Copenhagen Trial Unit's own administration is handling the daily expense allocation according to the business procedure from the Capital Region of Denmark, and meetings are held between the internal administration and the head of the department on a regular basis to ensure the controlling of these expense allocations. Meetings are also held between the head of the department and the administration to verify and control the monthly accounting for both the Government grant, and other revenue-based research grants from both domestic and foreign investigators, including EU grants. At these meetings, the budget is reviewed and revised in order to anticipate future expenses.

By combining work with randomised clinical trials (irregular activity, demanding periods while other periods may be less stressful) with work on systematic reviews (less demanding periods; work may wait until there is time) the level of stress is somewhat ironed out.

When projects collide, then meetings are held to give priority to those projects that should be cared most.

The Chief Financial Department at the Capital Region of Denmark has the overall responsibility for the accounting of the Copenhagen Trial Unit's accounts.

1.4.5 Relevant documents and additional information

In my function as Head of Administration of Research Projects in "Region Hovedstaden" I am glad to confirm, that CTU is an integrated part of the implemented procedures and control systems in "Region Hovedstaden".

Kind regards

Forskningsadministration
Region Hovedstaden
Center for Økonomi, Koncernregnskab
c/o Rigshospitalet, Glostrup
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Figure 1-4 Report from Rigshospitalet's financial officer.

2 Research production and quality

The Copenhagen Trial Unit has been involved in the conduct of more than 139 randomised clinical trials in which more than 126,000 participants were randomised. The Copenhagen Trial Unit hosts the Editorial Team Office of the Cochrane Hepato-Biliary Group) - one of the 54 global Collaborative Review Groups within the Cochrane Collaboration - as well as the Danish Clinical Research Infrastructures Network (DCRIN), the Danish coordinating hub of the Nordic Trial Alliance (NTA), and the Danish coordinating hub of the European Clinical Research Infrastructures Network (ECRIN).

During the 23 years of full activity (1996 to 2018), the core funding from the Hovedstadens Sygehusfællesskab (H:S) and the Danish state to the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group amounts to about DKK 175 million in 2018 DKK. This public investment has created about 1030 peer reviewed publications in various medical journal; 367 peer-reviewed protocols for Cochrane Hepato-Biliary Group protocols; and 218 Cochrane Hepato-Biliary Group systematic reviews, i.e. a total of about 1600 publications. This corresponds to about a public investment of DKK 110,000 (Euro 14,666) per publication. In addition, the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group have obtained research grants from both domestic and foreign investigators, including EU grants. This makes the cost for certain publication between 25% to 150% higher.

The yearly number of articles published according to PURE is shown in Figure 2-1. In addition, we have published 367 Cochrane protocols and 218 Cochrane systematic reviews in The Cochrane Library.

The number of citations to Copenhagen Trial Unit's publications is shown in Figure 2-2.

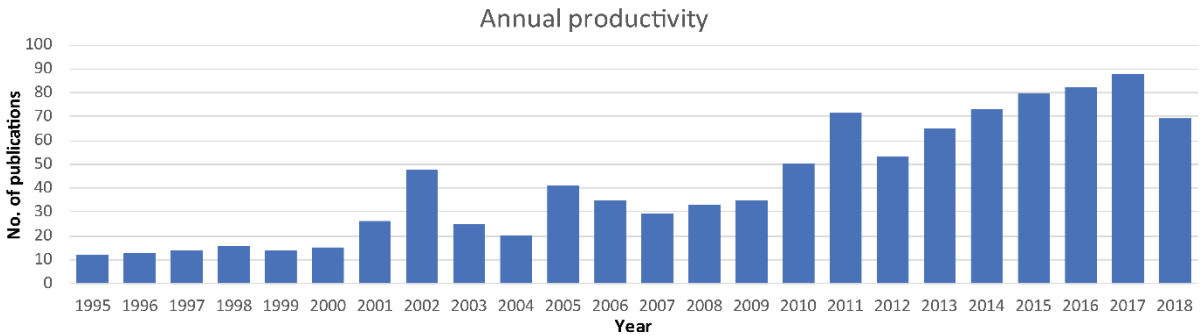

Figure 2-1 The development in publications per year from the Copenhagen Trial Unit.

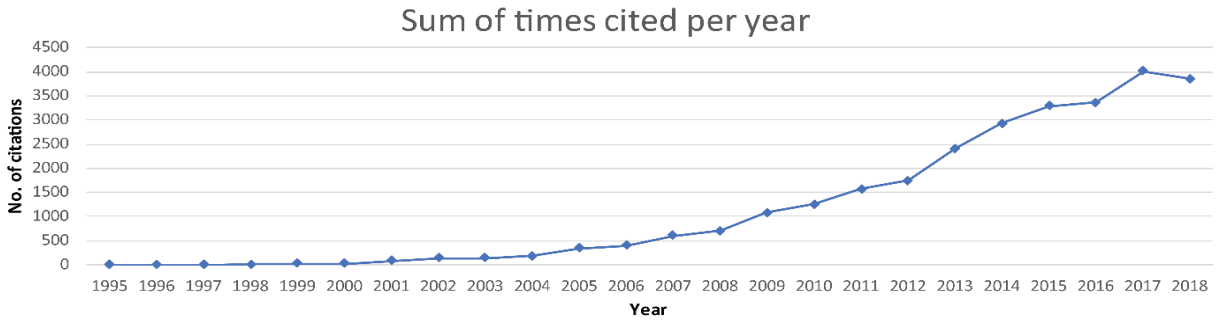

Figure 2-2 The development of citations per year. The Hirsch-index is 79 per March 1st, 2019.

2.1 Research production

2.1.1 The centre's publication list for the last seven years.

- *In addition, to the accounts of publications below, please provide a full list of all publications for the past seven years (01.01.2012-31.12.2018) for VIVEs analysis of citations. The list should be based on PURE, and exported from PURE in CSV file. It is expected that all publications are available in PURE for each researcher. If the publications are not found in PURE, they are not counted in the final evaluation.*

See attached file "2.1.1 - 1 - Publication list CTU 2012-2018.xls" for full list of Copenhagen Trial Unit publications. A full list of Cochrane Hepato-Biliary Group publications is in the attached file "2.1.1 - 2 - Publication list CHBG 2012-2018.xlsx" and "2.1.1 - 3 - Note to the CHBG publication list 2012-2018.pdf". The Cochrane Hepato-Biliary Group publications from authors employed at Copenhagen Trial Unit are found in both lists.

2.1.2 The centre's research production for the last five years?

- *Please count the yearly scientific output of PURE publications for the last five years in the main categories of publications presented in the table below. Please provide the count for each year from 2014-2018.*
    - *In the first table, please exclude publications by Danish Cochrane Review Groups affiliated with the centre*

Table 2-1 depicts the yearly scientific output from Copenhagen Trial Unit. At Rigshospitalet, it is not a requirement that the centres register their conference contributions in PURE, hence, the row for this type of publication is marked with "-" for all years. This, however, does not mean that the Copenhagen Trial Unit does not participate in conferences. During the years, we have participated and contributed to several conferences, presenting abstracts, posters, and having had the function of being chairman.

Table 2-1 Number of publications from the Copenhagen Trial Unit (excluding publications by the Cochrane Hepato-Biliary Group).

Publication type per year	2014	2015	2016	2017	2018	Total
Peer-reviewed journal articles	48	52	57	61	47	265
New Cochrane reviews	9	5	3	10	5	32
Updated Cochrane reviews	3	3	3	1	1	11
Cochrane protocols	2	9	8	7	9	35
Ph.D. or doctoral dissertations	4	4	6	7	1	22
Contributions to books (books and book chapters)	0	1	0	0	0	1
Conference contributions	-	-	-	-	-	-
Other publications and non-peer-reviewed dissemination of research (reports, letters, comments, etc.)	8	4	5	3	6	26
Total (excluding publications by the Cochrane Hepato-Biliary Group)	**74**	**78**	**82**	**89**	**69**	**392**

Figure 2-3 shows graphically the annual scientific production. About 90% of all publications (343/392) are peer reviewed publications.

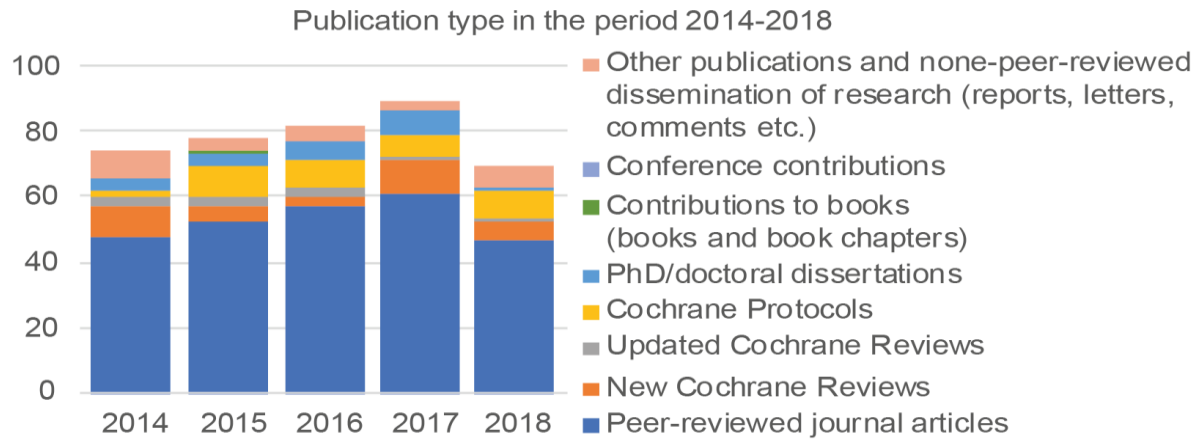

Figure 2-3 Publication type of Copenhagen Trial Unit publications in the period 2014-2018.

Table 2-2 depicts the yearly scientific output from the Cochrane Hepato-Biliary Group.

Table 2-2 Number of publications by the Cochrane Hepato-Biliary Group affiliated with the Copenhagen Trial Unit.

Publication type per year	2014	2015	2016	2017	2018	Total
Peer-reviewed journal articles	6	5	5	1	5	22[1]
New Cochrane reviews	17	7	5	17	9	55
Updated Cochrane reviews	4	5	2	7	3	21[2]
Cochrane protocols	12	33	19	15	25	104
Ph.D. or doctoral dissertations	2	1	0	0	0	3
Contributions to books (books and book chapters)	0	0	0	0	0	0
Conference contributions	2	2	2	3	0	9
Other publications and non-peer-reviewed dissemination of research (reports, letters, comments, etc.)	3	2	3	3	6	17[3]
Total by the Cochrane Hepato-Biliary Group affiliated with the centre	**46**	**55**	**36**	**46**	**48**	**231**

[1] Ten of these publications are also included in the list of publications from the Copenhagen Trial Unit.
[2] The first publication of an updated review could have been originally published before or after 2014. An updated review can also be updated twice from 2014 to 2018. Updates are usually required every second year since last date of search.
[3] Three of these publications are also included in the list of publications from the Copenhagen Trial Unit.

2.1.3 Number and type of studies in Cochrane reviews

- *If relevant, please reflect upon trends over the last five years in the number and the type of studies included in each Cochrane Review as well as the overall complexity of the reviews.*

The Cochrane Hepato-Biliary Group ranked 9th, 6th, 10th, 8th, and 6th in number of publications in The Cochrane Database of Systematic Reviews among all Cochrane review groups from 2013 to 2018. The production of Cochrane protocols for systematic reviews has been about 21 per year for the Cochrane Hepato-Biliary Group alone, and when taken together with the Copenhagen Trial Unit Cochrane protocols, this number is about 28. The production of Cochrane systematic reviews has been about 15 per year for the Cochrane Hepato-Biliary Group alone, and when taken together with the Copenhagen Trial Unit Cochrane reviews, this number is about 21. The fluctuations seen in the numbers are likely random. During the period, the types of systematic reviews have increased in complexity, now including more network meta-analysis systematic reviews and diagnostic test accuracy systematic reviews. Such types of reviews are generally more demanding, also because of their inherent methodologies. The Cochrane Hepato-Biliary Group has published methodological articles on both types of reviews (35-37).

Intervention reviews with meta-analysis of randomised clinical trials with parallel group design
These reviews usually compare an experimental intervention versus a control intervention, being placebo or no intervention, or one experimental intervention versus another or other interventions.

By the end of 2013, the Cochrane Hepato-Biliary Group has published 146 intervention reviews with meta-analyses of parallel group design trials, in which a total of 1669 randomised clinical trials were included.

From 2014 to the end of 2018, the Cochrane Hepato-Biliary Group has published 58 intervention reviews with meta-analysis of parallel group design trials (the number includes the new reviews plus the latest published version of an updated review), in which another 1463 randomised clinical trials were included. The number of included randomised clinical trials in these reviews spans from 0 (because randomised clinical trials were lacking) to 278 included randomised clinical trials.

Intervention reviews with network meta-analysis of randomised clinical trials
In 2014, the Cochrane Hepato-Biliary Group published its first protocol for a network meta-analysis review. By the end of 2018, the Cochrane Hepato-Biliary Group had 26 published protocols for network meta-analysis reviews. However, only 2 of these protocols could be developed further as reviews with network meta-analysis and were published in 2016 and 2017, respectively. This was due to the lack of randomised clinical trials of the planned interventions or lack of relevant outcome data in the included randomised clinical trials. The 2 published network meta-analysis systematic reviews include a total of 93 randomised clinical trials (26 and 67, respectively). Most of the planned as network meta-analysis review protocols have been further developed as intervention reviews with direct comparisons, assessing the comparative benefits and harms of different interventions.

Network meta-analysis reviews require a high level of statistical knowledge and experience as its analysis synthesises information over a network of comparisons to assess the comparative effects of more than two alternative interventions for the same condition, and in case of sufficient trials, they will contain direct and indirect evidence over the entire network. Thus, the estimates of intervention effect are based on all available evidence for those comparisons. This evidence may be direct evidence, indirect evidence, or mixed evidence. Reviews with network meta-analysis may provide relative intervention effects for all comparisons; and a ranking of the interventions.

Diagnostic test accuracy reviews of observational studies and/or randomised clinical trials of test accuracy
From 2014 to 2018, the Cochrane Hepato-Biliary Group has also published 8 diagnostic test accuracy reviews including a total of 153 observational studies (range from 2 to 71). Diagnostic test accuracy reviews are also complex and require a high level of statistical knowledge, in addition to a statistician in the authors' team. The assessment and the critical appraisal of the studies is also performed in a different way than the afore-mentioned review types. As there is no universal terminology for diagnostic study designs, an information specialist who can design an optimal search strategy is a key aspect of the success of identifying the relevant studies.

The complexity from title registration to publication of network meta-analysis reviews and diagnostic test accuracy reviews is also increased by the different editorial processes. Advice and peer review support on network meta-analyses reviews is obtained from Cochrane Methods Comparing Multiple Intervention Group, and on diagnostic test accuracy reviews, from the Cochrane Screening and Diagnostic Tests Methods Group. The additional editorial processes as well as the insufficient number of experts available to comment on these review types may prolong the time from title to protocol and review publication.

We know that on average each randomised clinical trial or study is published twice (1). As our reviews include 3378 studies, this would mean that the Cochrane Hepato-Biliary Groups published reviews include information from almost 7000 references to randomised clinical trials on hepato-biliary diseases. This represent about 50% of the assumed 14.000 randomised clinical trial publication published until end of 2018 (38). Completion of Cochrane reviews on all interventions requires substantial investment. On the other hand, the inclusion and coverage of about half of all randomised clinical trials within hepatology within 20 years shows that the job can be done.

2.1.4 Prioritising of Cochrane reviews

- *Please provide information about how Cochrane Reviews are prioritised and who is involved in setting the review questions*

At an editor meeting back in 2016 and during following meetings, it was decided that it should be mostly up to the Cochrane Hepato-Biliary Group editors, based on demographic approach, to propose priority reviews. Priority reviews are also defined as priority reviews based on replies to surveys from patient organisations and decision-makers. One of our Editors, Kurinchi S Gurusamy, has the most experience on how to identify priority topics for systematic reviews. Currently, the Cochrane Hepato-Biliary Group has defined the following reviews as priority topic for systematic reviews:

- Interventions for chronic hepatitis B.
- Interventions for chronic hepatitis C.
- Interventions for alcoholic liver disease.
- Interventions for non-alcoholic steatohepatitis.
- FibroTest for diagnosis of fibrosis in people without previously diagnosed liver disease.
- Pharmacological interventions for autoimmune liver disease.
- Pharmacological interventions for itching in people with primary biliary cirrhosis: a network meta-analysis.
- Surgery versus non-surgical treatment for gallstones.
- Transient elastography for diagnosis of fibrosis in people without previously diagnosed liver disease.
- Interventions for fatigue in people with cirrhosis.
- Aluminum adjuvants used in vaccines.
- Aluminum adjuvants used in vaccines versus placebo or no intervention.

For many years now, review author teams have usually been working on their systematic reviews on voluntary basis. And yet we have a large number of registered

titles, and protocols and reviews under development. However, recently, we have started requesting prospective authors, through the review proposal forms, to provide evidence on the importance of their proposed review title as well as how important the title is for people with the disease and the source of priority (an upcoming guideline, funders report, etc.) so that we can use this information in our review topic priority setting.

