Knowledge synthesis and implementation - the huge challenges of today and tomorrow

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European JBI symposium of
Evidence-Based Healthcare in the Czech Republic
Brno 13 December 2018
Conflicts of interest

– Till 31 Oct 2018

– 50% Cochrane Germany Foundation (tax-based charity)

– 50% Institute for Evidence in Medicine (for Cochrane Germany Foundation)

– Potential intellectual conflict:
  Long-lasting commitment to Evidence and Systematic Reviews
Contents

– Inflation of unnecessary trials and SRs

– Growing problem in the publication process: predatory journals

– Soft science?

  Real World Data (RWD), Big Data and Artificial Intelligence (AI)

– One world? Knowledge in English – implementation in ? language

– New science or better old science?
What is the optimal decision for the selection of the right diagnostic procedure or the best therapy?
Information from similar persons under same conditions
The path to the truth

Counterfactual thinking: What would happen if . . .
Two crucial targets

1. Minimization of systematic errors (risk of bias)

2. Control of random errors (play of chance)

Gold standard is not the randomized controlled trial but the criteria to control error and to maximize benefit
Transfer of Research into Practice

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

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

Evidence production

1968 McMaster Univ.
Hamilton, Canada
1971 Archie Cochrane, UK
1996 EBM in Germany
1998 Cochrane Germany
2018 Cochrane Czech Rep
Transfer of research results into practice

Patients / healthy persons
Research / studies / data

- Literature based synthesis (SR; Cochrane classic)
- Individual-patient-data-based synthesis (IPD SR)
- Access to trial reports (SR from authority data)

Trustworthy?
The trial deluge
RCTs (Reports) in Medline
Overall: 436,827

22 Sept 2017
The truth
RCTs (Reports) in Medline (PubMed)
Overall: 436,827

22 Sept 2017
AllTrials: Withholding results costs lives

On Lorcanide
Transfer of Research into Practice

Clinical studies (experimental, randomised, controlled, prospective)

Epidemiological studies (observational, retrospective)

Systematic Reviews

EBM

Health Technology Assessment (HTA)

Clinical Guidelines

Patient Information

Disease Management Programs (DMPs)

Clinical Pathways (CPs)
Unnecessary Trials and SRs
RCTs of aprotinin in cardiac surgery to stop bleeding

*Lancet* 2005

*Clinical Trials* 2005

1987

2002

Cited

2018 No stopping rule for trials

Ethics approval for unnecessary trials
Knowledge accumulation:
A good principle failing
RCTs in Medline (PubMed)
Gesamtanzahl: 436.827

Stand 22. 9. 2017
Systematic Reviews in Medline (PubMed; 22.09.2017)
Total: 94,885

<15% by Cochrane
Systems of wrong incentives, agendas driven by science and scientists' careers, maldevelopment of journals . . .
The problem of duplicate systematic reviews
Systematic reviewers should identify existing reviews as a compulsory first step

David Moher senior scientist
Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa Hospital, Ottawa, Canada ON K1H 8L6

Systematic reviews occupy a central position in evidence based medicine. They are the starting point of a well developed practice guideline. Some funders of randomised trials ask investigators for a strong rationale for their proposed trial, indicating that the best evidence is likely to be a well conducted and completely reported systematic review.¹ These reasons, and others, probably explain the popularity and publication trajectory of systematic reviews.² Does this translate into duplication of effort and waste? In a linked paper (doi:10.1136/bmj.f4501), using sound methodology and complete and transparent reporting, Siontis and colleagues examined this question.³

Having selected 73 meta-analyses published during 2010, the authors identified two thirds of them as having at least one overlapping meta-analysis. The good news is that duplication does not seem to have been a major problem. The authors report a median of two overlapping meta-analytic protocols. However, protocols of ongoing systematic reviews. However, an international prospective register for systematic review protocols now exists [PROSPERO; www.crd.york.ac.uk/PROSPERO], funded by the National Institute of Health Research and administered through the Centre for Reviews and Dissemination. The database contains 18 mandatory items and 22 discretionary ones.⁴ This information can be used to search for existing systematic review protocols. At the time of writing, 1871 records of review protocols exist from 65 countries and duplication seems to be rare. This number will probably increase substantially later this summer when Cochrane protocols are added to the register. With increasing international endorsement of the register by journals and funders,⁵ it is likely to help reduce unnecessary duplication.

