An Introduction to Cochrane Collaboration and its Impact on Medical Practices

Gerd Antes
Cochrane Germany (www.cochrane.de)
University Medical Center Freiburg

REHA-Kolloquium
Frankfurt 20. März 2017
Conflicts of interest

- The Cochrane Germany is a central unit of the University Medical Centre Freiburg
- G. Antes is 100% employed by the University Hospital
- Potential conflict: Long-lasting commitment to Evidence and Systematic Reviews
Contents

– Evidence to answer the crucial question: What works?

– Systematic reviews as key technology for knowledge synthesis

– Cochrane as host for global knowledge and rigorous methodology
Transfer of Research into Practice

Answers to medical questions
- Clinical (randomised / controlled) studies
- Epidemiological (observational) studies

Questions:
- Practicing physicians
- Health authorities, sickness funds, insurances, institutions
- Clinical research
- Patients

Body of Evidence

1968 McMaster Univ. Hamilton, Canada
1971 Archie Cochrane, UK
1993 Cochrane Collab.
1998 Cochrane Germany
The trial deluge
RCTs (Reports) in Medline
Overall: 419,020

September 2016
The truth
RCTs (Reports) in Medline (PubMed)  
Overall: 419,020

Freiburg Ethics Board  
2000-2002: 48% published until 2010  
J. Simes (1986)

September 2016

RCTs (Reports) in Medline (PubMed)

Freiburg Ethics Board
2000-2002:
48% published until 2010
J. Simes (1986)

2.5+ Mio. Patients

Only on paper

September 2016

Freiburg Ethics Board
2000-2002: 48% published until 2010
J. Simes (1986)
Transfer of Research into Practice

Clinical studies (experimental, randomised, controlled, prospective)

Epidemiological studies (observational, retrospective)

Systematic Reviews

Global

EBM

Health Technology Assessment (HTA)

Clinical Guidelines

Patient Information

Disease Management Programs (DMPs)

Clinical Pathways (CPs)

Local
The knowledge refinery
„All“ trials?

| identified | Not identified | Not published |

Review

Quality?
1. Framing the question (PICO)

2. Systematic search for evidence from relevant trials and studies

3. Critical appraisal of trials - inclusion

4. Summary and quantitative synthesis (if possible)

5. Interpreting and putting in context

**Updating!!**

Produce unbiased view of “all” evidence
Example
Thrombolysis after acute myocardial infarction

NEJM 1992

Forest Plot

Body of Evidence
Thrombolysis (Streptokinase) after myocardial infarction

**Forest Plot:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fletcher</td>
<td>1959</td>
<td>23</td>
</tr>
<tr>
<td>Dewar</td>
<td>1963</td>
<td>42</td>
</tr>
<tr>
<td>European 1</td>
<td>1969</td>
<td>187</td>
</tr>
<tr>
<td>European 2</td>
<td>1971</td>
<td>730</td>
</tr>
<tr>
<td>Heinkinheimo</td>
<td>1971</td>
<td>426</td>
</tr>
<tr>
<td>Italian</td>
<td>1971</td>
<td>321</td>
</tr>
<tr>
<td>Australian 1</td>
<td>1973</td>
<td>517</td>
</tr>
<tr>
<td>Frankfurt 2</td>
<td>1973</td>
<td>206</td>
</tr>
<tr>
<td>NHLBI SMIT</td>
<td>1974</td>
<td>107</td>
</tr>
<tr>
<td>Frank</td>
<td>1975</td>
<td>108</td>
</tr>
<tr>
<td>Valiere</td>
<td>1975</td>
<td>91</td>
</tr>
<tr>
<td>Klein</td>
<td>1976</td>
<td>23</td>
</tr>
<tr>
<td>UK Collab</td>
<td>1976</td>
<td>595</td>
</tr>
<tr>
<td>Austrian</td>
<td>1977</td>
<td>728</td>
</tr>
<tr>
<td>Australian 2</td>
<td>1977</td>
<td>230</td>
</tr>
<tr>
<td>Lassierra</td>
<td>1977</td>
<td>24</td>
</tr>
<tr>
<td>N Ger Collab</td>
<td>1977</td>
<td>483</td>
</tr>
<tr>
<td>Witchitz</td>
<td>1977</td>
<td>58</td>
</tr>
<tr>
<td>European 3</td>
<td>1979</td>
<td>315</td>
</tr>
<tr>
<td>ISAM</td>
<td>1986</td>
<td>1,741</td>
</tr>
<tr>
<td>GISSI-1</td>
<td>1986</td>
<td>11,712</td>
</tr>
<tr>
<td>Olsson</td>
<td>1986</td>
<td>52</td>
</tr>
<tr>
<td>Baroffio</td>
<td>1986</td>
<td>59</td>
</tr>
<tr>
<td>Schraiber</td>
<td>1986</td>
<td>38</td>
</tr>
<tr>
<td>Cribier</td>
<td>1986</td>
<td>44</td>
</tr>
<tr>
<td>Sainsous</td>
<td>1986</td>
<td>98</td>
</tr>
<tr>
<td>Durand</td>
<td>1987</td>
<td>64</td>
</tr>
<tr>
<td>White</td>
<td>1987</td>
<td>219</td>
</tr>
<tr>
<td>Bassand</td>
<td>1987</td>
<td>107</td>
</tr>
<tr>
<td>Vlay</td>
<td>1988</td>
<td>25</td>
</tr>
<tr>
<td>Kennedy</td>
<td>1988</td>
<td>368</td>
</tr>
<tr>
<td>ISIS-2</td>
<td>1988</td>
<td>17,187</td>
</tr>
<tr>
<td>Winsenberg</td>
<td>1988</td>
<td>66</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>36,974</td>
</tr>
</tbody>
</table>

