The campaign against CAM – a reason to be proud

Harald Walach
Research Professor in Psychology, University of Northampton

Summary

Does the campaign against CAM indicate that powerful factions feel threatened? A complacent CAM world has been slow to collect supporting data, but the waning of big pharma's once unassailable economic and clinical dominance may be a significant motivator for some who oppose integration. With biotech innovation slowing down, and adverse event scandals and research irregularities, users are distrusting flagship revenue-producing medications. As healthcare policy reshapes mainstream medicine we will need to understand the forces ranged against integrated medicine.

I have been involved in research in homeopathy, spiritual healing, CAM and mindfulness for two decades and am currently a research professor in psychology with the University of Northampton. I am President of the International Society for Complementary Medicine Research (www.iscmr.org), course leader of the MSc Transpersonal Psychology at the University of Northampton, editor of Research in Complementary Medicine/Forschende Komplementärmedizin (www.karger.com/fok) and Spirituality and Health International.

It should be obvious to everyone: for at least a few years now, there has been a concerted on-going campaign against complementary and alternative medicine (CAM). At first, it all seemed pretty innocuous: a meta-analysis published in *The Lancet*, claiming homeopathy was no better than placebo.[1] It was heavily criticised on methodological grounds,[2-4] and it contradicted *The Lancet*'s own tough criteria for publishing meta-analyses, but nevertheless, the editor of *The Lancet* proclaimed 'the end of homeopathy'. Then there was a letter (written without its consent on NHS-headed notepaper) calling on the NHS to cease offering CAM interventions such as homeopathy, as they are not 'evidence based'. Articles in the print media and elsewhere began to appear, stating that the NHS should only use evidence based interventions that are scientifically vindicated and that CAM, not being evidence based, should not be publicly supported. The homeopathic hospitals also came under pressure. And following enquiries based on the Freedom of Information Act, made to universities offering CAM courses, an article appeared first in Nature[5], then in the Times Higher Educational Supplement, demanding that those courses should not be taught in UK higher education institutions because CAM is not based on science. In addition, there have been requests for NICE to launch investigations into homeopathy/CAM. And on it goes.

Although homeopathy normally is at its centre, the campaign also extends to other branches of CAM: phytotherapy, osteopathy, acupuncture, spiritual healing and so on. So I think it is useful to stand back and observe what is going on here, and ponder the possible reasons for this backlash, as well as the way forward. I will do this in a series of steps. First, I will argue that part of the problem has to do with a certain complacency in the CAM community itself, and its fondness for being a cuddly counter-culture. But on its own, this is not sufficient explanation. Another reason is that this CAM counter-culture has established itself as an economic force. For CAM has grown stronger than its proponents realise: big enough in fact to have become a threat to the mainstream revenues of big pharma. It is hardly understandable why anyone should bother to campaign against CAM, unless what is happening behind the scenes is in fact not only a scientific debate, but represents a cultural, political, economic and paradigmatic struggle too. Let me point out several features of this process as I see it, and indicate some ways out of this polarised predicament.

CAM as counter-culture

Many doctors who turn to one or other CAM modality are dissatisfied with the restricted view offered by current medical training and paradigmatic understanding[6], which is based on a refined version of biological-mechanical engineering. The mainstream narrative runs like this. The body is a complex machine that functions according to mechanistic laws. We have not understood all of them, but we are on track to understanding them eventually. Meanwhile, we already have a pretty good understanding and are using this knowledge to hone our interventions, eg ever more finely crafted pharmaceutical agents that can target specific receptors and processes that have been identified to play a causal or at least important role in a particular disease process.

Take depression as an example. Biological psychiatry sees it as being due to compromised serotonin transmission; mainly too little serotonergic activity. So, using a little post-modern magic, it sets out to enhance this activity through selective serotonin re-uptake inhibitors (SSRIs). SSRIs exemplify the promise of the future: targeted drugs, developed on the basis of a causal biological theory, and manufactured to a scientifically rigorous standard. So, these drugs are developed, tested in blinded, randomised, placebo controlled studies of sufficient power, and marketed as the way to wipe depression off the planet; at least for those who can afford to buy them. And let us not forget the other side of the equation: those who produce SSRIs and similar drugs make huge profits because, since interventions for long-term conditions are very rarely designed to cure a disease once and for all, they normally have to be taken for a long time, sometimes lifelong. Hence big pharma is very big business indeed. Now, enter another interesting element: while other sectors of the economy thrive mainly on private consumption, pharmaceutical net earnings are largely from public sector money.

