

# Complementary and alternative medicine in paediatrics: a systematic overview/synthesis of Cochrane Collaboration reviews

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## Summary

**BACKGROUND:** A high prevalence of complementary and alternative medicine (CAM) use has been documented in children with chronic illnesses. Conversely, evidence-based medicine is considered an important contributor in providing the best quality of care.

**METHODS:** We performed a systematic overview/synthesis of all Cochrane reviews published between 1995 and 2012 in paediatrics that assessed the efficacy, and clinical implications and limitations of CAM use in children. Main outcome variables were: percentage of reviews that concluded that a certain intervention provides a benefit, percentage of reviews that concluded that a certain intervention should not be performed, and percentage of studies that concluded that the current level of evidence is inconclusive.

**RESULTS:** A total of 135 reviews were included – most from the United Kingdom (29/135), Australia (24/135) and China (24/135). Only 5/135 (3.7%) reviews gave a recommendation in favour of a certain intervention; 26/135 (19.4%) issued a conditional positive recommendation, and 9/135 (6.6%) reviews concluded that certain interventions should not be performed. Ninety-five reviews (70.3%) were inconclusive. The proportion of inconclusive reviews increased during three, *a priori*-defined, time intervals (1995–2000: 15/27 [55.6%]; 2001–2006: 33/44 [75%]; and 2007–2012: 47/64 [73.4%]). The three most common criticisms of the quality of the studies included were: more research needed (82/135), low methodological quality (57/135) and small number of study participants (48/135).

**CONCLUSIONS:** Given the disproportionate number of inconclusive reviews, there is an ongoing need for high quality research to assess the potential role of CAM in children. Unless the study of CAM is performed to the same science-based standards as conventional therapies, CAM therapies risk being perpetually marginalised by mainstream medicine.

**Key words:** children; complementary and alternative medicine (CAM); evidence-based medicine (EBM); Cochrane reviews; paediatrics

## Introduction

Complementary and alternative medicine (CAM) refers to a broad range of healing philosophies, approaches and therapies that exist largely outside the institutions where conventional medicine is taught and provided (exclusive definition). An increasing and generally high prevalence of CAM use by children and adolescents with chronic illnesses has been documented in industrialised countries [1–3]. While there are compelling data concerning increasing CAM use in adults, the use of CAM by children is not only less well studied, but also appears to have a considerable prevalence. CAM use by hospitalised children, as well as in outpatient settings, ranges from 1.8% to 84% [4–7]. A recent trial showed prevalence rates between 36% in general paediatrics and 61.9% in children with epilepsy [8]. Herbal medicine, homeopathy, reflexology and acupuncture are among the most popular treatments [9, 10]. The reasons for this high prevalence of use are diverse and might include dissatisfaction with conventional medicine and positive reports from friends and family [11, 12]. Children whose parents use CAM are almost five times more likely to use CAM than children whose parents do not use it [13].

Conversely, over the last two decades, evidence-based medicine (EBM) has substantially changed the approach to patients in clinical practice. EBM has contributed to improving the quality of medicine in general and in paediatrics in particular [14–16]. This development has led to the publication of a growing number of guidelines in the field of paediatrics [17, 18]. Moreover, with the advent and further development of EBM in modern medicine, clear and ambitious requirements for what is considered acceptable evidence have been defined. Today, the gold standard of

EBM is the randomised controlled trial and systematic reviews of randomised controlled trials. The further development and standardisation of EBM – by providing specific tools to assess the level of evidence – is constantly promoted by the Oxford Centre for Evidence-Based Medicine [<http://www.cebm.net/>].

In recent years, efforts have been made to apply rigorous scientific standards to CAM through various initiatives, one of which is the Cochrane CAM Field [[http://www.compmed.umm.edu/cochrane\\_about.asp](http://www.compmed.umm.edu/cochrane_about.asp)]. The Cochrane CAM Field, which was founded in 1996, is dedicated to facilitating the production of systematic reviews of randomised controlled trials in the field of CAM. It is also a member entity of the Cochrane Collaboration. It is noteworthy that a number of Cochrane reviews in the field of CAM [19] have demonstrated a clinical benefit for some aspects of CAM therapy [21].

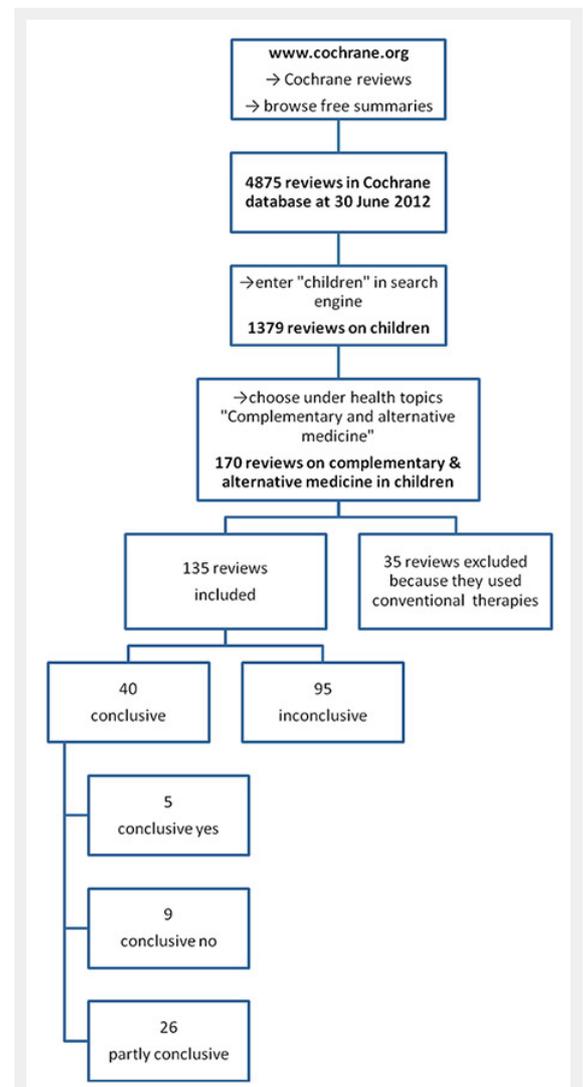
High-quality research and its perpetual critical assessment in accordance with EBM standards is the best way to clarify the role of CAM in the medical arena (diagnosis, therapy, funding, reimbursement, etc.). To date, no formal overview/synopsis of all published systematic Cochrane reviews in the field of CAM in children has been performed for physicians caring for children. Thus, the aim of this study was to provide the reader with a systematic overview/synthesis of Cochrane reviews assessing the efficacy, and the practical implications and limitations of CAM therapies in children.

