Ottawa Hospital
Research Institute
Institut de recherche
de l'Hôpital d'Ottawa

RRRG

Do we need a rapid review reporting guideline?

Is PRISMA-P helpful when generating a RR protocol?

David Moher
senior scientist, Ottawa Hospital Research Institute
associate professor, Department of Epidemiology and Community Medicine, University of Ottawa

4th February 2015

CADTH Rapid Review Summit: Then, Now, and in the Future

Vancouver, Canada

Competing interests

- Intellectual
  - Co editor-in-chief Systematic Reviews
    - And will be peddling the journal
  - Principal developer, PRISMA and PRISMA-P
  - Member of the PROSPERO advisory group
  - Lead editor for a book I'll be peddling☺
- *Fiscal*
  - *None*

Key questions to consider

- Is there evidence/rationale for developing RRRG?
  - Popularity or small niche market
  - Examining the publication record

Organizations producing Rapid Reviews

ISCRR
Institute for Safety, Compensation and Recovery Research

Penn Medicine

Canadian Centre on Substance Abuse
Centre canadien de lutte contre les toxicomanies
Partnership. Knowledge. Change.
Collaboration. Connaissance. Changement.

camh
Centre for Addiction and Mental Health

IHE
INSTITUTE OF HEALTH ECONOMICS
ALBERTA CANADA

Ontario
Health Quality Ontario

KAISER PERMANENTE®

Cochrane Innovations
Expect more

CADTH
Canadian Agency for Drugs and Technologies in Health

World Health Organization

UNITED STATES
DEPARTMENT OF VETERANS AFFAIRS

OREGON HEALTH & SCIENCE UNIVERSITY
OHSU

KCE
Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

Health Canada
Santé Canada

THE COCHRANE COLLABORATION COLLEGE FOR POLICY
AT GEORGE MASON UNIVERSITY

SYSTEMATIC REVIEWS

New thematic series

Open Access | Highly accessed

Advances in Rapid Reviews

Guest Editor: Prof Holger Schünemann

7556
Total accesses

Including:

34
Altmetric score

Editorial

Reviews: Rapid! Rapid! Rapid! …and systematic

Holger J Schünemann* and **Lorenzo Moja**

46
Altmetric score

Research

Using text mining for study identification in systematic reviews: a systematic reviews of current approaches

Alison O'Mara-Eves, James Thomas*, John McNaught, Makoto Miwa and **Sophie Ananiadou**

Read the full series: bit.ly/RapidReviews

The publication record

- It’s tarnished ☹☹☹☹☹
- There is considerable <u>avoidable</u> waste in the biomedical research industrial complex

International Journal of
Evidence-Based Healthcare

doi:10.1111/j.1744-1609.2012.00290.x *Int J Evid Based Healthc* 2012; **10:** 397–410

COMMENTARY

What is a rapid review? A methodological exploration of rapid reviews in Health Technology Assessments

Julie Harker MRes[1] and Jos Kleijnen MD PhD[1,2]

[1]*Kleijnen Systematic Reviews Ltd, York, UK; and* [2]*School for Public Health and Primary Care (CAPHRI), Maastricht University, Maastricht, The Netherlands*

Abstract

Aim Commissioners of Health Technology Assessments require timely reviews to attain efficacious decisions on healthcare and treatments. In recent years, there has been an emergence of 'rapid reviews' within Health Technology Assessments; however, there is no known published guidance or agreed methodology within recognised systematic review or Health Technology Assessment guidelines. In order to answer the research question 'What is a rapid review and is methodology consistent in rapid reviews of Health Technology Assessments?', a study was undertaken in a sample of rapid review Health Technology Assessments from the Health Technology Assessment database within the Cochrane Library and other specialised Health Technology Assessment databases to investigate similarities and/or differences in rapid review methodology utilised.

Method In a targeted search to obtain a manageable sample of rapid reviews, the Health Technology Assessment database of The Cochrane Library and six international Health Technology Assessment databases were searched to locate rapid review Health Technology Assessments from 2000 onwards. Each rapid review was examined to investigate the individual methodology used for searching, inclusion screening, quality assessment, data extraction and synthesis. Methods of each rapid review were compared to investigate differences and/or similarities in methodologies used, in comparison with recognised methods for systematic reviews.

Results Forty-six full rapid reviews and three extractable summaries of rapid reviews were included. There was a wide diversity of methodology, with some reviews utilising well-established systematic review methods, but many others diversifying in one or more areas, that is searching, inclusion screening, quality assessment, data extraction, synthesis methods, report structure and number of reviewers. There was a significant positive correlation between the number of recommended review methodologies utilised and length of time taken in months.

Conclusions Despite the number of rapid reviews published within Health Technology Assessments over recent years, there is no agreed and tested methodology and it is unclear how rapid reviews differ from systematic reviews. In a sample of Health Technology Assessment rapid reviews from 2000 to 2011, there was a wide diversity of methodology utilised in all aspects of rapid reviews. There is scope for wider research in this area to investigate the diversity of methods in more depth during each stage of the rapid review process, so that eventually recommendations could be made for clear and systematic methods for rapid reviews, thus facilitating equity and credibility of this type of important review methodology.

Key words: Cochrane Library, health technology assessment, methodology, rapid review, timeline plot.

Background

Over recent years, there has been demand from commissioners of Health Technology Assessments (HTAs), healthcare guidance and guidelines for reviews that are able to answer the stipulated research question rapidly, efficiently, competently and satisfactorily. While systematic reviews (SRs) remain the methodology of choice when summarising evidence by identifying, selecting, appraising and synthesising research findings in health and medical research,[1] they can often be time-consuming using many human and financial resources. There have been several HTA reports published by

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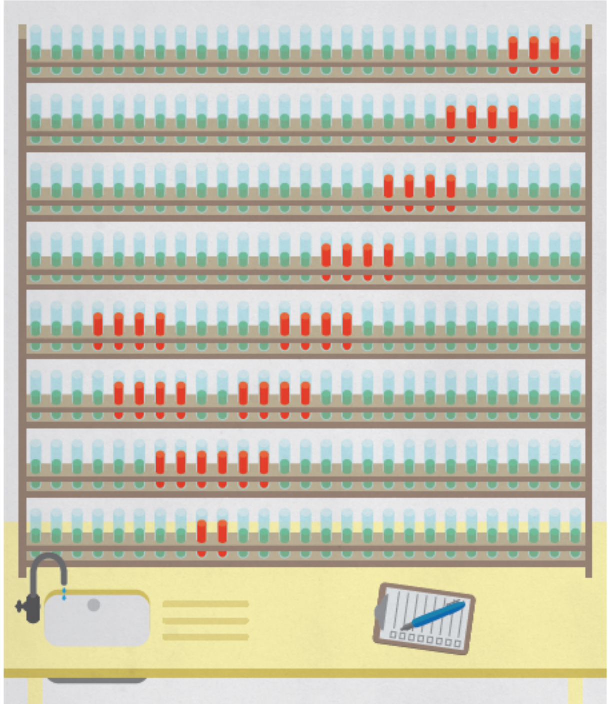
COMMENT



CHRIS RYAN/NATURE

NIH plans to enhance reproducibility

Francis S. Collins and **Lawrence A. Tabak** discuss initiatives that the US National Institutes of Health is exploring to restore the self-correcting nature of preclinical research.

A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring[1,2]. As leaders of the US National Institutes of Health (NIH), we share this concern and here explore some of the significant interventions that we are planning.

Science has long been regarded as 'self-correcting', given that it is founded on the replication of earlier work. Over the long term, that principle remains true. In the shorter term, however, the checks and balances that once ensured scientific fidelity have been hobbled. This has compromised the ability of today's researchers to reproduce others' findings.

Let's be clear: with rare exceptions, we have no evidence to suggest that irreproducibility is caused by scientific misconduct. In 2011, the Office of Research Integrity of the US Department of Health and Human Services pursued only 12 such cases[3]. Even if this represents only a fraction of the actual problem, fraudulent papers are vastly outnumbered by the hundreds of thousands published each year in good faith.