2.1.5 Teaching activities

- *If relevant, please account for teaching activities of researchers at the centre over the last five years*

Teaching and training go hand in hand, and to define exactly the character of the events is not always possible because of the different roles the Cochrane Hepato-Biliary Group Editorial Team office staff fulfils.

- Cochrane Hepato-Biliary Group Editorial Team office staff (Dimitrinka Nikolova (DN); Sarah Louise Klingenberg (SLK); and Christian Gluud (CG)) were taught in Cochrane methodology for the preparation of Cochrane reviews at the annual Cochrane colloquia organised by Cochrane (See attached file “2.1.5 - 1 - Teaching and Training activities for CHBG staff 2014-2018 (Colloquia).pdf”) during Cochrane staff meetings; or through the training Cochrane website for trainers or review authors; or webinars organised by Cochrane. As the best skills are acquired and mastered through the conscious preparation of systematic reviews, Cochrane Editorial Team office staff is continuously working on reviews (See attached file “2.1.1 - 2 - Publication list CHBG 2012-2018.xlsx”).
- Cochrane Hepato-Biliary Group Editorial Team office staff organised and presented Cochrane Hepato-Biliary Group reviews and other methodological papers at the Cochrane Hepato-Biliary Group bi-annual meetings and workshops, during the EASL (the European Liver meeting) and AASLD (the American Liver meeting) yearly meetings for EASL and AASLD attendants. In addition, teaching activities were performed at the Cochrane Hepato-Biliary Group exhibitor stand and via poster presentations. (See attached file “2.1.5 - 2 - Teaching and Training activities 2014-2018 for the CHBG.pdf”).
- Cochrane review results or lectures on evidence-based medicine were also presented in Denmark and Russia, at symposia or workshops in The Netherlands, Croatia, Serbia, Italy, and UK (none of these are mentioned earlier). Talks were delivered at meetings at the Danish Parliament, with The Danish Health Authorities, The Danish Drug Information Association, the Danish National Innovation Network (Biopeople), WHO in Copenhagen, the Italian Gastroenterology Society in Palermo, the Danish Endocrine society, Department of Public Health, Rigshospitalet. (See attached file “2.1.5 - 3 - Christian Gluud - Teaching activities by CG, other CTU or CHBG staff, CHBG editors.pdf”).
- Copenhagen Trial Unit/Cochrane Hepato-Biliary Group participated with presentations at the ECRIN/ECRAN meetings. (See attached file “2.1.5 - 3 - Christian Gluud - Teaching activities by CG, other CTU or CHBG staff, CHBG editors.pdf”).
- Three workshops on Diagnostic test accuracy reviews were organised and run in Gargano, Italy. (See attached file “2 2.1.5 - 2 - Teaching and Training activities 2014-2018 for the CHBG.pdf”).

- One team working visit, hosted by the first review author, took place in 2015 in Italy, to work on a Cochrane Hepato-Biliary Group systematic review. (See attached file “2.1.5 - 2 - Teaching and Training activities 2014-2018 for the CHBG.pdf”).

2.1.6 Training activities

- *If relevant, please account for training activities at the centre over the last five years*

- Between 2014 and 2018, the number of visits to the Cochrane Hepato-Biliary Group Editorial Team office was 32 (some people came more than once). People from Italy (3), Serbia (1), Russia (2), Croatia (3), Saudi Arabia (1), China (4), Germany (3), The Philippines (1), South Africa (1), Mexico (1), UK (1), Bosnia and Herzegovina (2) came to be trained or updated in systematic review methodology while working on systematic reviews. Two of the visitors (China) were Ph.D. students, with Christian Gluud and Janus C Jakobsen as mentors. (See attached file “2.1.6 - 1 - Visitors at the CHBG Editorial Team and CTU.pdf”).
- Cochrane Hepato-Biliary Group Editorial Team office staff organises twice-a-year web-based meetings with Cochrane Hepato-Biliary Group editors. The aim is mainly to discuss editorial work, to update editors on Cochrane methodology, and activities.
- The Cochrane Hepato-Biliary Group Editorial Team office issues twice-a-year a Cochrane Hepato-Biliary Group Newsletters. The aim is to inform CHBG members and other interested in the work of The CHBG of CHBG achievements/publications, past and future activities, and various other news such as useful information. All CHBG Newsletters are identifiable with the 8-digit code ISSN 1901-6301. The CHBG Newsletters are also archived and displayed at the CHBG website: hbg.cochrane.org. From 2014 to 2018, we have issued 10 Newsletters.
    - 2014;18(2):1-6
    - 2014;18(1):1-6
    - 2015;19(2):1-8
    - 2015;19(1):1-9
    - 2016;20(2):1-4
    - 2016;20(1):1-6
    - 2017;21(2):1-8
    - 2017;21(1):1-4
    - 2018;22(2):1-4
    - 2018;22(1):1-4
- The Managing Editor and the Co-ordinating Editor are keeping abreast Cochrane Hepato-Biliary Group Editors through regular e-mail correspondence.

2.1.7 Publication productivity

- *For the centre at large, please provide the average number of publications per researcher and the average number of publications per million of the budget for the last five years. Please use the information on total publications in divided with the number of researchers from Table 1-6 and the funding from government grant and total funding in Table 1-2.*
  In the first table, please exclude publications, employees and budgets of Danish Cochrane Review Groups affiliated with the centre

- *Please provide the same information for Danish Cochrane Review Groups affiliated with the centre, based on the information on total publications in the number of researchers from Table 1-7 and the funding from government grant and total funding in Table 1-3.*

Table 2-3 and Table 2-4 depicts the average number of publications per researcher, and the average number of publications per million of government grant and total funding, respectively.

Table 2-3 Average number of publications per researcher and per million DKK from the Copenhagen Trial Unit (excluding publications, personnel and budgets of the Cochrane Hepato-Biliary Group).

	2014	2015	2016	2017	2018
Average number of publications per employed researcher (FTE), including management	13.63	14.50	14.41	15.06	9.72
Average number of publications per 1 million DKK of government grant	12.26	13.03	13.58	14.41	11.15
Average number of publications per 1 million DKK of total funding	9.47	9.93	8.98	8.96	9.33

Table 2-4 Average number of publications per researcher and per million DKK for The Cochrane Hepato-Biliary Group affiliated with the Copenhagen Trial Unit.

	2014	2015	2016	2017	2018
Average number of publications per employed researcher (FTE), including management	17.62	21.07	14.29	18.25	19.05
Average number of publications per 1 million DKK of government grant	30.50	36.74	23.84	29.79	31.03
Average number of publications per 1 million DKK of total funding	30.50	36.74	23.84	29.79	31.03

2.2 Research Quality

2.2.1 Journals of publication

- *Please provide a list of the peer-reviewed journals in which the centre's researchers have published articles in the last five years and count the number of articles published in each of these journals for each of the last five years in a table like the one below.*
    - *In the first table, please exclude publications of Danish Cochrane Review Groups affiliated with the centre*

- *Please describe which international journals you consider as the top journals for the centre's research and provide information on potential strategies underlying the distribution of articles in the table above and/or for future publications in peer-reviewed journals.*

- *Please provide the same information for publications by employees at Danish Cochrane Review Groups affiliated with the centre*

Table 2-5 depicts the top 15 journals in which Copenhagen Trial Unit has published articles in the last five years. The full list consists of 109 different journals and is therefore attached as a separate excel document, please see attached file “2.2.1 - 1 - CTU Journals 2014-2018.xlsx”.

Table 2-6 depicts all journals in which Cochrane Hepato-Biliary Group has published articles in the last five years. We have ordered the journals based on the latest journal impact factor published by Thomson Reuters July 2018. Journals not found in the list by Thomson Reuters are categorised with “0” in the column “Journal impact factor”.

Table 2-5 Number of published peer-reviewed articles by journal published by the Copenhagen Trial Unit (excluding publications, personnel and budgets of the Cochrane Hepato-Biliary Group).

Journal name per year	Journal impact factor (JIF) (two-years JIF 2017)	2014	2015	2016	2017	2018	Total for all years
New England Journal of Medicine	79.258	3	1	0	0	1	5
Lancet	53.254	0	0	0	0	1	1
JAMA - Journal of the American Medical Association	47.661	0	0	1	0	0	1
World Psychiatry	30.000	0	0	1	0	0	1
Lancet Infectious Diseases	25.148	0	0	0	1	0	1
BMJ	23.259	0	3	0	1	3	7
Circulation (Baltimore)	18.880	0	1	0	0	0	1
American College of Cardiology. Journal	16.834	0	1	0	0	0	1
Intensive Care Medicine	15.008	2	5	4	0	2	13
Hepatology	14.079	1	0	0	0	0	1
Annals of Neurology	10.244	0	0	0	1	0	1
Theranostics	8.537	0	0	0	1	0	1
British Journal of Sports Medicine	7.867	1	0	0	0	0	1
Neurology	7.609	0	0	1	0	0	1
Alimentary Pharmacology and Therapeutics	7.357	0	0	1	0	0	1
Total publications in other journals	Median JIF of other	41	41	49	57	40	228

	journals: 2.413						
Total number of peer-reviewed articles	**Median JIF of all journals: 2.766 (min: 0, max: 79.258)**	**48**	**52**	**57**	**61**	**47**	**265**

As a rule of thumb, we try to publish in the best suitable journals regularly publishing clinical research or publishing on methodology. As the peer review system is not functioning optimally (e.g. the peer reviewers having too much focus on the smallness of P values), we often have to accept that the journal we first approach, may not accept the submitted paper, and then, we would try a more modest journal.

Table 2-6 Number of published peer-reviewed articles by employees at the Cochrane Hepato-Biliary Group affiliated with the Copenhagen Trial Unit.

Journal name per year	Journal impact factor (JIF) (two-years JIF 2017)	2014	2015	2016	2017	2018	Total for all years
Lancet (Letter)	53.254	1	0	0	0	0	1
BMJ	23.259	0	0	0	0	1	1
Hepatology	14.079	1	0	1	0	0	2
Clinical Gastroenterology and Hepatology	7.683	1	0	0	0	0	1
Alimentary Pharmacology and Therapeutics	7.357	1	0	1	0	0	2
Cochrane Database of Systematic Reviews	6.754	10	5	5	7	6	33
Current Opinion in Clinical Nutrition and Metabolic Care	4.534	1	0	0	0	0	1
Liver International	4.500	0	1	0	0	0	1
Journal of Clinical Epidemiology	4.245	0	0	1	0	0	1
European Journal of Internal Medicine	3.282	0	0	1	0	0	1
PLoS ONE	2.766	0	1	0	0	0	1
International Journal of Surgery	2.693	0	1	0	0	0	1

BMC Medical Research Methodology	2.524	1	0	0	1	0	2
BMJ Open	2.413	0	0	1	0	0	1
Medicine (Baltimore)	2.028	0	0	0	0	1	1
Sao Paulo Medical Journal	1.063	0	1	0	0	0	1
BMJ Evidence-based Medicine	-	0	0	0	0	1	1
Bibliotek for Læger	-	0	1	0	0	0	1
Journal of Clinical and Experimental Hepatology	-	0	0	0	0	1	1
Systematic Reviews	-	0	0	0	0	1	1
Total number of peer-reviewed articles	**Median JIF of all journals: 6.754 (min: 0, max: 53.254)**	**16**	**10**	**10**	**8**	**11**	**55**

2.2.2 Authorship order as indicator of involvement in research production

- *In health sciences, the first and last authorships are often considered the most prestigious. Please reflect whether this sort of reasoning is reflecting the way the authors are listed in the peer-reviewed articles published by your centre or other principles of authorship order are prominent.*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group follow the guidelines by the International Committee of Medical Journal Editors (ICMJE) for authorship (39), and advise researchers and collaborators to do the same. Regarding the order of authorship, the first author is the one who has had the major job with pulling the project through and usually the last author is the one with the idea or the major methodological insight. All authors should approve of the final manuscript submitted for publication.

The specific contributions should be listed under the section ‘Contributions of authors’. We encourage authors to discuss the by-line early in the preparation of the manuscript and to revise it, if needed, before submitting the final manuscript for publication.

2.3 Ph.D. activity

2.3.1 Ph.D. supervision responsibility

- *Please provide information whether the centre is expected to provide supervision for Ph.D.s and if so, how this supervision is provided*

One of Copenhagen Trial Unit’s main goals is to educate students, candidates, and researchers in evidence-based medicine, randomised clinical trials, meta-analyses, and trial sequential analysis. Supervising Ph.D.s is for us a great way to achieve this goal. Therefore, we do not only supervise when possible for Ph.D.s, or doctoral

dissertations or master dissertations, but we also assist as unofficial supervisors as much as possible for the aforementioned.

2.3.2 The number of Ph.D. projects that are initiated, ongoing, and defended dissertations

- *Please count the activity of Ph.D.s for the last five years according to the three categories: Ph.D.s that have been initiated, Ph.D.s that are ongoing and Ph.D.s that are publicly defended (dissertations). Please provide the number for each year in a table like the one below.*

Table 2-7 depicts the number of Ph.D.s supervised by employees at Copenhagen Trial Unit during the period from 2014-2018. A detailed list of Ph.D.s can be found in the attached file "2.3.2 - 1 - Ph.D., Doctoral dissertations and Master dissertations 2014-2018.xlsx".

Table 2-7 Official supervising by members of the Copenhagen Trial Unit staff of Ph.D. projects (excluding personnel of the Cochrane Hepato-Biliary Group).

Category per year	2014	2015	2016	2017	2018	Total
Ph.D.s initiated	4	3	0	1	1	9
Ph.D.s ongoing	4	5	7	3	3	22
Defended Ph.D. dissertations	1	3	1	4	1	10

As mentioned in section 2.3.1, Copenhagen Trial Unit does not only officially supervise Ph.D.s and others striving for a dissertation, but we also provide unofficial supervising for Ph.D.s, doctoral dissertations, and master dissertations. Table 2-8 displays the number of this type of work combined. A detailed list of these can be found along with the supervised Ph.D.s in the attached file "2.3.2 - 1 - Ph.D., Doctoral dissertations and Master dissertations 2014-2018.xlsx".

Table 2-8 Unofficial supervising by members of the Copenhagen Trial Unit staff of Ph.D. projects and doctoral dissertations (excluding personnel of the Cochrane Hepato-Biliary Group).

Category per year	2014	2015	2016	2017	2018	Total
Initiated	3	1	2	1	2	9
Ongoing	5	6	4	1	1	17
Defended Ph.D. dissertations and doctoral dissertations	4	2	3	5	1	15

In addition to the above, The Cochrane Hepato-Biliary Group supervised three Ph.D.s and one doctoral dissertation along with unofficial supervision for one doctoral dissertation from 2014-2018. These are also included in the detailed list in the attached file "2.3.2 - 1 - Ph.D., Doctoral dissertations and Master dissertations 2014-2018.xlsx".

2.3.3 Affiliation of Ph.D. fellows following the dissertation

- *Please provide the number of Ph.D. fellows that are employed at the centre following the public de and Ph.D.s that are no longer affiliated with the centre. This should be provided in table as the one below. Please also provide a list*

of the specific affiliations of the Ph.D.s that are not affiliated at the centre after the Ph.D. defence

From 2014 to 2018, no Ph.D. fellows were employed at Copenhagen Trial Unit after their defence (Table 2-9). However, the Copenhagen Trial Unit has maintained collaboration with a large number of the Ph.D.s, still doing research together and publishing work related to not only the topic of the Ph.D. but also additional projects. Table 2-10 shows the place of work of most of the Ph.D.s in 2018.

Table 2-9 Affiliation of Ph.D. fellows, doctoral these fellows, and master dissertation candidates (excluding the Cochrane Hepato-Biliary Group).

Category per year	2014	2015	2016	2017	2018	Total
Supervised Ph.D.s employed at the centre following the defence	0	0	0	0	0	0
Supervised Ph.D.s employed other places following the defence	1	3	1	4	1	10
Assisted Ph.D. projects, and supervised and assisted doctoral dissertations and master dissertations employed at the centre following the defence	0	0	0	0	0	0
Assisted Ph.D. projects, and supervised and assisted doctoral dissertations and master dissertations employed other places following the defence	4	2	3	5	1	15

Table 2-10 Employment of Ph.D. fellows not affiliated with the centre after the Ph.D. defence (excluding the Cochrane Hepato-Biliary Group affiliated with the centre).

