



# Developing efficient search strategies to identify papers on adverse events

Golder S\*, McIntosh HM, Duffy S, Glanville J

Centre for Reviews and Dissemination, THE UNIVERSITY of York, UK

\*spg3@york.ac.uk

The precision and sensitivity of five different approaches to searching for adverse events, and combinations of these approaches, were compared in a case study.

## Background

Systematic reviews and HTAs are increasingly incorporating evidence on adverse events. However, there is little published evidence on the most appropriate methods to identify reports of adverse events.

## Methods

A systematic review of the effectiveness and adverse effects of seven new anti-epileptic drugs was used as a case study. This review included a thorough search for studies of effectiveness and additional searches for adverse events.

Five different approaches to searching for adverse events evidence were identified from a search of the literature [1, 2] and from scanning technology appraisals produced at the Centre for Reviews and Dissemination (CRD). MEDLINE and EMBASE were

## Objectives

To assess the performance (in terms of precision and sensitivity) of different approaches to searching MEDLINE and EMBASE to identify studies of adverse events, for a systematic review.

searched using each of the 5 approaches and in each case the drug terms were ANDed with the strategy.

The results from MEDLINE and EMBASE were augmented with additional studies identified from reference lists, experts, submissions from drug companies, and a search on TOXLINE (using the drug terms only). The combined set of 84 relevant records (73 on EMBASE and 67 on MEDLINE) was used as a quasi gold standard against which the sensitivity and precision of more than 200 combinations of the five individual search approaches were tested in EMBASE and MEDLINE.

## Results

### Approach 1: Specified adverse events

Specified adverse events were identified from textbooks and CD-ROMS [3-7] and then searched for, using appropriate indexing terms with subheadings where available. In instances where no appropriate indexing term was available, text words were used to search in the title and abstract.

**Table 1: Precision and sensitivity of specified adverse event searches**

Database	Specified adverse events	Example (Ovid interface)	Precision	Sensitivity
MEDLINE	Indexing terms with "chemically induced" [chemically induced]	Exp liver diseases/ci	6.4%	20.9%
EMBASE	Indexing terms with "side-effect" [side effect]	Exp liver disease/si	2.5%	38.4%

This method proved more sensitive in EMBASE than MEDLINE (Table 1).

A browse of all the relevant papers suggests that if all the possible adverse events had been identified for the search this search approach would have been even more successful in EMBASE (Table 2).

**Table 2: Percentage of relevant papers with index terms for specific adverse events**

Database	Percentage of relevant papers with index terms for specified adverse events
MEDLINE	40.3%
EMBASE	84.9%

### Approach 2: Using adverse event subheadings

The subheadings, adverse events (ae), poisoning (po) and toxicity (to) were used in conjunction with a drug indexing term and as floating subheadings. The use of floating subheadings rather than linking terms to indexing terms proved useful in MEDLINE but not in EMBASE (Table 3).

**Table 3: Precision and sensitivity of adverse event subheadings searches**

Database	Search	Example	Precision	Sensitivity
MEDLINE	Subheadings linked to drug indexing terms *	vigabatrin/ae, po, to	12.1%	41.4%
MEDLINE	Floating subheadings*	ae.fs, to.fs, po.fs	6.0%	89.7%
EMBASE	Subheadings linked to drug indexing terms *	vigabatrin/ae, to	2.5%	80.8%
EMBASE	Floating subheadings	ae.fs to.fs	1.8%	80.8%

\*Analysis on Vigabatrin as only drug indexed in MEDLINE

### Approach 3: Using text words for "adverse events"

Text words denoting "adverse events" were searched for in the title and abstract using truncation where appropriate. Terms included were; safe, safety, side effect, undesirable effect, treatment emergent, tolerability, toxicity, adrs, adverse effect, adverse reaction, adverse event, adverse outcome (Table 4).

**Table 4: Precision and sensitivity of using text words to search for "adverse events"**

Database	Precision	Sensitivity
MEDLINE	4.4%	74.6%
EMBASE	2.9%	75.3%

### Approach 4. Using indexing terms for "adverse events"

Searching using available indexing terms for "adverse events" provided low sensitivity in both databases although the precision was higher in MEDLINE (Table 5).

**Table 5: Precision and sensitivity of using indexing terms for "adverse events"**

Database	Indexing terms	Precision	Sensitivity
MEDLINE	"drug toxicity"	8.3%	9.0%
EMBASE	"adverse drug reaction" "side effect"	1.1%	16.4%

### Approach 5: Searching by study design

Two approaches, identified in the literature, incorporated study designs into their search strategies and these strategies were tested in MEDLINE and EMBASE (Table 6).

**Table 6: Precision and sensitivity of published search strategies**

Database	Search Strategy	Precision	Sensitivity
MEDLINE	(ae or co or po or de).fs or case report and human/[1]	2.7%	86.6%
MEDLINE	Case control studies or cohort studies or clinical trial or drug indexing terms/ae and human[2]	5.1%	61.2%
EMBASE*	(ae or co).fs or case report and human/[1]	1.4%	80.8%
EMBASE	Case control studies or cohort studies or clinical trial or drug indexing terms/ae and human[2]	2.0%	86.3%

\* direct conversion from Badgett's suggested MEDLINE strategy.

### Most sensitive searches

In both MEDLINE and EMBASE the most sensitive search strategy with the highest precision contained a combination of the search approaches ORed together (Table 7).

**Table 7: Precision and sensitivity of highly sensitive searches**

Database	Search strategy	Precision	Sensitivity
MEDLINE	(Approach 1 OR Approach 2 (floating) OR Approach 3 OR Approach 4)	2.8%	97.0%
EMBASE	(Approach 1 OR Approach 3)	2.8%	98.6%

## Discussion

The searches for adverse events using a range of approaches provided relevant papers in addition to those found via the effectiveness searches.

Comparisons of the sensitivity and precision of five different search strategies and combinations of strategies suggest that thorough searching for adverse events requires a combination of different approaches. A very different approach may be required when searching EMBASE to MEDLINE as floating subheadings proved more successful in MEDLINE and adverse event indexing terms more successful in EMBASE.

## References

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