Evidence of effectiveness but not efficacy

- why many complementary therapies are so hard to accept for biomedicine

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"Background and aims"

My impression

• Integration of CAM into health care practice proceeding (at least in most in western industrialized countries)

• Scientific and academic debate on some major therapies heats up again

• Both proponents and adversaries (and those in between) claim their view is based on evidence from randomized clinical trials (RCTs)

My aims for today

• To explore why it is so hard for biomedicine to accept CAM therapies
Evidence from RCTs

• **Efficacy**: evidence of specific effects from placebo-controlled RCTs

• **Effectiveness**: evidence of an overall benefit from RCTs with more naturalistic comparator groups (no treatment, usual care/usual care alone, other treatment)
Overview of my presentation

• The general problem of interpreting evidence (Example: Do homeopathic remedies have clinical effects over placebo)

• The problem of specific effects, placebo, and of the dominance of efficacy over effectiveness

• Summary and conclusions
An attempt to summarize evidence from RCTs on homeopathy with as little interpretation as possible

Efficacy (effects over placebo)
- If you pool all available trials
  - homeopathy > placebo\(^1,3(2)\)
  - better and larger trials tend to yield less positive findings\(^1,2\)
- If analyzed per condition
  - few trials
  - inconsistent results\(^1,4\)

Effectiveness
- Few (mostly small) RCTs available, some evidence from observational studies

Major influences on prior beliefs

Scientific Theory: Low plausibility
Major influences on prior beliefs

- Scientific Theory: Low plausibility
- Practical Experience
Major influences on prior beliefs and Bayes factors

- Scientific Theory/Plausibility
  - Relevance
  - Knowledge
  - Interpretation
  - Systematic Empirical Evidence

- Practical Experience
  - Relevance
  - Kind/Amount of Experience
  - Interpretation
  - World Outlook Theories
  - Conflict of Interests
The evidence for homeopathy

There is a growing body of published research in good quality peer-reviewed journals showing that homeopathy has a positive effect.

This section of the website gives you a straightforward introduction to the kinds of evidence that exist for homeopathy and the range of conditions with positive evidence.

More research needed

Homeopathic research is still in its infancy. The body of
There is no scientific case for homeopathy: the debate is over

Edzard Ernst

Pharmacists who sell homeopathic remedies as anything other than placebos are putting their customers' health at risk.
We have to accept that different groups interpret evidence on controversial topics very differently (unless it is really unequivocal (???)).

Is it likely that further placebo-controlled trials or meta-analyses of such trials will settle the debate???
Overview of my presentation

• The general problem of interpreting evidence
  (Example: Do homeopathic remedies have clinical effects over placebo)

• The problem of specific effects, placebo, and of the dominance of efficacy
  over effectiveness

• Summary and conclusions
Legitimization (medical profession)

Why do we allow a physician to

• ask us to take off our clothes (coercion)?

• to stick needles into our body or even cut out an organ (bodily injury)?
Legitimization (medical professions)

Our situation

- We feel bad or worry about our health
- We cannot solve the problem alone

The physician has expert knowledge and skills and we rely that

- our well-being is primacy
- **what she/he does is the one correct thing to do (functional specificity)**
- she/he acts in affectively neutral

Therapeutic ideal: act only when necessary and with specific therapies

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1 Parsons T. The Social System. The Case of Modern Medical Practice. 1964
2 Comaroff J. Sociol Rev 1976;24:79-96
How biomedicine ensures functional specificity

- Scientific Theory/Plausibility
- Systematic Empirical Evidence
How biomedicine ensures functional specificity

- Scientific Theory/Plausibility
- Systematic Empirical Evidence

- Practical Experience

Academic and professional authority and power
In routine practice positive practical experience is often sufficient evidence of specific effects for the patient and the doctor.

But things get problematic:
- on the professional level
- when public money is spent
- when there are safety concerns

And much of conventional medicine not based on solid trial evidence has more scientific plausibility and more academic authority/power.
Why is the request stronger in case of CAM?

Controversial Theory/Low Plausibility

The lower the plausibility, the more need of strong evidence for efficacy (specific effects over placebo)
Beware of the placebo trap!!!

