

Review of the usefulness of contacting other experts when conducting a literature search for systematic reviews

R J McManus, S Wilson, B C Delaney, D A Fitzmaurice, C J Hyde, R S Tobias, S Jowett, F D R Hobbs

Department of Primary Care and General Practice, University of Birmingham, Birmingham B15 2TT
 R J McManus, *clinical research fellow*
 S Wilson, *research fellow*
 B C Delaney, *senior lecturer*
 D A Fitzmaurice, *senior lecturer*
 R S Tobias, *research associate*
 S Jowett, *research associate*
 F D R Hobbs, *professor*

continued over

BMJ 1998;317:1562-3

Introduction

Identifying relevant studies is "the most fundamental challenge" when compiling a systematic review.¹ Electronic databases, such as Medline, may detect only about half of papers identified by the gold standard of hand searching journals.¹ Hand searching requires a focus, usually the specialist literature,² which may not exist for newly developed fields or those that cross boundaries with other areas. We examined the usefulness of contacting other experts when searching for relevant references for a systematic review of a field where such a specialist focus does not exist.

Methods and results

As part of a systematic review undertaken in 1996, all published literature relating to "near patient testing" (any investigation performed in a clinical setting where the result is available without a sample being sent to a laboratory for analysis) in primary care was identified for 1986-95.³ Electronic databases were searched and secondary citations were collected from identified publications (see table). The search strategy is reported elsewhere.³ Indexes of abstracts from major international primary care scientific conferences were hand

searched. We sent a questionnaire to 194 academics in the United Kingdom (heads of academic departments of general practice and clinical chemistry and researchers identified from the previously mentioned abstracts) and to 152 commercial companies known to have an interest in near patient testing. The questionnaire requested key references from journals, unpublished data, and names of other workers in the field.

Overall, 156 (45%) questionnaires were returned completed (103 (53%) of those sent to academics and 53 (35%) of those sent to commercial companies). No unpublished data were offered.

Articles that did not report original data, were not relevant to primary care, or were not in English were excluded. Remaining articles were then judged by both an external and internal reviewer against standard appraisal criteria,⁴ with discrepancies being adjudicated on by a third reviewer (BCD). A verifying search did not identify any further key words or references.

The searches yielded 1286 citations comprising 1057 unique references potentially eligible for inclusion in the review. The table shows a breakdown of the results by source—102 references were relevant, of which 29 were of high quality. Of the 102 unique eligible references, 50 (49%) were identified by one of the electronic databases, 40 (39%) by people working in the field, and 31 (30%) by hand searches. Each of these sources produced a similar proportion of high quality papers.

The 1057 potential references came from 418 different publications, of which only 48 were found to contain relevant articles. Only one journal, the *BMJ*, contained more than 10% (11 articles) of the relevant references.

Comment

This study confirms that searching electronic databases may uncover only half of all relevant studies¹ and shows the importance of contacting other experts when compiling a systematic review. Over 300 of the references in this review were identified by experts working in the field, of which 40 were found subsequently to be eligible. Twenty four references (24% of the total number of eligible references) would have been missed entirely without the input of people working in the field.

The lack of sensitivity of electronic databases may be due to problems with indexing⁵: articles from journals that lie outside of the mainstream (which currently includes primary care) take some years to be electronically indexed; furthermore, near patient testing is an expanding field without unique medical subject headings (MeSH terms). The continuing work of the Cochrane Collaboration is improving this situation,⁵ but at the time of this study, making up the shortfall in articles by hand searching would not have been justifiable in terms of either time or money.