Count	Name of employment place following the public defence
2	Dept. of Intensive Care 4131, Rigshospitalet, Copenhagen, Denmark
1	Dept. of Anaesthesiology, Rigshospitalet, Copenhagen, Denmark
1	Dept. of Cardiothoracic Surgery, Rigshospitalet University of Copenhagen, Denmark
1	Dept. of Neurosurgery, University Hospital Copenhagen, Rigshospitalet, Denmark
1	Dept. of Anaesthesiology and Intensive Care Medicine, North Zealand Hospital, Hillerød, Denmark
1	Paediatric Department, North Zealand Hospital, Hillerød, Denmark
2	Dept. of Anaesthesiology, Herlev and Gentofte Hospital, Denmark
1	Dept. of Urology, Herlev and Gentofte Hospital. Denmark
1	Dept. of Radiology, Bispebjerg Hospital, Denmark
1	Zealand University Hospital, Roskilde, Denmark
1	Medical Department, Holbæk Hospital, Denmark
1	Dept. for occupational and preventive medicine, Holbæk Hospital, Denmark
1	Dept. of Anaesthesia and Intensive Care Medicine, Amager and Hvidovre Hospital, Denmark

1	Sports Orthopedic Research Center-Copenhagen (SORC-C), Arthroscopic Center, Department of Orthopedic Surgery, Amager-Hvidovre University Hospital, Denmark
1	Dept. for Child and Adolescent Psychiatry Southern Jutland, Aabenraa, Denmark, and Institute of Regional Health Research, University of Southern Denmark, Odense, Denmark
1	Lundbeck, Denmark
1	Dept. of Anaesthesia and Pain Medicine, Western Health, Gordon Street, Footscray, Victoria, Australia
1	Lund University Hospital, Sweden
1	Drug Regulatory Affairs Consulting OY, Finland
4	NA (Not known, Not employed now, or still affiliated to the university following their dissertation

3 Impact and relevance

3.1 Who are the centre's primary audiences/target groups in the Danish society?

- *Please list the organisations that the centre considers its primary target group*

The Copenhagen Trial Unit
The Copenhagen Trial Unit has since its opening in 1995 had a broad range of audiences and target groups. Ultimately, our aim is to improve treatment and health for patients in Denmark and worldwide through our four missions:

1) Support, coordinate, and conduct randomised clinical trials in the primary and secondary health-care sectors. The trials may have preventive, diagnostic, therapeutic, or care objectives.
2) Support, coordinate, and conduct systematic reviews of the literature based on meta-analyses, and participate in the international Cochrane Collaboration.

When conducting randomised clinical trials and systematic reviews, our audience and target groups are health researchers, broadly defined. We target both health researchers from academia and from industry. Moreover, we work with people with different educational backgrounds and specialties, such as physicians, nurses, physiotherapists, engineers. We have conducted trials in people with various diseases, from foot warts to schizophrenia. The Copenhagen Trial Unit welcomes collaboration with researchers from any region or hospital in Denmark or abroad.

We establish our collaboration with the respective party by stipulating that the randomised clinical trial and systematic review would be conducted according to the best available methodology ensuring low risk of bias (systematic error), low risk of random error (play of chance), and low risk of design errors. Moreover, we require transparency regarding trial protocols; statistical analysis plans, results, and anonymised patient data in order to ultimately benefit the patients. The Copenhagen Trial Unit prefers to do clinical research with the joint efforts of academic researchers at Danish universities and university hospitals, as well as small private start-ups. Our experience with development plans with pharmaceutical or medical device industries, or where these industries were involved as sponsors, have not always been positive because of their unwillingness to choose the most valid PICOTs for the systematic reviews and transparency of data.

3) Participate in the development of methods for randomised clinical trials and meta-analyses.

Development of trial and systematic review methodology is mostly conducted in collaboration with academic researchers. Ultimately, any new methodology developed by the Copenhagen Trial Unit targets all health researchers conducting trials and systematic reviews both nationally and internationally.

Examples of developments that the Copenhagen Trial Unit has participated in are:

- Development of thresholds for statistical and clinical significance in randomised trials and systematic reviews (26, 27).
- Trial Sequential Analysis as a tool for handling imprecision and risk of random errors in randomised trials and systematic reviews (40-42).
- Risk of bias and systematic review methodology (24, 43-45).

- Development of OpenClinica software for trials: this includes improving system stability, speed, and adding functionality for randomisation, monitoring, and various self-service capabilities. Also, customisation has been added for supporting medicine distribution, complex electronic case report forms (eCRF) controls, and data extractions.
- Full transparency in clinical research.

4) Educate students, candidates, and researchers in evidence-based medicine, randomised clinical trials, meta-analyses, and Trial Sequential Analysis. Education is targeting multiple groups.
   - In any collaboration with a specific trial or review, the Copenhagen Trial Unit educates our collaborators in the given methodology as part of the process. This is our main focus for education.
   - Furthermore, the Copenhagen Trial Unit is involved in and hosts many Ph.D. students and 'research year students' (scholars), who are supervised and educated in research methodology.
   - The Copenhagen Trial Unit hosts courses and seminars, and researchers from the Copenhagen Trial Unit are often invited to have teaching sessions during various courses relating to the conduct and methodology of clinical research.

The Cochrane Hepato-Biliary Group and its Cochrane products

The Cochrane Hepato-Biliary Group shares the same aims as the other Cochrane review groups, which is to provide reliable information to practitioners, researchers, policy and decision makers, and consumers in general. The Cochrane Hepato-Biliary Group strives to achieve this through production, maintenance, and international dissemination of hepato-biliary systematic reviews.

The Cochrane Hepato-Biliary Group publishes its products (protocols and reviews, 'added-value' products, such as podcasts, editorials, abstracts of the annual Cochrane Colloquium and for Cochrane Methods) in the Cochrane Library. Selected important reviews are also communicated in parallel in medical journals.

As Cochrane is an international organisation, registered as charity in the UK, the products of The Cochrane Hepato-Biliary Group and the remaining Cochrane groups alike, are intended to be used world-wide. However, studied interventions in Hepato-Biliary reviews may not necessarily have equal value for people from different countries. This could be due to, for e.g. the affordability of the interventions or disease prevalence.

People in Denmark have free access to the Cochrane Library and its products. However, for sure, there are still patients or consumers who are not aware of this, likely due to insufficient national media attention, or English language reading comprehension.

Most of the Cochrane Groups, like the staff at the Cochrane Hepato-Biliary Group Editorial Team office, are underpowered, lack the means for sufficient disseminating activities on their own, and are understaffed. So far, Cochrane has made huge efforts in establishing work relationships with international Cochrane groups and centres, and with various partners, on dissemination of Cochrane products, including

the Hepato-Biliary. This has led to publishing translations of Abstracts of Systematic Reviews into various languages, translations of Plain Language Summaries into various languages, translation of the Cochrane Review Database into Spanish, or publishing podcasts. Other products on the Cochrane Library are The 'Clinical questions and Clinical answers', 'Cochrane evidence', and 'the Journal Club'. The Cochrane Hepato-Biliary Group has no translations of any of the products into Danish.

The Cochrane Hepato-Biliary Group has been or is still in contact with more than 138 people (medical students, physicians at Danish hospitals, and others) from Denmark. One-hundred and one of these people are Cochrane Hepato-Biliary Group authors. Five of the 138 people have also the role of an editor of the Cochrane Hepato-Biliary Group. The Cochrane Hepato-Biliary Group Newsletter is issued bi-annually, with an aim to inform its members of the latest Hepato-Biliary Group's achievements (publications), past and present meetings and activities. Every Cochrane Hepato-Biliary Group Newsletter is sent to the Royal Danish Library and is identifiable with the 8-digit code ISSN 1901-6301. It is also uploaded on the Hepato-Biliary Group's website (hbg.cochrane.org).

3.2 Please describe the ways in which the centres' research and activities are used by and creates benefits in various parts of the Danish society. Include at least the following topics

- *Examples of potential impact on clinical practices and clinical guidelines within the past five years*

The Copenhagen Trial Unit
The CLARICOR trial published in BMJ (clarithromycin versus placebo for patients with stable coronary artery disease) surprisingly showed that clarithromycin increased mortality even at 10-years follow-up (46-48). Since the first results published in 2005, the Copenhagen Trial Unit has repeatedly informed the authorities of the possible adverse reactions of clarithromycin (meetings at European Medicines Agency (EMA), London, and Danish Medicines Agency; Copenhagen). At the time of the first publication of the results, the United States Food and Drug Administration (FDA) issued a safety alert. In 2018, the FDA has added a new warning to clarithromycin's label, advising prescribers to choose other antibiotics in patients with coronary artery disease. That happened after FDA had conducted a large observational study confirming CLARICOR's results. During the same period, the Danish and the European medicines agencies have changed nothing in their recommendations for the use of clarithromycin.

The 6S trial (hydroxyethyl-starch versus placebo infusion to septic patients) published in NEJM (49) and the subsequent systematic review in BMJ (50) has contributed to EMA and the 'Surviving Sepsis Campaign' (51) recommending not using hydroxyethyl-starch to septic, burned and critically ill patients and the EMA recommends monitoring perioperative patients receiving hydroxyethyl-starch products for kidney problems to at least 3 months after infusion of starch (52). Twice, the EMA Pharmacovigilance Risk Assessment Committee (PRAC) and the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) (http://www.hma.eu/352.html) have endorsed the recommendation to suspend the marketing authorisations of hydroxyethyl-starch solutions for infusion

across the European Union, but twice the European Union has opposed such a definite withdrawal.

The TTM-1 trial (cooling to 33 to 34 degrees Celsius versus 36 degrees Celsius to patients with out of hospital cardiac arrest) published in NEJM (53) has led the ICU department at Rigshospitalet to cool unconscious patients not to the previously recommended 33-34 degree Celsius but to 36 degrees Celsius. Several other ICUs in Europe and Australia have adopted this strategy as well (54). The TTM-2 trial, presently randomising patients, aims to determine if unconscious patients with out of hospital cardiac arrest should be cooled at all if the temperature is lower than 37.8 degrees (55).

The TRISS trial (patients in the intensive care unit (ICU) who had septic shock and a haemoglobin concentration of 9 g per decilitre or less to receive 1 unit of leukoreduced red cells when the haemoglobin level was 7 g per decilitre or less (lower threshold) or when the level was 9 g per decilitre or less (higher threshold) during the ICU stay) published in NEJM (56) and the subsequent systematic review published in BMJ (57) has contributed to the 'Surviving Sepsis Campaign' guidelines (51) recommending not to transfuse septic patients before the haemoglobin was 7.0 g/dl or less.

The SUP-ICU trial (patients admitted to the ICU for an acute condition (i.e., an unplanned admission) and who were at risk for gastrointestinal bleeding received 40 mg of intravenous pantoprazole (a proton-pump inhibitor) versus placebo daily during the ICU stay) published in NEJM (58) and the subsequent systematic review in Intensive Care Medicine (59) has led the ICU department at Rigshospitalet not to use proton pump inhibitors prophylactic to all patients at risk of gastrointestinal bleeding, but to reserve this intervention for patients exhibiting signs of gastrointestinal bleeding.

The Cochrane Hepato-Biliary Group

In the last five years more than 70 different Cochrane Hepato-Biliary Group systematic reviews, either published in The Cochrane Library or in paper journals, have been cited over 100 times in more than 30 international guidelines. Below is an overview per year covering a selection of these guidelines. A detailed list of the specific guidelines and the titles of reviews or publications cited is given in the attached file "3.2 - 1 - Guidelines and reviews.xlsx".

Table 3-1 Number of guidelines in which reviews and publications are cited.

Year	Number of guidelines citing Cochrane Hepato-Biliary Group reviews	Number of reviews cited
2014	7	16
2015	4	21
2016	8	40
2017	9	29
2018	4	9

This overview represents some of the major guidelines within the hepato-biliary field, but we are aware that there are guidelines from other countries or other societies not included here.

Furthermore, the Cochrane Hepato-Biliary Group systematic reviews have also been cited on several Wikipedia pages, e.g. reviews on biliary colic, capsule endoscopy, flumazenil, gastrointestinal bleeding, hepatic encephalopathy, hepatitis B, hepatitis B vaccine, hepatitis C, and paracetamol poisoning. A detailed list of the titles of the reviews used are given in the attached file “3.2 - 2 - Wikipedia and reviews.xlsx”.

- *Collaborations with public authorities within the past three years*

The Copenhagen Trial Unit and the Cochrane-Hepato-Biliary Group
Public authorities including the Capital Region of Denmark and the Danish Medicines Counsel have been benefiting by the research performed by the Copenhagen Trial Unit in terms of official advice and reports related to clinical research topics. As example, Jørn Wetterslev has delivered written contributions to the draft for Capital Region of Denmark research strategy 2018 (60). Moreover, in 2018, Jørn Wetterslev contributed with a written opinion to the Danish Medicines Counsel on the use of confidence intervals and point estimates in the assessment of new drugs and indication extensions (61).

We have participated in meetings in the Danish parliament regarding the lack of public money for independent clinical research.

- *Collaboration with hospitals and healthcare professionals within the past three years*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group
Both the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group provide accessible and credible information to support evidence-informed decision making in the healthcare sector. The research and activities are typically non-commercial or conducted with non-conflicted funding. We believe our research is particularly important for hospitals and healthcare professionals who experience difficulties knowing whether information on a given intervention or medicinal product is reliable, accurate and unbiased and unconstrained by commercial and financial interests.

Through the trials the Copenhagen Trial Unit have been involved in the last three years we have collaborated with hospitals across Denmark, Scandinavia, and Europe. Through the Cochrane Hepato-Biliary Group, we collaborate with physicians and methodologists or statisticians all over the world.

- *Participation in consulting, commissions, boards etc. within the past three years*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group
Christian Gluud is a member of the Scientific Board of ECRIN and Janus Christian Jakobsen is a member of the Panel of Methodologists anchored in the ECRIN Scientific Board. The aim of the ECRIN Scientific Board is to provide unbiased assessment of preventative, diagnostic and therapeutic interventions that might not

otherwise be investigated, and ultimately to optimise medical practice in Europe across all disease areas.

Jørn Wetterslev participated in the Adjudication Committees for the Poise II trial in 2014-2015. Christian Gluud is a member of the scientific steering committee of Centre for Research in Intensive Care (CRIC). Jørn Wetterslev is a member of the daily executive committee of CRIC.

- *Organisation of conferences, symposiums or other knowledge sharing initiatives within the past three years*

The Copenhagen Trial Unit
A cornerstone of the Copenhagen Trial Unit's mission is to teach trial methodology and evidence-based medicine. One way to achieve this is through knowledge sharing. During the past three years, the Copenhagen Trial Unit has offered courses and workshops, and has actively participated in conferences and symposia as listed in Table 3-2. A key event is ECRIN's celebration of International Clinical Trials Day, which has been organised as a yearly event by Christian and the Copenhagen Trial Unit since 2006. The latest event was in 2017.

Jørn Wetterslev has been a teacher in systematic reviews, bias and random errors in meta-analysis during educational courses for specialist in anaesthesiology in the last 10 years.

The Cochrane Hepato-Biliary Group
The Cochrane Hepato-Biliary Group has also performed educational and training activities on the methods used in Cochrane systematic reviews at local and international events; through establishing working relationships with medical institutions and Universities, and through collaboration with people from around the world visiting the Editorial Team Office, see Table 3-2 (for activities limited to the Cochrane Hepato-Biliary Group, please see attached file 2.1.5 - 2 - Teaching and Training activities 2014-2018 for the CHBG.pdf).

Mainly during the annual European Association for the Study of the Liver (EASL) and American Association for the Study of Liver Disease (AASLD) meetings, the Cochrane Hepato-Biliary Group has held some annual meetings and has manned stands at the exhibitions. At these annual meetings or symposia, affiliated events of the EASL and the AASLD meetings, Cochrane Hepato-Biliary Group authors have presented their reviews. The meetings are conducted as a research forum where attendants and presenters come into discussions. At the exhibition stands, the work of the Cochrane Hepato-Biliary Group is also presented to meeting attendants; this is achieved through posters on Cochrane methodology or of systematic reviews, brochures, copies of review abstracts and plain language summaries of reviews. People willing to work on reviews or people who are already authors are provided with the possibility to discuss various issues with the Editorial Team office staff. These could be on review types and review development to the software needed for developing the reviews. Meetings with Cochrane Hepato-Biliary Group editors, attending these international meetings, are also organised to discuss Cochrane Hepato-Biliary Group-related work.

Table 3-2 Conferences, symposiums, and knowledge sharing 2016-2018 for both the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group.

Date	Conference or symposium	CTU or CHBG organiser or participants
26 February 2016	Nordic Trial Alliance meeting Place: Oslo, Norway	Presenter: CG: Nordic clinical research transparency and registration
3-4 March 2016	ECRIN (European Clinical Research Infrastructures network) meeting CORBEL (Coordinated Research Infrastructures Building Enduring Life-science Services): Multi-stakeholder taskforce. Sharing patient-level clinical trial data. Place: Paris, France.	Participant: CG.
8 April 2016	Danish Society for Clinical Nutrition (DSKE) meeting. 25th yearly meeting in clinical nutrition. Place: Rigshospitalet, auditorium 2	Presenter: Joshua Feinberg. Nutrition support in hospitalised adults at nutritional risk. A Cochrane review with meta-analysis and trial sequential analysis.
13 April 2016	The 38th Bi-Annual CHBG Meeting. Joint workshop EASL (European Association for the Study of the Liver) – CHBG. April 13, 2016. 08:00 am to 11:00 am. Barcelona, Spain. The joint workshop was based on four CHBG reviews of interventions for different liver conditions (chronic hepatitis C; hospitalised liver patients; primary biliary cirrhosis; and hepatic encephalopathy). The harms and benefits of the different interventions for these conditions have been evaluated in the systematic reviews with meta-analysis, Trial Sequential Analysis, and network meta-analysis. Furthermore, a CHBG diagnostic accuracy test review on non-invasive diagnostic tests for oesophageal varices was presented. The learning objectives were to understand the powers and weaknesses of systematic reviewing outperforming even large single randomised clinical trials. Chair: Christian Gluud (Denmark) and Cecilia Rodrigues (Portugal)	Presenters from the CHBG Editorial Team (ET) office: Joshua Feinberg; CG.