CAM doctors and practitioners are people who out of instinct or insight are not satisfied with this mainstream narrative. They feel that human disease is more complex than the breakdown of a complex engine and that human suffering needs a different answer to Prozac.[7,8] Hence, they have shifted to what they see as 'holistic paradigms'. For example, homeopaths claim that all of a patient's symptoms have to be taken into account: acupuncturists and practitioners of traditional Chinese medicine purport to correct imbalances in a patient's system by regulating some mysterious life-force called Chi, which circulates in even more mysterious channels called meridians. In the case of homeopathy, the medications used generally contain no pharmaceutically active agents; in the second, treatment entails needles being stuck into those purported meridians, and taking herbs prescribed according to a diagnostic scheme that to the outsider seems as adventurous and unintelligible as the map to the treasure on Treasure Island. Other therapists have moved on to even more esoteric things: directing Ki, the Japanese little brother of the Chinese Chi, with their hands and thoughts; or tinkering with some deep-seated cell memories by manipulating, so they say, the matrix that holds all life and cells together; or touching and directing gently the pulses of the cerebrospinal fluid, having once learned to palpate its infinitely tiny undulations. Still others claim to talk directly to those in heaven responsible for the mess in a patient's body and to tell them to stop their messing around, and to call in the invisible sweeping brigades to clear out the spiritual litter. The diversity of approaches is as numerous as milestones on the roads through the Roman Empire, yet the theories behind them seem as unrelated as a Pictish warrior would be to a Numidian slave. Arguably, the only common ground between all these CAM approaches is the complexity of their models, their talk of flowing life-forces, and their relative irreconcilability with the mainstream narrative. So together, they form a counter culture to the mainstream narrative.

One could go to great lengths trying to understand why CAM narratives have gained such momentum at the end of the second millennium. One element of any explanation would have to include the fact that the mainstream narrative is defective, especially in chronic diseases.[9,10] Many patients do not experience the benefits promised by biomedicine. Many medications do not work for a lot of people, and in those for whom they do work, deeply unpleasant side effects are the price paid.[11] Often treatments are short-term, getting rid of one problem only to produce another one in its wake. Patients are not stupid. They often realise these problems sooner than doctors too enamoured of their own theories to see the situation as it is. But even the push given by these obvious deficiencies in the mainstream system and its narratives are not enough to explain the rise of CAM. There are also many pull factors. Patients have adopted a more holistic view of the world themselves, incorporating spirituality, ecology, body-mind connections and so on, and are seeking treatments that respect, reflect and ideally work with such a background model.[12] In such a situation, it is easy to create a veritable counter culture. It is then 'them', the stupid, reductionists of the mainstream culture, against 'us', the truly enlightened, insightful, holistic, patient-centred 'complex systems' therapists. It is easy, in such a culture, to start believing one's own ideas, to deposit one's critical mind with the receptionist and bask in patients' gratefulness. Are they not all benefiting from our treatments? We don't really need data to prove this, do we? Everyone can see it. Have we not cured so many difficult diseases that have been unsuccessfully treated by the best mainstream specialists in the fields? And sure enough the word goes around; cured patients tell their neighbours, friends, aunties and parents, and by sheer word of mouth, the clinics are full. What more proof do we want? Patients are voting with their feet. The stamping can be heard in the psychiatrist's office next door, who is wondering why the patient he put on Prozac the other week is now walking out of the homeopath's office, throwing him a slightly irritated and superior smile. The counter-culture created by CAM doctors and practitioners has been very successful. It has grown, patients like it, and

it has even started to produce some research output. But for the most part, CAM has been comparatively complacent. From my own perspective as a researcher, critical reasoning, systematic data collection and documentation, and planning of studies are strengths not uniformly possessed by all in the CAM field. Partly, this is due to the fact that the academic infrastructure which supports such work is largely lacking. Also, there is no immediate gain to be had from such work. And, it has to be said, there is a very subtle, narcissistic haughtiness: 'We are so much better than those mainstream guys. We do not need research: they do. Why should we bother, please, can anyone tell us? Let them come and ask us about our secret!'