Instead, a complex array of other factors seems to have contributed to the lack of reproducibility. Factors include poor training of researchers in experimental design; increased emphasis on making provocative statements rather than presenting technical details; and publications that do not report basic elements of experimental design[4]. Crucial experimental design elements that are all too frequently ignored include blinding, randomization, replication, sample-size calculation and the effect of sex differences. And some scientists reputedly use a 'secret sauce' to make their experiments work — and withhold details from publication or describe them only vaguely to retain a competitive edge[5]. What hope is there that other scientists will be able to build on such work to further biomedical progress?

Exacerbating this situation are the policies and attitudes of funding agencies, academic centres and scientific publishers. Funding agencies often uncritically encourage the overvaluation of research published in high-profile journals. Some academic centres also provide incentives for publications in such journals, including promotion and tenure, and in extreme circumstances, cash rewards[6].

Then there is the problem of what is not published. There are few venues for researchers to publish negative data or papers that point out scientific flaws in previously published work. Further compounding the problem is the difficulty of accessing unpublished data — and the failure of funding agencies to establish or enforce policies that insist on data access.

PRECLINICAL PROBLEMS

Reproducibility is potentially a problem in all scientific disciplines. However, human clinical trials seem to be less at risk because they are already governed by various regulations that stipulate rigorous design and independent oversight — including randomization, blinding, power estimates, pre-registration of outcome measures in standardized, public databases such as ClinicalTrials.gov and oversight by institutional review boards and data safety monitoring boards. Furthermore, the clinical trials community has taken important steps towards adopting standard reporting elements[7].

Preclinical research, especially work that uses animal models[1], seems to be the area that is currently most susceptible to reproducibility issues. Many of these failures have simple and practical explanations: different animal strains, different lab environments or subtle changes in protocol. Some irreproducible reports are probably the result of coincidental findings that happen to reach statistical significance, coupled with publication bias.

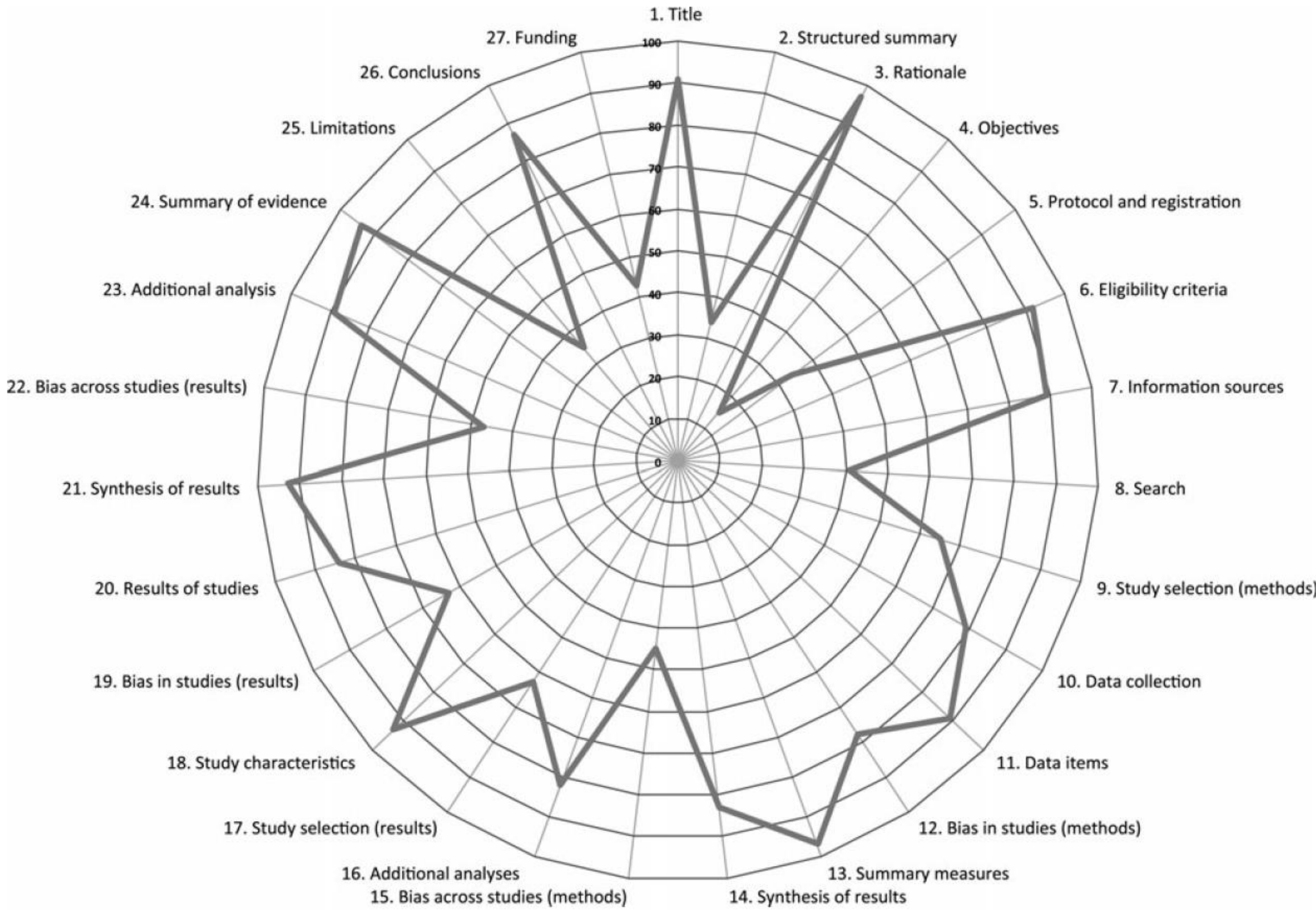


FIGURE 2. Star chart depicting proportions of adequately reported PRISMA items. A higher proportion meant that item was better reported.

Adie S, et al. Annals of Surgery 2015

and finally

- 80 consecutive studies
  - Subsequently published in Evidence Based Medicine (Oct 2005 for 12 months
  - 55 RCTs; 25 SRs
- intervention information missing from 41/80
- retrieved through additional methods

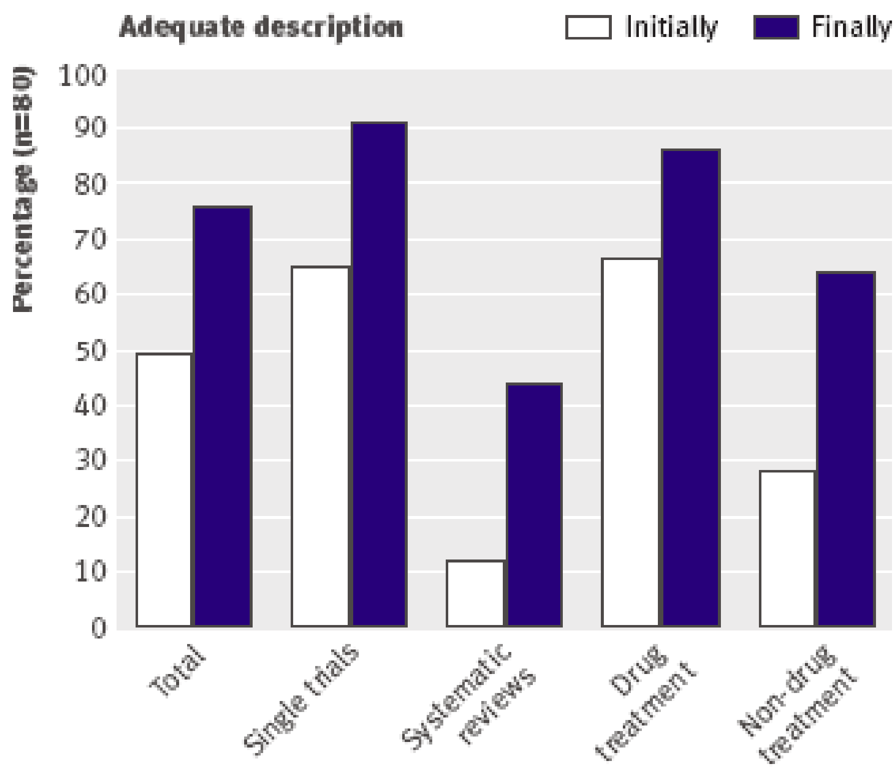


Fig 2 | Percentage of studies with sufficient description of treatment initially (based only on the published paper) and after supplementary information was obtained