Date	Conference or symposium	CTU or CHBG organiser or participants
13-16 April 2016	CHBG exhibition, Barcelona, Spain	
28-29 April 2016	STRIDER project investigator meeting. Place: London, UK	Participant: CG.
20 May 2016	ECRIN 2016 celebrations of The International Clinical Trials Day. Place: Prague, The Czech Republic	Chair: CG Personalised medicine
8 September 2016	Evidence-based medicine course. Place: Institute for Social Medicine and Epidemiology. Lübeck, Germany	CG: The evidence-based hierarchy of studies for health-care interventions – and the threats to their validity
1 November 2016	Danish Diabetes Academy Annual Day. Place: Sinatur Hotel Storebælt, Østerøvej 121, DK-5800 Nyborg	CG: Transparency and translation of clinical research: the significance for clinical practice
13 November 2016	The 39th Bi-Annual CHBG Meeting, affiliate event at the AASLD (American Association for the Study of Liver Diseases), The Liver Meeting®. Boston, MA; USA.	Presenters from the CHBG Editorial Team (ET) office: Joshua Feinberg (JF) presented a review on nutrition support which JCJ and CG also co-authored. Emil Eik Nielsen (EEN) presented a review on direct acting antivirals for chronic hepatitis C which JF, JCJ, SLK, DN, and CG also co-authored.
11-15 November 2016	CHBG exhibition, Boston, MA, USA	JF participated at the LIVER meeting with a poster “Cochrane Hepato-Biliary Systematic Review: Nutrition support in hospitalised adults at nutritional risk. Joshua Feinberg (DK), Emil Eik Nielsen (DK), Steven Kwasi Korang (DK), Kirstine Halberg Engell (DK), Marie Skøtt Rasmussen (DK), Kang Zhang (CN), Maria Didriksen (DK), Lisbeth Lund (DK), Niklas Lindahl (DK), Sara Hallum (DK), Ning Liang (CN), Wenjing Xiong (CN), Xuemei Yang (CN), Pernille Brunsgaard (DK), Alexandre Garioud (DK), Sanam Safi (DK), Jane Lindschou (DK),

Date	Conference or symposium	CTU or CHBG organiser or participants
		Jens Kondrup (DK), Christian Gluud (DK), and Janus C Jakobsen (DK).
25 November 2016	Copenhagen University. Place: Kommunehospitalet.	CG: Two lectures on evidence based-medicine.
30 March 2017 – 1 April 2017	4th World Congress on Controversies in Pediatrics (CoPedia). Place: Amsterdam, The Netherlands	Session Chair: CG + Presenter: CG (The benefits of methylphenidate for children and adolescents with attention-deficit hyperactivity disorder (ADHD): Are the results so special and are they valid?); The harms of methylphenidate for children and adolescents with attention-deficit hyperactivity disorder (ADHD): are the results so special and are they valid?
4-8 April 2017	Basic residential course: DIAGNOSIS: the pathway of a diagnostic test from bench to bedside. Place: Palazzo Feltrinelli, Gargnano, Lago di Garda, Italy.	Organised by Centro Interuniversitario “THOMAS C. CHALMERS and ALESSANDRO LIBERATI” – Italy; Università degli Studi di Milano; The Multiple Sclerosis and Rare Diseases of the CNS Group; The Copenhagen Trial Unit (CTU), The Cochrane Hepato-Biliary Group, Rigshospitalet, Copenhagen, Denmark. Tutors: DN and CG from CHBG ET office.
20-22 April 2017	CHBG exhibition at EASL, Amsterdam, The Netherlands.	DN, SLK
21 April 2017	Meeting with the EASL Governing Board, Amsterdam, The Netherlands	Aim: to discuss possibilities for educational joint CHBG/EASL meetings (presentations on methodology of systematic reviews and presentation of most recent or new CHBG reviews). Participants/representatives: DN and SLK
4 May 2017	The Danish Parliament (Folketinget).	CG participant in meeting for funding of clinical research:

Date	Conference or symposium	CTU or CHBG organiser or participants
		[Clinical trials save lives… who will pay?] Kliniske forsøg redder og forbedre liv… hvem vil betale?
31 July – 4 August 2017	NorWHO meeting. Place: United Nation's City, Copenhagen	CG: Antioxidant supplements and mortality. Results of a Cochrane systematic review.
11 August 2017	Hillerød Hospital. Inventing for Life. Thematic day on treatment of bacterial infections and antibiotics. Place: Konferencecenteret Pharmakon, Milnersvej 42, Hillerød	Presenters: CG and Naqash Javaid Sethi (NJS) (CTU): Clarithromycin as a secondary profylacsis for patients with coronary heart disease: the randomised placebo-controlled CLARICOR trial.
5 October 2017	Greta Castellini. Trial Sequential Analysis project. Italian meeting. Place: Mario Negri, Milan, Italy	CG: Risks of random errors in randomised clinical trials and how to control them.
10 October 2017 (13:00 to 15:00)	Internet presentation on Trial Sequential Analysis.	Participants: Editors of the Cochrane Anesthesia Group. Tutors: CG; Jørn Wetterslev (JW).
6-7 November 2017	Pharmacology workshop. Clinical Pharmacology and Biostatistics. Place: Copenhagen University, Institute of Pharmacology.	CG: Randomised clinical trials. Introduction and concepts; Meta-analysis; and Is the current development system suitable?
13-14 November 2017	Bristol Meta-analysis Workshop. Cochrane meta-analysis updating project meeting. Place: University of Bristol, Bristol. UK	Talk and discussion: 'For and against sequential updating' 14.11.2017. CG and Jonathan Sterne. Julian Higgins (chair)
20-24 November 2017	AASLD, CHBG exhibition during the LIVER® meeting, Washington, DC, USA	DN; CG.
15-17 December 2017	Evidence-based medicine course and workshop. Place: Rijeka, Croatia.	Organised by Davor Stimac (Croatia), Goran Poropat (Croatia), Goran Hauser (Croatia), and Christian Gluud (Denmark). This workshop is run for a second time. Tutors: Naqash Sethi (NS), JCJ, CG from The CHBG ET office
23-26 March 2018	Best of EASL. XXIII international Russian congress "Hepatology today". Moscow. Cochrane Hepato-Biliary Group clinical symposium.	Tutors and presenters: DN; CG. Lise Lotte Gluud (DK) and Chavdar Pavlov (RU) presented.

Date	Conference or symposium	CTU or CHBG organiser or participants
	Place: Moscow, Russia. Organised by the Russian Scientific Liver Society and EASL.	
4-5 April 2018.	London. Meeting for IMPROvED investigators	CG and Per Winkel participants.
12-14 April 2018	CHBG exhibition during EASL, Paris, France	DN; SLK; CG.
12-14 April 2018	CHBG presentation 'Chronic hepatitis C. Direct-acting antivirals for chronic hepatitis C review (available from the Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD012143. DOI: 10.1002/14651858.CD012143.pub3' during the "Critical reflection on landmark papers 2017" session. 13.04. 2018 from 17:30 to 18:00.	Presenter: CG. Opponent: Jean-Michel Pawlotsky (FR).
June 2018	CTU participated as partner in CRIC in the arrangement and organisation of Clinical Research Høring in Landstingssalen.	Jørn Wetterslev participant and partner
Summer 2018	The Scandinavian Society of Anaesthesiology and Intensive Care Medicine course.	Jørn Wetterslev has been a teacher in randomised clinical trials.
16-18 September 2018	Cochrane Colloquium 'Cochrane for all - better evidence for better health decisions'. Place: Edinburgh, UK	CG: Assessing imprecision in Cochrane systematic reviews: a comparison of GRADE and Trial Sequential Analysis.
Autumn 2018	Ph.D. course at Copenhagen University autumn 2018.	Jørn Wetterslev has been a teacher in randomised clinical trials.
8-9 November 2018	SafeBoosC investigator meeting. Place: Copenhagen	Participants: CG and JCJ
9-13 November 2018	AASLD, CHBG exhibition during the LIVER® meeting, San Francisco, CA, USA.	DN, Goran Bjelakovic
30 November 2018	Copenhagen University. Place: Kommunehospitalet.	CG: Evidence-based clinical practice – two lectures.
22 November 2018	Copenhagen Trial Unit, Copenhagen.	Janus C. Jakobsen Workshop on bias

- *Other ways the centres' research and activities are used by and creates benefits in the Danish society within the past three years*

The Copenhagen Trial Unit
Clinical research is often funded by industry and regularly involves development of a narrow pipeline of commercially attractive medicinal products or devices. The Copenhagen Trial Unit believes that, in an ideal setting, clinical research should be independent from funding resources in order to avoid any negative effects of vested interests.

Independent (and non-commercial) trials are in our experience typically initiated by academic researchers. The academic researchers must rely on public funding to conduct research they deem important to advancing medical practice. Unfortunately, the usual consequence is that academic trials are underfunded, making them too small and short-lived to provide high-quality evidence and reliable estimates of the long-term balance of risks and benefits.

To increase the likelihood of success, the Copenhagen Trial Unit offers our collaborators to apply for funding as a collaborative act. Our goal is to enable high-quality academic trials focusing on general public-health issues of limited interest to industry. This is particularly important since many public-health issues may not be addressed due to the obvious lack of economic incitement in interventions that are non-medicinal, e.g. physical exercise or dietary interventions in heart disease and diabetes. In the last three years, we have been involved in many non-medicinal trials, including trials on psychotherapy, rehabilitation (physical training/exercise) and surgical procedures.

3.3 Visitors, secondments etc. at the centre in the past three years?

- *Please provide information on the number of visitors, secondments etc. at the centre during the past three years.*

The Copenhagen Trial Unit and The Cochrane Hepato-Biliary Group
The two centres have had a number of visitors in the past. Please see Table 3-3 below for details. For more details on visitors, please see attached file "2 2.1.6 - 1 - Visitors at the CHBG Editorial Team and CTU.pdf".

Table 3-3 Visitors in the years 2016-2018 in both the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group.

Date	Visitor	Purpose
25-30 January 2016	Jonathan Nyong, UCL Cochrane Heart Group	Trial Sequential Analysis training
1 February – 1 August 2016	Joshua Rose-Hansen Feinberg	Research year medical student
1 February – 1 August 2016	Emil Eik Nielsen	Research year medical student

Date	Visitor	Purpose
1-15 February 2016	Daria Varganova, Uljanovsk, Russia.	To learn Cochrane review methodology including how to develop a Cochrane protocol for a systematic review, how to critically read and comment on a protocol, and how to develop a protocol into a systematic review. Here the visit was sponsored by EASL mentorship programme. The programme aims at enhancing scientific exchange and personal development relationships across European countries.
1-22 February 2016	Prof. Chavdar Pavlov, Moscow, Russia	Work on 'Ultrasonography for diagnosis of alcoholic cirrhosis in people with alcoholic liver disease' review. Work on an invited editorial regarding the already published Transient elastography for diagnosis of stages of hepatic fibrosis and cirrhosis in people with alcoholic liver disease review published also in Alimentary Pharmacology & Therapeutics.
16 April – 26 September 2016	Greta Castellini, Milan, Italy	Ph.D. student research fellow, Cochrane methodology in Cochrane systematic reviews.
Spring 2016	Frederic Keus, Consultant, Research Unit, Dpt. Intensive Care, University Hospital Groningen, The Netherlands	Collaboration on Horizon 2020 application
Spring 2016	Iwan van der Horst, Consultant, Research Unit, Dpt. Intensive Care, University Hospital Groningen, The Netherlands	Collaboration on Horizon 2020 application
6 June – 4 July 2016	Sheema Muhssen Hamza, Denmark.	Apprenticeship
18-19 September 2016	Jane Campos, Ermita Manila, the Philippines.	To learn about the updated methods in Cochrane systematic review preparation. Work on the review "Clevudine in people with chronic hepatitis B virus infection
20 September	Prof. Chavdar Pavlov, Moscow, Russia	To work on DTAR (Diagnostic test accuracy review) protocols

Date	Visitor	Purpose
– 21 October 2016		for systematic reviews. Recipient of EASL Sheila Sherlock Physician Scientist Fellowship (received April 2015, work 2016 and 2017). Project title: Diagnostic test accuracy systematic reviews of non-invasive fibrosis tests for patients with alcoholic liver disease and chronic hepatitis C.
20 September – 21 October 2016	Daria Leonidovna Varganova, Uljanovsk, Russia.	To learn and be trained in Cochrane methodology for preparation of Cochrane systematic reviews; extract data from randomised clinical trials for inclusion in the 'Glucocorticosteroids for people with alcoholic hepatitis' Cochrane systematic review.
25 January – 14 February 2017	Goran Bjelakovic, Nis, Serbia.	To update two Cochrane systematic reviews on vitamin D assessing the effect of vitamin on prevention of cancer and mortality. Work on the Cochrane review entitled "Vitamin D supplementation for chronic liver diseases in adults".
10 February 2017	Jian Ping Liu, Beijing, PR of China. CHBG editor and author.	To discuss preparation of reviews on Chinese medicinal herbs and education/training of two Chinese Ph.D. students
24 March – 16 April 2017	Anouk Pels, The Netherlands	To write the statistical analysis plan for the Dutch Strider trial
19 April 2017	Anne Marie Halstensen, project coordinator, Oslo Hospital Service, Norge	To discuss the set-up of a trial unit in Oslo.
1 June 2017 to 31 October 2017	Bart Hiemstra, The Netherlands	Ph.D. research period at research institution
1 August 2017 – 1 August 2018	Naqash Sethi, Denmark	Research year medical student
1 August 2017 – 1	Sanam Safi, Denmark	Research year medical student

Date	Visitor	Purpose
August 2018		
14 August – 9 September 2017	Kasper Højgaard Thybo; Denmark	Ph.D. research period at research institution
20 October 2017 – 20 December 2018	Ning Liang, Ph.D. student. Beijing, PR of China	To work on traditional Chinese medicine Cochrane reviews and methodological papers. Work on Radix Sophorae flavescentis for chronic hepatitis B and Radix Sophorae flavescentis versus antiviral drugs for chronic hepatitis B. Currently undertaking a Ph.D. study at the Center for Evidence-based Chinese Medicine, Beijing University of Chinese Medicine (BUCM).
20 October 2017 – 26 October 2018	DeZhao Kong, Ph.D. student. Beijing, PR of China	To work on traditional Chinese medicine Cochrane reviews and methodological papers. Work on “Acupuncture for chronic hepatitis B” and “Xiao Chai Hu Tang, a Chinese herbal medicine formula”, for chronic hepatitis B. Currently undertaking a Ph.D. study at Liaoning University of Traditional Chinese Medicine (LUTCM).
21 January – 17 February 2018	Goran Bjelakovic, Nis, Serbia.	To work on a review on vitamin A and mortality.
22-23 February 2018	Ian van der Horst, Consultant, Research Unit, Dpt. Intensive Care, University Hospital Groningen, The Netherlands	Collaboration on Horizon 2020 application
22-23 February 2018	Frederic Keus, Consultant, Research Unit, Dpt. Intensive Care, University Hospital Groningen, The Netherlands	Collaboration on Horizon 2020 application
26 February to 9 March 2018	Chikwendu Jeffrey Ede, Johannesburg, South Africa.	To be trained in Cochrane systematic review techniques including trial sequential analysis. Work on “Surgical portosystemic shunts versus devascularisation procedures

Date	Visitor	Purpose
		for prevention of variceal rebleeding in people with hepatosplenic schistosomiasis" review. Dr Ede's entire visit to Copenhagen Trial Unit was financed through a grant sourced from a South African organization
6-9 March 2018	Ana-Maria Sopic, Marko Claric, Tea Stimac, Rijeka, Croatia.	To discuss future work on reviews and involvement of young physicians from Rijeka, Croatia
28 May 2018	Anne Pitkäranta, Juha Aarvala, Ilkka Talvio, Raimo Skottman and Satu Nikander PIF, Mia Bengström Clinical Research Institute, Helsinki University Hospital, Finland	Learning about the Copenhagen Trial Unit Research and structure
28 May 2018	Sweedish delegation; Anne-Sophie Fröjmark, Chris Heister, Jan-Ingvar Jönsso, Marika Hellqvist Greberg, Anne-Sophie Fröjmark, Sweden	Create an overview of Danish life science
25 July 2018	EuroHYP Steering Committee	EuroHYP, end of trial, break randomisation code
1 August – 26 October 2018	Beatriz Sanchez-Jimenez, Toluca, Mexico	To be taught and to work on two review protocols. 'Antibiotic prophylaxis versus placebo or no intervention for people with cirrhosis' and variceal bleeding and 'Antibiotic prophylaxis for people with cirrhosis and variceal bleeding'.
5-7 October 2018	Kurinchi Selvan Gurusamy, London, UK	To work on methodological issues related to Trial Sequential Analysis
4 September 2018 – 2 September 2019	Jehad Barakji, Denmark	Research year student
1-30 November 2018	Camilla Funch Steugaard, Valdemar Uhre, Denmark	Research students conducting a systematic review on cognitive behavioural therapy in children and adolescents with obsessive compulsive disease

Date	Visitor	Purpose
6-28 November 2018	Svjetlana Grgic, Mostar, Bosnia and Herzegovina.	To be trained in Cochrane methodology of systematic review preparation. Work on the systematic review protocol "Antibiotics for people with cholangitis or cholecystitis or both". Their visit is sponsored by their own institutions 'University Hospital Center Mostar' and 'University of Mostar, School of Medicine'.
6-28 November 2018	Filipa Markotic, Mostar, Bosnia and Herzegovina.	To be trained in Cochrane methodology of systematic review preparation. Work on the systematic review protocol "Antibiotics for people with cholangitis or cholecystitis or both". Their visit is sponsored by their own institutions 'University Hospital Center Mostar' and 'University of Mostar, School of Medicine'.
24 April – 3 October 2018	María Hdez, Denmark	Apprenticeship
7 March – 24 May 2018	Signe Goul Svendsen, Denmark	Apprenticeship

3.4 Web hits, downloads of Cochrane reviews and media activity

- *The number of web hits for your centre per year in the past three years*

The Copenhagen Trial Unit
For the website www.ctu.dk, there have been a total of 25,282 sessions (meaning an average of 8,427 per year, and more than 23 sessions per day) through the main browsers (Chrome, Safari, Firefox, Internet Explorer, Edge, YaBrowser) during the period 1 January 2016 to 31 December 2018.