Another factor contributing to duplication is the relentless
Open access, data sharing . . .
A new enemy?
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>
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<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>
Open-Access

– Author fees are business model for new journals

– Immediate consequence:
  growth, equivalent to loss of quality in a limited market
Tangled web. The location of a journal's publisher, editor, and bank account are often continents apart.
Predatory journals: Ban predators from the scientific record

Jeffrey Beall

*Nature* 534, 326 (16 June 2016) | doi:10.1038/534326a
Published online 15 June 2016

**Subject terms:** Publishing · Peer review

Predatory journals are threatening the credibility of science. By faking or neglecting peer review, they pollute the scholarly record with fringe or junk science and activist research. I suggest that every publishing stakeholder could contribute to reining in these journals.

Universities and colleges should stop using the quantity of published articles as a measure of academic performance. Researchers and respectable journals should not cite articles from predatory journals, and academic library databases should exclude metadata for such publications.
Mehr als 5000 deutsche Wissenschaftler haben in scheinwissenschaftlichen Zeitschriften publiziert

More than 5000 German scientists published in predatory journals

Including directors of institutions, the rector of a university . . .


Die Recherchen zeigen: Pseudowissenschaftliche Verlage nutzen den Publikationsdruck, der auf Wissenschaftlerinnen und Wissenschaftlern lastet, und sprechen sie per E-Mail an. Die

Closely linked to “Presentations at World Congress for Urology . . . . . ”
Joint statement of

v.-Humboldt-St
DFG
Fraunhofer
HRK
DAAD
Helmholtz

(25 July 2018)

– Complaints: scientists deceived, damaged trust into science

– Self-repair of science is sufficient

– Emphasis that articles in those journals may be high quality
Surprised and downplaying the issue

– No statement before July 2018

– Who focusses on “Fake Science“ ignores the real problems

– Storm in a teacup: predatory journals are irrelevant

– Presentations and texts from G. Antes describing Predatory Journals since October 2015
Perspective

Current Incentives for Scientists Lead to Underpowered Studies with Erroneous Conclusions

Andrew D. Higginson1, *, Marcus R. Munafò2,3, *

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* a.higginson@exeter.ac.uk (ADH); marcus.munafo@bristol.ac.uk (MRM)

Abstract

We can regard the wider incentive structures that operate across science, such as the priority given to novel findings, as an ecosystem within which scientists strive to maximise their fitness (i.e., publication record and career success). Here, we develop an optimality model that predicts the most rational research strategy, in terms of the proportion of research effort spent on seeking novel results rather than on confirmatory studies, and the amount of research effort per exploratory study. We show that, for parameter values derived from the scientific literature, researchers acting to maximise their fitness should spend most of their effort seeking novel results and conduct small studies that have only 10%–40% statistical power. As a result, half of the studies they publish will report erroneous conclusions. Current incentive structures are in conflict with maximising the scientific value of research; we suggest ways that the scientific ecosystem could be improved.
Medical and scientific publishers have lost their moral voice. Do they have the courage to reclaim it? There is little sign of it as yet.

Today's medical/scientific publishing industry operates in a moral vacuum. It has betrayed its Enlightenment values. Time to remoralise.
The main library at the University of Göttingen, which says it will hold firm in negotiations with Elsevier.

about prices included in most contracts.

Formal talks with Elsevier began in August to draft a contract that would take effect on 1 January. To increase pressure on the publisher, more than 60 participating organizations canceled their online subscriptions effective 31 December. After DEAL rejected Elsevier’s offer in early December, several universities warned staff that access could be disrupted starting 1 January. Though some German universities had subscriptions allowing them to continue to access papers published through the end of 2016, others, such as Braunschweig University of Technology, have been cut off completely. “Despite the loss of immediate full-text access, our scientists are supportive and have welcomed the measures” to push for more open access, says Katrin Stump, director of the university’s library.