## Methods and clinical questions

We conducted a systematic literature overview/synopsis including reviews from the Cochrane Review Group (CRG) from 1995 (launch of the Cochrane Database of Systematic Reviews in London by the British Minister for Health) until June 2012 (fig. 1). Initially, all Cochrane reviews in the general field of CAM in children provided by the CRG were screened for potential eligibility (i.e. whether they pertained to the field of CAM), using the operational definition of CAM with the inclusion of dietary supplements as detailed by Wieland and co-workers [22]. Of note, for many of these categories the operationalisation is clear-cut (e.g. any therapy described as ‘homeopathy’ or ‘homeopathic’ would be considered CAM). In some cases, however, the context of the therapy determines whether the therapy itself would be considered CAM or not (e.g. hyperbaric oxygenation is a standard treatment for carbon monoxide poisoning, but is an alternative treatment for

multiple sclerosis) [22]. If then considered pertinent to the field of CAM in children, the reviews were subsequently included in the data synopsis (fig. 1).

The following data were retrieved from the CRG database: (1) date of publication; (2) origin of publication by continent/country (address of corresponding author was used for this purpose); (3) number of included studies/participants; and (4) type of intervention (pharmacological, nonpharmacological, etc.).



**Figure 1**  
Flow chart of study inclusion.

**Table 1:** Characteristics of included reviews with a “positive” recommendation [24–28].

Year of first publication	Continent	Country	Author	Therapy mode	Title	Studies included	Patients included
2004	Asia	China	Anna Lee	Traditional Chinese medicine	Stimulation of the wrist acupuncture point P6 for preventing postoperative nausea and vomiting	40	4,858
2011	Asia	China	Qiukui Hao	Dietary supplements	Probiotics for preventing acute upper respiratory tract infections	14	3,451
2010	Asia	Pakistan	Zohra S Lassi	Dietary supplements	Zinc supplementation for the prevention of pneumonia in children aged 2 months to 59 months	6	7,850
2007	Europe	Germany	Rudolf A Kley	Dietary supplements	Creatine for treating muscle disorders	14	364
1998	Africa	South Africa	G Justus Hofmeyr	Dietary supplements	Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems	13	15,730



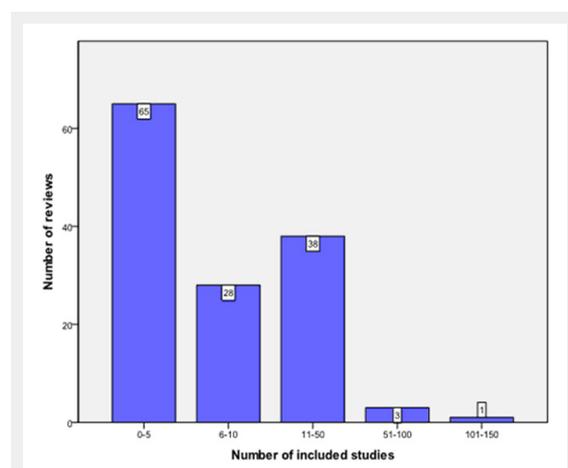
sidered eligible and 135 reviews were subsequently included (figs 1 and 2). Thirty-five Cochrane reviews were excluded because they dealt with conventional therapies (fig. 1).

The origin of Cochrane reviews by continent was as follows: Europe (45), Asia (40), Australia (26), North America (16) and Africa (8). Figure 3 depicts the country of origin of the included reviews. A wide range in the number of included studies/patients was noticed (fig. 4). Eighty-six reviews assessed dietary supplements; other fields included traditional Chinese medicine (16/135), physical therapy (12/135), and various other forms of CAM (figs 5 and 6). Only 5/135 (3.7%) reviews gave a clear recommendation in favour of a certain intervention (table 1 [24–28]), 26/135 (19.4%) issued a conditional positive recommendation, while 9/135 (6.6%) reviews concluded that certain interventions should not be performed (table 2 [29–37]). Ninety-five reviews (70.3%) were inconclusive. Conclusive reviews were significantly associated with the number of included studies ( $p < 0.01$ ; table 3). The proportion of inconclusive reviews increased during three, *a priori*-defined, time intervals (1995–2000: 15/27 [55.6%]; 2001–2006: 33/44 [75%]; and 2007–2012: 47/64 [73.4%]). The three most common criticisms with regard to quality of the included studies were: more research needed (82/135), low methodological quality (57/135) and small number of study participants (48/135; fig. 7).

