Complementary medicine: Where is the evidence?

Edzard Ernst, MD, PhD, FRCP (Edin.)
Peninsula Medical School, Universities of Exeter and Plymouth, Exeter, UK

Practice recommendations

Herbal medicines have been submitted to systematic reviews more frequently than any other complementary therapy, and it is here where the most positive evidence can be found.

There is not much research into potential serious risks of complementary medicine. Possible risks range from the toxicity of herbs to vertebral artery dissection or nerve damage after chiropractic manipulation.

Currently the Cochrane Library contains 34 systematic reviews of complementary medicine: 20 of herbal medicines, 7 of acupuncture, 3 of homeopathy, 2 of manual therapies, and 2 of other forms.

Complementary or alternative medicine has moved from the fringe of health care toward its center; recent figures show that in Germany, for instance, no less than three quarters of the general population use at least 1 complementary therapy.¹ In the United States, the equivalent figures have increased from 33% in 1990 to 42% in 1997.²

Virtually all survey data agree that those most fascinated with complementary medicine are predominantly female, affluent, middle-aged, and well-educated. Seventy-eight percent of all Medicaid programs provide coverage of at least 1 form of complementary medicine.³

At the same time, critics of complementary medicine often insist there is no good evidence to support these therapies,⁴,⁵ and that it is a waste of resources and a misuse of science to try establishing an evidence base for therapies that are essentially nonscientific, irrational, and implausible fads.⁶ But is this really true?

RESEARCH IN COMPLEMENTARY MEDICINE

Over the last 30 years, the level of original research activity in complementary medicine has increased considerably.⁷ The best quality of
## TABLE

### Cochrane reviews in complementary medicine with (tentatively) positive results

<table>
<thead>
<tr>
<th>First author (primary studies)*</th>
<th>Therapy</th>
<th>Indication</th>
<th>Reservations*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furlan (8)</td>
<td>Massage</td>
<td>Low back pain</td>
<td>More studies required, some trials of poor quality</td>
</tr>
<tr>
<td>Green (4)</td>
<td>Acupuncture</td>
<td>Lateral elbow pain</td>
<td>More studies required, most trials of poor quality</td>
</tr>
<tr>
<td>Linde (7)</td>
<td>Acupuncture</td>
<td>Asthma</td>
<td>Evidence only positive for peak expiratory flow rate, effect size small</td>
</tr>
<tr>
<td>Linde (27)</td>
<td>St John’s wort (Hypericum perforatum)†</td>
<td>Depression</td>
<td>Some trials of poor quality, few equivalence studies</td>
</tr>
<tr>
<td>Little (11)</td>
<td>Various herbal medicines</td>
<td>Rheumatoid arthritis</td>
<td>More studies required, some trials of poor quality</td>
</tr>
<tr>
<td>Little (5)</td>
<td>Various herbal medicines</td>
<td>Osteoarthritis</td>
<td>More studies required, some trials of poor quality</td>
</tr>
<tr>
<td>Melchart (26)</td>
<td>Acupuncture</td>
<td>Headache</td>
<td>Evidence positive only for migraine headaches, effect size small</td>
</tr>
<tr>
<td>Pittler (7)</td>
<td>Kava (Piper methysticum)†</td>
<td>Anxiety</td>
<td>Concern over safety</td>
</tr>
<tr>
<td>Pittler (13)</td>
<td>Horse chestnut (Aesculus hippocastanum)†</td>
<td>Chronic venous insufficiency</td>
<td>Scarcity of long-term studies</td>
</tr>
<tr>
<td>Pittler (4)</td>
<td>Feverfew (Tanacetum parthenium)†</td>
<td>Migraine prevention</td>
<td>More studies required, effect size small</td>
</tr>
<tr>
<td>Pittler (2)</td>
<td>Globe artichoke (Cynara scolymus)†</td>
<td>Hypercholesterolemia</td>
<td>More studies required effect size small</td>
</tr>
<tr>
<td>Vickers (7)</td>
<td>Oscillococcinum</td>
<td>Influenza</td>
<td>More studies required, effect size small</td>
</tr>
<tr>
<td>Wilt (21)</td>
<td>Saw palmetto (Serenoa repens)†</td>
<td>Benign prostate hypertrophy</td>
<td>Effect size moderate, scarcity of long-term studies</td>
</tr>
<tr>
<td>Wilt (18)</td>
<td>African prune (Pygeum africanum)†</td>
<td>Benign prostate hypertrophy</td>
<td>Scarcity of long-term studies</td>
</tr>
<tr>
<td>Wilt (4)</td>
<td>Cernilton†</td>
<td>Benign prostate hypertrophy</td>
<td>More studies required, scarcity of long-term trials</td>
</tr>
<tr>
<td>Wilt (4)</td>
<td>Beta-sitosterols†</td>
<td>Benign prostate hypertrophy</td>
<td>More studies required, scarcity of long-term trials</td>
</tr>
</tbody>
</table>

All data extracted from The Cochrane Library, 2003. “More studies required” means that volume of data was small; “trials of poor quality” means that the average quality of the evidence was lowered by flawed studies; “effect size” describes the difference in clinical response to active and control treatment.

*As expressed by authors of respective review.
†Plant-based treatments.
Herbal medicines are submitted for more systematic reviews and have the most positive evidence for or against the effectiveness of any therapy is usually provided by Cochrane reviews.\textsuperscript{8,9}

**Cochrane reviews**

Currently the Cochrane Library contains 34 systematic reviews and 35 protocols of complementary medicine\textsuperscript{10} (depending on what one considers complementary/alternative and what mainstream, this figure might vary marginally). Twenty of the reviews are of herbal medicines, 7 of acupuncture, 3 of homeopathy, 2 of manual therapies, and 2 of other forms of complementary medicine. Twelve reviews include a meta-analytic approach.