Glasziou P, et al. BMJ 2008;336;1472-1474

Key questions to consider

- Are there scientific barriers to development?
  - Terminology
  - Diversity of product

Spectrum of Rapid Review Products

i.	ii.	iii.	iv.	v.	vi.	vii.
Evidence brief (snapshot)	Rapid Evidence Map (scoping) (primary studies and/or SRs, HTAs, or CPGs)	Rapid Evidence Map (SRs, HTAs, or CPGs)	Rapid Review (Primary studies only)	Rapid Review (SRs, HTAs, or CPGs + primary studies)	Rapid Review (SRs, HTAs, or CPGs)	Traditional SR – done quickly (shortened timeframe only)

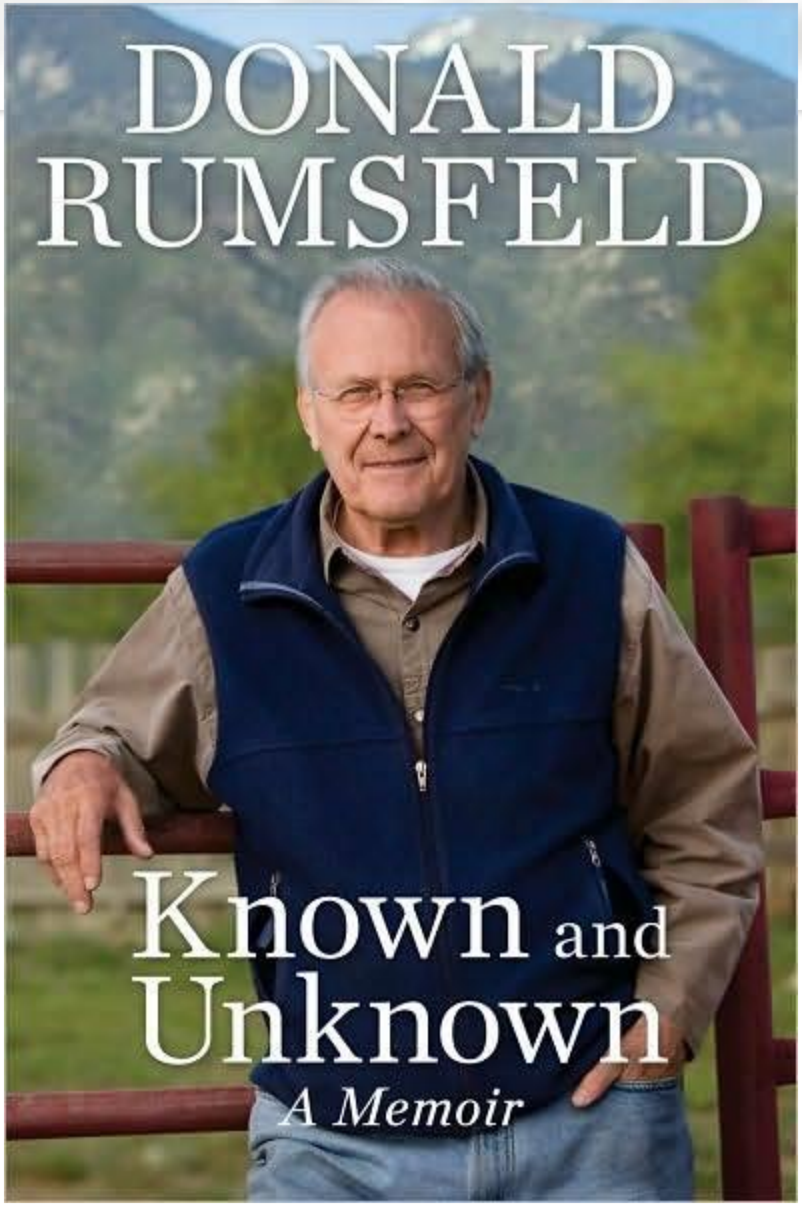
Evidence Briefs - 24 hrs-3 wks; short and concise

Variety of rapid review products – from a rapid evidence map or scoping (ii-iii) based on '**off the shelf evidence**' +/- primary studies to rapid reviews using 'off the shelf sources of evidence' +/- primary studies

Traditional SR but within a shortened timeframe – no corners cut (but report format)

Key questions to consider

- What's the best practice for developing the RRRG?


DONALD
RUMSFELD
Known and
Unknown
A Memoir

WHAT IS A RAPID REVIEW?

There is broad agreement as to what is a systematic review

Spectrum of Rapid Review Products

i.	ii.	iii.	iv.	v.	vi.	vii.
Evidence brief (snapshot)	Rapid Evidence Map (scoping) (primary studies and/or SRs, HTAs, or CPGs)	Rapid Evidence Map (SRs, HTAs, or CPGs)	Rapid Review (Primary studies only)	Rapid Review (SRs, HTAs, or CPGs + primary studies)	Rapid Review (SRs, HTAs, or CPGs)	Traditional SR – done quickly (shortened timeframe only)

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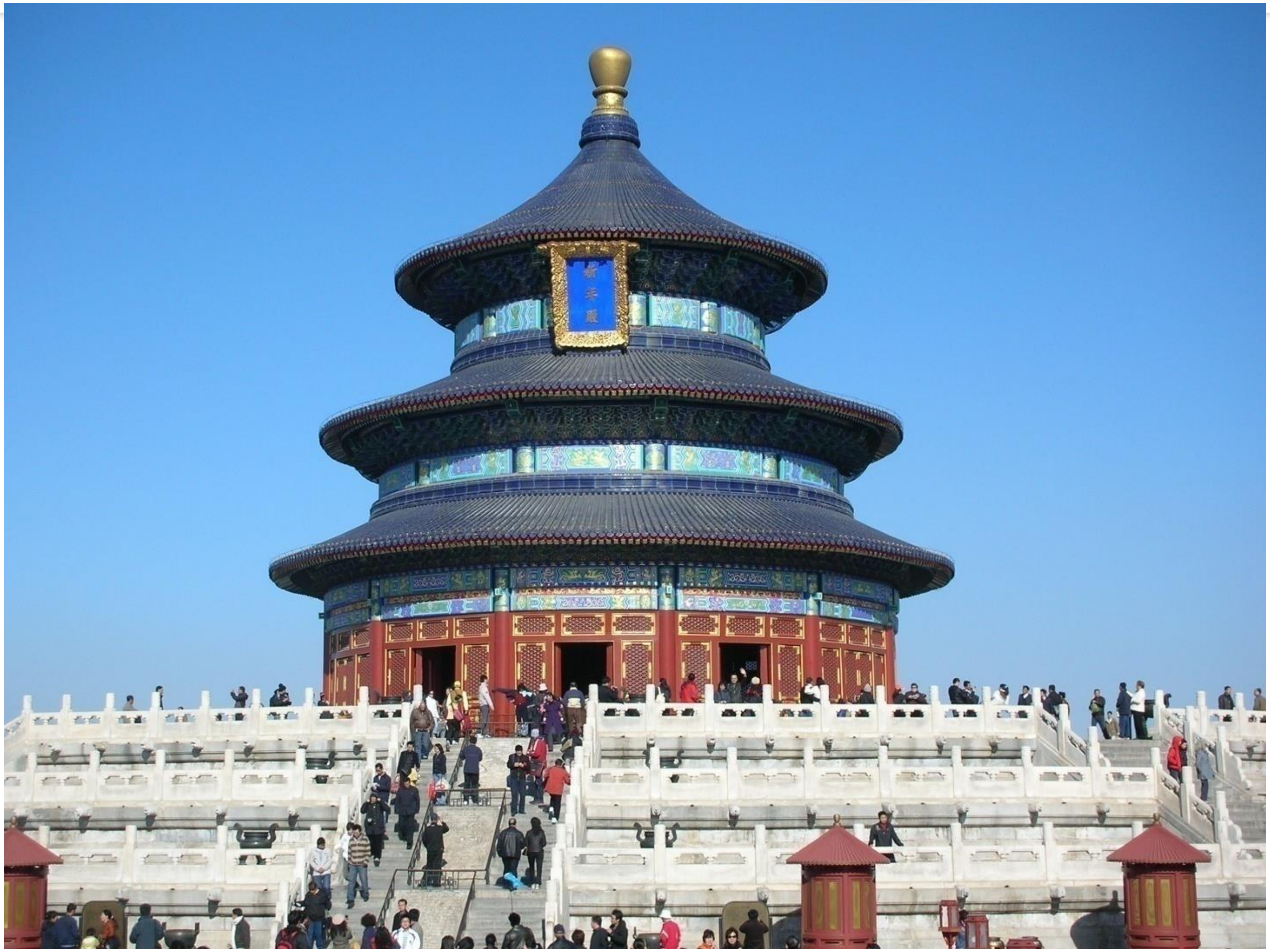