The Cochrane Hepato-Biliary Group
For the Cochrane Hepato-Biliary Group website https://hbg.cochrane.org/, there have been a total 2,228 sessions in year 2016, 2,142 sessions in year 2017, and 2,317 sessions in year 2018. The sessions originate from 104 countries. Between 2014 to 2018, in Denmark, there have been 658 new visitors with 1208 sessions with 4.09 pages per session.

- *The number of Cochrane reviews, that have been downloaded by Danish IP-addresses (.dk) in the past three years*

The number of full text downloads from Danish IP addresses during the last three years is available for all Cochrane reviews only. It was not possible to obtain data only for the Cochrane Hepato-Biliary Group reviews.

Full text access in Denmark
- 2016: 102,738 downloads
- 2017: 88,774 downloads
- 2018: 92,552 downloads

For Cochrane Hepato-Biliary Group reviews the most recent (2017) data pack provided by Wiley gives the number of full text downloads globally. It was not possible to obtain data only for Denmark.

Cochrane Hepato-Biliary Group downloads globally
- 2015: 46,304 downloads
- 2016: 69,181 downloads
- 2017: 98,766 downloads

- *The number of times employees at the centre have been cited in Danish media in the past three years*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group
The number of citations in Danish media is not readily available at the present, but can be achieved from Infomedia A/S

The list below covers non-systematic media participation for Janus Christian Jakobsen and Christian Gluud:

Janus Christian Jakobsen:
- 2017: (January) Interview about the effects of antidepressants Danish TV2 NEWS
- 2017: (January) Interview about the effects of antidepressants Danish radio P1
- 2017: (January) Interview about the effects of antidepressants Danish radio P3
- 2017: (January) Interview about the effects of antidepressants Danish TV2 (morning news)
- 2017: (January) Interview about the effects of antidepressants Politiken
- 2017: (January) Interview about the effects of antidepressants Jyllandsposten
- 2017: (January) Interview about the effects of antidepressants Videnskab DK
- 2017: (June) Interview about the effects of antidepressants Videnskab DK
- 2017: (June) Interview about the effects of direct-acting antivirals. MED PAGE
- 2017: (June) Interview about the effects of antidepressants BMJ
- 2017: (June) Interview about the effects of antidepressants The Guardian
- 2017: (June) Interview about the effects of antidepressants. Danish Radio P3
- 2018: (October) Interview in the Swedish newspaper ‘Aftonbladet’ about antidepressants to young people.
- 2019: Participation in a documentary DR1. Planned to be broadcasted April 2019.

Christian Gluud

- 2017: (December): Interview about the effects of clarithromycin. Videnskab DK
- 2017: (March) Interview about the effects of antidepressants. Politiken
- 2017: (November) Interview about the effects of clarithromycin. Dagens Medicin
  2017: (March) Interview about effects of antioxidants/vitamins. Jyllands-posten

3.5 User-friendly summaries of reviews and other tailored research knowledge

- *Please reflect upon the centre's policy for making user-friendly summaries of reviews or other tailored written versions of publications to communicate research knowledge to the primary target groups in the Danish society*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group
Cochrane publications are a major output of the Copenhagen Trial Unit's research. As a Cochrane policy, each publication has a plain language summary addressed to the lay public. Each summary includes at least information about the condition, the intervention, the outcomes in question, and a summary of the main findings of the review, including an assessment of the certainty of the evidence.

Moreover, Copenhagen Trial Unit research has been often communicated to the public via the Videnskab.dk website, in a user-friendly format.

3.6 The centre's impact on the public debate in Denmark?

- *Please reflect upon the centre's impact on the public debate in Denmark and give examples*

The Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group
The Copenhagen Trial Unit strives to base all its research on a 'results-driven' approach rather than an 'hypothesis-driven' approach. This chosen approach rules out the intention to deliberately impose or dictate pre-specified opinions to the public and ultimately to the patients. In many cases, the research we conduct end up showing that there is not enough evidence to either support or refute a given intervention. These types of results are important to the scientific eye but seldom create public debate. In some cases, the evidence accumulates, and evidence quality is enough to make reliable estimates of the long-term balance of risks and benefits of a given intervention, and at times, these research findings have turn out to be controversial in the public opinion. The Copenhagen Trial Unit has been involved in the public debate through several media channels, as exemplified in the following.

In February 2017, the Copenhagen Trial Unit published a systematic review on selective serotonin reuptake inhibitors (SSRIs) (62). The study concluded that SSRIs might have statistically significant effects on depressive symptoms, however, SSRIs significantly increase the risk of both serious and non-serious adverse events and the potential small beneficial effects seem to be outweighed by harmful effects. These findings triggered a substantial public debate in several media channels.

Another example of the impact of the Copenhagen Trial Unit on the public debate involves the findings on vitamin and mineral supplements, which sow doubts about the common beliefs that vitamin and minerals supplementations are necessary for good health. Christian Gluud participated in the BBC Horizon documentary on the matter: BBC Horizon 25.10. 2018: Trial - Vitamin Pills: Miracle or Myth?

The systematic reviews on methylphenidate for children and adolescents (63) have been used in another BBC documentary, the famous The Doctor Who Gave Up Drugs (BBC One) by Dr Chris van Tulleken. He holds our Cochrane review in his hands.

In March 2017, the Copenhagen Trial Unit published a systematic Cochrane review on the effects of direct-acting antivirals (DAAs) for hepatitis C (64). This was the first systematic review assessing the clinical effects of DAAs. The results from the Cochrane review and the BMJ article discussing the review results, received tremendous attention both in Denmark (interview in national radio, several articles, etc.) and internationally.

Currently, the Copenhagen Trial Unit is involved in two out of five planned systematic reviews (involving randomised clinical trials and animal studies) on aluminium adjuvants used in vaccines. The yet to be findings of these systematic reviews, regardless of the outcome, will most likely stir a public debate. In times where the World Health Organisation has deemed anti-vaccine sentiments one of the major threats to global health in 2019, these on-going systematic reviews are not likely welcomed by some public entities, as their mere existence imply a lack of information or evidence concerning aluminium adjuvants. Nonetheless, the Copenhagen Trial Unit considers this research essential for the public health. We have been contacted by international newspapers including Le Monde and Le Figaro, and by the French Embassy in Copenhagen regarding the expected publication dates, which we believe highlights the level of global interest, degree of information needs, and concern.

Although the public opinions on the above matters have been diverse, it is plausible to believe that the debate will help driving science forward also by encouraging more researches and doctors to shed light on the relationship between the beneficial effects and harms of these interventions and interventions in general.

4 Collaboration and partnerships

4.1 National collaborations and partnerships

4.1.1 The centre's formal collaborations and partnerships in Denmark

- *Please list the centre's national collaborations during the last five years.*
- *Please describe the role(s) of the centre in each of its national collaborations.*
- *Please describe the achieved output of each of the national collaborations.*

Table 4-1 Lists all national collaborations and partnerships for the Copenhagen Trial Unit.

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
1	**Center for Research in Intensive Care (CRIC)** (CRIC includes international collaborators from The Netherlands, Sweden, Norway, Finland, Iceland, United Kingdom of Great Britain, Italy, Switzerland, and Spain)	Anders Perner Anders.Perner@regionh.dk Professor, M.D., Ph.D.,	Intensive care	CTU is a partner in CRIC. Protocol template(s), protocol and protocol article writing, randomisation, eCRFs, data management, statistical analysis plan, statistical analyses, participated in article writing	Four trials completed: 6S, TRISS, CLASSIC, SUP-ICU Three trials ongoing: HOT-ICU, AID-ICU, CLASSIC. 41 publications	FC: Danish Research Council and Innovation Fund Denmark. Partner contract. JW co-supervisor for 6 completed Ph.D.s CG in advisory board of CRIC	Department of Intensive Care, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				JW member of all the trials Steering Committees			
2	**Postoperative pain management group**	Jørgen B. Dahl Joergen.Berg.Dahl@regionh.dk Associate professor, M.D., Dr. Med. Sci.	Pain research	Protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, statistical analyses, article writing. JW member of all the trials Steering Committees	Three trials completed: PANSAID-Trial, Hyperalgesia-1, Hyperalgesia-2 Three systematic reviews: Gabapentin, Pregabalin 15 publications	FC for PANSAID JW Supervisor for Ph.D.s: MLF and MSH	Department of Anaesthesiology and Intensive Care Medicine, Bispebjerg and Frederiksberg Hospitals, Copenhagen, Denmark
3	**Airway handling in the anaesthetised surgical patient**	Lars Hyldborg Lundstrøm: lars_hyldborg@hotmail.com Associate Professor, M.D., Ph.D.	Difficult airway handling in the operative patient	Protocol template(s), protocol and protocol article writing, randomisation, statistical	One cluster randomised trial: DIFFICAIR-Trial Eight register studies	FC for DIFFICAIR (Tryg Fonden DK) JW Supervisor	Department of Anaesthesiology, Copenhagen University Hospital, Nordsjællands Hospital,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				analysis plan, statistical analyses, article writing JW member of the trial Steering Committees	15 publications	for Ph.D.s: LLH and AKN	Dyrehavevej 29, Hillerød 3400, Denmark
4	**PROXI Trial Group**	Christian S. Meyhoff christian.sahlholt.meyhoff@regionh.dk Chief Physician, M.D., Ph.D.	Perioperative oxygen in non-cardiac surgery	Protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, participating in article writing JW member of all the trials Steering Committees	One trial completed: PROXI One trial ongoing: VIXIE 11 publications	FC for PROXI, NC for VIXIE JW Supervisor for Ph.D. Christian S. Meyhoff	Department of Anaesthesiology and Intensive Care Medicine, Bispebjerg and Frederiksberg Hospitals, Copenhagen, Denmark
5	**Copenhagen Insulin Metformin Trial-Group**	Steen Madsbad Sten.Madsbad@regionh.dk Professor, M.D., Dr. Med. Sci.	Diabetes Mellitus - Type 2	Protocol and protocol article writing, randomisation, eCRFs,	One 2x3 Factorial Randomised clinical trial in type 2	FC for CIMT CG member of Steering Group	Department of Endocrinology, Hvidovre Hospital, Copenhagen

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				statistical analysis plan, statistical analyses, participating in article writing CG and JW members of the trial Steering Committees	diabetes mellitus patients 5 publications	JW previously also member of Steering Group	University Hospital, Hvidovre, Denmark
6	**Health related fitness in adolescents with congenital heart disease**	Susanne Hwiid Klausen suhk@regionsjaelland.dk Chief Research Nurse, cand. scient. san., Ph.D.	Physical activity in adolescents	Protocol template(s), protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, statistical analyses, participated in article writing	One trial completed: PREVAIL-Trial 3 publications	FC for PREVAIL-Trial JW co-supervisor for Ph.D. SHK	Roskilde Hospital, Roskilde, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				JW member of the trial Steering Committee			
7	**Pulmonary protection during coronary artery bypass grafting (CABG)**	Katrine Buggeskov katrine.buggeskov@gmail.com M.D., Ph.D.	Pulmonary perfusion during Coronary Artery Bypass Surgery and heart-lung cardiopulmonary bypass circulation	Protocol template(s), protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, statistical analyses, participated in article writing JW member of the trial Steering Committees	One trial completed: The PP-Trial One Cochrane systematic review 4 publications	FC JW co-supervisor for Ph.D. KB	Department of Cardiothoracic Anaesthesiology, The Heart Centre, Rigshospitalet, Copenhagen, Denmark
8	**Prostacyclin in subarachnoid haemorrhage**	Rune Rasmussen rune333@gmail.com M.D., Ph.D.	Stroke research	Protocol and protocol article writing, statistical analysis plan,	One trial completed: Prostacyclin for Subarachnoid	NC	Department of Neurosurgery, The Neuroscience Centre, and Department of

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				participated in article writing JW member of the trial Steering Committee	Haemorrhage-Trial 3 publications		Neuroanaesthesia, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
9	**Interventions in type 2 diabetes**	Bianca Hemmingsen biancahemmingsen@hotmail.com M.D., Ph.D.	Diabetes Mellitus - Type 2	Protocol and protocol article writing, statistical analysis plan, statistical analyses, participated in article writing	6 systematic reviews.	FC for two of the reviews (Tryg Fonden DK) CG & JW supervisors for Ph.D. Bianca Hemmingsen	Department of Endocrinology and Nephrology, Nordsjællands University Hospital, Hillerød, Denmark
10	**Review and trials group**	Arash Afshari Arash.Afshari@regionh.dk Chief Physician, Ph.D.	Postoperative agitation in children. Immuno-coagulatory interventions in intensive care	Protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, data management,	One trial completed: The Clonidine -Trial 3 systematic reviews.	FC for the Clonidine Trial JW co-supervisor for Ph.D. Arash Afshari	Department of Anaesthesiology, Juliane Marie Centre, Copenhagen University Hospital,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				statistical analyses, participated in article writing JW member of the trial Steering Committee			Rigshospitalet, Copenhagen, Denmark
11	**Psychiatry depression group**	Ulla Knorr ulla.knorr@regionh.dk M.D., Ph.D.	Impact of SSRI on psyche and endocrinology of relatives to depressed Predictors of depression	Protocol and protocol article, randomisation, eCRFs, statistical analysis plan, statistical analyses, participated in article writing JW member of the trial Steering Committee	Two trials completed: AGENDA-Trial, Relapse of Depression Trial 1 systematic review completed: Saliva cortisol for prediction of depression	FC for AGENDA and Relapse of Depression Trial CG Supervisor for Ph.D. UK	Psychiatric Centre Copenhagen, Rigshospitalet, Copenhagen University Hospital, Denmark
12	**Transfusion in Vascular Surgery**	Anders Møller dr.andersm@gmail.com M.D., Ph.D. student	Transfusion triggers in vascular surgery	Protocol template(s), protocol and protocol article writing,	One trial completed: TV-Trial Two register studies	FC for TV-Trial JW co-supervisor for	Department of Anaesthesia and Intensive care, Slagelse Hospital,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				randomisation, eCRFs, statistical analysis plan, statistical analyses, participated in article writing JW member of the trial Steering Committee	ongoing: Register study from The Danish Vascular Surgery Database,	Ph.D. student AM	Slagelse, Denmark Research, Rigshospitalet, Copenhagen, Denmark
13	**Child and Adolescent Mental Health Centre, Bispebjerg Hospital, Copenhagen**	Anne Katrine Pagsberg Anne.Katrine.Pagsberg @regionh.dk Associate Professor; M.D., Ph.D.	Children with affective and psychotic disorders	Protocol development and approvals from authorities, randomisation, Trial Master File, data management, statistics, trial monitoring, Data Monitoring and Safety Committee, and	One trial completed (TEA trial). One trial initiated (TECTO trial) One systematic review ongoing. 2 publications to date.	FC for both TEA trial and TECTO trial	Research unit Child and Adolescent Mental Health Centre, Lersø Park Allé 107, 2100 Copenhagen Ø, Denmark www.psykiatri-regionh.dk/Forskningsenheden-boerne-og-ungdomspsykiatri

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				systematic reviews. CG member of both trial Steering Committees.			
14	**Rehabilitation for patients with severe acquired brain injury**	Kirsten Møller kirsten.moeller.01@regionh.dk Professor, M.D., Ph.D., Dr. Med. Sc., EDIC, Christian Riberholt: christian.gunge.riberholt@regionh.dk Ph.D. student	Brain injury	Trial protocol article, randomisation, statistics, and trial reporting. Systematic review. CG member of the trial Steering Committee.	One trial initiated (TIM-TBI trial) One systematic review initiated. 1 publication to date.	FC CG and JCJ Ph.D. supervisors	Department of Neuroanaesthesiology, The Neuroscience Centre and Institute for Clinical Medicine, Faculty of Health Sciences, University of Copenhagen, Denmark
15	**Prevention of obesity in overweight children**	Inge Lissau inlis18@gmail.com Senior Research Scientist, Ph.D.	Childhood obesity	Two systematic reviews	No publications to date. Four expected.	FC	Clinical Research Centre, Hvidovre Hospital, Copenhagen University Hospital, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
16	**Department of Neurology, Bispebjerg and Frederiksberg Hospitals**	Hanne Christensen Hanne.Krarup.Christensen@regionh.dk Professor, M.D., Dr. Med. Sci. Christian Ovesen: Christian.Aavang.Ovesen@regionh.dk MD, Ph.D.-student	Neurology	Protocol template(s), protocol and protocol article writing, statistical analysis plan, statistical analyses, article writing, systematic review	One ongoing trial (sub-study of the TICH-2 trial (Patch-it trial) and one systematic review 1 publication.	FC CG is Ph.D. supervisor.	Department of Neurology, Bispebjerg and Frederiksberg Hospitals, Copenhagen University Hospital, Denmark
17	**Cardio-thoracic surgery**	Christian Carranza christian@thoraxkir.dk Head of Department, M.D.	Cardio-thoracic surgery	Protocol development and publication, randomisation, data management, statistics and two systematic reviews. CG is a member of the trial Steering Committee.	One trial initiated (NEO trial). Two systematic reviews initiated. 1 publication to date.	FC	Department of Cardio-thoracic Surgery, The Heart Centre, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
18	**Psychotherapeutic Center Stolpegård**	Marianne Lau mariannelau@dadlnet.dk Head of Department, M.D., Dr. Med. Sci. Sebastian Simonsen sebastian.simonsen@regionh.dk Head of Research, Ph.D.	Psychiatry	Protocol and protocol article writing, randomisation, statistical analysis plan, statistical analyses, article writing, systematic review. CG is a member of trial Steering Committees for F-EAT and IBT FearFighter. JCJ member of the trial Steering Committee for MBT trial	One trial completed (F-EAT trial) One trial completed (IBT FearFighter trial). One trial ongoing (MBT-trial) and one ongoing systematic review. 3 publications to date.	FC	Stolpegaard Psychotherapy Centre, Mental Health Services, Stolpegårdsvej 20, 2820 Gentofte Capital Region of Denmark, Gentofte, Denmark
19	**Aluminium adjuvants**	Mette Kenfelt Mette@Kenfelt.dk Patient representative	Vaccine adjuvant research	Conduct of five systematic review involving	Two protocols for systematic reviews in	NC.	Department of Occupational and Environmental

