Bibliometric analysis of randomized trials in complementary medicine

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SUMMARY. Objective: To determine the following features of randomized trials in complementary medicine: the extent to which they are indexed on Medline, the journals in which they are published, dates of publication, the therapies and conditions most commonly the focus of study. Design: Bibliometric analysis of the registry of randomized trials of the Cochrane Collaboration field in Complementary Medicine. Outcome measures: The number of trials in each category. Results: There were 3774 randomized trials on the registry of which 3072 (81%) were indexed on Medline. However, only about a third of these references could be easily found with a Medline search. Trials were published in a total of 965 different journals. Most trials (84%) were published in a conventional medical journal. The number of trials is increasing rapidly, having approximately doubled every 5 year period since 1965. There was a large variation in the number of trials for different complementary therapies. There were a high number of trials in acupuncture (554), herbal medicine (804) and meditation and relaxation techniques (643) but few trials in aromatherapy (47) and osteopathy (18). There were many trials in cardiovascular disease (501), musculoskeletal disorders (386) and surgery-related symptoms (293), but few in fatigue disorders (11). Conclusion: Medline is an incomplete source of randomized trials in complementary medicine. Searching of Medline could be significantly enhanced by changes to keywords and improved data on type of publication. The conditions and therapies subject to trials in complementary medicine do not provide an accurate reflection of clinical practice.

INTRODUCTION

The Cochrane Collaboration is an international network of individuals dedicated to preparing, maintaining and disseminating systematic reviews of the effects of health care interventions.[1] One of the main products of the collaboration is a CD-ROM called the 'Cochrane Library.' In principal, this allows a health practitioner or consumer rapid access to the best evidence on the effectiveness of a particular treatment. For example, a doctor considering whether to give steroids to a pregnant women in danger of going into premature labour who typed in 'premature labour steroids' would at present retrieve a systematic review of all randomized trials comparing the outcome of pregnancies in women given steroids to those of women not given steroids. This review concludes that giving steroids to women expected to deliver preterm 'reduces mortality, respiratory distress syndrome and intraventricular haemorrhage in preterm infants.' The Cochrane Library is an important tool in the on-going attempt to base medical decisions on the best available evidence.

The complementary medicine 'field' of the Cochrane Collaboration was established in 1995. Its overall aim is to make sure that reviews on complementary medicine (CM) interventions are published on the Cochrane library, that these reviews include all relevant information and that they are conducted to the highest possible standards. One of the field's main functions has been to establish a database (or registry) of randomized trials (RCTs) in CM. Details of trials listed on the registry are forwarded to reviewers carrying out systematic reviews.

The registry has been created by downloading data from databases such as Medline and EMBASE. The basic method of searching a database is to use what are known as keywords. Each record on the database is identified by a set of keywords which describe the type of article. For example, a study on relaxing imagery for childbirth, might have the keywords 'relaxation techniques'; 'labor', 'pain' and 'randomized controlled trial' Keywords are

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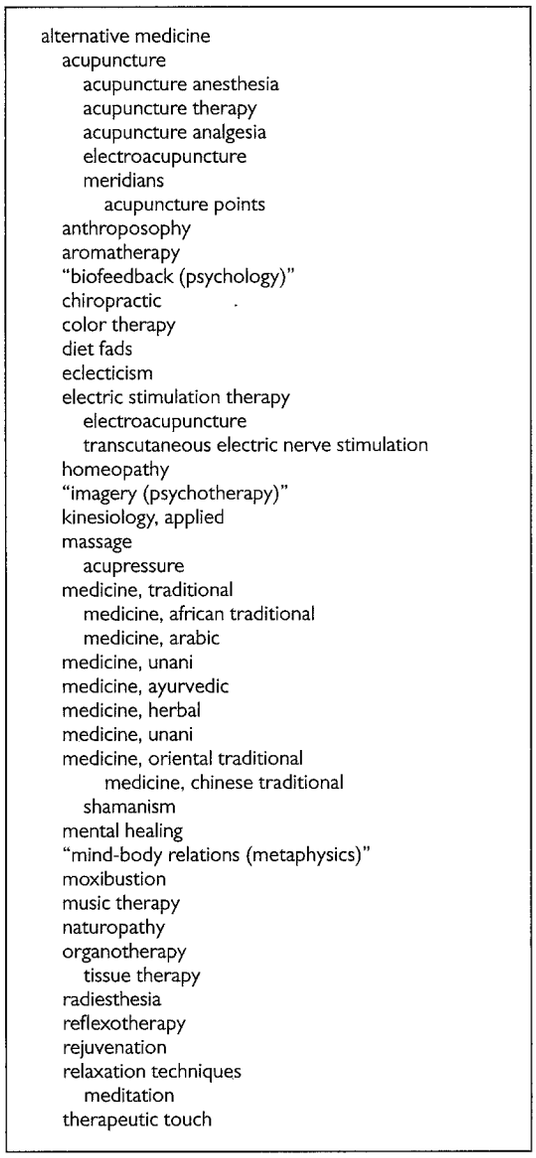