- Scientific content
- Format of product(s)

Defining a reporting guideline

- “a checklist, flow diagram, or explicit text to guide authors in reporting a specific type of research, developed using explicit methodology”

OPEN ACCESS Freely available online PLoS MEDICINE

Guidelines and Guidance

Guidance for Developers of Health Research Reporting Guidelines

David Moher[1,2]*, Kenneth F. Schulz[3], Iveta Simera[4], Douglas G. Altman[4]

1 Ottawa Methods Centre, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada, 2 Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada, 3 Family Health International, Research Triangle Park, North Carolina, United States of America, 4 Centre for Statistics in Medicine, University of Oxford, Oxford, United Kingdom

Introduction

Publishing health research is a thriving, and increasing, enterprise. On any given month about 63,000 new articles are indexed in PubMed, the United States National Library of Medicine's public access portal for health-related publications. However, the quality of reporting in most health care journals remains inadequate. Glasziou and colleagues [1] assessed descriptions of given treatments in 80 trials and systematic reviews for which summaries were published during one year (October 2005 to October 2006) in *Evidence-Based Medicine*, a journal that is aimed at physicians working in primary care and general medicine. Treatment descriptions were inadequate in 41 of the original published articles, which made their use in clinical practice difficult if not impossible to replicate. This is just one of numerous examples of a large and disturbing literature indicating the general failure in quality of reporting health research [2–6]. Many publications lack clarity, transparency, and completeness in how the authors actually carried out their research.

Inadequate reporting is problematic for several reasons. If authors do not provide sufficient details concerning the conduct of their study, readers are left with an incomplete picture of what was done. As such, they are not able to judge the reliability of the results and interpret them. There are also ethical and moral reasons for reporting research adequately [7].

review. And research funders can benefit from introducing reporting guidelines into the research application system [11]. Ensuring clear and complete reporting of funded research through the use of reporting guidelines should facilitate more efficient use of the new findings and bring better returns on research investments. There are enormous potential benefits of good reporting. However, despite the impressive recent upsurge in the number and range of reporting guidelines, the literature on how individual guidelines were developed remains sparse [12,13] and there is no generic guidance on how to develop one.

In this paper we update and expand upon an earlier effort to outline a strategy for developing reporting guidelines that was published only in Spanish [14]. We recognize that there is no single best or correct approach. However, this paper benefits from our collective experiences of helping to develop more than ten reporting guidelines over the last 16 years, over which period these ideas have evolved considerably. If reporting guidelines are to be useful and more widely disseminated, they need to be developed using robust and widely accepted methodologies.

This strategy assumes the involvement of an executive group to facilitate the guideline development and the expectation of having a face-to-face meeting as part of the reporting guideline development. We propose 18 steps to occur in five phases, which are outlined in Table 1.

Table 1. Recommended steps for developing a health research reporting guideline.

Step	Item Number	Detail
Initial steps	1	Identify the need for a guideline
	1.1	Develop new guidance
	1.2	Extend existing guidance
	1.3	Implement existing guidance
	2	Review the literature
	2.1	Identify previous relevant guidance
	2.2	Seek relevant evidence on the quality of reporting in published research articles
	2.3	Identify key information related to the potential sources of bias in such studies
	3	Obtain funding for the guideline initiative
Pre-meeting activities	4	Identify participants
	5	Conduct a Delphi exercise
	6	Generate a list of items for consideration at the face-to-face meeting
	7[a]	Prepare for the face-to-face meeting
	7.1	Decide size and duration of the face-to-face meeting
	7.2	Develop meeting logistics
	7.3	Develop meeting agenda
	7.3.1	Consider presentations on relevant background topics, including summary of evidence
	7.3.2	Plan to share results of Delphi exercise, if done
	7.3.3	Invite session chairs
	7.4	Prepare materials to be sent to participants prior to meeting
	7.5	Arrange to record the meeting
The face-to-face consensus meeting itself	8[a]	Present and discuss results of pre-meeting activities and relevant evidence
	8.1[a]	Discuss the rationale for including items in the checklist
	8.2	Discuss the development of a flow diagram
	8.3[a]	Discuss strategy for producing documents; identify who will be involved in which activities; discuss authorship
	8.4	Discuss knowledge translation strategy
Post-meeting activities	9[a]	Develop the guidance statement
	9.1	Pilot test the checklist
	10	Develop an explanatory document (E&E)
	11	Develop a publication strategy
	11.1	Consider multiple and simultaneous publications
Post-publication activities	12[a]	Seek and deal with feedback and criticism
	13[a]	Encourage guideline endorsement
	14	Support adherence to the guideline
	15	Evaluate the impact of the reporting guidance
	16	Develop Web site
	17	Translate guideline
	18	Update guideline

Five stages

- Initial steps
  - Seek relevant evidence on the quality of reporting in published research articles
- Pre-meeting activities
  - Conduct a Delphi exercise
  - Involve decision makers and patients
- Face-to-face meeting
  - Discuss the development of checklist (and flow diagram)
- Post meeting activities
  - Pilot test checklist
  - publication
- Post publication activities
  - Develop a toolkit

ELSEVIER

Journal of Clinical Epidemiology ■ (2011) ■

Journal of Clinical Epidemiology

REVIEW ARTICLE

Describing reporting guidelines for health research: a systematic review

David Moher[a,*], Laura Weeks[a], Mary Ocampo[a], Dugald Seely[b], Margaret Sampson[c], Douglas G. Altman[d], Kenneth F. Schulz[e], Donald Miller[f], Iveta Simera[d], Jeremy Grimshaw[a], John Hoey[g]

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[b]*Research and Clinical Epidemiology, Canadian College of Naturopathic Medicine, Toronto, Ontario, Canada*
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Accepted 29 September 2010

Abstract

Objective: To describe the process of development, content, and methods of implementation of reporting guidelines for health research.
Study Design and Setting: A systematic review of publications describing health research reporting guidelines developed using consensus.
Results: Eighty-one reporting guidelines for health research were included in the review. The largest number of guidelines do not focus on a specific study type ($n = 35$; 43%), whereas those that do primarily refer to reporting of randomized controlled trials ($n = 16$; 35%). Most of the guidelines ($n = 76$; 94%) include a checklist of recommended reporting items, with a median of 21 checklist items (range: 5−64 items). Forty-seven (58%) reporting guidelines were classified as new guidance. Explanation documents were developed for 11 (14%) reporting guidelines. Reporting-guideline developers provided little information about the guideline development process. Developers of 50 (62%) reporting guidelines encouraged endorsement, most commonly by including guidelines in journal instructions to authors ($n = 18$; 36%).
Conclusions: Reporting-guideline developers need to endeavor to maximize the quality of their product. Recently developed guidance is likely to facilitate more robust guideline development. Journal editors can be more confident in endorsing reporting guidelines that have followed these approaches.