**Cumulative Forest Plot:**

- z = -2.28, P = 0.023
- z = -2.69, P = 0.0071
- z = -3.37, P < 0.001
Open questions

– No accepted stopping rule

– Have all relevant trials been identified and considered?

Need „all“ (!) relevant trials:
2016 no reliable method and procedure
RCTs of aprotinin in cardiac surgery to stop bleeding

Lancet 2005
Clinical Trials 2005
Benefit?
Harm?
Costs?
Research in context
findings? How can we improve the accessibility and usability of research findings, and data availability? And, finally, how can we further raise awareness and continue discussions on the topic of research productivity?

As a first step, we are strengthening our requirement to put research into context. Knowing and rigorously assessing the context and value of research will help editors make decisions about whether to publish a paper, and will help readers to interpret the importance of published research in addressing unanswered questions and building an evidence base. From Jan 1, 2015, all research papers, apart from systematic reviews and meta-analyses, submitted to any journal in The Lancet family must include a Research in context panel with an enhanced structure and subheadings (panel). Editors will use this information at the first assessment stage and
Leaving things out

Selective reporting =

1. Hiding whole trials (classical publication bias)

2. Hiding (or distorting) information from trials which are published

3. Spin: Interpretations which have nothing to do with the trial results
Striving for quality:
Trial registration as basis for transparency
“Research Registration and Publication and Dissemination of Results

35. Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

36. Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty . . . . . . .
The Cochrane Collaboration (since 1993)

Trusted evidence. Informed decisions. Better health

Independent network of 36000+ contributors from science and health professions
Systematic Reviews
Leading principle: Minimizing bias

Risk of Bias
The Cochrane Library

- free searching and abstracts
- updating system

Cochrane is

- a charity under UK law
- member of WH assembly
- organized globally in entities

Total Records

<table>
<thead>
<tr>
<th>Total Records</th>
<th>9520</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>955,738</td>
</tr>
<tr>
<td></td>
<td>15,764</td>
</tr>
<tr>
<td></td>
<td>36,795</td>
</tr>
<tr>
<td></td>
<td>16,372</td>
</tr>
<tr>
<td></td>
<td>15,015</td>
</tr>
<tr>
<td></td>
<td>78</td>
</tr>
<tr>
<td></td>
<td>114</td>
</tr>
</tbody>
</table>

Cochrane Library Counts
September 2016

7004 reviews
2516 protocols

Impact Factor 2015: 6.103 (vorläufig)
Cochrane Reviews can be withdrawn from the active database when they become out of date or are replaced by new Cochrane Reviews in a similar subject area.