Fig. 1 The alternative medicine tree on Medline

arranged in 'trees'. Each tree is a related group of concepts which become more specific as one moves down the tree (Fig. 1). Records are identified by the most specific keyword possible. For instance, a paper on electric stimulation in acupuncture would be identified by 'electroacupuncture' but not by 'acupuncture' or 'alternative medicine'. One can, however, search all branches of a tree (a technique known as 'exploding') to retrieve all records on a broad topic. As keywording is not always 100% accurate, the searches used by the Cochrane field include searching for particular words in the title or abstracts of papers.

Another important source of RCTs is 'hand-searching.' This is when journals are checked page by page to determine whether they have published any RCTs. Handsearching is the most reliable method of finding RCTs as many such trials are not described as such on databases such as Medline.

In April 1998, the field undertook a bibliometric analysis of the registry. Our questions were as follows:

1) what proportion of CM RCTs are listed on Medline, the world's leading bibliographic database?
2) can CM RCTs on Medline be identified easily?
3) in what types of journal are CM RCTs published?
4) how has the number of CM RCTs changed over the years?
5) which therapies and conditions are most commonly the focus of CM RCTs?.

METHODS

Question 1. CM RCTs and Medline

One of the database fields on the registry specifies the source of the record, for example, the database from which it was downloaded. If the record was not obtained from Medline, extensive attempts are made to double-check whether the record can, in fact, be found on this database. If so, the Medline recorded is downloaded and the duplicate deleted. We searched the registry to count the number of records obtained from Medline to estimate the proportion of CM RCTs which are listed on this database.

Question 2. Identifying CM RCTs on Medline

The way to find CM RCTs on Medline would be to search the entire alternative medicine tree by 'exploding' alternative medicine as a keyword, find all records described as 'randomized controlled trial' in the publication type field and combine the two. All records on the registry list the original Medline keywords and publication type. To answer whether CM RCTs on Medline can be identified easily, we searched the registry for Medline-indexed RCTs which had a keyword in the alternative medicine tree and 'randomized controlled trial' as publication type.

Question 3. Journals publishing CM RCTs

The journals listed on the database were categorised as 'complementary medicine' or 'conventional medicine' by a researcher with good knowledge of the CM literature. For the purposes of this study, trials which were unpublished, or published in conference proceedings and the like, were classed as 'non-periodical publications' which, in turn, was classified as conventional. To determine where CM RCTs are published, we counted the number of complementary and conventional journals publishing RCTs as well as the number of trials published in each.

Question 4. Publication date of CM RCTs

The year of publication of each RCT was identified and grouped into categories of 5 years starting in 1965.

I. NUTRITION
I.I Any form of supplementation with vitamins, minerals or fatty acids to treat or prevent disease apart from:
I.I.I Treatment of deficiency disease (defined as any disease caused by levels of intake of a nutrient which are persistently lower than RDA)
I.I.II prevention of neural tube defects
I.I.III treatment of premature infants
I.I.IV treatment of cancer with b and d vitamin derivatives
I.I.V treatment and prevention of osteoporosis with calcium vitamin D
I.I.VI vitamin e or essential fatty acids to treat dermatological conditions
I.I.VII essential fatty acids to treat or prevent cardiovascular disease
I.I.VIII magnesium supplementation for cardiovascular disease
I.I.IX treatment and prevention of measles using vitamin A
I.I.X prevention of eye disease
I.I.XI prevention of cancer in those not at increased risk
I.I.XII treatment of insulin dependent diabetes mellitus
I.I.XIII treatment of disease in developing countries
I.II Elimination of any food from the diet other than when that food is not thought to cause disease by conventionally understood allergic mechanisms or by raising or reducing levels of an identifiable substance in the body apart from:
I.II.I Treatment or prevention of coeliac disease, ulcer
I.III Adherence to any of following diets: Hay, Dong, macrobiotic, high fibre for weight loss, Cambridge, vegetarian, vegan, "stone age", raw foods, essential fatty acid diet for multiple sclerosis