Officials at the University of Göttingen said in December that they are committed to holding firm; the university would work with researchers to obtain papers through an interlibrary loan and other online sources, they said. (Researchers also have an illegal option: downloading papers from Sci-Hub, a site hosting pirated papers that cite breast cancer treatment meetings.)
A further obstacle: The language
Transfer of Research into Practice

Answers to medical questions

• Clinical (randomised / controlled) studies
• Epidemiological (observational -) studies

Knowledge Translation

English language

5% of world population anglophone

Implementation: local/national languages
Seriously underfunded

1000+ lay language summaries in German

Am häufigsten besuchte Themen:

1. Oral verabreichtes Misoprostol zur Einleitung der Wehenbeginn
2. Die Behandlung des Thoracic Outlet Syndroms (Schultergürtelkompressionssyndrom)
3. Manuelle Therapie und Übungen bei Frozen Shoulder (Adhesive Kapuzen, Schultersteife)
4. Kontinuierliche passive Bewegungsbewegung
5. Impfstoffe zur Vorsorgung gegen Grippe bei Erwachsenen
6. Hemmepathisches Oscillococcinum zur Vorsorgung und Behandlung von Grippe und grippalähnlichen Erkrankungen
7. Rehabilitation für Menschen mit Demenz nach der Operation eines Oberschenkelhalteschnitts
Trusted Answers

Trip medical database, a smart, fast tool to find high quality clinical research evidence.

Searched over 125,000,000 times
Over 70% of clinical questions answered
Unmatched content
Millions of articles items indexed & uniquely ranked
Twenty years of learning & fine tuning
Observational studies “sufficient“: Real world data
Risk of bias assessment tools

Welcome to our pages about risk of bias tools for use in systematic reviews.

- Go to ROBINS-I tool (Risk Of Bias in Non-randomized Studies of Interventions)
- Go to RoB 2.0 tool (revised tool for Risk of Bias in randomized trials)
- Go to ROBINS-E tool (Risk Of Bias in Non-randomized Studies of Exposures)

Feedback is welcome to julian.higgins@bristol.ac.uk
The new competitor:
Big data, artificial intelligence, personalized medicine.
Big Data:

A Revolution That Will Transform How We Live, Work and Think

Kenneth Cukier
Viktor Mayer-Schönberger
Big Data Hype: The Mantras

Big Data

– can analyze unstructured data

– can easily solve every problem by using more data

– needs ownership moving from owner to user

– cannot reproduce results because everything is changing every second: real-time results

– The era of causality is over, now is the era of correlation (enabled by unlimited access to data)
The End of Theory. The Data Deluge Makes the Scientific Method Obsolet

Science in megalomania
How Big Data makes us and our life predictable

The End of Randomness
Transfer of research results into practice

- Patients / healthy persons
- Research / studies / data
- Data drilling
- Big data
- Individual-data-based synthesis (IPD SR)
- Knowledge Systems
- Artificial Intelligence
- Deep learning system
- Machine learning
- Dr. Watson
- Access to trial data or trial reports (SR from authority data)
- Literature based synthesis (SR; Cochrane classical)
- Application / benefit
IBM pitched its Watson supercomputer as a revolution in cancer care. It’s nowhere close

By CASEY ROSS @CaseyRose and IKE SWETLITZ @ikesweetlitz SEPTEMBER 5, 2017

“Their marketing and PR has run amok—to everyone’s detriment.”

Why Everyone Is Hating on IBM Watson—including the People Who Helped Make It
Large amounts of electronic patient records... will help to avoid any wrong diagnosis and treatment.
A new Science(ability)?

(October 2nd, 2016) Big Data, Innovation, Personalised Medicine and co. - Are these the hallmarks of a new science(ability) in medicine? An essay by Gerd Antes, Freiburg.

If one is to believe what one reads in editorials, comments or opinion articles in scientific journals, then we are at the beginning of a golden age for patients and healthy people. Patients are diagnosed much earlier and more correctly, and then treated accurately, efficiently and free of side effects by personalised medicine. Healthy people aren’t at all at risk because they will be proactively identified and treated as healthy from the first place by perfect preventative healthcare.