Keywords: Systematic review; Reporting guidelines; Research methodology

1. Introduction

More than 60,000 articles are indexed monthly in PubMed, the United States National Library of Medicine's public access portal to the health-related journal literature. Given the large and growing volume of published articles, readers commonly find research reports that fail to provide a clear and transparent account of the methods and adequate reporting of the results. If authors do not provide sufficient details concerning the conduct of their study, readers

Financial disclosure: Funding support was obtained from the Canadian Institutes of Health Research (http://www.cihr-irsc.gc.ca). Professor Altman is supported by Cancer Research UK, Dr Moher by a University of Ottawa Research Chair, and Dr Schulz by Family Health International. The funders had no role in study design, data collection, and analysis; decision to publish; or preparation of the manuscript. All researchers are independent from relevant funding agencies.

Author contributions: Drs Moher, Sampson, Altman, Schulz, Miller, Simera, Grimshaw, and Hoey contributed to the design and planning of the systematic review, including securing funding. Drs Weeks and Seely and Ms Ocampo conducted data screening and extraction and prepared the results, with assistance from Dr Moher. Dr Moher prepared the first draft of this manuscript, and all coauthors contributed to revised drafts and have approved this final version. Dr Moher is the guarantor.

Competing interests: Drs Moher, Schulz, Simera, Hoey, and Professor Altman are all members of the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) Network Steering Group.

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doi: 10.1016/j.jclinepi.2010.09.013

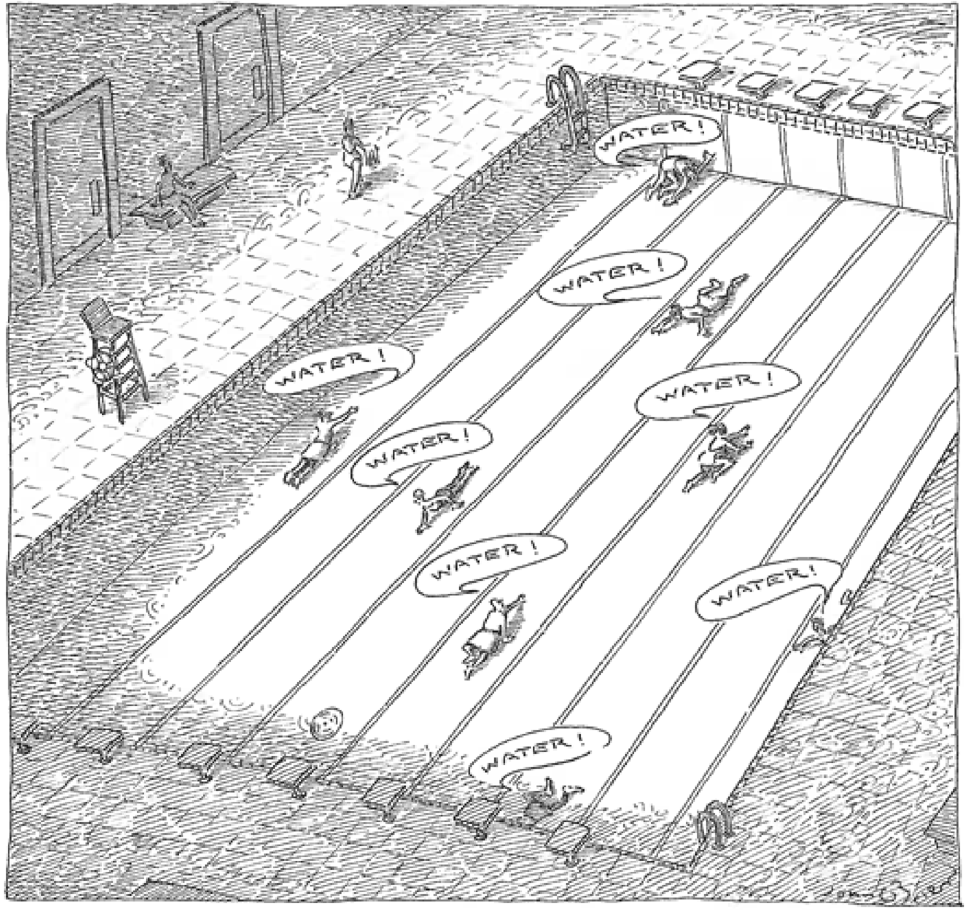
Moher D et al. JCE 2011; 64(7):718-42

Publishing RRRG

- Multiple journals versus a single one
  - Diversity of audience (multiple)

Toolkit

- Translation policy
- 5-10 minute Youtube for each item
- Link to bank of examples
- Link 'appropriate' creative commons licence
- More clearly outline optimal endorsement and implementation strategies for individual and group journals
  - Example letters
  - Example communication strategy across journals


WATER!
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Evolving format

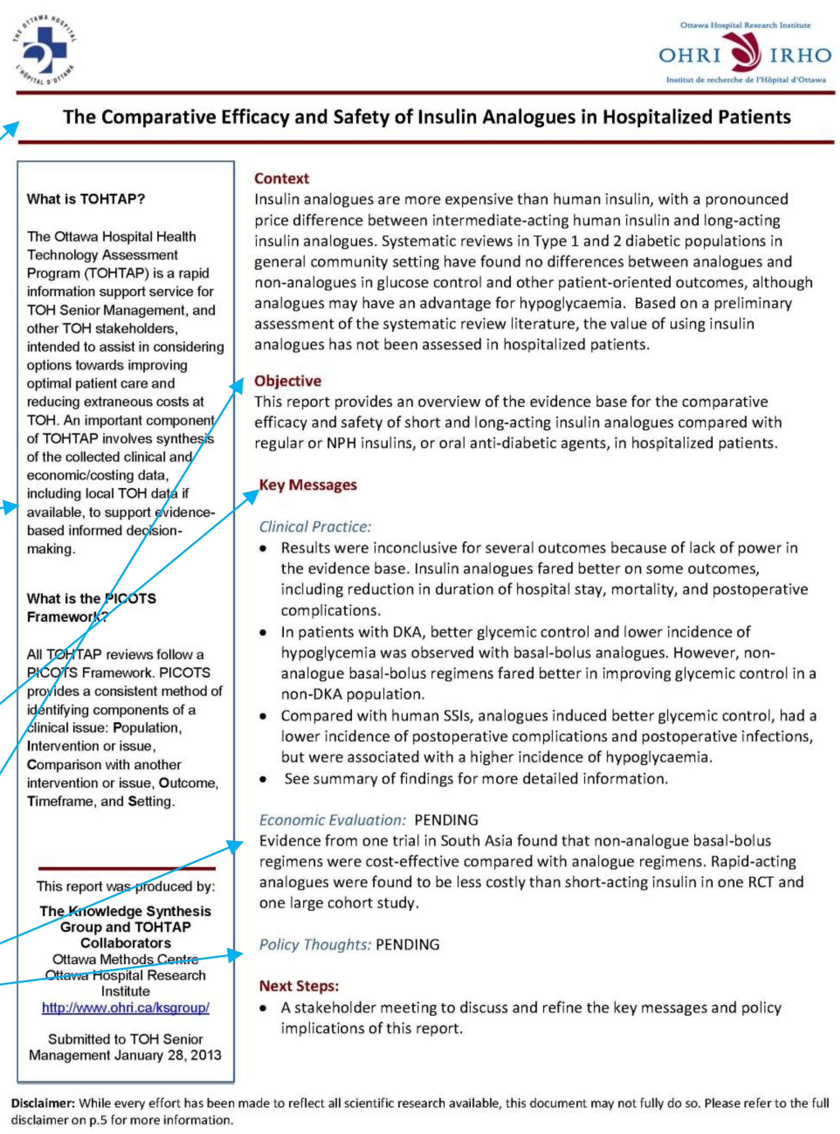
Primary research question as the title

Informative sidebar outlines the program; PICOTS framework; and our group as the producer

“Key messages” section aims to summarize overall findings

Brief context, objectives, plus, a section on economic & policy implications

Reference to the disclaimer (versus full disclaimer upfront)



Ottawa Hospital Research Institute
OHRI IRHO
Institut de recherche de l'Hôpital d'Ottawa

The Comparative Efficacy and Safety of Insulin Analogues in Hospitalized Patients

What is TOHTAP?