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Sesilje Bondo Petersen bondo@sesilje.dk Postdoc, cand. scient., Ph.D.		randomised clinical trials (three reviews) and animal studies (two reviews)	humans completed. Two systematic reviews in humans under development. Two protocols for animal studies under development. 2 publications to date.	Collaboration is established based on common interests in this research field and only documented as listed authors on the published protocols. CTU will be first and last author on the systematic reviews and will contribute with most of the work.	Medicine; Bispebjerg Hospital, Copenhagen university hospital, Copenhagen, Denmark
20	**Department of Psychiatry, Rigshospitalet**	Klaus Martini klaus.martiny@regionh.dk Associate Professor, Dr. Med. Sci.	Depression research	Protocol and protocol article writing, randomisation, eCRFs,	One ongoing pilot trial. Launch of RoomLight	FC	Department of Psychiatry, Rigshospitalet, Copenhagen, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				statistical analysis plan, statistical analyses, article writing. JCJ member of all trial Steering Committees	RCT in spring 2019. 1 publication under development		
21	**SIUTIT**	Preben Homøe prho@regionsjaelland.dk Associate Professor, Dr. Med. Sci.	Otitis research	Protocol and protocol article writing, randomisation, eCRFs, statistical analysis plan, statistical analyses, article writing. JCJ member of the trial Steering Committee	One trial (SIUTIT) ongoing. 1 publication.	FC	Department of Otorhinolaryngology and Maxillofacial Surgery, Zealand University Hospital, Køge, Denmark
22	**CIRE**	Lis Adamsen la@ucsf.dk Professor, Ph.D.	Cancer rehabilitaion	Randomisation and data management.	Data management in 10 projects	FC	Department of Public Health,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				Consultancy services, no collaboration.	in the period (Children, FC Prostata, Luft, Pace-AL, Proluca Feasibility, Proluca RCT, Proluca Nej-sigere, Sedentary Pilot, Sedentary RCT, Sedentary Colorektal). No publications.		University of Copenhagen, Øster Farimagsgade 5, opg. B, 1014 Copenhagen K, Denmark
23	**CopenHeart and SheppHeart-CABG group**	Selina Kikkenborg Berg selina.kikkenborg.berg @rh.regionh.dk Professor, R.N., M.S.N., Ph.D., FESC	Rehabilitation after heart disease	Protocol development, randomisation, statistics, and systematic reviews	6 trialss completed (CopenHeart-RFA, CopenHeart-VR, CopenHeart-	FC with the CopenHeart group and the SheppHeart-CABG group.	The Heart Centre, Rigshospitalet, Copenhagen University Hospitals, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				CG is a member of the 6 trials Steering Committees	IE, CopenHeart-SF, SheppHeart-CABG pilot trial, and SheppHeart-CABG trial. 3 systematic reviews. 10 publications to date		
24	**Discontinuation of benzodiapine use in schizophrenia**	Lone Baandrup Lone.Baandrup@regionh.dk Postdoc, M.D., Ph.D.	Schizophrenia	Protocol development, randomisation, data management, statistics, and a systematic review CG is a member of the trial	1 trial completed (SMART trial) 1 systematic review completed 2 publications.	FC	Centre for Neuropsychiatric Schizophrenia Research & Centre for Clinical Intervention and Neuropsychiatric Schizophrenia Research, Mental Health Centre Glostrup, Mental

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				Steering Committee			Health Services – Capital Region of Denmark, Denmark
25	**SafeBoosC**	Gorm Greisen Gorm.Greisen@regionh.dk Professor, M.D., Dr. Med. Sci. Mathias Hansen: mathias.safeboosc@gmail.com, Ph.D.student	Neonatology	Protocol development, randomisation, data management, statistics, project management, reporting. Systematic reviews. CG and JCJ are members of the trial Steering Committee.	1 pilot trial completed. 1 phase II trial completed. 1 phase III trial is being planned. 1 systematic review completed. 8 publications to date	FC with the Danish Strategic Research Council	Department of Neonatology, Rigshospitalet, Copenhagen University Hospital, Denmark
26	**Psychiatric Centre Copenhagen**	Merete Nordentoft d198080@dadlnet.dk Professor, M.D., Ph.D., Dr. Med. Sci.	Psychiatry	Protocol development, randomisation, publications,	6 trials completed (IMR, DiaS, SHERPA,	FC.	Mental Health Center Copenhagen, Mental Health Services Capital

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Lene Falgaard Eplov Lene.Falgaard.Eplov@regionh.dk Head of research, M.D., Ph.D.		systematic review.	CHANGE, FOCUS, IPS) 12 publications		region of Denmark, University of Copenhagen, Denmark
27	**Psychiatric Centre Copenhagen**	Helene Speyer Helene.Speyer@regionh.dk Senior registrar, Ph.D.	Psychiatry	Protocol for systematic review and systematic review	Systematic review submitted	NC	Psychiatric Research Unit, Psychiatric Centre Copenhagen Psychiatric Centre Copenhagen, Mental Health Services in the Capital Region of Denmark
28	**Department of Cardiology, Holbæk Hospital**	Michael Hecht miheo@regionsjaelland.dk Professor, M.D., Dr. Med. Sci.	Cardiology	Protocol and protocol article writing, randomisation, statistical analysis plan, statistical	Two planned trials (DanAF and one unnamed trial), two planned prognostic studies, four	NC	Department of Cardiology, Holbæk Hospital, Smedelundsgade 60, 4300 Holbæk, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				analyses, participating in article writing, systematic reviews JCJ member of the trial Steering Committees.	systematic reviews. 4 publications.		
29	**ImmuReM**	Ole Bjarne Christensen: ole.bjarne.christiansen @regionh.dk Professor, M.D., Dr. Med. Sci.	Fertility	Systematic review	One systematic review completed 2 publications.	FC.	The Fertility Clinic, Rigshospitalet, Denmark
30	**Juliane Marie Centre for Children, Women and Reproduction**	Jette Led Sørensen jette.led.soerensen@rh.regionh.dk Associate professor, M.D. M.Sci., Ph.D. Flemming Bjerrum: fbjerrum@gmail.com M.D., Ph.D.	Training and education for health personnel	Protocol development, randomisation, data management.	2 completed trials (In situ, off situ simulation trial, and procedure-to-procedure transfer trial) 3 publications	FC	Juliane Marie Centre for Children, Women and Reproduction (JMC) Rigshospitalet, Copenhagen University Hospital, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
31	**ACT**	Søren Dalsgaard sdalsgaard@econ.au.dk M.D., Ph.D.	Child psychiatry	Protocol development, randomisation, data management, statistical analysis plan.	1 trial completed (ACT trial). 1 publication.	FC	Child and Adolescent Psychiatry, Department of Clinical Research University of Southern Denmark, Denmark
32	**NEWBORN**	Pernille Due pdu@si-folkesundhed.dk Professor, Head of department, Dr. Med. Sci. Vibeke Koushede: vibe@si-folkesundhed.dk Senior researcher, MPH, Ph.D.	Maternity care	Protocol development, randomisation, statistics. CG member of the trial Steering Committee.	1 trial completed (NEWBORN trial). 2 publications	FC.	The National Institute of Public Health and Centre for Intervention Research, Copenhagen, University of Southern Denmark, Denmark
33	**PREVEX**	Niels Erik Ebbehøj Niels.Erik.Ebbehoej@regionh.dk	Dermatology	Protocol development. Randomisation, statistics, medical writing.	1 trial completed (PREVEX trial) 2 publications	FC.	The Department of Occupational and Environmental Medicine,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Head of Department, M.D., Dr.Med. Sci., Dipl Med Tox		CG member of the trial Steering Committee.			Bispebjerg Hospital, Copenhagen University Hospital, Denmark
34	**Center for Evidensbaseret Psykiatri (CEBP), Slagelse, Denmark**	Ole-Jacob Storebø ojst@regionsjaelland.dk Professor, Cand. Psych., Ph.D.	Psychiatry	Protocols for systematic reviews and final publications of systematic reviews and extensive correspondence on these	Methylphenidate reviews on benefits and harms CG Advisory Board Center for Evidensbaseret Psykiatri (CEBP) Methods research on nocebo (active placebo) Methods research on impact of control		Centre for Evidence-Based Psychiatry (CEBP), Slagelse, Denmark

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
					interventions on the effects of psychology interventions 17 publications		
35	**Statistical analyses**	Jørgen Hilden jhil@sund.ku.dk Associate professor	Trial statistics	Collaboration regarding statistical analyses of the CLARICOR trial	Long term follow-up of the CLARICOR trial 7 publications	NC	Section of Biostatistics, University of Copenhagen, Denmark
36	**Ph.D.-student at CRIC and CTU**	Marija Barbateskovic marija.barbateskovic@ctu.dk MSc, Ph.D.-student	Intensive care	JW and JCJ are Ph.D. supervisors	5 systematic reviews ongoing 5 publications	FC with University of Copenhagen	Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark
37	**Scholar at CTU**	Joshua Feinberg wtv945@alumni.ku.dk MD	Nutrition and cardiology	JCJ scholar supervisor	4 systematic reviews 4 publications	NC	Copenhagen Trial Unit, Centre for Clinical Intervention Research,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
							Rigshospitalet, Copenhagen, Denmark
38	**Scholar at CTU**	Emil Nielsen emil.eik.nielsen@gmail.com MD	Cardiology	JCJ scholar supervisor	4 systematic reviews 4 publications	NC	Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark
39	**Scholar at CTU**	Naquash Sethi naqash.sethi@ctu.dk MD-student	Cardiology	JCJ scholar supervisor	3 systematic reviews 3 publications	NC	Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark
40	**Scholar at CTU**	Sanam Safi sanam.safi@ctu.dk MD-student	Cardiology	JCJ scholar supervisor	3 systematic reviews 3 publications	NC	Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet,

#	National collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other research activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
							Copenhagen, Denmark
41	**Scholar at CTU**	Ulver Lorenzen ulversl@gmail.com MD-student	Cardiology	JCJ scholar supervisor	2 systematic reviews 2 publications	NC	Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark

Table 4-2 All national collaborations and partnerships for the Cochrane Hepato-Biliary Group.

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
1	**Joshua Feinberg**	Editor	Denmark	Expertise in hepatology; vascular diseases; and cardiology.	Author (systematic reviews and journal articles) Peer reviewer; Presenter at international AASLD CHBG affiliated events' meetings. Editor.	Published about 12 systematic protocols and reviews. Some of the reviews are with the CHBG and some are with other Cochrane Groups. Has published Cochrane reviews in paper journals.	Unpaid	Dr Joshua Feinberg Copenhagen Trial Unit, Centre for Clinical Intervention Research Department 7812, Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, 2100 Copenhagen, Denmark Email: wtv945@alumni.ku.dk Dr Joshua Feinberg MD, Department of Medicine Glostrup University Hospital, Valdemar Hansens Vej 1-23,2600 Glostrup, Denmark

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
2	**Lise Lotte Gluud**	Editor	Denmark	Hepatology/ Gastroenterolgy	Author (systematic reviews) Peer reviewer; Editor; Course presenter (CHBG symposium, April 2018. Moscow, Russia)	Has published more than 20 systematic protocols and reviews. Some of the protocols and reviews are with the CHBG and some are with other Cochrane Group. Has published Cochrane reviews in paper journals.	Unpaid	Dr Lise Lotte Gluud, MD, DMSc Consultant Gastrounit, Medical Division Copenhagen University Hospital Hvidovre Kettegaards Alle 30 2650 Hvidovre Denmark Phone: +45 38621964 Email: Lise.lotte.gluud.01@regionh.dk
3	**Janus C Jakobsen**	Deputy Co-ordinating Editor	Denmark	Various expertise, including Hepatology/ Gastroenterolgy	Author (systematic reviews) Peer reviewer; Editor.	Has published more than 40 protocols and reviews. Some of the protocols and reviews are with the CHBG and some are with	Paid 30%	Dr Janus C Jakobsen Medical Doctor, PhD Cochrane Hepato-Biliary Group, Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 7812,

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
						other Cochrane Groups. Has published Cochrane reviews in paper journals. Has published journal articles on methodology of randomised clinical trials, systematic reviews, and Trial Sequential Analysis with CHBG Editorial Team office staff.		Rigshospitalet, Copenhagen University Hospital, Blegdamsvej 9, DK-2100 Copenhagen, Denmark, Phone: +45 26186242 Email: jcj@ctu.dk Email 2: janusjakobsen@mac.com
4	**Emil Eik Nielsen**	Editor	Denmark	Various expertise, including hepatology/ gastroenterolgy	Author (systematic reviews) Peer reviewer;	Has published more than 10 systematic protocols and reviews.	Unpaid	Dr Emil Eik Nielsen Copenhagen Trial Unit, Centre for Clinical Intervention Research

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
					Presenter at international AASLD CHBG affiliated events' meetings. Editor.	Some of the protocols and reviews are with the CHBG and some are with other Cochrane Groups.		Department 7812, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9 2100 Copenhagen Denmark Email: Emil.eik.nielsen@gmail.com
5	**Luit Penninga**	Deputy Co-ordinating Editor	Denmark	Surgery Hepatology/ Gastroenterolgy	Author (systematic reviews) Peer reviewer; Editor.	Has published more than 28 protocols and reviews. Some of the protocols and reviews are with the CHBG and some are with other Cochrane Groups.	Unpaid	Mr. Luit Penninga, Ph.D. Department of Surgery and Transplantation C2122 Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9 DK-2100 Copenhagen Denmark Phone: +45 3545 2122

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
								Email: LP@ctu.dk Email 2: luitpenninga@hotmail.com
6	**Sarah Louise Klingenberg**	Information Specialist	Denmark	Biochemistry Trained in systematic review preparation	Author; Performs searches for reviews; Handsearcher (past); Translator; Consumer.	Has published about 9 protocols and reviews with the CHBG and another Cochrane group.	100% paid by the CHBG	Cochrane Hepato-Biliary Group Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 7812, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9 DK-2100 Copenhagen Denmark Phone: + 45 3545 7168

#	Cochrane Hepato-Biliary Editorial Team. National Collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact details
7	**Dimitrinka Nikolova**	Mana ging Editor	Denmark	M.A. in English Philology and English Language and Literature Trained in systematic review preparation and writing	Author (systematic reviews) Peer reviewer; Consumer; Translator; Handsearcher (past); Presenter; Editor.	Author of about 40 intervention protocols and reviews with the CHBG and other Cochrane groups. Co-author on methodological papers.	100% paid by the CHBG	Cochrane Hepato-Biliary Group Copenhagen Trial Unit, Centre for Clinical Intervention Research, Department 7812, Rigshospitalet, Copenhagen University Hospital Blegdamsvej 9 DK-2100 Copenhagen Denmark Phone:+ 45 3545 7169

4.2 International collaborations and partnerships

4.2.1 The centre's formal collaborations and partnerships internationally

- *Please list the centre's international collaborations during the last five years*
- *Please describe the role(s) of the centre in each of its international collaborations.*
- *Please describe the achieved output of each of the international collaborations.*

Table 4-3 Lists all international collaborations and partnerships for the Copenhagen Trial Unit.