The 34 reviews comprise a total of 286 clinical, mostly randomized and often placebo-controlled, double-blind studies. In 1999, the Cochrane Library listed more than 4000 controlled trials of complementary medicine and a further 4000 awaited assessment.\textsuperscript{11}

The single largest Cochrane review of complementary medicine is a meta-analysis of randomized clinical trials of St John’s wort for depression, based on 27 primary studies with a total of 2291 patients.\textsuperscript{12} Seven of the 34 Cochrane reviews are “negative”—ie, do not suggest a positive clinical effect of the intervention under evaluation. Eleven are entirely inconclusive and 16 draw at least tentatively positive conclusions (Table). Given the dire funding situation for research in complementary medicine,\textsuperscript{13} this evidence base is remarkable.

**Other reviews**

The Cochrane database may be the best but certainly is not the only source of systematic reviews of complementary medicine. My unit has published about 100 systematic reviews (a full list is available from the author), and most were not in the Cochrane format.

Linde and Willich have analyzed selected systematic reviews of acupuncture, homeopathy, and herbal medicine, and have shown that their methodological approach differed considerably.\textsuperscript{14}

**METHODS OF REVIEWING COMPLEMENTARY MEDICINE**

The conclusions of these methodologically diverse articles were still surprisingly consistent.\textsuperscript{15} Some maintain that complementary medicine cannot be evidence-based in the conventional sense of the word\textsuperscript{16}; that “softer” types of evidence need to be taken into consideration as well\textsuperscript{17}; that placebo effects must not be dismissed as nonbeneficial\textsuperscript{18}; that the healing encounter includes significant factors that may never be quantifiable\textsuperscript{19}; that “the scientific method cannot measure hope, divine intervention, or the power of belief.”\textsuperscript{20}

And, obviously, research in complementary medicine “must consider social, cultural, political, and economic contexts.”\textsuperscript{21}

The debate about what constitutes the best research methods for complementary medicine has been going on for decades. There are no simple answers except that, like in any type of scientific inquiry, there are no intrinsically good or bad methods, only good and bad matches between the research question posed and the methodology employed.\textsuperscript{22}

Herbal medicines have been submitted to systematic reviews more frequently than any other complementary therapy, and it is in this area where most of the positive evidence can be found (also outside Cochrane reviews).\textsuperscript{23}

The medical conditions treated with complementary medicine are often chronic benign diseases for which existing conventional treatments fail to offer a cure or a risk-free reduction of symptoms (Table). Given the popularity of complementary medicine and the economic importance of these conditions, it
seems ill-conceived to argue against further research in this area.\textsuperscript{6}

Firm conclusions of the Cochrane (or other) reviews of complementary medicine are often hampered by the paucity of primary studies; 10 of the 16 reviews in Table are based on fewer than 10 primary studies. The average methodological quality of the primary data is in some but by no means all disappointing.\textsuperscript{24–26}

**Problems in testing complementary medicine**

There is little doubt that rigorous trials of complementary medicine can pose formidable problems.\textsuperscript{22} What, for instance, is an adequate placebo for a study of massage therapy, and how should one blind patients in such a trial? The biggest obstacle to good research is perhaps the notorious lack of research funding in this area, which is all the more acute because costs can be particularly high for trials of time-intensive forms of complementary medicine.\textsuperscript{13}

The average size of the overall therapeutic effect associated with complementary medicine is usually modest and the numbers needed to treat are often high. In other words, the difference between benefit from complementary medicine and no therapy or placebo may be statistically significant but critics might argue that it is of debatable clinical relevance.\textsuperscript{5} Even minor adverse effects would therefore critically disturb the delicate balance of risk and benefit.\textsuperscript{23}

**Assessing the risks**

It follows that the potential risks of complementary medicine require careful attention and more systematic study. Our fragmentary knowledge indicates that the issues are complex.\textsuperscript{27} They range from toxicity of herbs to vertebral artery dissection or nerve damage after chiropractic manipulation.

They also include more subtle indirect hazards. Some practitioners of complementary medicine, for instance, tend to advise their clients against employing important medical interventions.\textsuperscript{28} At present there are no reliable incident figures regarding serious adverse effects of complementary medicine,\textsuperscript{5,23,27} rendering this area perhaps the most urgent topic for further research.

**Moving forward**

At a time when healthcare systems universally are strapped for money, the decision whether to integrate complementary medicine into routine medicine will undoubtedly be influenced by economic considerations. Virtually all research on this issue is inconclusive or flawed or both.\textsuperscript{29} We therefore cannot be sure whether such an integration would save public funds or cost extra money.

In the US, about 41 million people have no health insurance and are thus not covered for even the most basic health care. About the same number of Americans are underinsured. In this situation, it seems difficult to argue without convincing data that the integration of complementary medicine would present a solution to the economic problems in healthcare.

In conclusion, during recent years the evidence in support of complementary medicine has been considerably strengthened, primarily through numerous Cochrane reviews\textsuperscript{10} and other documents.\textsuperscript{7,23,30} A large range of promising interventions could be at our fingertips. At a time when whole populations are voting with their feet in favor of complementary medicine,\textsuperscript{1,2} it would be in everyone’s interest to invest in rigorous research of this area.

**References**

1. Institut für Demoskopie Allensbach. Naturheilmittel: Wichtigste Erkenntnisse aus Allensbacher Trendstudien. [Natural cures: The most important conclusions...