The Ottawa Hospital Health Technology Assessment Program (TOHTAP) is a rapid information support service for TOH Senior Management, and other TOH stakeholders, intended to assist in considering options towards improving optimal patient care and reducing extraneous costs at TOH. An important component of TOHTAP involves synthesis of the collected clinical and economic/costing data, including local TOH data if available, to support evidence-based informed decision-making.

What is the PICOTS Framework?

All TOHTAP reviews follow a PICOTS Framework. PICOTS provides a consistent method of identifying components of a clinical issue: **P**opulation, **I**ntervention or issue, **C**omparison with another intervention or issue, **O**utcome, **T**imeframe, and **S**etting.

This report was produced by:

The Knowledge Synthesis Group and TOHTAP Collaborators
Ottawa Methods Centre
Ottawa Hospital Research Institute
http://www.ohri.ca/ksgroup/

Submitted to TOH Senior Management January 28, 2013

Context

Insulin analogues are more expensive than human insulin, with a pronounced price difference between intermediate-acting human insulin and long-acting insulin analogues. Systematic reviews in Type 1 and 2 diabetic populations in general community setting have found no differences between analogues and non-analogues in glucose control and other patient-oriented outcomes, although analogues may have an advantage for hypoglycaemia. Based on a preliminary assessment of the systematic review literature, the value of using insulin analogues has not been assessed in hospitalized patients.

Objective

This report provides an overview of the evidence base for the comparative efficacy and safety of short and long-acting insulin analogues compared with regular or NPH insulins, or oral anti-diabetic agents, in hospitalized patients.

Key Messages

Clinical Practice:

- Results were inconclusive for several outcomes because of lack of power in the evidence base. Insulin analogues fared better on some outcomes, including reduction in duration of hospital stay, mortality, and postoperative complications.
- In patients with DKA, better glycemic control and lower incidence of hypoglycemia was observed with basal-bolus analogues. However, non-analogue basal-bolus regimens fared better in improving glycemic control in a non-DKA population.
- Compared with human SSIs, analogues induced better glycemic control, had a lower incidence of postoperative complications and postoperative infections, but were associated with a higher incidence of hypoglycaemia.
- See summary of findings for more detailed information.

Economic Evaluation: PENDING

Evidence from one trial in South Asia found that non-analogue basal-bolus regimens were cost-effective compared with analogue regimens. Rapid-acting analogues were found to be less costly than short-acting insulin in one RCT and one large cohort study.

Policy Thoughts: PENDING

Next Steps:

- A stakeholder meeting to discuss and refine the key messages and policy implications of this report.

Disclaimer: While every effort has been made to reflect all scientific research available, this document may not fully do so. Please refer to the full disclaimer on p.5 for more information.

Specifics of PICOTS elements (in detail)

Key question(s)

Snapshot of evidence (literature search findings)

Abbreviations (front & centre)

PRIMSA Flow diagram (anchors the report)

PICOTS Framework

Population: Adult patients hospitalized with either hyperglycemia; a prior diagnosis of type 1 or type 2 diabetes, but not receiving NPH or regular insulin; or newly diagnosed with type 1 or type 2 diabetes. We excluded studies of non-diabetic pregnant patients and patients with gestational diabetes.

Intervention: Rapid-acting, long-acting, or mixed insulin analogues.

Comparator: Short or intermediate-acting insulin, or any oral anti-diabetic medication.

Outcomes: The following outcomes were evaluated: hyperglycemia; hypoglycemia (symptomatic or glucose < 4 mmol/L); acute length of hospital stay; surgical site infection; mortality, and economic impact (e.g. cost-effectiveness, cost-benefit, cost-utility). We also extracted information on utilization to inform cost analyses.

Timing: Outcomes were evaluated within 30 days of hospital admission. If the duration of follow-up was unclear, but was limited to the period of hospitalization (and likely to be 30 days or less), then we still extracted data for those outcomes.

Setting: We only included those studies that examined hospitalized patients. Studies from general community settings were excluded.

Abbreviations

AMI = acute myocardial infarction
CABG = coronary artery bypass graft
CEA = cost-effectiveness analysis
CI = confidence interval
DKA = diabetic ketoacidosis
DM = diabetes mellitus
ICER = incremental cost-effectiveness ratio
IV = intravenous
MD = mean difference
NPH = neutral protamine Hagedorn
RCT = randomized controlled trial
RR = relative risk
SC = subcutaneous
SSI = sliding scale insulin

Key Questions

1. In adult patients admitted to an acute-care hospital, do rapid or long-acting insulin analogues reduce the total time spent in a state of hyperglycemia (> 11 mmol/L) and/or the frequency of hyperglycemic episodes during hospitalization compared with insulin (regular or NPH) or oral anti-diabetic medications, among those who are:
   a. Non-diabetic, but who experience a state of hyperglycemia due to acute or chronic illness?
   b. With type 1 or type 2 diabetes, but who are not receiving regular or NPH insulin?
   c. With newly diagnosed type 1 or type 2 diabetes?
2. In adult patients admitted to an acute-care hospital, do rapid or long-acting insulin analogues improve other outcomes (i.e. hypoglycemia, acute length of hospital stay, surgical site infection, and mortality) during hospitalization compared with insulin (regular or NPH) or oral anti-diabetic medications, among those who are:
   a. Non-diabetic, but who experience a state of hyperglycemia due to acute or chronic illness?
   b. With type 1 or type 2 diabetes, but who are not receiving regular or NPH insulin?
   c. With newly diagnosed type 1 or type 2 diabetes?
3. Compared with insulin (regular or NPH) or oral anti-diabetic medications, what are the economic impact(s) of use of rapid or long-acting insulin analogues for the period of hospitalization?

Snapshot of the Evidence

- Out of approximately 3,000 citations screened, 23 primary studies were relevant (16 RCTs and 7 cohort studies)[1-23] (PRISMA diagram).
- Most studies were from the United States. A few studies were from India, France, Sweden, Israel, Australia, and Brazil.
- Sample sizes ranged from 20[2] to 35,049[23]
- Population: surgery (6 studies)[5,8,12,15,21,22]; Type 2 diabetics (16 studies)[1-3,5,6,8,9,11,12,14,16-18,21-23]; DKA (4 studies)[1,10,19,20]; continuous tube feeding (1 study)[9]; CABG/cardiac surgery/AMI (4 studies)[2,7,13,16]

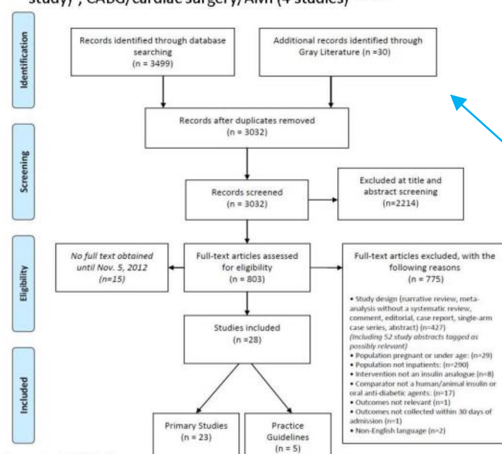


Figure 1. PRISMA flow

2

Results:
Listed as' 'Summary of Findings:
- Aim is to limit text

For each key question the following are highlighted:

a) Evidence based identified (by study design; region)
b) Risk of bias assessment findings
c) Population

In tabular format, outcomes are listed alongside their findings

Summary of Findings

How do rapid-acting insulin analogues compare with short-acting insulin?