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
1	**Target Temperature Management (TTM) in cardiac arrest patients** (TTM includes includes international collaborators from The Netherlands, Sweden, Norway, United Kingdom of Great Britain, Italy, Switzerland.)	Niklas Nielsen niklas.nielsen@med.lu.se Chief Physician, associate professor, University of Lund, M.D., Ph.D.	Out of hospital cardiac arrest	Protocol and protocol article writing, randomisation, statistical analysis plan, statistical analyses, participated in article writing JW member of the trial Steering Committee for TTM-1 JCJ member of the trial Steering	TTM-1 and TTM-2 trials (ongoing), 1 systematic review, 31 publications	FC for financing the Danish patients in TTM-1 (Tryg Fonden DK) JW Supervisor for Ph.D. Niklas Nielsen	Department of Anaesthesiology and Intensive Care, Helsingborg Hospital, Helsingborg, Sweden

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				Committee for TTM-2			
2	**Intensive Care Research Unit Groningen University Hospital**	Frederic Keus f.keus@umcg.nl Consultant, M.D., Ph.D.	Intensive Care	Protocol template(s), protocol and protocol article writing, statistical analysis plan, statistical analyses, participated in article writing	One observational study completed: The SICS-I Study 15 systematic reviews in intensive care and methodology for meta-analysis	NC CG Supervisor for Ph.D. F Keus	Department of Critical Care, University Medical Center, Groningen, The Netherlands
3	**Meta-analyses with and without TSA**	Georgina Imberger gimberger@gmail.com Chief Physician, M.D., Ph.D.	Meta-analysis methodology	Protocol template(s), protocol, statistical analysis plan, statistical analyses,	Four systematic reviews: N2O in anaesthesia, PEEP in anaesthesia, type 1 error in meta-analysis	FC JW Faculty supervisor for Ph.D. GI	Department of Anaesthesia & Perioperative Medicine, Monash University, Melbourne, Victoria, Australia

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				participated in article writing	with and without Trial Sequential Analysis		
4	**Dept. Clinical Epidemiology at McMaster University, Ontario, Canada**	PJ Devereaux philipj@mcmaster.ca Professor, M.D., Ph.D.,	Postoperative complications in non-cardiac surgery	Recruiting of sites in DK for the POISE-II trial and JW participating in the events adjudication committee	One trial completed: POISE-2 (2x2 factorial RCT of aspirin and clonidine vs placebo) 2 publications	FC for JW to participate in the international adjudication committee	Health Research Methods, Evidence and Impact, Medicine, HHSC, Hamilton General Hospital, DBCVSRI, Rm. C-116, 237 Barton St. E. Hamilton Ontario L8L 2X2, Canada
5	**Cardiology systematic review group**	Sripal Bangalore sripalbangalore@gmail.com Director, Professor, M.D., Ph.D.	Cardiology interventions	Statistical analysis plan, statistical analyses, Trial Sequential Analysis, article writing	Three systematic reviews	NC	Cardiac Catheterization Laboratory, Cardiovascular Clinical Research Center, New York University School of Medicine, The Leon H. Charney Division of

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
							Cardiology, New York, NY 10016, US.
6	**EUROHYP-1**	H.B. van der Worp H.B.vanderWorp@umcutrecht.nl MD, Professor	Stroke research	Protocol development, statistical analysis plan, statistical analysis CG member of Steering Committee	One trial (EuroHYP-1) completed, results being published. 3 publications.	FC (EU 7th Framework Programme funded trial).	Department of Neurology, Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, Utrecht, The Netherland Universitaetsklinikum Erlangen, University Hospital Erlangen, Maximiliansplatz 2, Erlangen 91054, Germany.
7	**ECRIN**	Jacques Demotes jacques.demotes@ecrin.org	European Clinical Research	1) Facilitate the conduct of academic	1) Initiation and conduct of 5 trials and	FC	ECRIN, Paris BioPark, 5 rue

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Director General, professor, M.D. Vittorio Bertele vittorio.bertele@marionegri.it Laboratory Head, Laboratory of Drug Regulatory Policies, Mario Negri	Infrastructures Network 1) multinational trials in Denmark 2) coordination of the annual International Clinical Trials Day 3) Integrating Activities 4) Scientific Board	multinational trials in Denmark. Services as regulatory affairs and GCP monitoring. 2) Organisation and coordination of International Clinical Trials Day in 2014, 2015, and 2016. 3) First author on one article, last author on all articles.	studies during the period (RESCUE ESES, DISCHARGE, TENSION, MACUSTAR and R-Link) 2) CG member of the ECRIN Scientific Committee. – 3) Four publications, systematic literature reviews on rare disease, nutrition, medical devices, and general barriers to	NC of membership of Scientific Committee.	Watt, 75013 Paris, France. Mario Negri Institute, Milan, Italy (Istituto di Ricerche Farmacologiche Mario Negri, Via La Masa 19 - 20156 Milano, Italia)

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				4) Member of scientific board (CG), permanent member of the panel of methodologists (JCJ)	conduct of clinical trials (see below).		
8	**STRIDER Consortium Group**	Katie Groom Associate professor, M.D., Ph.D.	Obstetrics, fetal growth restriction	Protocol and protocol article writing, statistical analysis plan, statistical analyses, participated in article writing. Individual patient data meta-analysis and randomised trial (Dutch Strider Trial)	Five randomised trials under publication Individual patient data meta-analysis planned.	FC	University of Auckland, M&HS BUILDING 503 - Bldg 503 Level 2, Room 263B 85 Park RD, Grafton, Auckland, 1023, New Zealand

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				JCJ and CG members of the trial Steering Committee			
9	**CAASA Consortium Group**	Lehana Thabane ThabanL@mcmaster.ca Professor/Associate Chair, Ph.D.	Biostatistics	JCJ leading three large methodological consensus studies describing valid statistical analysis methodology for randomised clinical trials involving Delphi methodology	Under publication	NC	McMaster University. Biostatistics Unit/FSORC 50 Charlton Avenue East St Joseph's Healthcare-Hamilton 3rd Floor Martha Wing, Room H325 Hamilton, Ontario L8N 4A6 Canada
10	**IMPROvED study**	Louise Kenny: l.kenny@ucc.ie Professor, vice chancellor	Pre-eclampsia	Project governance, statistics, GCP monitoring	One ongoing observational study trying to develop biomarkers for preeclampsia	FC (FP-7 funded study)	University College, Cork, Ireland University of Liverpool, UK

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
				CG member of Steering Committee PW and JCJ statistical Analyses			
11	**COST Action - Improving the efficiency of clinical trials**	Shaun Treweek streweek@mac.com Professor of Health Services Research, Health Services Research Unit, University of Aberdeen	Trial methodology	Partner	International methodological collaboration In spite of substantial investments in clinical research, more than 85% may be considered waste. The poor evidence base to support trial design, conduct, analysis, and	NC (EU-application)	Health Services Research Unit University of Aberdeen Office 306, 3rd Floor, Health Sciences Building Foresterhill Aberdeen AB25 2ZD UK

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
					reporting means that trials are inefficient, sometimes to the point of irrelevance. The central research questions of the COST Action are: What is the optimal approach to systematically identify gaps in knowledge in trial design, conduct, analysis, and reporting? What is the best way to		

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
					generate evidence to fill those gaps? How can we disseminate evidence effectively to improve trial efficiency in Europe?		
12	**Cardiology rehabilitation systematic reviews**	Rod Taylor rod.taylor@gla.ac.uk Professor, M. Sci., Ph.D.	Cardiology rehabilitation	Statistical analysis plan, statistical analyses, Trial Sequential Analysis, article writing	One publication submitted.	NC.	Chair of Population Health Research, MRC/CSO Social and Public Health Sciences Unit, University of Glasgow, Top floor, 200 Renfield Street, Glasgow, G2 3AX; Mobile: + 44 (0)7968 152537
13	**Cardiology intervention**	Claudio Bravo	Cardiology interventions	Statistical analysis plan,	3 publications	NC	Bravo:

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
	systematic reviews and network meta-analyses	claudiobravo26@gmail.com Cardiology fellow, M.D. Deepak L. Bhatt dlbhattmd@post.harvard.edu Professor, M.D., MPH, FACC, FAHA, FSCAI, FESC		statistical analyses, Trial Sequential Analysis, article writing	4 to 5 more ongoing.		Montefiori Health system, Newark, New jersey Mobile: +1 (908) 902 5746 Bhatt: Executive Director of Interventional Cardiovascular Programs, Brigham and Women's Hospital Heart & Vascular Center Professor of Medicine, Harvard Medical School 75 Francis Street, Boston, MA 02115

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
							Phone: 1-857-307-1992
14	**Systematic reviews and methodology research within vascular surgery**	Giel G Koning gg.koning@bernhoven.nl Head of department, M.D., Ph.D., FEBVS	Vascular surgery	Statistical analysis plan, statistical analyses, Trial Sequential Analysis, article writing	One protocol published. One systematic review in draft.	NC	Department of Surgery Bernhoven Hospital Nistelrodeseweg 10 5406 PT, Uden, the Netherlands
15	**Transparency – Nordic Trial Alliance**	Pierre Lafolie pierre.lafolie@sll.se NTA project coordinator; M.D: Ph.D. And Maria Nilsson maria.nilsson@nordforsk.org Special Advisor and Leader of Health and Welfare Programme	Certainty of evidence	CG leading the project with representatives from all Nordic countries	One report.	FC with NordForsk	NordForsk Maria Nilsson, Special Adviser and Leader of the Health and Health and Welfare Programme NordFrosk, Stensberggata 25, NO-0170 Oslo, Norway

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
							Work +47 993 80 264
16	**Transparency – CORBEL consensus on sharing of individual patient data from clinical trials**	Christian Ohmann Christian.Ohmann@med.uni-duesseldorf.de Professor, Ph.D.	Certainty of evidence	CG partner.	Several international meetings. One publication.	NC	ECRIN Paris
17	**Transparency – Cochrane should also share data**	Clive E Adams clive.adams@nottingham.ac.uk Chair of Mental Health Services Research, Co-ordinating Editor Cochrane Schizophrenia Group	Certainty of evidence	CG partner	One publication.	NC	Mental Health Services Research, University of Nottingham, Nottingham, UK Tel: +44 (0)115 82 31274
18	**Barriers towards rare diseases and clinical trials**	Ana Rath ana.rath@inserm.fr Dr., Director Coordinator of RD-ACTION, European Joint Action on Rare Diseases 2015-2018	Rare diseases.	CTU leader; systematic reviews of rare diseases and clinical trials.	One review published.	FC via ECRIN and EU	INSERM, US14 - Orphanet Plateforme Maladies Rares, 96 rue Didot, 75014 Paris, France

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Coordinator of HIPBI-RD - Harmonizing information on phenomics for a better interoperability in the rare diseases field Member of the Revision Steering Committee of the WHO's International Classification of Diseases (ICD11) Scientific coordinator of Support-IRDiRC, Scientific secretariat of the International Rare Diseases Research Consortium					
19	**Barriers towards medical devices and clinical trials**	Edmund A.M. Neugebauer edmund.neugebauer@mhb-fontane.de Univ.- Prof. Dr. Prof. h.c. Dr. h.c.	Medical devices.	CTU leader; systematic reviews of medical devices and clinical trials.	One review published.	FC via ECRIN and EU	Campus Neuruppin Fehrbelliner Str 38 16816 Neuruppin Tel. 03391 39 14100

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Dean and CEO Brandenburg Medical School Theodor Fontane & Seniorprofessur for Health Services Research Witten/Herdecke University					
20	**Barriers towards nutrition and clinical trials**	Martine Laville martine.laville@univ-lyon1.fr Professor of Nutrition	Nutrition.	CTU leader; systematic reviews of nutrition and clinical trials.	One review published.	FC via ECRIN and EU	Hospices Civils de Lyon, Lyon 1 University, Lyon, France
21	**Threats towards clinical research and how to overcome them**	Silvio Garattini silvio.garattini@marionegri.it Professor, Director	Clinical research.	CTU leader; systematic reviews of threats towards clinical research and how to evade these threats.	One review published.	FC via ECRIN and EU	Mario Negri Institute Via Giuseppe La Masa, 19 20156 Milano, Italy +39 02 390141 +39 02 3546277 mnegri@marionegri.it www.marionegri.it

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
22	**Program in Placebo Studies, Harvard Medical School**	Irving Kirsch: irvkirsch@gmail.com Ph.D., Professor Emeritus of Psychology, Associate Director, Program in Placebo Studies, Harvard Medical School	Depression research	Cooperation	Three studies planned	NC.	University of Connecticut (USA), Plymouth University (UK), and University of Hull (UK)
23	**Ronald Koretz**	Ronald Koretz rkoretz@msn.com Professor Emeritus of clinical medicine	Hepatitis research	Collaboration	One systematic review, one study. Several letters to the editors.	NC.	Granada Hills, CA, USA
24	**Comparison of imprecision estimated with GRADE and Trial Sequential Analysis in Cochrane systematic reviews**	Lorenzo Moja mojal@who.int Technical Officer Secretariat of the Model List of Essential Medicines Department of Essential Medicines and Health Products	Methodological research	Methodological expertise and medical writing.	One oral presentation. Two methodological publications.	NC	Department of Essential Medicines and Health Products World Health Organization Geneva, Switzerland Office: +41 (0)22 791 3756

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		World Health Organization Greta Castellini gre.caste@gmail.com PT, MSc, Ph.D. student Department of Biomedical Sciences for Health, University of Milan Unit of Clinical Epidemiology, IRCCS Orthopedic Institute Galeazzi,					Mobile: +41 (0)79 506 9223 Department of Biomedical Sciences for Health, University of Milan Unit of Clinical Epidemiology, IRCCS Orthopedic Institute Galeazzi, Via R.Galeazzi 4, 20161 Milano +02 66214780
25	**Trial Sequential Analysis of systematic review for estimating number of participants in future**	Jo Leonardi-Bee Jo.Leonardi-Bee@nottingham.ac.uk Professor of Medical Statistics & Epidemiology Interim Course Director for Masters in Public Health and Masters in	Methodological research	Methodological expertise and medical writing	One publication in draft.	NC	Division of Epidemiology and Public Health School of Medicine The University of Nottingham

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
	randomised clinical trials	Public Health (International Health) programmes Division of Epidemiology and Public Health School of Medicine The University of Nottingham Ravinder Claire Ravinder.Claire@nottingham.ac.uk Ph.D. student Division of Primary Care, School of Medicine University of Nottingham					Room C117, City Hospital campus Hucknall RoadNottingham NG5 1PB+44 (0) 115 82 31388 Division of Primary Care, School of Medicine University of Nottingham Room 1502, Tower Building University Park Nottingham, NG7 2RD +44 (0) 115 74 86682
26	Clinical relevance assessment of animal preclinical research	Kurinchi Gurusamy k.gurusamy@ucl.ac.uk Professor of Evidence-based Medicine and	Methodological research	Methodological expertise and medical writing	Two publications in draft.	NC.	Royal Free Hospital, Royal Free Campus, UCL, Rowland Hill Street,

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
		Surgery MBBS MRCS Ph.D. Director of Surgical and Interventional Trials Unit University College London			Network meta-analyses in draft Multiple editorial tasks		London. NW3 6DH
27	**Comparison of imprecision estimated with GRADE and Trial Sequential Analysis in health technology assessments or systematic reviews**	Gerald Gartlehner gerald.gartlehner@donau-uni.ac.at Professor, Dr., MPH Head of the Department for Evidence-based Medicine and Clinical Epidemiology	Methodological research	Methodological expertise and medical writing	One methodological publication. Another methodological study being considered.	NC	Danube University Krems Department for Evidence-based Medicine and Clinical Epidemiology Dr.-Karl-Dorrek-Straße 30 3500 Krems Austria +43 (0)2732 893-2910
28	**Systematic reviews**	Arturo Marti-Carvajal arturo.marti.carvajal@gmail.com Professor, M.D., M. Sci., Ph.D.	Systematic reviewing	Methodological expertise and medical writing	Two systematic reviews.		Universidad de Carabobo, UC Location Valencia, Venezuela

#	International collaboration	Contact persons	Topic or field of research	Copenhagen Trial Unit's (CTU) contributions	Trials or systematic reviews or other activities since 2014	Collaboration with formal contract (FC) or no contract (NC)	Contact address
29	**Haematologic research**	Aurellio Maggio md.amaggio@gmail.com Professor, M.D.	Methodological research	Methodological expertise and medical writing	Two publications. A third is under development.		Campus of Hematology Franco and Piera Cutino, AOOR Villa Sofia-V. Cervello, Palermo, Italy 00390916802012

The international collaborators for the Cochrane Hepato-Biliary Group can be seen in Table 4-4.

Table 4-4 International collaborations and partnerships for the Cochrane Hepato-Biliary Group.