The gaps in the CAM database and in the mainstream narrative

On a scientific gut-level type of evidence, CAM is quite successful in open, uncontrolled, general practice. [11,13-18] We do not have many studies, but those which we have demonstrate that roughly 60–70% of all patients visiting CAM doctors say they feel significantly improved after roughly three months. Rarely do we know how that would compare to conventional practice, but the real-world comparative studies which we do have show that some CAM practice is just as good as conventional practice, sometimes better, and often cheaper. There are many studies I would love to see done, which could provide very good gut-level evidence for CAM, which have not been done so far:

- long-term, real-world comparative studies, looking into the follow-up costs and proneness to deteriorations and chronicity in patients treated by diverse CAM modalities and conventional practice
- pragmatic randomised studies in cost-intensive chronic diseases comparing CAM care with conventional care
- longitudinal studies of children and other patients who follow a minimal intervention strategy, sound dietary advice and healthy living, compared with the standard conventional interventionist, could-not-be-bothered and doesn't-really-matter attitude of (bad) GP practice.

No such trials are underway. If they were, it is likely they would have provided the data we now don't have, and which now makes CAM vulnerable to attack.

The gut-level real-world effectiveness of CAM has an older brother: the real-world unsuitability of some major gunships of conventional pharmaceutical wisdom. Although most pharmaceutical interventions have gone through rigorous RCTs and survived (otherwise they would not be on the market), many don't stand the test of time or of real life: patients don't like them because of their side effects; doctors don't like them because they are unpredictable in their efficacy for individual patients; the public purse does not like them because their efficacy is too small compared to their costs (and the danger of the side effects). The latter has been the reason why NICE refused to take any of the newly-developed anti-dementia drugs on to the books for public reimbursement. For examples of the first two reasons let's again look at the classic case: SSRIs. It was with an unprecedented public advertising campaign that SSRIs were hailed as happy pills, the wonder drugs that would wipe out depression and sadness. The perception, even of the educated public, was that at least one problem could now be fixed. But when we look at more recent literature, we find two striking counter-examples. Two meta-analyses, conducted independently but on roughly similar material and with the same intention, have shown that the effects of SSRIs were grossly overstated. [19,20] Not overestimated; overstated. Both meta-analyses had used material that had to be submitted for regulatory purposes to the FDA, but had otherwise been unpublished. Both found that the public image presented by the published data was comparatively favourable, an effect size of roughly $d = 0.7 – 0.9$ of a standard deviation vis-à-vis placebo (such an effect size is a dimensionless measure of a difference between the treated groups and the control groups, in this case of placebo controls, standardised by the common standard deviation: this is why one can express the difference as a proportion of a standard deviation). However, both meta-analyses found that this effect size dropped to $d = 0.3$ standard deviations, once all unpublished studies were taken into account, because of course in the majority of cases the unpublished studies were negative. To put this figure into perspective; NICE has stipulated that in the case of depression an effect worth paying for out of public funds is $d = 0.5$, half a standard deviation. We have conducted a meta-analysis on the effects of mindfulness meditation in health conditions. [21] Control groups in those studies were mostly weak, such as waiting list controls, and we have found a robust effect size of $d = 0.53$. Our distant healing study, where patients with chronic fatigue syndrome received distant healing or had to wait, was also about $d = 0.3$ in effect size between those who received healing and those who had to wait.[22] A third of a standard deviation is really a small effect. It might be important, if the disease is very difficult to treat, or the intervention comparatively cheap. But it is surely too small an effect to be advertised widely as a breakthrough.

The second of the two SSRI meta-analyses made an even more disconcerting point: most of the effects of anti-depressants really are due to the placebo effect, ie the perception and hope of the patient to have received good treatment. Arguably, this is also a major vehicle for therapeutic effects in CAM[23], and my view would be that the best therapist is the one who can produce the strongest placebo effect with the least effort and side effects: for one definition of a placebo effect really is a self-healing response.