Placebo-controlled trials investigate whether the postulated mechanism of action makes a clinical difference! They directly link (scientific) theory and empirical evidence! If the mechanism is not fully clear, defining an adequate placebo is impossible!
Low back pain and sciatica in over 16s: assessment and management (2016)

https://www.nice.org.uk/guidance/ng59
• Acupuncture had the most robust evidence for effects over usual care (effectiveness)
• It was the only non-drug therapy which had any reasonable evidence of effects over sham (efficacy/specific effects)!!!! But the size of these effects was below the pre-defined threshold for clinical relevance

https://www.nice.org.uk/guidance/ng59
The GDG first discussed the necessity of a body of evidence to show specific intervention effects, that is, over and above any contextual or placebo effects. It was therefore agreed that if placebo-controlled evidence (or sham acupuncture) is available, this should inform decision making in preference to contextual effects, but that the effect sizes compared with usual care would be important to consider if effectiveness relative to placebo, or sham, has been demonstrated. This approach is consistent with that taken in the recent osteoarthritis NICE guideline.

https://www.nice.org.uk/guidance/ng59
The logic (???) of the GDG

• If there is placebo-controlled(???) evidence (efficacy) ignore evidence over usual care (effectiveness - where specific and „contextual“ effects cannot be separated)

Actually there WAS evidence of specific effects, but there were too small

![Diagram showing the comparison between Acupuncture and Placebo (Sham) vs. Usual Care in terms of specific effect (efficacy) and overall effect (effectiveness).]
The logic (???) of the GDG

• If there is placebo-controlled(???) evidence (efficacy) ignore evidence over usual care (effectiveness - where specific and „contextual“ effects cannot be separated)
  Actually there WAS evidence of specific effects, but there were too small

• If there is no placebo-controlled evidence (efficacy), then evidence of effectiveness is sufficient
Functional specificity is fundamental for legitimate care

BUT

Is the primary goal of health care being science-based or being effective?
Accumulating evidence that the placebo paradox is reality in case of acupuncture. Which treatment would you prefer?

Adapted from Walach. J Alternat Complement Med 2001;7:213
Accumulating evidence „the placebo paradox“ can be real: The example of acupuncture and drugs in migraine prophylaxis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean (SE)</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacological placebo</td>
<td>1.79 (0.08)</td>
<td>[1.55-2.08]</td>
</tr>
<tr>
<td>Sham acupuncture</td>
<td>0.95 (0.17)</td>
<td>[0.68-1.33]</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>0.70 (0.17)</td>
<td>[0.50-0.98]</td>
</tr>
<tr>
<td>No treatment</td>
<td>4.35 (0.37)</td>
<td>[2.10-8.99]</td>
</tr>
</tbody>
</table>

Meissner et al. JAMA Intern Med 2013;173:1941
Linde et al. Cochrane Library 2016
Functional specificity is fundamental
Effectiveness is fundamental

BUT

Many CAM therapies should re-consider the focus of their traditional theories of specific effects…
…because we need a good explanation for this difference!
My time is up .... Summary & Conclusions (I)

• Evidence from RCTs is NOT interpreted in an empty space. It depends on what we/science currently know/believe and what else we consider important.

• Functional specificity is central to legitimizing a therapy. Believing in functional specificity is crucial for a provider! Explaining and showing this remains important for CAM therapies! If you fail this is a problem!

• I think it is ok that more evidence of effectiveness is needed when evidence of efficacy is weak and the plausibility of "specific" effects is low. But how much evidence of effectiveness is then needed????

• While more evidence from RCTs is always nice, the major challenge is on the level of theories.
My time is up .... Summary & Conclusions (II)

• While placebo/sham controls have a role the concept of placebo interventions and placebo effects is often highly misleading and an obstacle to logic thinking.

• In my view quite a number of CAM therapies are quite reductionistic and mechanistic in their theories. Do not commit the same error as biomedicine!

• Apart for mind-body therapies/lifestyle therapies theories in textbooks of CAM therapies rarely reflect the current state in science (neurosciences, psychology, sociology, anthropology, bio-psycho-social model, …). Do not commit the same error as biomedicine!

• Many CAM therapies have components/aspects which are likely to strengthen "placebo/context" – try to include these aspects better into the theories (then, maybe, they are no longer placebo but specific effects)
Thank you for listening!
Thanks to all the many homeopaths, acupuncturists, naturopaths, other CAM people, CAM researchers, skeptics, EBM people, lab researchers, general practitioners for the countless discussions...

Some of the books that strongly influenced my view:
Sociology of Science - B. Latour: Science in Action, 1987; Pandora’s Hope, 1997
An Anthropological Analysis of Medicine - B. Good: Medicine, Rationality and Experience, 1994
Non-specific effects in Psychotherapy - B. Wampold & Z. Imel: The Great Psychotherapy Debate. 2nd ed. 2015
Evolutionary Perspective on Placebo Effects - F. Benedetti: The Patients’ Brain, 2011
Specifics of General Practice - R. Braun: Wissenschaftliches Arbeiten in der Allgemeinmedizin, 1988

Some of the texts that strongly influenced my view:
T. Parsons in The Social System, 1964: Chapter The Case of Modern Medical Practice

Many other articles by Grünbaum, Goodman, Howick, Walach, Hyland, Heusser, and so many others...

If anyone is aware of a good epistemological text on the role of practical experience in natural sciences, please tell me!