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
1.	**Omar Abdel-Rahman**	Editor	Canada/Egypt	Surgery; oncology (Unresectable hepatocellular carcinoma; Advanced biliary tract carcinoma)	Author; Peer reviewer; Editor.	Has published about 6 systematic reviews with protocols. Some of the protocols and reviews are with the CHBG and some are with other Cochrane Groups.	Unpaid	Dr Omar Abdel-Rahman Senior Clinical Fellow Department of Oncology University of Calgary and Tom Baker Cancer Center Calgary Alberta T2N 4N1 Canada Phone: 403-521-3810 Mobile Phone: +20201008541806 Email: omar.abdelrhman@med.asu.edu.eg Email 2: omar.abdelsalam@ahs.ca

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
2.	**Goran Bjelakovic**	Editor	Serbia	Hepatology/ Gastroenterology	Author (systematic reviews and journal articles) Peer reviewer; Editor; Course organiser and presenter at evidence-based medicine courses (Nish) and international EASL and AASLD CHBG affiliated events' meetings.	Has published 16 systematic reviews with protocols. Some of the protocols and reviews are with the CHBG and some are with other Cochrane Groups. Has published Cochrane reviews in paper journals.	Unpaid editor	Prof Goran Bjelakovic, MD Dr.Med.Sci Professor Department of Internal Medicine Medical Faculty, University of Nis Zorana Djindjica 81 18000 Nis Serbia Phone: +381 18 53 23 81 Mobile Phone: +381 641 192 823 Email: goranb@junis.ni.ac.rs

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Received the Serbian Medical Society award for the best scientific publication in 2014: Vitamin D supplementation for prevention of cancer in adults. Cochrane database Syst Rev.2014;6. Art.No. CD007469. Co-authors from Denmark: Lise Lotte Gluud; Dimitrinka Nikolova, Kate Whitfield; Jørn			

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appoint ment	Contact address
					Wetterslev; Christian Gluud Received the Serbian Medical Society award for the best scientific publication in 2017: Vitamin D supplementation for chronic liver diseases in adults. Cochrane database Syst Rev.2017;11. Art.No. CD011564. Co-authors from Denmark: Dimitrinka			

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Nikolova, Christian Gluud Peer reviewer; Editor.			
3.	**Giovanni Casazza**	Statistical Editor	Italy	Expertise in hepatology/gastroeneterology	Author (systematic reviews and journal articles) Peer reviewer; Editor; Course organizer and presenter at CHBG evidence-based medicine workshops (Gargano).	Has published more than 30 protocols and reviews, and journal articles. 11 of the systematic protocols and reviews (including Diagnostic test accuracy reviews and intervention reviews) are with the CHBG.	Unpaid	Prof Giovanni Casazza Statistician Dipartimento di Scienze Biomediche e Cliniche "L. Sacco" Università degli Studi di Milano via GB Grassi 74 20157 Milan Italy Phone: +39 0250319653 Email: giovanni.casazza@unimi.it

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
4.	**Agostino Colli**	Deputy Co-ordinating editor	Italy	Expertise in hepatology/gastroeneterology	Author (systematic reviews and journal articles) Peer reviewer; Editor; Course organizer and presenter at CHBG evidence-based medicine workshops (Gargano).	Author of 14 published and ongoing Diagnostic test accuracy protocols and reviews and intervention systematic protocols and reviews. Has published journal articles with CHBG Editorial Team office staff.	Unpaid	Dr Agostino Colli, MD Director until 2018 (now retired but still working as editor with the CHBG) Department of Internal Medicine A Manzoni Hospital ASST Lecco Via dell'Eremo, 9/11 23900 Lecco Italy Phone: +39 0341 489 670 Email: colliagostino@gmail.com
5.	**Brian R Davidson**	Editor	UK	Surgery/hepatology and gastroenetrology	Author (systematic reviews and journal articles)	Author of about 100 published and ongoing Diagnostic test accuracy	Unpaid	Prof Brian R Davidson Professor of HPB and Liver Transplant Surgery

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Peer reviewer; Editor.	protocols and reviews and intervention systematic protocols and reviews. Has published journal articles with CHBG Editorial Team office staff.		Department of Surgery Royal Free Campus, UCL Medical School Pond Street London NW3 2QG UK Phone: +44 207 830 2757 Email: b.davidson@ucl.ac.uk
6.	**Mirella Fraquelli**	Editor	Italy	Hepatology/Gastroeneterology	Author (systematic reviews and journal articles) Peer reviewer; Editor;	Published about 12 protocols and 1 systematic review with the CHBG. Has published journal articles with CHBG Editorial Team office staff.	Unpaid	Dr Mirella Fraquelli Consultant Gastroenterologist Gastroenterology and Endoscopy Unit Fondazione IRCCS Cà Granda - Ospedale Maggiore Policlinico, Department of Pathophysiology and

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Course organizer and presenter at CHBG evidence-based medicine workshops (Gargano).			Transplantation, Università degli Studi di Milano Via F. Sforza, 35 20122 Milan Italy Phone: ++390255033369 Mobile Phone: +39 338 6733495 Email: mfraquelli@yahoo.it
7.	**Vanja Giljaca**	Editor	UK	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor;	Author of about 20 published and ongoing Diagnostic test accuracy protocols and reviews and intervention systematic protocols and reviews with the	Unpaid	Dr Vanja Giljaca, MD, PhD Consultant Gastroenterologist Directorate of Surgery, Department of Gastroenterology University Hospitals Birmingham NHS

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Course organizer and presenter at CHBG evidence-based medicine workshops (Rijeka).	CHBG and other Cochrane groups.		Foundation Trust, Birmingham Heartlands Hospital Bordesley Green East Birmingham B9 5SS UK Mobile Phone: +44 74 91470029 Email: vanja.giljaca@gmail.com
8.	**Kurinchi Selvan Gurusamy**	Deputy Co-ordinating Editor	UK	Various expertise, including Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor;	Has published more than 150 systematic protocols and reviews. Some of the protocols and reviews are with the CHBG and some	Unpaid	Prof Kurinchi Selvan Gurusamy, MBBS MRCS PhD Professor of Evidence-based Medicine and Surgery/ Course tutor in MSc in Evidence-based

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Presenter at international EASL CHBG affiliated events' meetings.	are with other Cochrane Groups. Has published Cochrane reviews in paper journals. Has published journal articles with CHBG Editorial Team office staff.		Healthcare/Short-course in Systematic reviews Division of Surgery and Interventional Science UCL 9th Floor, Royal Free Hospital Rowland Hill Street London NW3 2PF UK Phone: +44 207 794 0500 ext 33943 Mobile Phone: +44 (0)7545075003 Email: k.gurusamy@ucl.ac.uk
9.	**Goran Hauser**	Editor	Croatia	Hepatology/Gastroeneterology	Author (systematic reviews)	Has published about 6 reviews with the CHBG.	Unpaid	Dr Goran Hauser Medical doctor

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Peer reviewer; Course organizer and presenter at CHBG evidence-based medicine workshops (Rijeka). Editor.			Department of Gastroenterology Clinical Hospital Centre Rijeka Kresimirova 42 51 000 Rijeka Croatia Phone: 385 51 658 122 Email: goran.hauser@medri.uniri.hr
10.	**Ronald L Koretz**	Editor	USA	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor. Presenter at CHBG EASL and	Published 3 systematic protocols and reviews with the CHBG and another Cochrane Group. Has published Cochrane reviews, letters, and	Unpaid	Prof Ronald L Koretz (retired) 16847 Colven Road Granada Hills CA CA 91344 USA Phone: +1 818 360 2708 Mobile Phone: +1 818 378 4474

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					AASLD affiliated meetings.	comments in paper journals.		Email: rkoretz@msn.com Email 2: rkoretz@email.msn.com
11.	**Jian Ping Liu**	Editor	P.R. of China	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Translator (Data extractor) Editor.	Has published more than 30 systematic protocols and reviews. Some of the protocols and reviews are with the CHBG and some are with other Cochrane Groups. Has published Cochrane reviews in paper journals.	Unpaid	Prof Jian Ping Liu, MD, PhD Director Centre for Evidence-Based Chinese Medicine Beijing University of Chinese Medicine 11 Bei San Huan Dong Lu, Chaoyang District 100029 Beijing China Phone: +86 10 64286760 Email: jianping_l@hotmail.com

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
12.	**Goran Poropat**	Editor	Croatia	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor.	Author of about 15 published and ongoing Diagnostic test accuracy protocols and reviews and intervention systematic protocols and reviews with the CHBG and other Cochrane groups.	Unpaid	Dr Goran Poropat, M.D. Department of Gastroenterology Clinical Hospital Centre Rijeka Kresimirova 42 51000 Rijeka Croatia Phone: 0038551658122 Mobile Phone: +385981634541 Email: goran_poropat@yahoo.com
13.	**Daniele Prati**	Editor	Italy	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor.	Recently appointed (end of 2018). Ongoing work on two CHBG reviews.	Unpaid	Dr Daniele Prati Director Department of Transfusion Medicine and Hematology Ospedale Alessandor Manzoni

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
								Lecco Italy Phone: +39 0341 489870 Email: daniele.prati@policlinico.mi.it
14.	**Rosa G Simonetti**	Editor	Italy	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor.	Has published about 5 systematic protocols and reviews with the CHBG.	Unpaid	Dr Rosa G Simonetti (retired) v.G. Perrotta 4 I-90145 Palermo Italy Phone: + 39 91 6802764 Mobile Phone: +39 335 8369 575 Email: simonettimarino@gmail.com

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
15.	**Davor Štimac**	Editor	Italy	Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer; Editor.	Author of about 15 published and ongoing Diagnostic test accuracy protocols and reviews and intervention systematic protocols and reviews with the CHBG and other Cochrane groups.	Unpaid	Prof Davor Štimac, MD, Ph.D. Department of Gastroenterology Clinical Hospital Centre Rijeka Kresimirova 42 51000 Rijeka Croatia Phone: +385 516 58122 Email: davor.stimac@ri.t-com.hr Email 2: davor.stimac@medri.uniri.hr
16.	**Stefano Trastulli**	Editor	Italy	Surgery Hepatology/Gastroeneterology	Author (systematic reviews) Peer reviewer;	Has published about 10 systematic protocols and reviews with another Cochrane group.	Unpaid	Mr Stefano Trastulli Resident in General Surgery Department of General Surgery

#	Cochrane Hepato-Biliary Editorial Team. National and International collaboration	Role	Country	Topic or field of research	Contributions to the Cochrane Hepato-Biliary Group (CHBG)	Cochrane Hepato-Biliary systematic reviews or other research activities since 2014	Form of appointment	Contact address
					Editor.			University of Perugia Terni Italy Phone: +39 0744/205201 Email: stefano.trastulli@hotmail.it

4.3 Own assessment of national and international collaborations

4.3.1 How does the centre's collaborations cohere with the centre's goals/vision and strategy?

- *Please reflect upon the importance of the centre's collaborations for accomplishing the centre's goals/vision and for succeeding with its strategy.*

During its existence, the Copenhagen Trial Unit has collaborated with a leading array of both national and international collaborators and partners. During the last seven years this, collaboration has been intensified in several ways.

The Copenhagen Trial Unit has participated as a national partner in Centre for Research in Intensive Care (CRIC: http://www.cric.nu/) within a 5-year contract with CRIC and Innovation Fund Denmark to accomplish four large multicentre trials (SUP-ICU, HOT-ICU, AID-ICU, and CLASSIC-II) (58, 65-67) within intensive care and to summarise the existing evidence for the interventions addressed in these trials in a number of systematic reviews both before and after the trials were completed. This collaboration is also based on several international collaborators participating in the trials and systematic reviews.

The Copenhagen Trial Unit has participated in European Clinical Infrastructures Network (ECRIN) (68-71) and Nordic Trial Alliance (NTA) (34) to improve and harmonise conditions for doing multi-national and multicentre clinical research in Europe and Scandinavia (21, 72). The Copenhagen Trial Unit has prioritised to participate in international trial collaborations as well when these exhibited high scientific standards, e.g. the Target Temperature Management-1 (TTM-1) (53) and -2 (TTM-2) Trials (55) and the POISE-2 Trial (73, 74). These endeavours have led to six publications in NEJM of the main results of these trials and several systematic reviews published in JAMA, BMJ, Intensive Care Medicine, and Acta Anaesthesiologica Scandinavica summarising the evidence base for the investigated interventions. Parallel with this, the Copenhagen Trial Unit has participated in overviewing the scientific evidence base for all interventions in intensive care through two systematic reviews of the methodological quality and the risk of random errors of 467 reviews and meta-analyses published for interventions within intensive care concluding that the evidence base is of low quality and the risks of random errors are high within this research field (24). We are embarking on a similar project within vascular surgery.

The Copenhagen Trial Unit's goals and visions relate intensely to the wish for improving the evidence base for medical interventions both qualitatively and quantitatively for the betterment of patients. We have tried and succeeded in entering long-lasting national and international collaborations to improve and harmonise clinical research in Europe with a systematic approach for evaluating existing and new interventions in research fields as cardiology, endocrinology, neurosurgery, intensive care medicine, perioperative medicine, pain research, psychiatry, obstetrics, etc. For several of our trials and systematic reviews, their results have helped change clinical practice, see chapter 3 of this report.

The Cochrane Hepato-Biliary Group has at the end of December 2018 published more than 367 peer reviewed protocols for systematic reviews and 218 peer

reviewed systematic reviews in The Cochrane Database of Systematic Reviews (The Cochrane Library). This has been achieved through an international collaboration between editors; peer reviewers; and author teams from around the world. Many of these systematic reviews have had their results referred to in clinical guidelines, see Chapter 3 of this report. In addition, The Cochrane Hepato-Biliary Group Controlled Trials Register contains 15,689 records of randomised clinical trials or quasi-randomised clinical trials. This would not have been possible without world-wide collaborative efforts and activities expressed through handsearching paper journals and electronic searches for identification of relevant hepato-biliary publications on randomised and controlled clinical studies. Source information and data extraction from publications on non-English language studies would not have been possible without the collaborative efforts of translators.

The Cochrane Hepato-Biliary Group Editorial Team office staff collaborates with more than 2180 people around the world (more than 70 countries) who may have one or more roles with the Group. This role may be of a peer reviewer; translator; consumer; review author; statistician, editor; or Cochrane Hepato-Biliary Group assistants. Not all peer reviewers are registered with The Cochrane Hepato-Biliary Group. However, during the years, we have worked with at least 800 people who were given the role of a peer reviewer; i.e. commented on Cochrane Hepato-Biliary Group protocols and reviews submitted to the Cochrane Hepato-Biliary Group Editorial Team office for publication.

- *Please reflect upon which areas of improvement you see, e.g. should the balance between national/international be changed; should output, focus, size of collaborations be different?*

The Copenhagen Trial Unit has in parallel with the efforts to evaluate specific medical interventions engaged in projects trying to improve the methodological standards of doing and interpreting results of trials and systematic reviews (26, 27). This has been done in projects for developing templates for eCRF within OpenClinica applicable to multinational multicentre trials and in Trial Sequential Analysis (TSA) (www.ctu.dk/tsa) of meta-analyses in systematic reviews (29, 40-42). The finalisation of several large trials using the eCRF template for intensive care trials including integrated tools for screening and randomisation has been well received by clinicians resulting in high data quality and finalisation of the trials within the scheduled time frame (usually less than 2 years). Tools for randomisation of patients and daily data collection is essential for the accomplishment of the trials in a population of extremely sick patients in a hectic environment. In addition, the implementation of TSA in all the systematic reviews of interventions aimed to be addressed in future trials shows that the Copenhagen Trial Unit has contributed to improved quality of systematic reviews particularly regarding the evaluation of risk of random errors in meta-analyses (29, 42).

Therefore, the Copenhagen Trial Unit has tried and, so far, reached our preliminary goals of assisting and initiating high quality, multicentre randomised clinical trials within multiple medical research fields, among critically ill patients, among cardiology patients, among children, and improving the methods and infrastructure of these trials. Further, the Copenhagen Trial Unit has participated in and conducted an increasing number of systematic reviews and improved the quality of systematic

reviews by use of Trial Sequential Analysis especially before and after the initiation and finalisation of large trials.

From the beginning, the Copenhagen Trial Unit has anticipated that many clinical questions can only be investigated and answered in large multicentre trials not confined to the Danish population and sites. The international cooperation seems essential for reaching evidence-based recommendations of the use or no use of interventions in all specialties of clinical medicine. The Copenhagen Trial Unit has engaged in international multicentre trials and collaborations on summarising the evidence both within and outside Cochrane. The Copenhagen Trial Unit has tried to influence, from an evidence-based perspective, the conditions and methods of how data are acquired and interpreted within international collaborations initiated both within and outside Denmark (24, 26, 27, 29, 40-42). We still, however, anticipate assisting national investigators in important research as our primary obligation, but we also increasingly suggest Danish investigators to participate in international collaborations as well as to extend their proposed trials to sites in Europe and Scandinavia. We do this in order to raise the methodological quality and statistical power to detect or reject clinically relevant intervention effects on patient centred outcomes as all-cause mortality, serious adverse events, and health-related quality of life. The balance between national and international engagements is difficult to anticipate and plan and will be determined by the nature of the clinical questions posed and the methods necessary to answer them. However, we are quite sure that the international collaborations in the years to come will be even more important and will require more resources from the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group in order to meet requests from the Danish society for evidence-based treatment modalities.

So, for the following three years, we wish the public investments in the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group to gradually increased with 33% per year to about double the present investment. About 75% of the total investment should go to clinical trials in the Copenhagen Trial Unit and the remaining 25% should be invested in the Cochrane Hepato-Biliary Group. The argumentation for such an expansion is that most of the tasks the Copenhagen Trial Unit and the Cochrane Hepato-Biliary Group are responsible for and work with are performed by too few people. Accordingly, such functions are vulnerable to disease and accidents. Moreover, with increased staff and funds, we will be able to conduct more research with higher certainty.

5 References

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6 Attachments

- 2.1.1 - 1 - Publication list CTU 2012-2018.xls
- 2.1.1 - 2 - Publication list CHBG 2012-2018.xlsx
- 2.1.1 - 3 - Note to the CHBG publication list 2012-2018.pdf
- 2.1.5 - 1 - Teaching and Training activities for CHBG staff 2014-2018 (Colloquia).pdf
- 2.1.5 - 2 - Teaching and Training activities 2014-2018 for the CHBG.pdf
- 2.1.5 - 3 - Christian Gluud - Teaching activities by CG, other CTU or CHBG staff, CHBG editors.pdf
- 2.1.6 - 1 - Visitors at the CHBG Editorial Team and CTU.pdf
- 2.2.1 - 1 - CTU Journals 2014-2018.xlsx
- 2.3.2 - 1 - Ph.D., Doctoral dissertations and Master dissertations 2014-2018.xlsx
- 3.2 - 1 - Guidelines and reviews.xlsx
- 3.2 - 2 - Wikipedia and reviews.xlsx