So, the emperor really has no clothes, it seems. SSRIs have been denuded of their mythical status. One might now say: well surely this awkward situation with the placebo effect only applies in clinical trials. So to settle the question of what happens in real world practice, the

biggest outcome study in psychiatric history was launched, called the STAR*D trial .[24] It was a complex, non-blinded, non-randomised outcome study that sought to reflect normal practice in a large number of outpatient clinics in the US. The treatment protocol started with a simple SSRI, followed up those patients who did not benefit from it with a more complex, or perhaps a mix of two SSRIs, or an SSRI and an another type of anti-depressant, then moved on stepwise moving from simple and less invasive drugs to more recent and more complicated ones, four steps in all. The results of this very complex and long-winded study can briefly be summarised. After step one 33% experienced a sustained recovery, 33% later relapsed, and 16% of all patients had intolerable side effects. After each further step, the recovery rate became poorer, and the side effects worse. Overall, it was possible to gain a sustained recovery in 43% of all patients, and after the first step, the succeeding three steps taken together could only produce an incremental sustained recovery rate of 6%. Thus, in real life, less than 50% of all depressed patients seeing a psychiatrist will experience a sustained recovery with any one of the modern anti-depressant drugs. (One editor has taken this result as a proof that the current paradigm of biological psychiatry and pharmacological treatment of depression is just plain wrong [25]). At the end of the research paper there is a lengthy (more than one page of small print) conflict of interest statement which I use in my lectures to sensitise students to the problem of financial stakes that the pharmaceutical industry holds in the steering of research, in the forging of paradigms, and in the maintenance of the status quo.

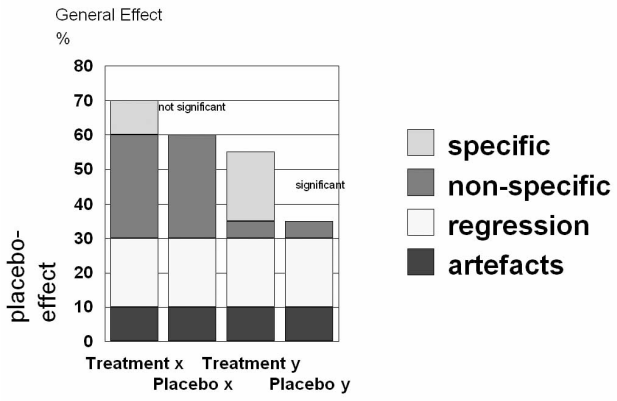
Evidence and the efficacy paradox

So it seems the mainstream narrative is not all that clean, sober or convincing. Yet trusted evidence for efficacy can be shown for all of those medications. In that sense, they are 'evidence based'. But what do we really mean by 'evidence'? Is it a question of whether something is better than placebo in a highly artificial, experimental setting? Or is it a question of whether an intervention is useful, accepted and effective long term in real-life conditions without producing too many side effects? If scrutinised properly, the term 'evidence based' is a battle cry that can mean quite different things to each of the warring sides. Let us make this clear with an example. I have pointed to a paradox, which I call the efficacy paradox .[26,27] This arises, because we normally view efficacy only in terms of a difference between a treatment and a control; normally placebo. If this difference is large enough, in relation to the sample size of a study, we call it significant and say the treatment is efficacious. If it is too small, we say the treatment is not efficacious. At no point in the equation do we consider the absolute effect of a treatment. This, however, is the only effect that matters to a patient. If a patient is seeing a doctor, he or she wants to know what the chances are that whatever the doctor decides to do – giving a pill, praying, putting on leeches, sticking in needles, dropping some sugar globules free from active molecules and a lot of purported information in her bag, sticking magnetic coils into her shoes – her symptoms are going to subside. Now we have an obvious paradox in the situation where a treatment appears very effective overall but a clinical trial shows these outcomes differ very little from those of patients in a control group given a placebo treatment. Perhaps this is because the non-specific effects of the treatment are large, but the specific effects are very small. By virtue of our current definition of efficacy we would have to call this treatment ineffective. The paradox is that another treatment, though it might have much less overall effectiveness, (and hence the patient's chances of seeing the symptoms vanish are less) might be called efficacious because there is a significant difference when compared with placebo.

