Searching for Systematic Reviews of Adverse Effects

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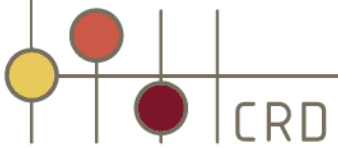
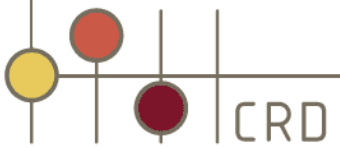
Background

- Systematic reviews traditionally examine beneficial intended effects
- Few systematic reviews address adverse effects
- Risk of unbalanced conclusions
- Guidance on including adverse effects in systematic reviews
- Lack of empirical evidence for methods



Survey of Systematic Reviews of Adverse Effects

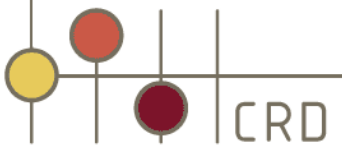
- **Aims and Objectives**
  - To describe methods used over past 10 years
  - To inform future guidance
  - To identify areas for further research
- **Inclusion Criteria**
  - Primary outcome of an adverse effect or effects
- **Data Extraction**
  - Types of studies, search strategies, resources searched, quality assessment, data pooling



Searching for Adverse Effects

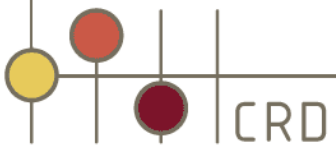
- Sensitive searches for primary studies of adverse effects requires combination of;
  - Text words in title and abstract
    - Adverse effect, side effect, safety, harm etc
  - MeSH
    - Drug Toxicity, Drug hypersensitivity
  - Subheadings/Qualifiers
    - Adverse effect, toxicity, complications

(See Badgett 1999, Derry 2001, Golder 2004, Wieland 2005)



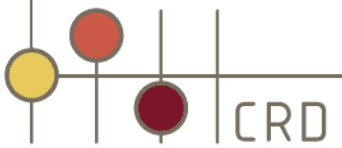
Databases Searched

- **Cochrane Database of Systematic Reviews (CDSR)**
  - Cochrane Library
- **Database of Abstracts of Reviews of Effects (DARE)**
  - Cochrane Library
  - CRD Website (more up to date)



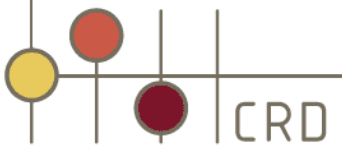
Searching Cochrane Review and DARE Abstracts

- Abstracts of Cochrane Reviews and DARE reviews:
  - “no information on the incidence of adverse effects are included”
  - “it would have been appropriate to include mention of adverse effects”
  - “the adverse effects of the treatment were not assessed in this review”
  - “Relative risk (RR) estimates were..”
- No abstract for records in progress in DARE



CDSR via the Cochrane Library (1)

#1 Any MeSH descriptor with qualifier: AE
#2 Any MeSH descriptor with qualifier: DE
#3 Any MeSH descriptor with qualifier: CO
#4 Any MeSH descriptor with qualifier: PO
#5 Any MeSH descriptor with qualifier: TO
#6 Any MeSH descriptor with qualifier: CI
#7 MeSH descriptor Drug Hypersensitivity explode all trees
#8 MeSH descriptor Drug Toxicity explode all trees
#9 MeSH descriptor Product Surveillance, Postmarketing explode all trees



CDSR via the Cochrane Library (2)

#10 (safe or safety or adverse or tolerability or toxicity or toxic or adrs or adr or tolerance or tolerate or harm or harms or harmful or complication* or risk or risks) near/20 objective* in Abstract

#11 (side next effect*) near/20 objective* in Abstract

#12 (undesirable next effect*) near/20 objective* in Abstract

#13 (treatment next emergent) near/20 objective* in Abstract

#14 (safe or safety or adverse or tolerability or toxicity or toxic or adrs or adr or tolerance or tolerate or harm or harms or harmful or complication* or risk or risks) in Record Title

#15 (side next effect*) in Record Title

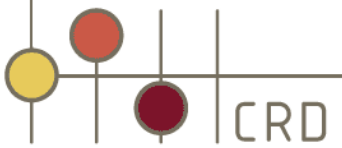
#16 (undesirable next effect*) in Record Title