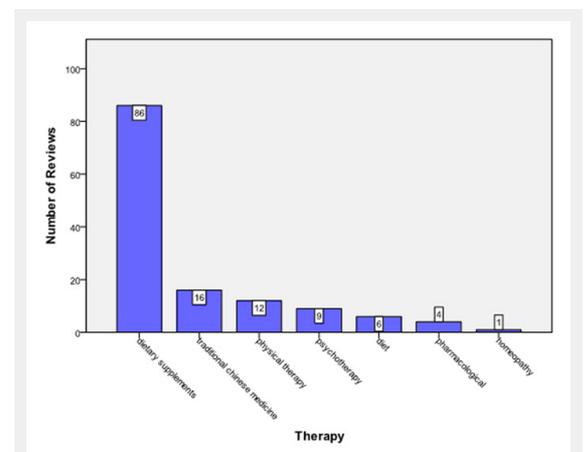
### Discussion

The results of our study do not provide consistent evidence to suggest that CAM is effective for a variety of paediatric conditions. In our study, only a minority of systematic re-

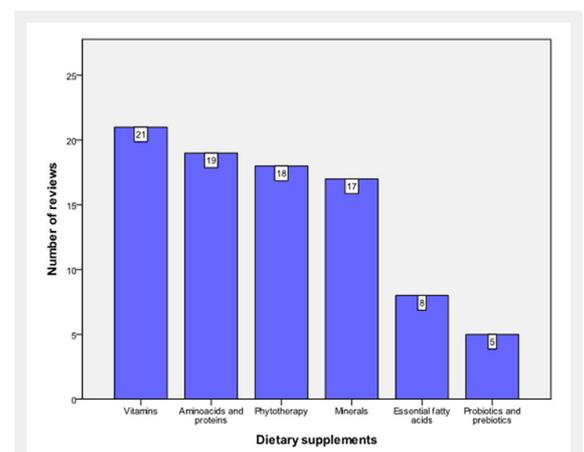
views provided data to answer the question as to whether a certain intervention should or should not be performed (5 positive, 9 negative, 26 partly conclusive). The results of these reviews will provide the physician at the bedside with invaluable information about both optimal and unnecessary or potentially harmful treatment modalities, as detailed in table 1 and table 2. Moreover, and of note, our study also demonstrated that by far the largest proportion of systematic Cochrane reviews were inconclusive (95/135), and failed to provide any recommendation with regard to a specific intervention / clinical question. In fact, previous reports have also demonstrated that for some conditions, CAM seems to worsen symptoms (e.g. in children with stridor treated with acupuncture [38]).



**Figure 4**  
Number of studies included in Cochrane reviews.



**Figure 5**  
Types of intervention assessed in Cochrane reviews.



**Figure 6**  
Types of dietary supplements assessed in Cochrane reviews.

		Number of included studies			
		0–10	11–150	Total	
Recommendation:	Conclusive	Number	17	23	40
		% of total number	12.6%	17.0%	29.6%
	Inconclusive	Number	76	19	95
		% of total number	56.3%	14.1%	70.4%
Total		Number	93	42	135
		% of total number	68.9%	31.1%	100.0%

The disproportionately high number of inconclusive reviews, when compared with other paediatric subspecialties [39, 40], strongly emphasises that CAM needs to undergo the same rigorous evaluation process with standardised techniques as conventional medicine (i.e. randomised controlled trials), in order to substantiate scientifically its role in modern medicine [2]. Inconclusive reviews usually conclude that, after an extensive literature search and appraisal, “insufficient trial evidence was found to guide clinical practice”. One possible and important way to increase research quality and overcome common reasons for failure to generate specific recommendations (most importantly low number of study participants) will be the formation of national and international research networks.

Although defining clinical uncertainty and thereby generating new research questions is a fundamental driving force for EBM, clinicians at the bedside will find this frustrating and unhelpful. However, by identifying important gaps in the evidence, Cochrane reviews have the potential to promote high-quality randomised controlled trials in the field of CAM (as has been demonstrated in other fields of medicine, e.g. collaborative quality improvement initiatives such as the WOMBAT collaboration in Australasia (see: <http://www.wombatcollaboration.net/>) [41, 42]).

If the above outlined approach is bound to be successful, one would expect an increasing number of high quality (and probably conclusive) reviews that are based on sophisticated research data. However, the number of inconclusive reviews over the 18-year study period increased (from 15/27 [55.6%] to 33/44 [75%], and finally to 47/64 [73.4%]; a relative increase from 1995 to 2012 of 32.3%). Interestingly, a positive association was seen between the number of included studies/reviews and conclusiveness, which is line with reports from other specialities (surgery) [43].

It is also noteworthy that the vast majority of reviews published in the CRG database originate from western, industrialised countries (fig. 2), with the largest proportion of Cochrane reviews originating from the United Kingdom. Thus, the recommendations issued in these reviews are most applicable to the field of CAM as practised in industrialised countries, and will only in part be useful for the majority of children being cared for in the developing world. The substantial proportion of reviews from the United Kingdom may in part be attributed to the fact that

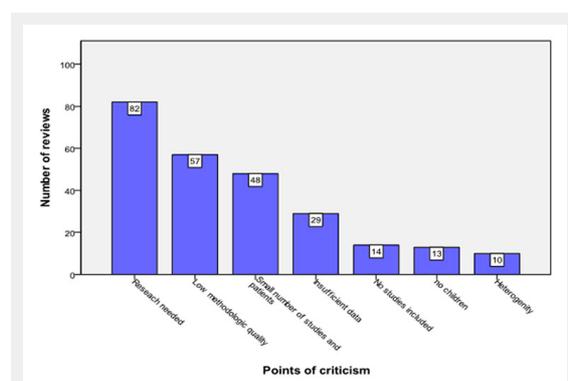
the Centre for Evidence-Based Medicine is located in Oxford, England, and that the use of EBM plays an important role in the provision of healthcare in the United Kingdom. However, other underlying factors – both political and administrative ones – related to the British National Health Service may also contribute to this phenomenon.

Also of note, the majority of reviews evaluated interventions assessing “dietary supplements”. This may in part be attributable to the fact that large randomised controlled trials require adequate funding, which in many circumstances can best be provided by pharmaceutical companies. Importantly, recent research by the Cochrane collaboration has demonstrated that results of drug and device studies may be distorted through sponsorship by manufacturing and pharmaceutical companies (i.e. more favourable results and conclusions than with sponsorship by other sources) [44]. Other inventions in the field of CAM that may merit critical assessment in a randomised clinical trial may not find adequate sponsorship. Therefore, adequate funding from independent organisations will be vital to tackle and solve this issue.