Clearly, something is wrong here. The paradox arises because the pharmacological paradigm is only interested in differences, and makes the wrong assumption that the placebo effect is always a stable entity, like the Arch-meter buried in the vaults of Paris, which will always read one meter. But on the contrary, the placebo effect is highly variable, and dependent on context, patients, practitioners and so on. Hence the conventional efficacy paradigm is really measuring with a measuring rod that is shrinking and expanding as we measure. Hence what we call efficacy really is only one aspect of efficacy, namely efficacy against placebo. It is interesting for regulators, because it tells them whether there is anything specific in a new intervention that is worth considering at all, given that side effects have to be taken into account. But real-world effectiveness is the whole bar, all the effects, non-specific ones included. This is all the main consideration for patients; plus the side-effects, plus the costs, plus the longevity of therapeutic effects.

Until recently this efficacy paradox was just a nice thought to play around with. But for a couple of years now, we know it is real. The large German acupuncture studies have all been three-armed. [28-30] They tested

Figure 1 – Illustration of Efficacy Paradox: Treatment X is supposed to be not statistically superior to its control, Placebo X, hence deemed 'ineffective', although the overall effectiveness is higher, while Treatment Y is said to be statistically superior to its Placebo Y and hence effective. The paradox arises, because the variability of the size of non-specific effects is not taken into account.



acupuncture versus sham acupuncture (a minimal kind of acupuncture that inserts needles superficially in points agreed by specialists to be non-therapeutic), versus the best that conventional therapy could offer. The trials considered migraine prevention, osteoarthritis of the knee, and chronic low back pain. While acupuncture outcomes were not significantly different from placebo acupuncture, in two of the studies both acupuncture and sham acupuncture were nearly twice as effective as conventional treatment, with a large effect size and high statistical significance. The conventional treatment offered here was best evidence based, according to guidelines, and delivered to a high standard by well-trained doctors. It was not delivered as a hopefully weaker control, for the expectation originally was that it represented the standard and that acupuncture would be lucky to measure up to it. As it happened acupuncture, but also sham acupuncture, were not only statistically but also clinically more effective than conventional, guideline-supported, best evidence based treatment.

What are we to make of this? Abandon conventional back pain treatment, which in this case consisted of a mix of painkillers, mobilisation, physiotherapy, back training and patient education? Should we just advise doctors to stick needles into patients anywhere, just not too deep, tell patients this is the most recent Chinese gimmick and that it will cure them, let them rest for 20 minutes while the next 10 patients are getting their needles put in, and that's it? Probably not. But these German acupuncture studies tell us three things: (i) on what swampy and treacherous ground we tread when we use the word 'evidence'; (ii) how surprisingly strong CAM treatments, even apparently silly ones, can prove to be once studied; (iii) how badly the deck is really shuffled and biased in favour of the all too powerful conventional crowd.

Conclusion: Be proud, not afraid, fight back and don't duck.

Now let us pull the arguments and facts together. Fact 1: We have a mounting campaign against CAM treatments. The battle is said to be between 'evidence based' treatments versus 'non-evidence based' treatments. Fact 2: (though CAM has not done its homework and collected strong enough data to make the point) CAM might be quite useful in real life, even though its specific effects might not be strong enough to show specific in an RCT. By its very nature CAM produces quite strong non-specific effects; in fact to a degree that in some comparative trials its results can dwarf the best of what conventional evidence based treatments have to offer. But then we run into problem number one: there is hardly any data to prove this, and problem number two: such data are not easy and cheap to come by. They need considerable study, skill and money. For example, the German acupuncture trials cost roughly 10 million Euros. Fact 3: that some recent flagship medications and projected frontrunners in the income generation machinery of big pharma have recently come under severe attack. SSRIs are much less effective than stated; actually less effective than NICE demands, and quite costly in terms of side effects. Anti-dementia drugs have cost billions to develop, and given nothing in return, as NICE has slashed them. And then there is Fact 4: big pharma is reeling from a series of extremely expensive side-effect scandals, starting with hormone replacement therapy, and ending with COX2 inhibitors.

So I have come to the conclusion that big pharma is scared, and I would argue that the current witch hunt to weed out allegedly non-evidence based practices is the consequence of twin developments. On the one hand the favour CAM has found with the public, and on the other the increasing pressure that the pharmaceutical companies have come under. So big pharma is doing the only sensible thing it can by attacking where it knows its enemy is weakest: for its lack of data. I think a second conclusion is inescapable: that CAM as a movement and as a culture should be proud and ashamed at the same time. Proud, because little David has got big Goliath scared. But at the same time ashamed that we have lost so much valuable time through complacency and narcissistic self-indulgence.