Golden future or empty promises?
Solutions?
Since 2011
2017 access to 85% of articles behind paywall

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...to remove all barriers in the way of science

enter URL, PMID / DOI or search string

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knowledge to all
no copyright
open access

Sci-Hub
support the project

The project is supported by user donations. Imagine the world with free access to knowledge for everyone - a world without any paywalls. Donate for this vision to become true. Make your contribution to the battle against copyright laws and information inequality. Even the smallest donation counts.

Send contribution to the Bitcoin address:
1K4t2vS5S2xFjZ6PofYnbgZewjoeqbg1TM
Sprechen Sie Deutsch?

The EQUATOR Network is proud to launch its German pages this week. Now, German-speaking researchers around the world will find resources for better research reporting more easily and quickly, says Shona Kirtley, EQUATOR’s Information Manager, who coordinated the effort: “When we were approached about translating our resource pages to German, we were delighted to help and felt that it built well on previous work”.

The previous work she mentions are the EQUATOR web pages in Spanish and Portuguese, which were made available in 2015 and 2016, through the support of PAHO (Pan American Health Organization). These are among the most accessed pages in the EQUATOR website. The EQUATOR Network hopes the same success will happen with the German pages.

“Full and transparent reporting is key to make research usable. Providing more resources to those whose first language is not English is vital in the campaign (spearheaded by the REWARD initiative) to reduce waste in research”, said Gary Collins, director of the UK EQUATOR Centre. “The EQUATOR website has become a reference resource about research integrity around the world. Following translations of the website into Spanish and Portuguese, this new German translation is another important milestone to provide information to authors whose first language is not English.”

EQUATOR in German is composed of a set of 26 pages with information on reporting guidelines, guidance on scientific writing, ethics and good practice guidelines and toolkits.
<table>
<thead>
<tr>
<th>Orthodox</th>
<th>The new world</th>
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<tbody>
<tr>
<td>– clearly defined question</td>
<td>– unplanned, unintended</td>
</tr>
<tr>
<td>– prospective</td>
<td>– <strong>quality</strong> of results?</td>
</tr>
<tr>
<td>– based on protocol</td>
<td>– reproducibility?</td>
</tr>
<tr>
<td>– good scientific practice</td>
<td>– principles of modeling?</td>
</tr>
<tr>
<td>– quality</td>
<td>– significance, clinical relevance</td>
</tr>
<tr>
<td>– overarching principle: risk-of-bias</td>
<td>– results under <strong>uncertainty</strong>?</td>
</tr>
<tr>
<td>– rigid methodology</td>
<td>– non-transparent!</td>
</tr>
<tr>
<td>– reproducibility</td>
<td>– <strong>clinical outcome</strong>?</td>
</tr>
<tr>
<td>– transparence, data sharing</td>
<td>– renaissance of surrogates</td>
</tr>
<tr>
<td>– crisis of science</td>
<td></td>
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<tr>
<td>– Basic model: incremental progress, research in context</td>
<td>Basic model: disruptiv</td>
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</tbody>
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From Experiment to Real World Data XXL

<table>
<thead>
<tr>
<th>Level der Evidenz</th>
<th>Systematic Reviews</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Experimental studies</td>
</tr>
<tr>
<td>II</td>
<td></td>
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<tr>
<td>III</td>
<td>Observational studies</td>
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<tr>
<td>IV</td>
<td></td>
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<tr>
<td>V</td>
<td>Big Data (AI)</td>
</tr>
</tbody>
</table>

Bias

http://www.cebm.net
Summary

- Enormous progress to use knowledge from trials and studies: Global knowledge – local implementation

- Evidence world based on systematic reviews as key technology for knowledge synthesis and translation

- Erosion and damage of key concepts in current development: serious confrontation with the old quality world of EBM clinical epidemiology

- Return to quality and quality assessment as leading principle
May 2013 in German
(English: Testing Treatments)

pdf and als html free on
de.testingtreatments.org

– www.cochrane.de

– www.cochrane.org

– www.thecochranelibrary.com
Czech National Centre for Evidence-Based Healthcare and Knowledge Translation

Congratulations