Given the limited financial and human resources that are nowadays available in the medical arena, future emphasis must be on conditions for which new treatment modalities would have an important impact on the health system, children, families and healthcare workers. While some therapeutic modalities, such as homeopathy and reiki, are based on beliefs that lie outside the scope of science and may lack scientific plausibility [45], it is noteworthy that lack of scientific plausibility is not always and necessarily equivalent to a lack of efficacy. Moreover, it is important to take into consideration the clinical context of using certain therapies [22]: while vitamin preparations may be considered CAM therapies under certain circumstances, they may represent standard therapy in other clinical situations (vitamin K administration to prevent haemorrhagic events in neonates), they may have profound immunological properties (probiotics), or may be characterised as strong growth factors (vitamin A for lung development) [46].

It will be important that future research addresses safety issues, as well as assessing effectiveness of CAM in children. This is of great importance since CAM is commonly considered by its users as a safe medical method, and this contributes to its widespread prevalence. Therefore, prior to issuing recommendations for or against the use of some CAM in children, more rigorous testing of therapies using standardised techniques and systematic reporting of adverse events in practice and research needs to be put in place [47], as is the case for conventional medicine [48]. For children, this is a particularly relevant because they are unable to give informed consent to treatment, and therefore rely upon appropriate decisions about their care being made on their behalf [38].

Of note, adverse events with CAM may extend beyond the actual treatments themselves. It has been demonstrated that children who consult naturopathy and chiropractic practitioners are significantly less likely to receive the recommended vaccinations and are significantly more likely to suffer from a vaccine-preventable disease [49]. Also, the use of CAM products may lead to unintentional household



**Figure 7**

Most common criticisms in Cochrane reviews.

poisoning, although symptoms of toxicity are usually mild [50].

However, it is important to note that some inherent weaknesses may be applicable to our data synopsis. First, Cochrane reviews themselves may be at risk of suffering from major weaknesses with regard to both clinical relevance (e.g. inclusion of primary trials that do not reflect clinical or “best” practice) and biased data [19, 51].

Second, a further possible shortcoming of our study was that we did not include data from sources other than the Cochrane database (e.g. randomised controlled trials and meta-analyses published in another form in the medical literature), thus possibly failing to provide a larger perspective on the current status of EBM in the field of CAM in children. Nevertheless, it is important to note that systematic reviews / meta-analyses as provided by the Cochrane Collaboration are considered to be scientific reports of the highest quality. Moreover, by performing this comprehensive analysis of all relevant Cochrane reviews in this field, we most likely have included the vast majority of all relevant randomised controlled trials. Although we used an up-to-date definition of CAM as provided by Wieland and co-workers [22], this operationalisation cannot be considered to be exhaustive, and will be subject to expansion over time.

In conclusion, based on our findings and in line with previous studies [2, 38], there is a need for more high quality research in children to assess whether there is a potential role for CAM in children. This will probably result in more systematic reviews that will come to clear conclusions (i.e. in favour or against a certain intervention or treatment modality, etc.). Moreover, the use of systematic reviews as provided by the CRG plays an important role in providing and disseminating the best available evidence in the field of CAM, thus contributing to the provision of good medical care at the bedside. The provision of high-quality data on the efficacy of CAM therapies in children will enable the physician to inform both patients and parents about potentially beneficial CAM options, especially if they involve less risk or fewer adverse effects than conventional therapy [21].

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**Authors' contribution:** SM and NS contributed equally to the manuscript. Sascha Meyer and Nicole Schroeder were chief investigators. They were responsible for the study design, data analysis and data synthesis. Sascha Meyer was responsible for writing the manuscript. Ludwig Gortner, Sven Gottschling, Alexander Larsen and Georg Kutschke were involved in data retrieval and data analysis. They contributed to writing the manuscript. Stefan Gräber provided statistical expertise.

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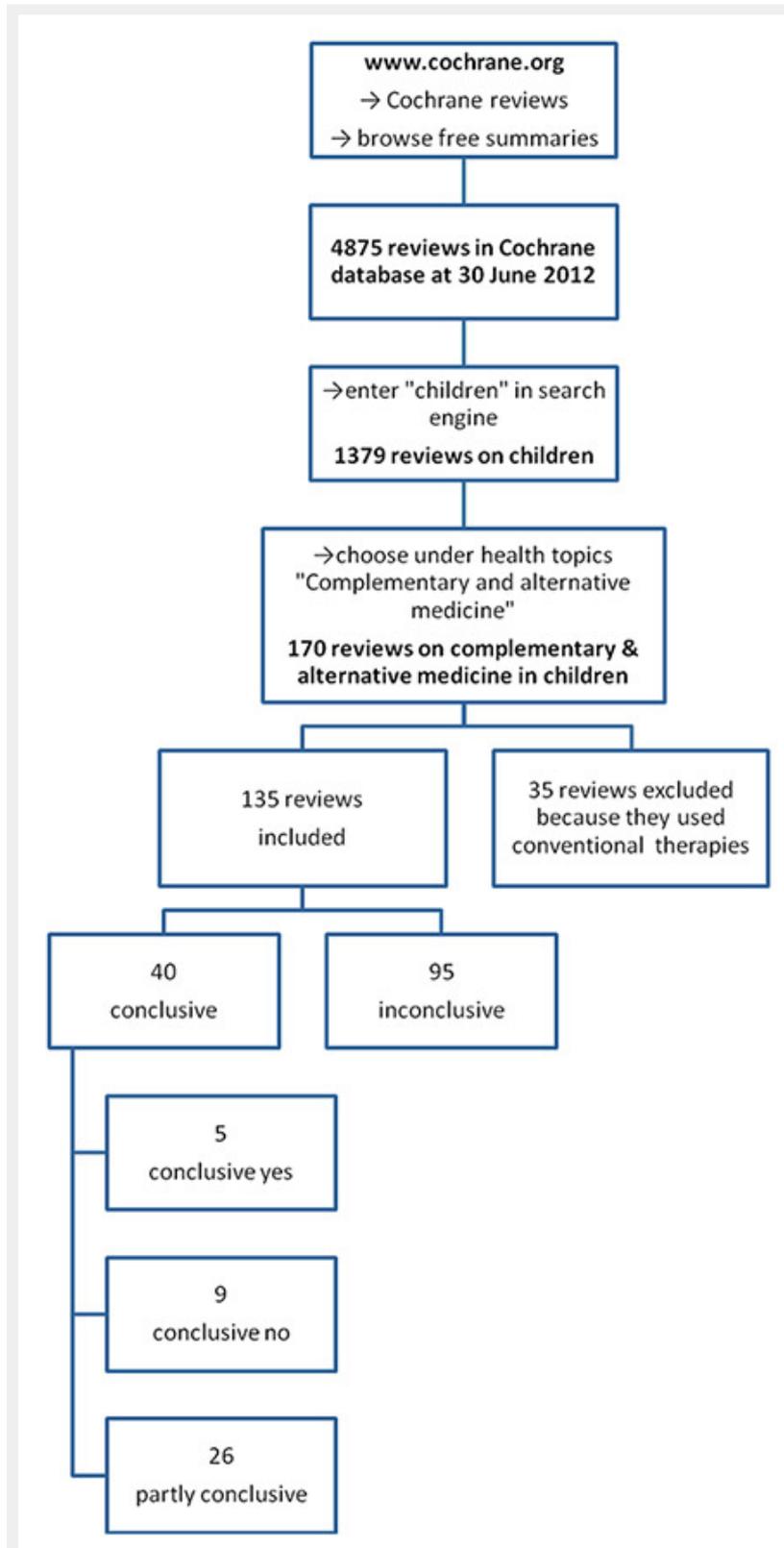
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## Figures (large format)