> I have come to the conclusion that big pharma is scared.

I have a suspicion that whoever rides into battle for big pharma does so because they are well protected and well paid. Like the mercenary Lombard Riders of fifteenth century Europe big pharma's troops are feared because they are well trained and well equipped. These mercenaries generally decided the battles, but they were also quick to swap sides if pay was lacking or their side's luck turned. The most dangerous moment for a fencer (according to my daughter who is a fencer, and told me this recently) is the attack, because it is then that they have to drop their guard, and so this is when the counter-attack happens. I would argue that we should start striking back now for the attack has opened an avenue for counter-attack. So have we asked the pertinent questions about conflicts of interest in research; have we investigated where the money is coming from that supports the anti-CAM campaigners; have we found out enough about the funding structures that keep those groups afloat, and the dinners and cocktail parties where promises and nice ideas are exchanged?

It is time for a counter-campaign; for some critical analysis, some investigative journalism, some discourse and social analysis to uncover the background that supports the campaign against CAM. I also suggest we start collecting the sort of data whose absence allowed the campaign to begin in the first place: data about CAM's real world outcomes and effectiveness. And I think it would be wise to demonstrate to our colleagues struggling with the realities of conventional medical practice just how short-sighted and silly the current concept of evidence really is,

since it is only modelled along the lines of pharmacological research. I am quite sure they will listen. After all, they have roughly the same problems as we do.[31] Only those who live in ivory towers and feed on the food lifted up to them in baskets, who do not have to care for patients and don't have to solve practical problems, can indulge in abstract debates about evidence, while the rest of their colleagues have to actually deal with people who are suffering, solve clinical problems and avert human disaster. This is the territory where we can meet, and where practical, sober, sound data collected in the real world will begin to speak clearly.

Acknowledgement
I thank Lionel Milgrom for critically reading a first draft and improving the language.

References

1 Shang A, Huwiler-Münteler K, Nartey L, Jüni P, Dörig S, Sterne JAC, Pewsner D, Egger M. Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *The Lancet* 2005; 366: 726–732.

2. Lüdtke R, Rutten ALB. The conclusions on the effectiveness of homeopathy highly depend on the set of analyzed trials. *Journal of Clinical Epidemiology* 2008; 61:1197-1204.

3. Walach H, Jonas W, Lewith G. Letter to the Editor: Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. *The Lancet* 2005; 366: 2081.

4. Fisher P, Bell IR, Belon P, *et al*. Letter to the Editor: Are the clinical effects of homoeopathy placebo effects? *The Lancet* 2005; 366:2082.

5. Giles J. Degrees in homeopathy slated as unscientific. *Nature* 2007; 444: 352–353.

6. Barrett B, Marchand L, Scheder J, Appelbaum D, Chapman M, Jacobs C,Westergaard R, St.Clair N. Bridging the gap between conventional and alternative medicine. Results of a qualitative study of patients and providers. *Journal of Family Practice* 2000; 49: 234–239.

7. Hyland ME. The intelligent body and its discontents. *Journal of Health Psychology* 2002; 7: 21–32.

8. Hyland ME. A brief guide to extended network entanglement theory as a theory of healing and its empirical predictions. *Forschende Komplementärmedizin und Klassische Naturheilkunde* 2003; 10: 201–206.

9. Furnham A. Explaining health and illness: Lay perceptions on current and future health, the causes of illness, and the nature of recovery. *Social Science and Medicine* 1994; 39: 715–725.

10. Vincent C, Furnham A. Why do patients turn to complementary medicine? An empirical study. *British Journal of Clinical Psychology* 1996; 35: 37–48.

11. Güthlin C, Lange O, Walach H. Measuring the effects of acupuncture and homoeopathy in general practice: An uncontrolled prospective documentation approach. *BMC Public Health* 2004; 4 (6).

12. Astin JA. Why patients use alternative medicine. Results of a national study. *Journal of the American Medical Association* 1998; 279: 1548–1553.

13. Riley D, Fischer M, Singh B, Haidvogl M, Heger M. Homeopathy and conventional medicine: An outcomes study comparing effectiveness in a primary care setting. *Journal of Alternative and Complementary Medicine* 2001; 7: 149–159.

