Clinical trials registers and clinical trials results registers: their contribution as health information sources to evidence-based healthcare decision-making

Carol Lefebvre  
Senior Information Specialist  
UK Cochrane Centre  
National Institute for Health Research  
Oxford, UK  

Julie Glanville  
Project Director - Information Services  
York Health Economics Consortium Ltd  
University of York  
York, UK  

ICML, Brisbane, September 2009
Presentation overview
Introduction

- Decisions about the effectiveness of healthcare interventions should be based on sound evidence, such as a systematic review of randomized controlled trials.
- Access to the results of trials, however, is problematic.
- Not all trials are published.
- Those that are published may be difficult to locate if they are published only in the grey literature or in journals that are not indexed in major databases.
- Those that are indexed may be hard to locate due to poor description or inadequate indexing.
- Those that are easily identifiable may not necessarily show the same results as other trials conducted on that topic, due to publication bias.
What are trials registers? (1)

• Databases of trial records
• Record is trial information – not bibliographic citation
• Typical citation record – e.g. MEDLINE:
  – AU, TI, SO, YR
• Typical trials register record:
  – PI, study name, recruitment status etc.
What are trials registers? (2)

Examples:

• ClinicalTrials.gov

• Current Controlled Trials *meta*Register of Controlled Trials (*mRCT*)

• WHO Clinical Trials Search Portal (to trials registers)
  – International Clinical Trials Registry Platform Search Portal (ICTRP)
What info is included in a typical clinical trials register? (1)

- Title
- Study design (RCT or otherwise)
- Single- or multi-centre study
- Treatment and comparator(s)
- Trial ID number
- Name / contact details of Principal Investigator (PI)
- Open (recruiting) or closed
- Ongoing or completed
What info is included in a typical clinical trials register? (2)

- Participants
  - included
  - excluded
- Location
- Timescale – when will it be completed
- Interim / final results (links)
- Links to publications
- Sponsor / links to sponsor or trial web site
Types of trials and results registers

- National and international trials registers
- Pharmaceutical industry trials registers
- Subject-specific trials registers
- Trials results registers
National and international trials registers (1)

- Association of the British Pharmaceutical Industry (ABPI) – Pharmaceutical Industry Clinical Trials database:
  - www.cmrinteract.com/clintrial/

- Australian New Zealand Clinical Trials Registry: also searchable under the International Clinical Trials Registry Platform Search Portal from the WHO
  - www.anzctr.org.au/

- CenterWatch Clinical Trials Listing Service:
  - www.centerwatch.com/

- ClinicalTrials.gov register: also searchable under the International Clinical Trials Registry Platform Search Portal from the WHO
  - clinicaltrials.gov/
National and international trials registers (2)

- Current Controlled Trials metaRegister of Controlled Trials (mRCT) – active registers:
  - [www.controlled-trials.com/mrct/](http://www.controlled-trials.com/mrct/)

- Current Controlled Trials metaRegister of Controlled Trials (mRCT) – archived registers:
  - [www.controlled-trials.com/mrct/archived](http://www.controlled-trials.com/mrct/archived)

- European Medicines Agency (EMEA):
  - [www.emea.europa.eu/index/indexh1.htm](http://www.emea.europa.eu/index/indexh1.htm)
National and international trials registers (3)

- International Clinical Trials Registry Platform Search Portal (from the WHO):
  - [www.who.int/trialsearch](http://www.who.int/trialsearch)

- International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Clinical Trials Portal:

- International Standard Randomised Controlled Trial Number Register: also searchable under the International Clinical Trials Registry Platform Search Portal from the WHO
  - [www.controlled-trials.com/isrctn/](http://www.controlled-trials.com/isrctn/)
Pharmaceutical industry trials registers

- AstraZeneca Clinical Trials web site (also includes trial results):
  - www.astrazenecaclinicaltrials.com/
- Bristol-Myers Squibb Clinical Trial Registry (also includes trial results):
  - www.bms.com/clinical_trials/Pages/clinical_trial_registry.aspx
- Eli Lilly and Company Clinical Trial Registry (also includes trial results)
  - www.lillytrials.com/
- GlaxoSmithKline clinical trial register (also includes trial results):
  - http://www.gsk-clinicalstudyregister.com/
- NovartisClinicalTrials.com:
  - www.novartiscclinicaltrials.com/webapp/etrials/home.do
- Roche Clinical Trial Protocol Registry (links to trial results database):
  - www.roche-trials.com/registry.html
- Wyeth Clinical Trial Listings (links to trial results sources):
  - www.wyeth.com/ClinicalTrialListings
Trials results registers

• ClinicalTrials.gov
  – www.clinicaltrials.gov

• International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Clinical Trials Portal:

• PhRMA Clinical Study Results Database:
  – www.clinicalstudyresults.org

• Bristol-Myers Squibb Clinical Trial Results:
  – http://www.bms.com/clinical_trials/results/Pages/default.aspx