**Figure 1**

Flow chart of study inclusion.

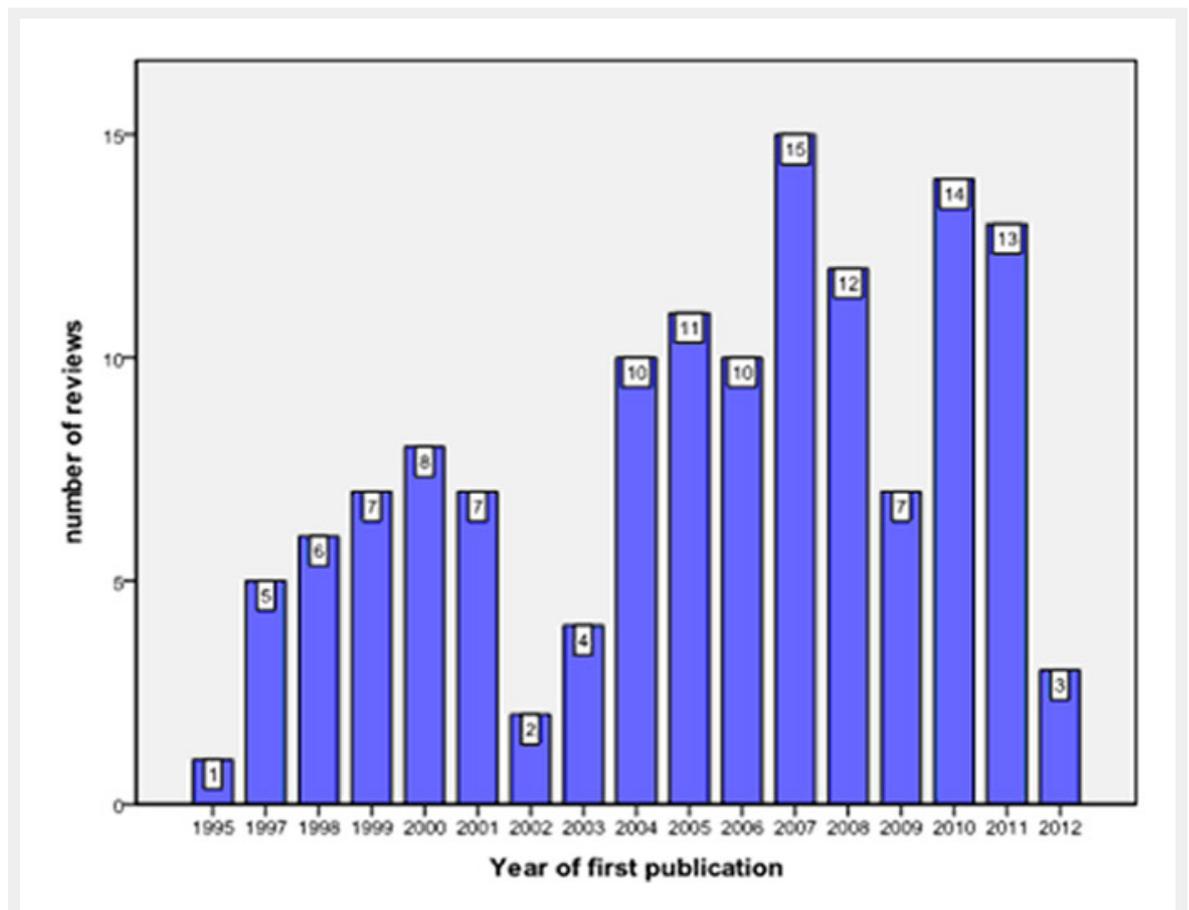