#17 (treatment next emergent) in Record Title

#18 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18

DARE via the Cochrane Library

#1 Any MeSH descriptor with qualifier: AE
#2 Any MeSH descriptor with qualifier: DE
#3 Any MeSH descriptor with qualifier: CO
#4 Any MeSH descriptor with qualifier: PO
#5 Any MeSH descriptor with qualifier: TO
#6 Any MeSH descriptor with qualifier: CI
#7 MeSH descriptor Drug Hypersensitivity explode all trees
#8 MeSH descriptor Drug Toxicity explode all trees
#9 MeSH descriptor Product Surveillance, Postmarketing explode all trees
#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9



DARE via CRD Website

(safe or safety or adverse or tolerability or toxicity or toxic or adrs or adr or tolerance or tolerate or harm or harms or harmful or complication$ or risk or risks)/xoa OR

side(w)effect$/xoa OR

undesirable(w)effect$/xoa OR

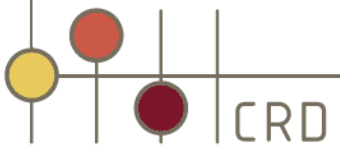
treatment(w)emergent/xoa OR

(safe or safety or adverse or tolerability or toxicity or toxic or adrs or adr or tolerance or tolerate or harm or harms or harmful or complication$ or risk or risks)/ttl OR