Results of various types of search

| Search | No of articles identified | No of articles eligible in review | Unique articles identified | High quality articles* |
|--------------------------------------|---------------------------|-----------------------------------|----------------------------|------------------------|
| Electronic databases | | | | |
| BIDS Science Citation Index | 185 | 32 | 15 | 5 |
| Medline | 335 | 20 | 11 | 9 |
| Embase | 40 | 11 | 5 | 4 |
| CINAHL | 48 | 0 | 0 | 0 |
| BIDS index to conference proceedings | 32 | 0 | 0 | 0 |
| GPLit | 26 | 0 | 0 | 0 |
| DHSS | 18 | 0 | 0 | 0 |
| PsychLit | 10 | 0 | 0 | 0 |
| Total No of articles | 694 | 63 | 31 | 18 |
| No of unique articles | 581 | 50 | 31 | 15 |
| Survey of expert network | | | | |
| Academics | 297 | 37 | 20 | 7 |
| Commercial organisations | 43 | 4 | 3 | 2 |
| Total No of articles | 340 | 41 | 23 | 9 |
| No of unique articles | 338 | 40 | 23 | 9 |
| Hand searching† | | | | |
| Abstracts | 44 | 0 | 0 | 0 |
| Reports | 29 | 7 | 1 | 2 |
| References | 129 | 24 | 20 | 8 |
| Total No of articles (all unique) | 202 | 31 | 21 | 10 |
| Overall results | | | | |
| Total citations identified | 1236 | 135 | 75 | 37 |
| Total unique references‡ | 1057 | 102 | 75 | 29 |

*Eligible papers scoring 4 or 5 for methodology (one point was given for each of the following: an independent blind comparison to a reference standard; an appropriate spectrum of patients in the sample; reference standard performed on all patients; test methods described sufficiently to permit replication; likelihood ratios quoted).

†Limited hand search of published abstracts of international primary care meetings, and bibliographies of publications identified from above sources.

‡Excluding overlaps between the three search methods.

This study has quantified the contribution of experts to a systematic review and has found them to be an essential source for identifying literature. We suggest that appropriate experts should be consulted when performing a systematic review in a developing field that does not have a clearly defined specialist literature.

Contributors: RJMCM participated in the analysis, wrote the first draft, and coordinated the redrafting and the editing of the paper. SW participated in the study design and coordinated the analysis. BCD participated in the study design, reviewed the initial search results and supervised the project. DAF participated in the study design and reviewed the initial search results. CJH participated in the study design and the analysis. RST participated in the design of the search strategy and in identifying and obtaining relevant citations from the searches. SJ participated in identifying and obtaining citations, designed the database used, entered the data and participated in the data analysis. FDRH participated in the study design and in obtaining national competitive funding to perform the work. All the authors contributed to redrafting and editing of the final paper. FDRH will act as guarantor.

Funding: Health Technology Assessment Programme.
Competing interests: BCD has received research funding and sponsorship to attend meetings from Cortecs. DAF has received research funding from Roche Diagnostics and has been sponsored to attend conferences by Nycomed UK and Roche Diagnostics. FDRH has received research grants from Nycomed UK, Roche Diagnostics, and Cortecs.

Aggressive Research Intelligence Facility, Edgbaston, Birmingham B16 9PA
C J Hyde, director

Correspondence to: Dr McManus rj.mcmanus@bham.ac.uk

- 1 Chalmers I, Dickersin K, Chalmers TC. Getting to grips with Archie Cochrane's agenda. *BMJ* 1992;305:786-8.
- 2 Jadad AR, McQuay HJ. Searching the literature. Be systematic in your searching. *BMJ* 1993;307:66.
- 3 Hobbs FDR, Delaney BC, Fitzmaurice DA, Wilson S, Hyde CJ, Thorpe GH, et al. A review of near patient testing in primary care. *Health Technol Assessment* 1997;1(5).
- 4 Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? *JAMA*; 271:389-91.
- 5 Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. In: Chalmers I, Altman DG, eds. *Systematic reviews*. London: BMJ Publishing, 1995.

(Accepted 16 July 1998)

Drug points

Anaphylaxis induced by gabexate mesylate

Yoshihiro Matsukawa, Susumu Nishinarita, Takashi Horie, Sensuke Naruse, Nihon University School of Medicine, Oyagochi-Kamimachi Itabashi, 173 Tokyo, Japan

Gabexate mesylate (molecular weight 417) is a protease inhibitor^{1,2} and has an effect against shock.³ Ten cases of shock induced by gabexate mesylate have, however, been reported (Ono Pharmaceutical Company and Nichiiko Pharmaceutical Company, personal communication). We report an additional case and an analysis of the clinical features of the 11 cases.