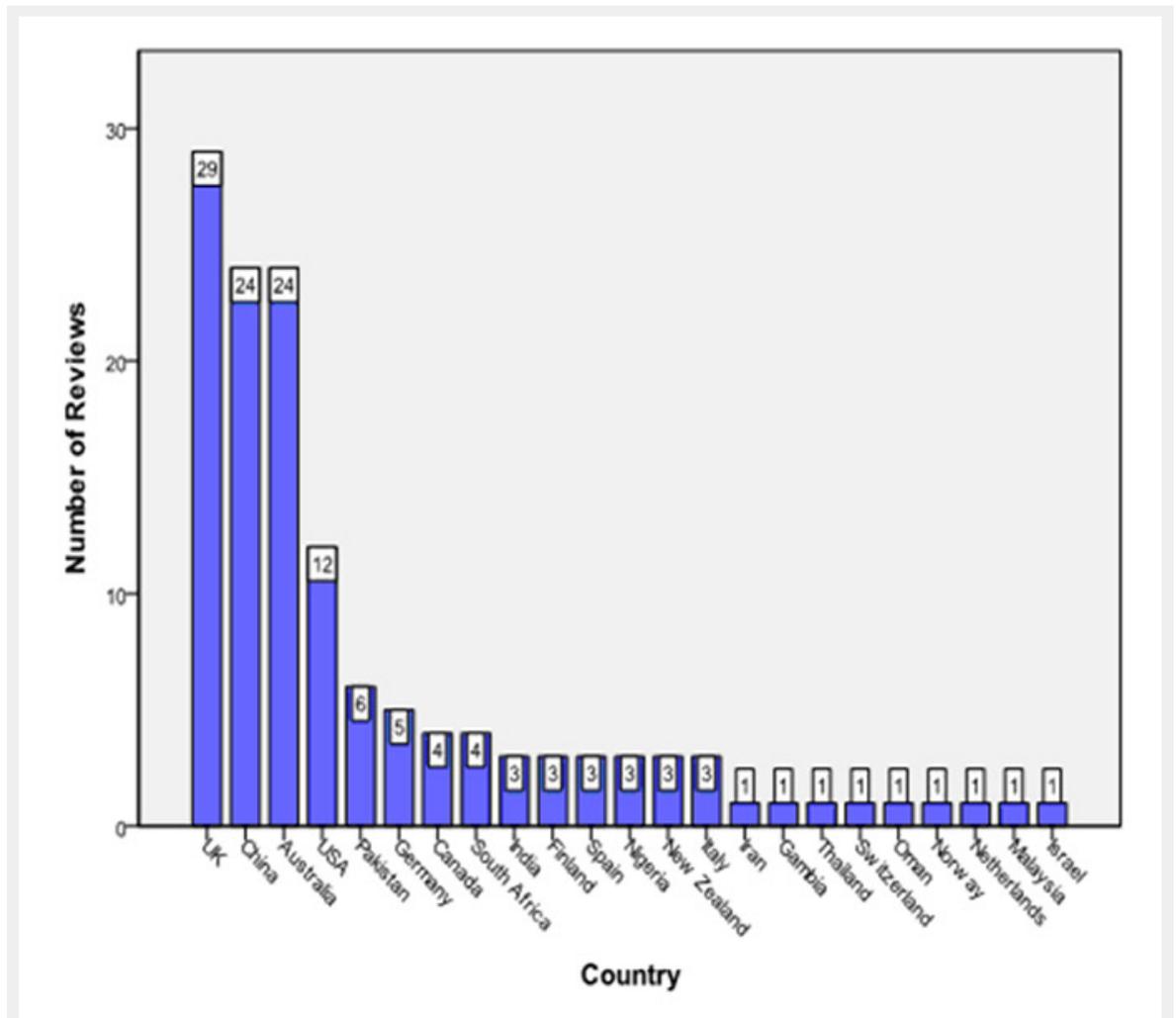
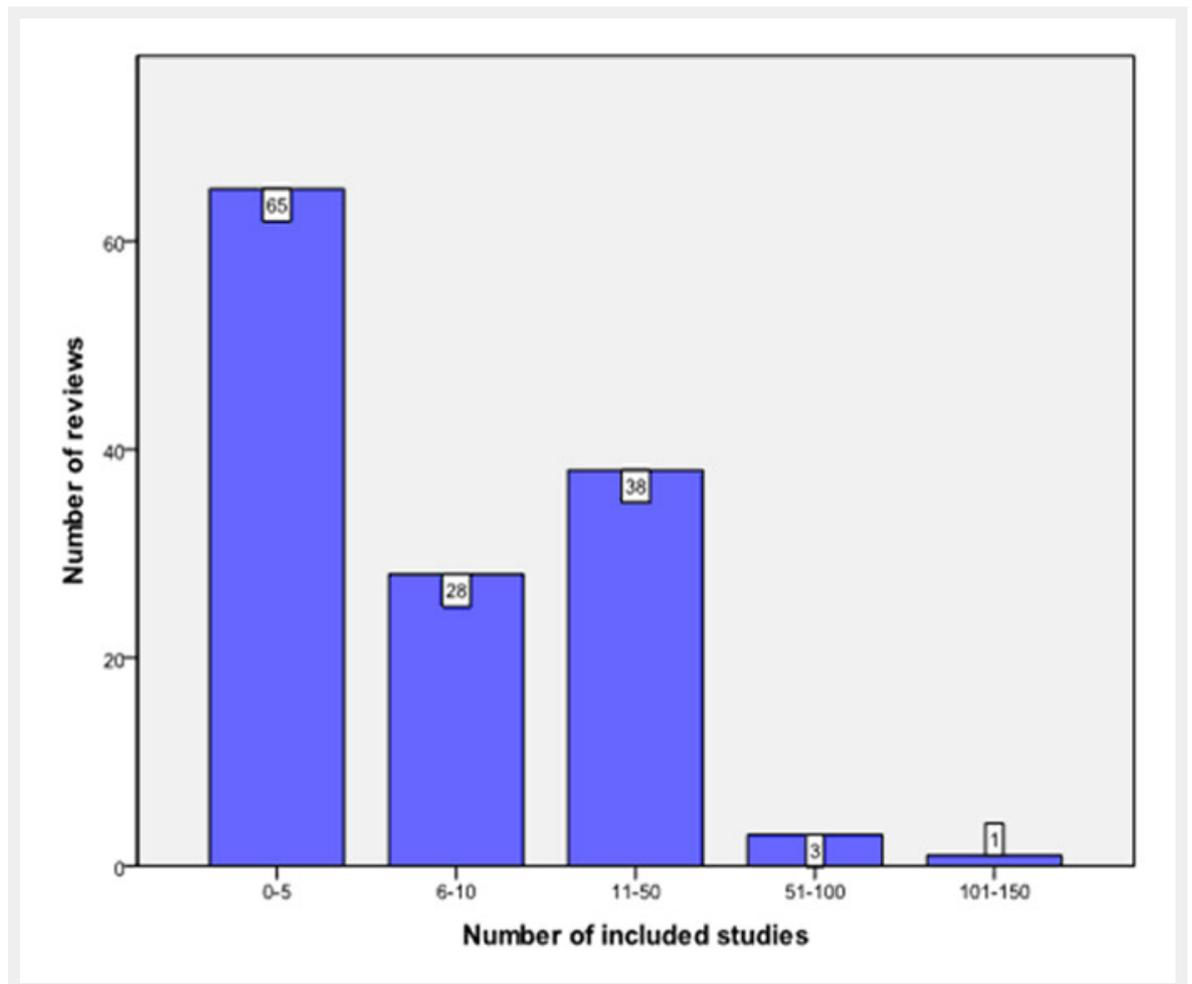