side(w)effect$/ttl OR

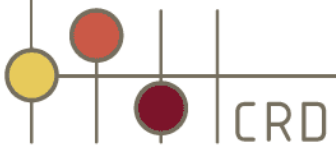
undesirable(w)effect$/ttl OR

treatment(w)emergent/ttl

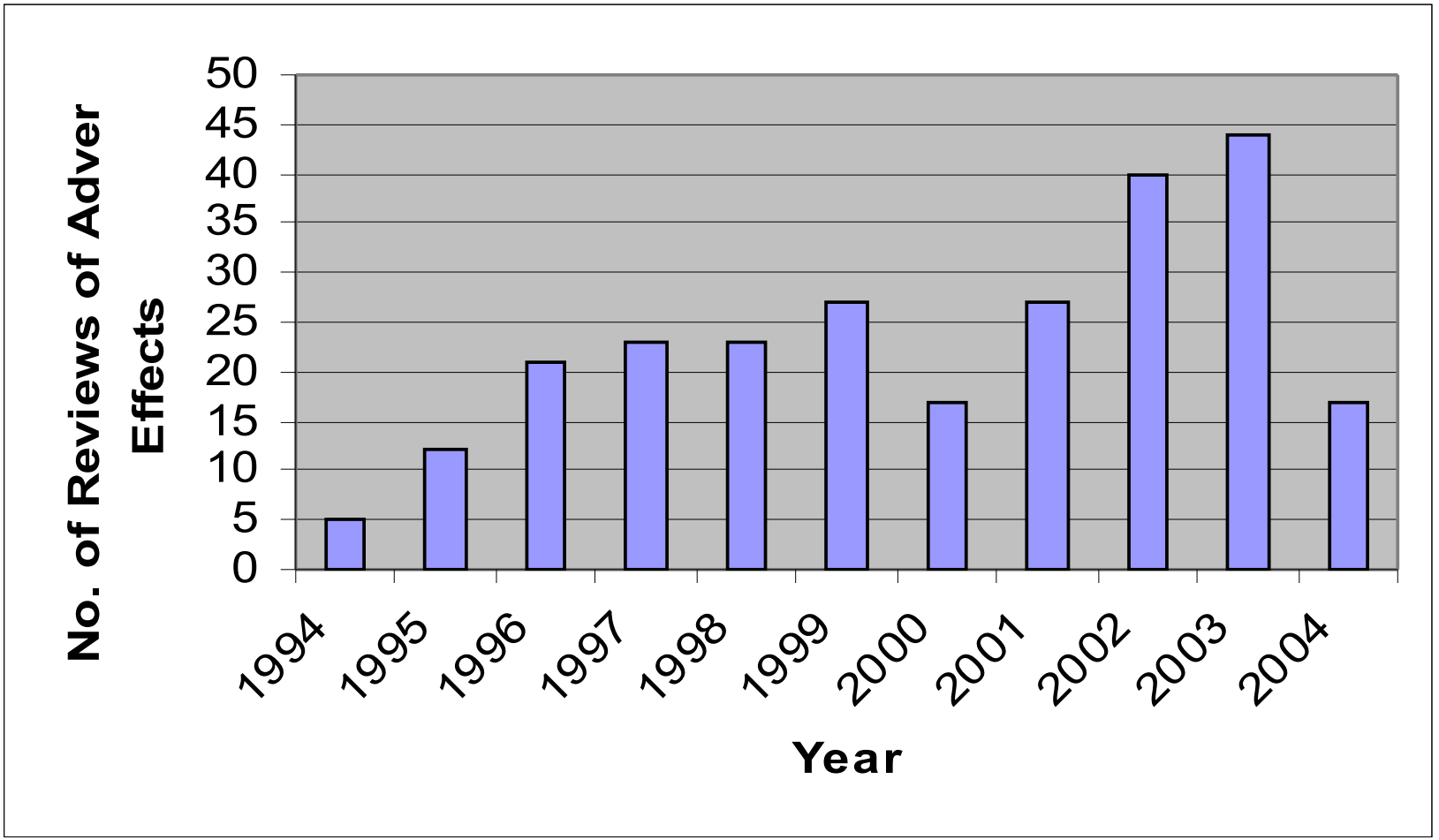


Results

- 3539 unique records sifted
- 257 relevant records
  - 246 relevant records from DARE
  - 11 relevant records from CDSR



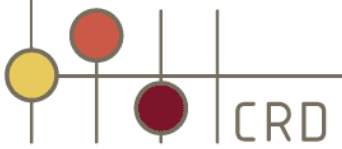
Results


No. of Reviews of Adver Effects
50
45
40
35
30
25
20
15
10
5
0
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003
2004
Year

CRD

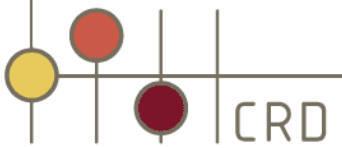
Increasing Precision in CDSR

- Search Strategy
  - floating subheading
    - “adverse effects” OR
  - abstract
    - ‘adverse near/20 objective’
- Increased precision from 0.8% to 3%



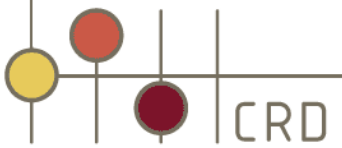
Increasing Precision in DARE

- Search Strategy
  - Floating subheadings
    - “adverse effects” OR “drug effects” OR “chemically induced” OR
  - Record title
    - risk or side effect or complication* or harm or tolerability or safety OR
  - ‘Outcomes assessed in the review’ field
    - risk
- Increased precision from 13% to 17%



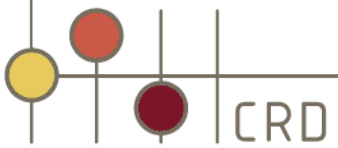
Increasing Sensitivity

- Scanned
  - 2249 Cochrane Reviews
  - 4919 DARE Reviews
- Missing papers
  - 8 DARE records in progress
  - 10 full DARE abstracts
  - 3 Cochrane Reviews
- Additional Terms
  - Hazards in title, abstract
  - RISK FACTORS in MeSH



Conclusions

- Different databases allow different search options
  - Cochrane Library – unable limit to sections of abstract
  - CRD Website – unable to float subheadings/qualifiers
- Unable to achieve 100% sensitivity due to inconsistent terminology and poor indexing
- To retrieve all systematic reviews of adverse effects on CDSR or DARE need scan all records
- Searching for studies where adverse effects are a secondary outcome is likely to be even more difficult



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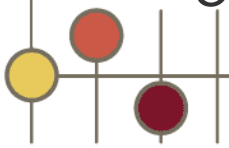
- Wieland S, Dickersin K. Selective exposure reporting and Medline indexing limited the search sensitivity for observational studies of adverse effects of oral contraceptives. *Journal of Clinical Epidemiology.* 2005;58:560-567.



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