Evidence base: 7 RCTs (n = 444; France, India and United States)[1,6,10,17-20] and 1 Cohort Study (n = 35 049; United States)[23]

Risk of bias assessment: RCTs - No obvious concerns but missing information precluded full assessment; Cohort – 8/9

Population: Type 1 or 2 DM; DKA

Outcome	Findings
Glycemic Control	• Inconclusive (4 RCTs meta-analyzed and 1 large cohort study)
Hypoglycemia	• Inconclusive: Number of patients with hypoglycemia (4 RCTs meta-analyzed and 1 large cohort study) • Inconclusive: Number of hypoglycemic events (3 RCTs meta-analyzed)
Duration of Hospital Stay	• Inconclusive (5 RCTs meta-analyzed) – favours analogue in subgroup of patients with Type 2 diabetes (non-DKA population) **MD (days) = -1.06, 95% CI -1.22, -0.90** • Favours analogue (1 large cohort study) **Crude MD (days) = -1.00, 95% CI -1.14, -0.86***
Mortality	• Zero events (4 RCTs) • Favours analogue (1 large cohort study): **Crude RR = 0.44, 95% CI 0.39, 0.50**
Postoperative Complications/ Wound Infections	• No evidence available
Utilization/Cost/CEA	• Similar utilization patterns across treatment arms (7 RCTs) • Lower cost with Lispro SC vs. Regular IV for treatment of DKA (1 RCT) **MD ($) = -1299.00, 95% CI -1843.40, -754.60** • Lower cost with analogue vs. human bolus (1 large cohort study) **Crude MD ($) = -12 197.00, 95% CI -13 084.92, -11309.08**

* After adjustment for confounders, the lower bound reduction in duration of hospital stay was as low as 11 hours and as high as 21 hours.

How do basal-bolus analogues compare with basal-bolus insulin?

Evidence base: 4 RCTs (n = 547; India and United States)[3,10,11,22] and 1 Cohort Study (n = 22; United States)[4]

Risk of bias assessment: RCTs – No obvious concerns but missing information precluded full assessment; Cohort – 4/9

Population: Type 2 DM with majority undergoing surgery; DKA; non-critically ill diabetic patients

Outcome	Findings
Glycemic Control	• Favours analogue for treatment of DKA (1 RCT) **MD (mmol/L) = -3.60, 95% CI -4.74, -2.46** • Favours non-analogue when regular insulin is administered three times daily (1 RCT and 1 cohort) **Severe hyperglycemia: 28.9% analogue vs. 12.9% non-analogue** **Values in target range (7.8-10 mmol/L): 24% analogue vs. 69% non-analogue**
Hypoglycemia	• Inconclusive: Number of patients with hypoglycaemia (2 RCTs meta-analyzed) – favours analogue in subgroup of patients with DKA: **RR = 0.36, 95% CI 0.14, 0.88** • Inconclusive: Number of hypoglycemic events (3 RCTs meta-analyzed for <2.2 or < 2.8 mmol/L and 2 RCTs meta-analyzed for <3.9 mmol/L or 2.2-3.3 mmol/L) – favours analogue in subgroup of patients with DKA: **Rate Ratio = 0.35, 95% CI: 0.16, 0.77**

Brief summary of the methods used: searches; sources; eligibility criteria; screening/ extraction methods; study types included; dates; risk of bias assessment

Collaborators

Acknowledgements

	analyzed) – favours Regular SSI vs. Glulisine + Glargine in subgroup of surgery patients: **RR = 6.17, 95% CI 1.42, 26.91** • Favours Regular SSI vs. Glulisine + Glargine: Number of hypoglycemic events < 3.3 mmol/L (2 RCTs meta-analyzed) **Pooled Rate Ratio = 3.98, 95% CI: 1.31, 12.12** • Favours Aspart SSI vs. NPH SSI (1 cohort study): **5 events/31 patients in analogue group and 28 events/52 patients in NPH group**
Duration of Hospital Stay	• Inconclusive (3 RCTs meta-analyzed)
Mortality	• Inconclusive (2 RCTs)
Postoperative Complications/ Wound Infections	• Favours analogue for postoperative complications (1 RCT) **RR = 0.36, 95% CI 0.18, 0.72** • Favours analogue for any postoperative infection (1 cohort study) **RR = 0.34, 95% CI 0.13, 0.89** • Inconclusive for wound infection (2 RCTs meta-analyzed)
Utilization/Cost/CEA	• Higher utilization with analogue (3 RCTs and 1 cohort study) **Range of 20-50 units for analogue and 7-12.5 units for Regular SSI** • No cost data available

Methods

Search strategies were developed by a trained information retrieval specialist and were implemented in Ovid Medline, Embase, and The Cochrane Library (inception – Aug 22, 2012). Retrieved records were systematically screened in duplicate at two levels. We included comparative experimental or observational study designs, and practice guidelines, health technology assessments, and systematic reviews. We used the Cochrane risk of bias tool to assess the risk of bias of RCTs and the Newcastle-Ottawa scale (score out of 9) to assess observational studies. We meta-analyzed RCTs with similar broad intervention and comparator groups. Findings described as inconclusive mean that the effect estimate crossed the null and there was a lack of power in the evidence base. This report was conducted over 12 weeks (Sept.-Dec. 2012).

Additional Materials Available Upon Request

- Full report
- Level 1 screening form
- Level 2 screening form
- Search strategies
- List of excluded studies
- List of relevant non-English citations
- Evidence table of primary studies
- Evidence table of practice guidelines

TOHTAP Collaborators: Dr. Alan Forster, Mr. Mike Tierney, Dr. Rakesh Patel, Dr. Erin Keely, Mr. Mario Bedard

Report should be cited as: Singh K, et al. The Comparative Efficacy and Safety of Insulin Analogues in Hospitalized Patients. The Ottawa Hospital Health Technology Assessment Program; Feb. 1, 2013. Report no. 1

Acknowledgments: The authors thank Chantelle Garritty, Raymond Daniel, Manvinder Kaur, Hadeel Alyacoob, Mohammed Golfam, Katrina Sullivan, Fatemeh Yazdi, and James Galipeau for their assistance with screening, data verification, database management, and report compilation.

Additional documents available upon request

Report Citation information including authors

Shorter disclaimer

Effects of Performing Complex Pediatric Intracavitary (IC) Surgical Procedures in Specialized versus Non-specialized Centers in High Risk Children: Cochrane Response Rapid Review

What is a Cochrane Response Rapid Review?

A Cochrane Response Rapid Review is an *abbreviated* and *accelerated* version of current systematic review methods with certain concessions made in relation to the systematic review process in order to accommodate an expedited turnaround time. Although not intended to replace a full systematic review, the rapid evidence summary retains transparency to ensure replication, preference for highest quality studies, and adoption of consensus standards for quality indicators of individual primary and secondary studies. All Cochrane response protocols are peer-reviewed by members of the Cochrane Response Consortium, and Cochrane Innovations Executive.

What is the PICOTS Framework?

All Cochrane Response Rapid Reviews follow a PICOTS Framework. PICOTS provides a consistent method of identifying components of a clinical issue: Population, Intervention or exposure, Comparison with another intervention or issue, Outcome, Timeframe, and Setting.

This report was produced by:

The Knowledge Synthesis Group and Cochrane Collaborators
Ottawa Methods Centre
Ottawa Hospital Research Institute
http://www.ohri.ca/ksgroup/

Submitted to CHA
April 12, 2013

Context

This review is being conducted as part of Cochrane Innovations Rapid Response program. **The Children's Hospital Association (CHA) has undertaken an initiative** to develop a system of care for infants, children, adolescents and their families with surgical needs. The aim is to optimize outcomes by matching patient needs prospectively defined with appropriate resources, and by improving the coordination of care for surgical patients within a given region. As such, the CHA has requested a rapid review to assist in informing pediatric surgical initiatives. Findings from this exercise will inform the **U.S. Task Force for Children's Surgical Care discussions.**

Objectives

CHA is interested in development of a rapid review that addresses the effects of performing certain pediatric surgical procedures in specialized centers. The population of interest would be children who are at **high risk** because of their **age or co-morbidities, primary condition requiring surgery**, or because the procedure they require is **rarely performed or highly complex.**

Key Messages

- From this rapid review of observational studies, the identified evidence signals that specialization compared with non-specialization may be generally effective for reducing mortality after pediatric cardiac surgery.
- For other outcomes and surgeries findings are ambiguous because:
  i. Results were inconsistent across studies (i.e., a mix of positive , negative , or non-significant findings); or
  ii. There was lack of clarity as to whether the results favoured specialization, non-specialization, or showed equivalence of surgical services (i.e., the majority of studies were statistically non-significant)
- Given the potential shortcomings of the rapid review process, and the limitations of analyses from observational studies, conducting a full systematic review in order to confirm our findings may be warranted.