14. Thompson EA, Reilly D. The homeopathic approach to symptom control in the cancer patient: a prospective observational study. *Palliative Medicine* 2002; 16: 227–233.

15. Jena S, Witt CM, Brinkhaus B, Wegscheider K, Willich SN. Acupuncture in patients with headache. *Cephalalgia* 2008; 28 (9): 969–980.

16. Witt C, Keil T, Selim D, Roll S, Vance W, Wegscheider K, Willich SN. Outcome and costs of homoeopathic and conventional treatment strategies: A comparative cohort study in patients with chronic disorders. *Complementary Therapies in Medicine* 2005; 13: 79–86.

17. Witt CM, Lüdtke R, Baur R, Willich SN. Homeopathic medical practice: Long term results of a cohort study with 3981 patients. *BMC Public Health* 2005; 5: 115.

18. Witt CM, Reinhold T, Jena S, Brinkhaus B, Willich SN. Cost-effectiveness of acupuncture treatment in patients with headache. *Cephalalgia* 2008; 28(4): 334–346.

19. Kirsch I, Deacon BJ, Huedo-Medina TB, Scoboria A, Moore TJ, Johnson BT. Initial severity and antidepressant benefits: A meta-analysis of data submitted to the food and drug administration. *PLoS Medicine* 2008; 5(2): e45.

20. Turner EH, Matthews AM, Linardatos E, Tell RA, Rosenthal R. Selective publication of antidepressant trials and Its influence on apparent efficacy. *New England Journal of Medicine* 2008; 358: 252–260.

21. Grossman P, Schmidt S, Niemann L, Walach H. Mindfulness based stress reduction and health: A meta-analysis. *Journal of Psychosomatic Research* 2004; 37: 35–43.

22. Walach H, Bösch H, Lewith G, Naumann J, Schwarzer B, Haraldsson E, Wiesendanger H, Nordmann A, Tomasson H, Prescott P, Bucher HC. Efficacy of distant healing in patients with chronic fatigue syndrome: A randomised controlled partially blinded trial (EUHEALS) *Psychotherapy and Psychosomatics* 2008; 77: 158–166.

23. Walach H, Jonas WB. Placebo research: The evidence base for harnessing self-healing capacities. *Journal of Alternative and Complementary Medicine* 2004; 10(Suppl. 1): S103–S112.

24. Rush JA, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G,Thase ME, Lavori PF, Lebowitz BD, McGrath PJ, Rosenbaum JF, Sackeim HA, Kupfer DJ, Luther J, Fava M. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: A STAR*D report *American Journal of Psychiatry* 2006; 163: 1905–1917

25. Fava GA, Tomba E, Grandi S. The road to recovery from depression – don't drive today with yesterday's map. *Psychotherapy and Psychosomatics* 2007; 76: 260–265.

26. Walach H, Falkenberg T, Fonnebo V, Lewith G, Jonas W. Circular instead of hierarchical – Methodological principles for the evaluation of complex interventions. *BMC Medical Research Methodology* 2006; 6(29).

27. Walach H. Das Wirksamkeitsparadox in der Komplementärmedizin. *Forschende Komplementärmedizin und Klassische Naturheilkunde* 2001; 8: 193–195.

28. Haake M, Muller HH, Schade-Brittinger C, Basler HD, Schafer H, Maier C, Endres HG, Trampisch HJ, Molsberger A. German acupuncture trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. *Archives of Internal Medicine* 2007; 167 (17): 1892–1898.

29. Diener HC, Kronfeld K, Boewing G, Lungenhausen M, Maier C, Molsberger A, Tegenthoff M,Trampisch HJ, Zenz M, Meinert R, for the GERAC Migraine Study Group. Efficacy of acupuncture for the prophylaxis of migraine: A multicentre randomised controlled clinical trial. *Lancet Neurology* 2006; 5: 310_316.

30. Scharf H-P, Mansmann U, Streitberger K, Witte S, Krämer J, Maier C, Trampisch HJ, Victor N. Acupuncture and knee osteoarthritis. *Annals of Internal Medicine* 2006; 145: 12–20.

31. Rawlins M. De Testimonio – On the evidence for decisions about the use of therapeutic interventions. The Harveian oration. Delivered before the Fellows of the Royal College of Physicians of London on 16 October 2008. London: Royal College of Physicians.