II PSYCHOLOGICAL INTERVENTIONS
II.I Any form of talking therapy, counselling or social support other than:
II.I.I treatment of any form of mental health problem including problem behaviour (eg. obesity)
II.I.II peer support/self-help groups
II.I.III non-specific social support

III HYDROTHERAPY
III.I Bathing in water in which salts or plant products have been added
III.II Bathing in water chosen because of a high-concentration of salts
III.III Bathing in natural springs and spas
III.IV Bathing in alternatively warm and then cool water or hot air and cool water.
III.V Any of the following: sitz baths, wraps, hydrogalvanic baths, carbon dioxide baths, underwater jet massage, mud packs, hyperthermia.

Fig. 2 Therapies which can sometimes be described as complementary medicine

Question 5. Therapies and conditions for CM RCTs

Each record on the registry is keyworded with at least one specific CM therapy. The therapies listed on the registry include some which constitute a 'grey area' between complementary and conventional medicine. For example, some forms of nutritional medicine are clearly conventional (vitamin C for scurvy); others are more appropriately described as CM (gluten free diet for schizophrenia). Details of these grey areas are given in Figure 2. Searches were conducted on the registry to determine the number of RCTs conducted in each therapy. Keyword searches were also conducted to determine the number of RCTs conducted in a variety of different condition areas. There was some element of double-counting as certain trials involved conditions in more than one area (for example, a trial of relaxation therapy for anxiety in cancer patients).

RESULTS

At the time that the searches were conducted, the registry listed a total of 3774 RCTs of CM interventions. Of these, 3072 (81%) were listed on the Medline database. However, only about a third (34%) of these references have both 'randomized controlled trial' as publication type and a keyword in the alternative medicine tree (Table 1).

Trials were published in a large number of different journals (Table 2). The journals publishing the largest number of trials were the Journal of Manipulative and Physiological Therapeutics; (104); Biofeedback and Self Regulation (70); American Journal of Chinese Medicine (56); American Journal of Acupuncture (36); Forschende Komplementarmedizin (36); International Journal of Clinical & Experimental Hypnosis (32); Complementary Therapies in Medicine (30); Acupuncture in Medicine (26); American Journal of Clinical Hypnosis (25); Alternative Therapies in Health and Medicine (21). This list in some respects reflects the journals which have been handsearched and it may be that there are CM journals yet to be handsearched which contain a significant number of RCTs. One hundred and forty-five studies fitted the category of 'non-periodical publication.' These included dissertations, unpublished reports, conference proceedings and book chapters.

The number of CM RCTs is increasing rapidly, approximately doubling every 5 years (Table 3). There was wide variation in the number of RCTs published in each therapy (Table 4). Details of the number of CM RCTs by condition is given in Table 5.

DISCUSSION

Our finding was that approximately 80% of CM RCTs can be found on Medline contrasts with some

Table 1 Record type on Medline

	Yes	No	%
Randomized controlled trial	2151	921	70%
Keyword in the alternative medicine 'tree'	1641	1431	53%
Randomized trial and alternative medicine keyword	1050	2022	34%

Table 2 Source of CM RCTs

Type of journal	Number of Journals	Number of trials	
Complementary Medicine	60	622	16%
Conventional Medicine	905	3152	84%
Total	965	3774	100%

Table 3 Date of publication

Date	Number	Proportion of total
No date	29	1%
Before 1965	8	0%
65–69	25	1%
70–74	58	2%
75–79	212	6%
80–84	356	9%
85–89	685	18%
90–94	1297	34%
1995–	1104	29%

Table 4 Number of RCTs by therapy

Acupuncture	554
Aromatherapy (but not massage)	47
Biofeedback	305
Electric stimulation therapy	280
Herbal medicine	804
Homeopathy	213
Hypnosis	250
Manipulative Therapies	195
– Osteopathy	18
– Chiropractic	106
– Manipulative therapy not specified	71
Meditation and relaxation techniques	643
Massage	160
Unconventional nutritional techniques	402
Talk therapies	338
Other	217
Number with >1 therapy	634