Figure 2

Number of Cochrane reviews published between 1995 and 2012.

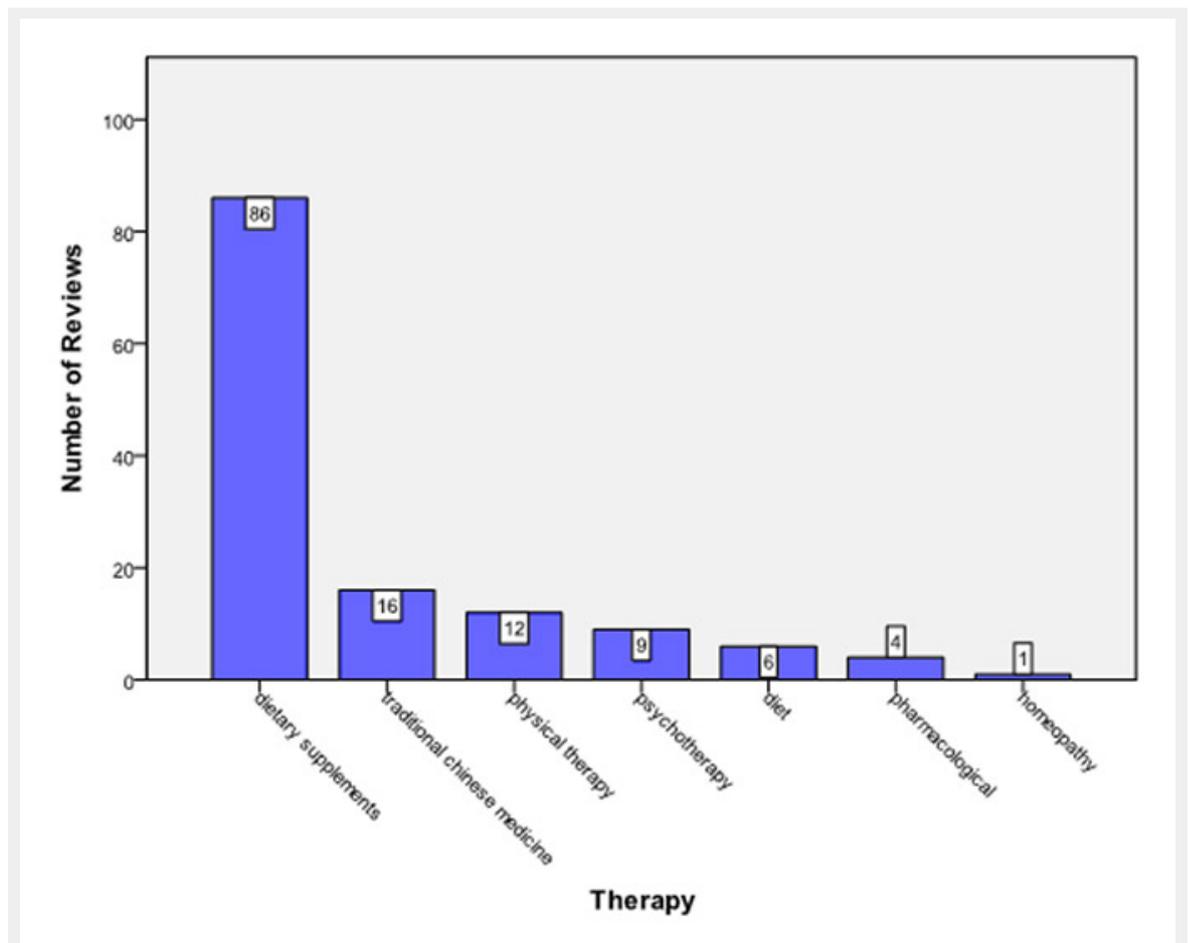


**Figure 3**  
Origin of Cochrane reviews by country.

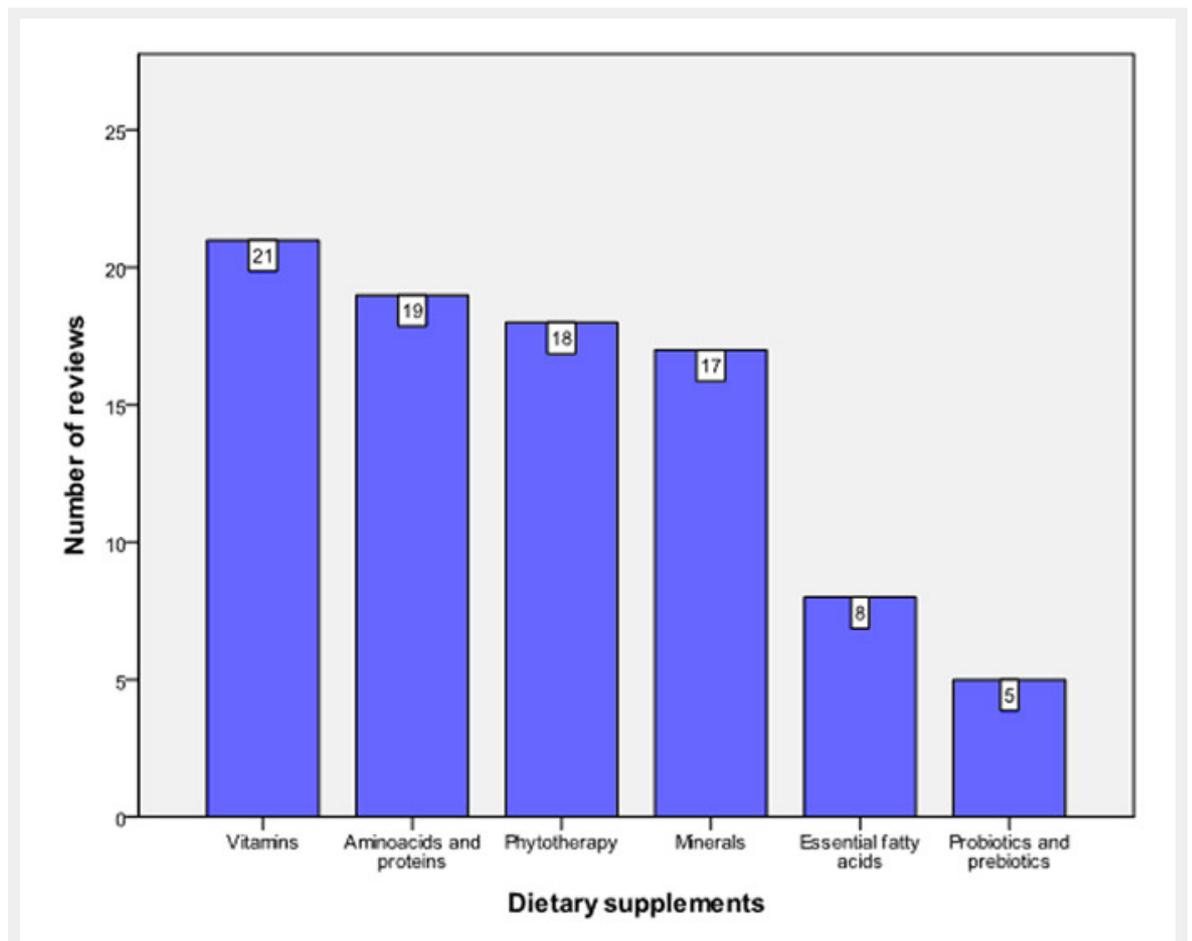


**Figure 4**

Number of studies included in Cochrane reviews.