Policy Implications

- Given the findings with cardiac surgery, policy decision-makers need to determine whether to generalize these findings to other complex, high risk (non-cardiac) conditions in the pediatric population.
- Further investigation may be needed to determine if other 'lower acuity' conditions (e.g., appendicitis) requires surgical specialty care.

"It's come to my attention that you have a life outside the office."

Is PRISMA-P helpful when generating a RR protocol?

Moher *et al. Systematic Reviews* 2015, **4**:1
http://www.systematicreviewsjournal.com/content/4/1/1

SYSTEMATIC REVIEWS

RESEARCH Open Access

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement

David Moher[1*], Larissa Shamseer[1], Mike Clarke[2], Davina Ghersi[3], Alessandro Liberati[^], Mark Petticrew[4], Paul Shekelle[5], Lesley A Stewart[6] and PRISMA-P Group

Abstract

Systematic reviews should build on a protocol that describes the rationale, hypothesis, and planned methods of the review; few reviews report whether a protocol exists. Detailed, well-described protocols can facilitate the understanding and appraisal of the review methods, as well as the detection of modifications to methods and selective reporting in completed reviews. We describe the development of a reporting guideline, the Preferred Reporting Items for Systematic reviews and Meta-Analyses for Protocols 2015 (PRISMA-P 2015). PRISMA-P consists of a 17-item checklist intended to facilitate the preparation and reporting of a robust protocol for the systematic review. Funders and those commissioning reviews might consider mandating the use of the checklist to facilitate the submission of relevant protocol information in funding applications. Similarly, peer reviewers and editors can use the guidance to gauge the completeness and transparency of a systematic review protocol submitted for publication in a journal or other medium.

Background

Systematic reviews are the reference standard for synthesizing evidence in health care because of their methodological rigor. They are used to support the development of clinical practice guidelines and inform clinical decision-making. They are becoming increasingly common; in 2010, 11 new reviews were estimated to be published daily [1]. Ideally, systematic reviews are based on pre-defined eligibility criteria and conducted according to a pre-defined methodological approach as outlined in an associated protocol.

The preparation of a protocol is an essential component of the systematic review process; it ensures that a systematic review is carefully planned and that what is planned is explicitly documented before the review starts, thus promoting consistent conduct by the review team, accountability, research integrity, and transparency of the eventual completed review. A protocol may also reduce arbitrariness in decision-making when extracting and using data from primary research, since planning provides an opportunity for the review team to anticipate potential problems. When clearly reported protocols are made available, they enable readers to identify deviations from planned methods in completed reviews and whether they bias the interpretation of a review results and conclusions. Bias related to the selective reporting of outcomes has been characterized as a serious problem in clinical research, including systematic reviews [2-7].

Until recently, systematic review protocols were generally available only through select organizations, such as The Cochrane [8] and Campbell Collaborations and the Joanna Briggs Institute, for which the preparation of a protocol is mandatory. Outside of these organizations, the existence of a protocol is infrequently reported in completed reviews [9,10]. Fewer than half of 300 systematic reviews indexed on MEDLINE in November 2004 (most recent generalizable sample; 2014 update underway) report working from a protocol [10], 80% of which are non-Cochrane affiliated. Of the non-Cochrane therapeutic reviews, only 11% mentioned the existence of a protocol [10]. The majority of reviews in health care are

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Table 3 PRISMA-P 2015 checklist: recommended items to include in a systematic review protocol[a]

Section/topic	Item #	Checklist item
ADMINISTRATIVE INFORMATION		
Title		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number
Authors		
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor/ funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data		
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned

the bmj

BMJ 2014;349:g7647 doi: 10.1136/bmj.g7647 (Published 2 January 2015)

RESEARCH METHODS & REPORTING

Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation

Larissa Shamseer[1], David Moher[1], Mike Clarke[2], Davina Ghersi[3], Alessandro Liberati (deceased)[4], Mark Petticrew[5], Paul Shekelle[6], Lesley A Stewart[7], the PRISMA-P Group

[1]Ottawa Hospital Research Institute and University of Ottawa, Canada; [2]Queen's University Belfast, Ireland; [3]National Health and Medical Research Council, Australia; [4]University of Modena, Italy; [5]London School of Hygiene and Tropical Medicine, UK; [6]Southern California Evidence-based Practice Center, USA; [7]Centre for Reviews and Dissemination, University of York, UK

Dedication: The PRISMA-P 2015 initiative is dedicated to our colleague Alessandro Liberati (1954–2012), who passed away while PRISMA-P 2015 was under development and whose contributions to this work were invaluable.

Abstract

Protocols of systematic reviews and meta-analyses allow for planning and documentation of review methods, act as a guard against arbitrary decision making during review conduct, enable readers to assess for the presence of selective reporting against completed reviews, and, when made publicly available, reduce duplication of efforts and potentially prompt collaboration. Evidence documenting the existence of selective reporting and excessive duplication of reviews on the same or similar topics is accumulating and many calls have been made in support of the documentation and public availability of review protocols. Several efforts have emerged in recent years to rectify these problems, including development of an international register for prospective reviews (PROSPERO) and launch of the first open access journal dedicated to the exclusive publication of systematic review products, including protocols (BioMed Central's *Systematic Reviews*). Furthering these efforts and building on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines, an international group of experts has created a guideline to improve the transparency, accuracy, completeness, and frequency of documented systematic review and meta-analysis protocols—PRISMA-P (for protocols) 2015. The PRISMA-P checklist contains 17 items considered to be essential and minimum components of a systematic review or meta-analysis protocol.

This PRISMA-P 2015 Explanation and Elaboration paper provides readers with a full understanding of and evidence about the necessity of each item as well as a model example from an existing published protocol. This paper should be read together with the PRISMA-P 2015 statement. Systematic review authors and assessors are strongly encouraged to make use of PRISMA-P when drafting and appraising review protocols.

Introduction

Systematic reviews hold a unique place in healthcare. They help form the basis for developing practice guidelines and they provide information on gaps in knowledge, thus informing future research efforts. This information is relevant to stakeholders across the health system. The rigour and trustworthiness of systematic reviews is, in large part, based on the a priori planning and documentation of a methodical approach to conduct (that is, a protocol).

A systematic review protocol is important for several reasons: (1) it allows systematic reviewers to plan carefully and thereby anticipate potential problems; (2) it allows reviewers to explicitly document what is planned before they start their review, enabling others to compare the protocol and the completed review (that is, to identify selective reporting), to replicate review methods if desired, and to judge the validity of planned methods; (3) it prevents arbitrary decision making with respect to inclusion criteria and extraction of data; and (4) it may reduce duplication of efforts and enhance collaboration, when available.

Various international organizations such as the Cochrane and Campbell Collaborations and the Agency for Healthcare Research and Quality (AHRQ) regularly require and publish protocols. However, outside of such organizations, few protocols are published in traditional journals and most reports of completed reviews (89%) do not mention working from a protocol[1] (2014 update under way). Many experts have called for improved documentation and availability of review protocols. In response, experts (some of whom are authors on this document) launched an international, prospective register for systematic review protocols (PROSPERO, www.crd.york.ac.uk/prospero/) through the Centre for Reviews and Dissemination at the University of York (UK) in February 2011, in which more than 5000 systematic review protocols from 69 countries have been registered as of December 2014. In February 2012, the

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ADMINISTRATIVE INFORMATION

- Title
- Identification
  - 1a Identify the report as a protocol of a systematic review
- Update
  - 1b If the protocol is for an update of a previous systematic review, identify as such
- Registration
  - 2 If registered, provide the name of the registry (e.g., PROSPERO) and registration number

Eligibility criteria

  - 8 Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review
- Information sources
  - 9 Describe all intended information sources (e.g., electronic databases, contact with study authors,
- trial registers, or other grey literature sources) with planned dates of coverage
- Search strategy
  - 10 Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated

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QUESTIONS