Table 5 Number of RCTs for various conditions

Anxiety	253
Cardiovascular disorders	501
Fatigue	11
GI disorders	248
Headache/migraine	161
Infection	118
Mental Health	263
Musculoskeletal disorders	386
Neoplasms (cancer)	195
Respiratory disorders	212
Skin disorders	234
Surgery	293
Women's Health	127

previous research. Kleijnen and Knipschild[2] undertook three systematic reviews of controlled trials in CM and calculated the proportion of studies in each which were listed in Medline. They found that only 17%, 36% and 31% of trials were Medline-indexed for reviews on homoeopathy, ascorbic acid for common cold and ginkgo biloba for cerebral insufficiency respectively. The lower sensitivity of these authors' Medline searching compared to the current study may be explained, at least in part, by wider inclusion criteria: Kleijnen and Knipschild included non-randomized trials and it may be that these are more commonly found in non-Medline journals. Support for this view comes from a meta-analysis restricted to RCTs of acupuncture[2] in which 83 of 98 papers were listed on Medline. This is a very similar proportion (81%) to our finding. However, it is likely that the proportion of RCTs on Medline varies depending on the type of trial. For example, Kleijnen and Knipschild[2] reported that whereas almost all (91%) of the best (randomized) studies of ascorbic acid for the common cold were either listed in Medline or cited by Medline-listed papers, only 68% of the better homoeopathy studies could be found in this way.

Our finding that approximately one-third of the CM RCTs on Medline could be located by standard search methods highlights two aspects of Medline which need improving: the identification of RCTs in the 'publication type' field and the keywording of CM. The National Library of Medicine, which produces Medline, is aware that many RCTs on Medline are not described as such and are working with the Cochrane Collaboration to attempt to resolve this problem: the results of Cochrane handsearching activities are being forwarded to the National Library of Medicine to enable the 'retagging' of records as randomised trials.

The difficulties of CM keywording are more complex. CM records are not picked up by searches of the alternative medicine 'tree' for several reasons. Firstly, some keywords, 'hypnosis' or 'drugs, Chinese herbal', for example, do not appear in the alternative medicine tree. Secondly, certain keywords refer to both conventional and

CM interventions. For example, the keyword 'manipulation, orthopedic' is used to describe both spinal manipulation of the type used by chiropractors and fracture reduction as used by orthopaedic surgeons. Thirdly, some papers are not identified by any keyword which could be recognized as CM. Papers on the needling of trigger points, for example, are keyworded by terms such as 'injections' and 'implants, artificial'.

The conditions investigated in CM RCTs is varied. There a large number of trials in musculoskeletal disorders. There is evidence that these conditions are commonly found in patients presenting to CM practitioners. In a retrospective survey of UK acupuncturists, Wadlow[4] found that about one in three presented with musculoskeletal pain. A similar figure was reported by Harris and Pooley[5] in a survey of shiatsu practitioners and in a study of CM in a general practice setting, Paterson[6] reported that 66% of referrals were for musculoskeletal conditions. On the other hand, fatigue, which is reported by 38% of shiatsu patients[5] and is the presenting condition for 7% of acupuncture patients appears relatively under-researched. The high number of trials in surgery may be explained in terms of the ease of undertaking research in this area. It is easier, say, to recruit 100 patients undergoing minor surgery and measure levels of nausea for 6 hours than to recruit 100 rheumatoid arthritis patients measure levels of pain for 6 months. The number of trials in cardiovascular disease, stroke, hypertension, angina, intermittent claudication, is a surprise, particularly as these disorders do not commonly present in CM clinical practice.[4–6]

The large variation in the number of trials published in different CM therapies is provocative, particularly the disparity between osteopathic and chiropractic research. Over five times as many trials stated 'chiropractic' than 'osteopathy' in the abstract, title or keywords. It is tempting to speculate whether this results from the development of a research infra-structure for chiropractic: specialist research units within chiropractic institutions. The number of trials on herbal medicine may be misleading. Most, perhaps all, trials involved the administration of a single herb, something which does not match the day-to-day practise of medical herbalists. Similarly, many of the aromatherapy trials involved practices, such as the use of mouth rinses with essential oil fractions, not widely used by practitioners. In conclusion, there is evidence that CM RCTs do not provide an accurate reflection of CM clinical practice either with respect to the conditions treated or the therapies employed.

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