Cochrane Database of Systematic Reviews:
Systematic Reviews in Medline (PubMed)
Total: 42063

<20% von Cochrane
Knowledge accumulation: backfiring?
Policy Points:

-Currently, there is massive production of unnecessary, misleading, and conflicted systematic reviews and meta-analyses. Instead of promoting evidence-based medicine and health care, these instruments often serve mostly as easily produced publishable units or marketing tools.

-Suboptimal systematic reviews and meta-analyses can be harmful given the major prestige and influence these types of studies have acquired.

-The publication of systematic reviews and meta-analyses should be realigned to remove biases and vested interests and to integrate them better with the primary production of evidence.
A new enemy?
Open access, data sharing . . .
List of Predatory Publishers 2014

By Jeffrey Beall

Released January 2, 2014

The gold (author pays) open-access model has given rise to a great many new online publishers. Many of these publishers are corrupt and exist only to make money off the author processing charges that are billed to authors upon acceptance of their scientific manuscripts.

There are two lists below. The first includes questionable, scholarly open-access publishers. Each of these publishers has a portfolio that ranges from just a few to hundreds of individual journal titles.

The second list includes individual journals that do not publish under the platform of any publisher — they are essentially standalone, questionable journals.

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of publishers</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>18</td>
</tr>
<tr>
<td>2012</td>
<td>23</td>
</tr>
<tr>
<td>2013</td>
<td>225</td>
</tr>
<tr>
<td>2014</td>
<td>477</td>
</tr>
<tr>
<td>2015</td>
<td>693</td>
</tr>
<tr>
<td>2016</td>
<td>923</td>
</tr>
</tbody>
</table>

Number of predatory publishers, 2011-2016.
A strong barrier: language
Most frequently visited SRs

1. Oral verabreichtes Misoprostol zur Einleitung der Wehentätigkeit
2. Die Behandlung des Thoracic Outlet Syndroms (Schultergürtelkompressionssyndrom)
3. Manuelle Therapie und Übungen bei Frozen Shoulder (Adhäsive Kapsulitis, Schultersteife)
4. Kontinuierliche passive Bewegungsbehandlung
5. Impfstoffe zur Vorbeugung gegen Grippe bei Erwachsenen
6. Homöopathisches Oscillococcinum® zur Vorbeugung und Behandlung von Grippe und grippeähnlichen Erkrankungen
7. Rehabilitation für Menschen mit Demenz nach der Operation eines Ober schenkelhalsbruchs
Schweizer erhalten kostenfreien Zugang zur Cochrane Library

Donnerstag, 7. Januar 2016


Möglich macht dies eine sogenannte Nationallizenz für die Cochrane Library, die für jeden Computer in der Schweiz gilt. Sie wird finanziert durch die Schweizerische Akademie der Medizinischen Wissenschaften (SAMW), das Bundesamt für Gesundheit (BAG) sowie durch Beiträge von Universitätsbibliotheken und Spitäler. Das Netzwerk „Cochrane“ erstellt seit über 20 Jahren systematische Reviews, in denen die Forschungsergebnisse zu Fragen der Gesundheitsversorgung zusammengefasst werden. Diese Reviews sind international als Qualitätsstandard anerkannt und geben den aktuellen Wissensstand wieder.
The biggest challenge: Updating
Updating of systematic reviews is generally more efficient than starting all over again when new evidence emerges, but to date there has been no clear guidance on how to do this. This guidance helps authors of systematic reviews, commissioners, and editors decide when to update a systematic review, and then how to go about updating the review.

The solution?
Living Systematic Reviews: An Emerging Opportunity to Narrow the Evidence-Practice Gap
Interventions for enhancing medication adherence
Article first published online: 20 NOV 2014 | DOI: 10.1002/14651858.CD000011.pub4
Summary

– Systematic reviews as key technology knowledge accumulation to provide evidence for medical decisions

– Cochrane is an international network to support the production of systematic reviews and to develop rigorous methodology
Register now for your early bird ticket!

Cochrane South Africa is delighted to be hosting the 2017 Global Evidence Summit. The event aims to advance the use of reliable research evidence in addressing some of the world’s most serious health and social challenges.