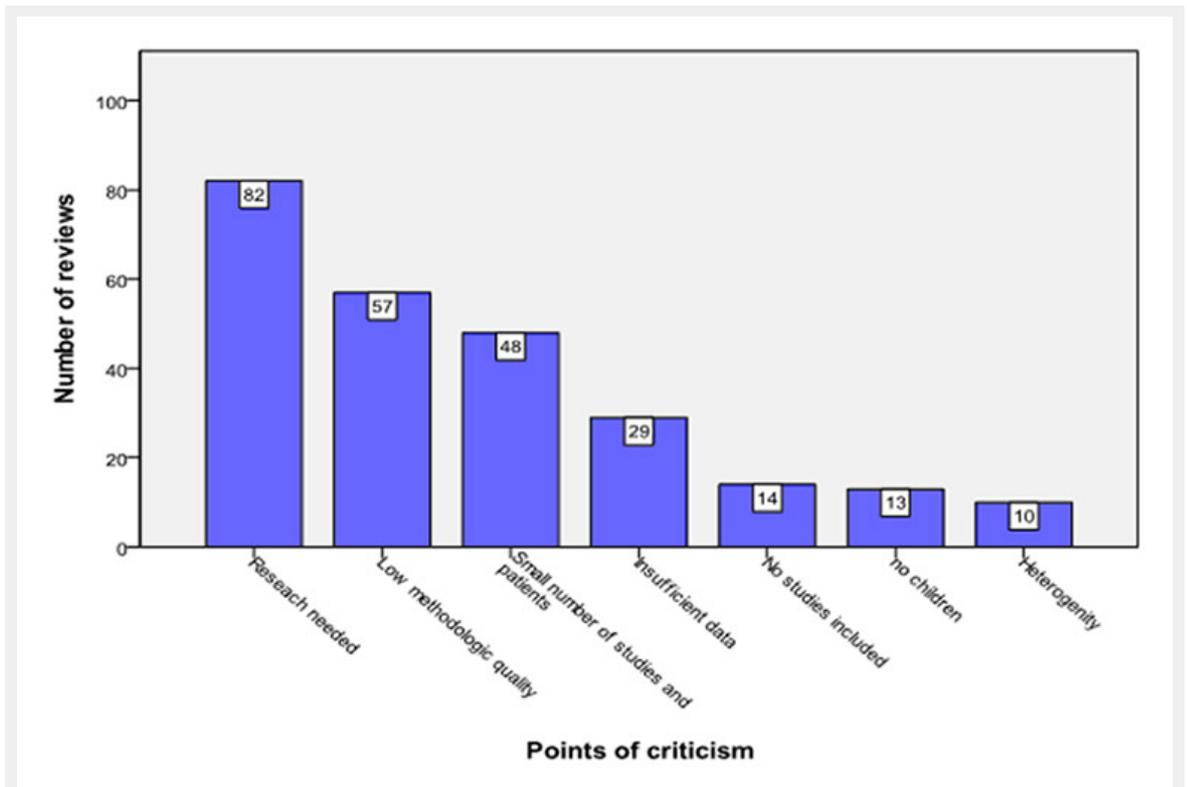


**Figure 5**  
Types of intervention assessed in Cochrane reviews.



**Figure 6**

Types of dietary supplements assessed in Cochrane reviews.



**Figure 7**  
Most common criticisms in Cochrane reviews.