• Eli Lilly and Company Clinical Trial Registry:
  – www.lillytrials.com/

• Roche Clinical Trials Results Database:
  – www.roche-trials.com/results.html

• Wyeth Clinical Trial Results:
  – www.wyeth.com/ClinicalTrialResults now re-directed to:
  – www.clinicaltrials.gov
  – www.clinicalstudyresults.org
Brief history of trials registers – selected highlights (1)

• Pre 1990s
  – Very few national, international or industry trials registers
  – A number of subject-specific trials registers
  – Trials results registers not available
  – No ‘enforcement’ of trial registration
Brief history of trials registers – selected highlights (2)

• Current Controlled Trials web site launched (1998)
  – Current Controlled Trials metaRegister of Controlled Trials
  – The International Standard Randomised Controlled Trial Number Register scheme launched as the first online service that provided unique numbers to randomized controlled trials in all areas of health care and from all countries around the world
Background and brief history – selected highlights (3)

- ClinicalTrials.gov - initiated as a result of the Food and Drug Administration Modernization Act of November 1997 – launched in 2000.

The legislation required the Department of Health and Human Services, through the NIH, to establish a registry of clinical trials for both federally and privately funded trials “of experimental treatments for serious or life-threatening diseases or conditions”. – subsequently extended to all conditions.
Background and brief history – selected highlights (4)

- The support of registration at inception by the leading medical journal publishers (ICMJE) and their refusal to subsequently publish reports of trials not properly registered


Background and brief history – selected highlights (5)

• The World Health Organization (WHO) launched the International Clinical Trials Registry Platform Search Portal in May 2007 to search across a range of trials registers which now includes:
  • Australian New Zealand Clinical Trials Registry (ANZCTRN)
  • Chinese Clinical Trial Register (ChiCTR)
  • ClinicalTrials.gov
  • Clinical Trials Registry - India (CTRI)
  • German Clinical Trials Register (DRKS)
  • Iranian Registry of Clinical Trials (IRCT)
  • ISRCTN.org
  • Sri Lanka Clinical Trials Registry (SLCTR)
  • The Netherlands National Trial Register (NTR)
Background and brief history – selected highlights (6)

• The US National Institutes for Health (NIH) Public Access Policy
  - voluntary until December 2007 but now requires that “all investigators funded by the NIH submit or have submitted for them to the National Library of Medicine's PubMed Central an electronic version of their final, peer-reviewed manuscripts upon acceptance for publication to be made publicly available no later than 12 months after the official date of publication”.

• www.publicaccess.nih.gov/policy.htm
Background and brief history – selected highlights (7)

• Registers of the *results* of completed trials
  - a more recent phenomenon, following on from ongoing trials registers

Recent legislation in the US known as Section 801 of the Food and Drug Administration Amendments Act 2007 (FDAAA 801), enacted in September 2007, called for expanding ClinicalTrials.gov and adding a clinical trial results database.
Current controversies

• Controversy persists:
  – Institute for Quality and Efficiency in Health Care (IQWIG) press release 10 June 2009

“Pfizer conceals study data”
  – “Drug manufacturer hinders the best possible treatment of patients with depression
  – The pharmaceutical company Pfizer is concealing data on the effect of a drug (Edronax® containing the agent reboxetine) for the treatment of depression. Despite repeated requests by the Institute for Quality and Efficiency in Health Care (IQWiG), Pfizer has refused to provide a complete list of all published and unpublished trials on reboxetine. The Institute discovered through its own literature search that the drug approved in Germany has been tested in at least 16 trials. However, in 9 of these 16 trials, key information is missing that would enable an evaluation of reboxetine's performance.”
Current controversies

- “Merck, Schering-Plough Reach Vytorin Settlement With State AGs”
- 17 July 2009
- “Merck & Co., Schering-Plough Corp. and their cholesterol joint venture Merck/Schering-Plough Pharmaceuticals reached a civil settlement with the attorneys general (AGs) of 35 states and the District of Columbia concerning the companies’ promotion of the drugs Vytorin and Zetia and the alleged delay in releasing the results of a related clinical trial.
- According to the state enforcement officials, a nearly two-year delay in the release of the full results of the so-called ENHANCE clinical trial violated state consumer protection laws.
- Under the terms of the new agreement … the companies must:
  - obtain preapproval from the FDA for all DTC advertisements;
  - comply with FDA suggestions to modify their drug advertising;
  - register their clinical trials and post the trials’ results;
  - comply with other detailed rules to prevent the deceptive use of clinical trial results.”
- [abridged by CLF]
Conclusions

Librarians need to be aware of the importance of clinical trials - and clinical trials registers - in particular clinical trials results registers - as an adjunct to the more traditional sources such as databases and journals in completing the evidence picture.