A 59 year old woman (case 7 in table) developed pancreatitis in 1975. She visited our clinic because of epigastralgia in October 1996. Laboratory tests showed raised concentrations of amylase (123 IU/l in serum, 857 IU/l in urine; normal values <120 IU/l and <700 IU/l). She received an infusion of gabexate mesylate (100 mg), which resolved her symptoms. She re-experienced abdominal pain in February 1997, which was relieved with the same treatment. This time, however, she developed urticaria after the gabexate mesylate infusion. She developed another bout of epigastralgia one week after this episode. She again developed urticaria 10 minutes after the initiation of the infusion and subsequently experienced chest constriction. Injection of hydrocortisone caused no improvements. Finally, she became pale and drowsy. Her systolic blood pressure fell to 90 mm Hg and became normal 30 minutes after receiving additional injections of hydrocortisone and noradrenaline (norepinephrine). Results of a lymphocyte stimulation test against gabexate mesylate were negative. Her serum concentration of IgE was within the normal range.

Ten of the 11 patients were re-exposed to gabexate mesylate. Nine patients developed eruptions. In three patients urticaria preceded the signs of anaphylaxis. Shock developed within 30 minutes after the challenge in all patients, with the signs of anaphylaxis—that is, hypotension and erythema or urticaria induced by the hypersecretion of histamine (table). All patients recovered from the shock, although two patients required intubation and artificial ventilation.

Patients who are repeatedly treated with gabexate mesylate should be carefully monitored for at least 30 minutes after administration of the drug. Use of

Clinical manifestations of shock induced by gabexate mesylate

| Case | Age (years) | Sex | Blood pressure (mm Hg) | Eruption | Urticaria | Disturbance in consciousness | Time of onset (minutes) |
|------|-------------|-----|------------------------|----------|-----------|------------------------------|-------------------------|
| 1 | 26 | F | 60/0 | ++ | NR | - | <5 |
| 2 | 46 | F | UD | + | NR | + | <30 |
| 3 | 46 | M | 50/0 | NR | NR | - | <5 |
| 4 | 48 | M | UD | + | + | + | <5 |
| 5 | 54 | M | 60/0 | ++ | NR | - | <5 |
| 6 | 57 | M | 60/0 | + | + | - | 5 |
| 7* | 59 | F | 90/0 | ++ | ++ | + | <30 |
| 8 | 60 | M | 55/26 | ++ | NR | - | 5 |
| 9 | 65 | M | UD | ++ | NR | + | 5 |
| 10 | 73 | F | 80/42 | NR | NR | NR | 5 |
| 11 | 76 | F | 44/0 | + | + | + | 30 |

NR = not reported; UD = not detectable. *Current case.

corticosteroids and adrenaline (epinephrine) and respiratory care seems to be adequate for treating such patients.

- 1 Buchler M, Malfertheiner P, Uhl W, Scholmerich J, Stockmann F, Adler G, et al. Gabexate mesilate in human acute pancreatitis. *Gastroenterology* 1993;104:1165-70.
- 2 Cavallini G, Tittobello A, Frulloni L, Masci E, Mariani A, DiFrancesci V. Gabexate in Digestive Endoscopy—Italian Group. Gabexate for the prevention of pancreatic damage related to endoscopic retrograde cholangiopancreatography. *N Engl J Med* 1996;335:919-23.
- 3 Novelli GP, Casali R, Bonizzoli M, Giorgi L, Lemma M, Piscitelli P. Antioxidant action of gabexate mesilate (FOY) in an experimental model of endotoxin shock. *Minerva Anestesiol* 1995;61:509-13.

Endpiece Orifices

First, there are orifices where we hear. For the area round the ear is hollow and hears nothing but noise and shouting. But whatever penetrates through the membrane to the brain is clearly heard there. This is the only perforation through the membrane which encloses the brain. At the nostrils there is no (such) opening but a soft area, like sponges. For this reason we hear over a greater distance than we smell.

Hippocrates, *Places in Man*, edited and translated by Elizabeth M Craik, 1998

Submitted by Ann Dally, Wellcome Institute for the History of Medicine