

'Proof' against homeopathy in fact supports Homeopathy

Suppose a salesman visits you with a basket of more than a hundred apples. You ask: 'are they all good?' Out of your sight, the salesman takes eight apples out of the basket. He shows you the apples and they look fine to you. 'This is the proof that all apples are all good', the salesman says. You ask: 'can I take some too?' and you take out eight rotten apples out of the basket, just like that. 'That means nothing, because I have just proven that all apples are fine', the salesman answers.

You may not believe it, but the editors of the leading medical Journal '*The Lancet*' cheated likewise and think this trick will mean the end of homeopathy. On 27 August 2005, *The Lancet* published a study, which purposed to prove that homeopathy is nothing more than a placebo effect.¹ With a selection of eight out of 110 studies on the efficacy of homeopathy, medical science is of the opinion that they can prove millions of satisfied users wrong. This basket of apples was therefore welcomed by opponents of homeopathy: for them good apples are studies that show no effect of homeopathy and rotten apples are studies with positive results for homeopathy.

Background

We have little knowledge on the underlying mechanisms of homeopathy. The theory that ill-making materials can cure as well is commonly accepted, for example in vaccination. But homeopathic medicinal products that are still effective after a process of high dilution and succession is beyond the current understanding of biomedicine. Yet, homeopathy has been used worldwide for centuries, especially by patients with chronic complaints. These patients have wide experience with conventional medicine and notice that conventional medicinal products may reduce their symptoms, but their complaints often recur in time. By using homeopathic treatment, complaints may disappear completely, while the treatment hardly causes any serious side effects.

In 1999, a number of complementary forms of medicine, including homeopathy, were provisionally included in the Swiss compulsory health insurance. Meanwhile, a large research programme was started to study the effectiveness and cost-effectiveness of these complementary treatments. The programme was known as the Programm Evaluation Komplementärmedizin (PEK). One of the institutions was the Institut für Sozial und Preventiv Medizin (ISPM) and it was this institution which carried out the meta-analysis

discussed here. However, the outcome of the meta-analysis was announced in the public press, back in August 2003. The methods and the conclusion of this meta-analysis in particular, received a lot of criticism from the PEK management. The PEK management noticed that different treatments for different diseases cannot be approached as if it concerns one treatment for one disease. This criticism is not mentioned or discussed in the *Lancet* publication.

The provocation

Up to 1990 sceptics thought that the problem of homeopathy could be solved quickly: perform a double-blind study and one will see that it does not work. But that was a rude awakening. In 1991 the first reports showed that quite a lot of research on homeopathy had been done and that '...a conventional method with comparable results would be acknowledged'.² At a jubilee lecture of the *Lancet* in 1998, the Dutch epidemiologist Jan Vandembroucke presented a portrayal of the available double-blind studies on homeopathy of that time. The higher dots represent the studies of better quality, the dots to the right represent studies with a strong positive result. Thus the dots towards the top right (Figure 1) represent the most convincing studies. The graphic is adapted from an analysis of 89 homeopathic studies by Linde.³ Vandembroucke challenged his audience to come up with a conventional treatment with better results.⁴

Fraud

Homeopathy is hard for sceptics to accept. We also know some that double-blind randomized studies are not as unquestionable as may be assumed. Studies performed by researchers linked to pharmaceutical companies have more positive results than studies performed by others. Editors of medical journals discovered that they are being deceived: scientists were paid to attach their names to studies, withhold negative results and give a better picture of study results than justified. For instance, some antidepressants are ineffective and increase the chance of suicide.^{5,6} Based on the positive outcomes of studies supported by the pharmaceutical industry, one might assume that positive outcomes of homeopathic studies are biased also. However, homeopathy has no research infrastructure. Most research is performed in cooperation

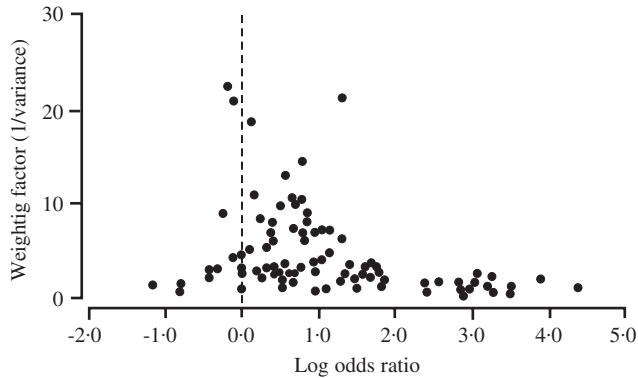


Figure 1.

with conventional research institutes and to obtain sufficient patients one needs the cooperation of conventional doctors. It is therefore unlikely that negative outcomes remain unpublished.

Objectivity

The objectivity of the evaluation of research is also questionable. In 2001 Ezzo *et al* analysed 160 evaluations of conventional studies performed by the renowned Cochrane Institute. They concluded that only a small number of conventional treatments are based on solid scientific research (RCTs) and that the evaluation of the research is highly subjective.⁷ Evaluation of homeopathic studies can also count on subjectivity, by opponents in particular. The head of the ISPM (the institute that performed the meta-analysis), and senior author of *The Lancet* paper, Egger, is known as opponent of homeopathy for years. When you analyse all available literature, it is almost impossible to claim that homeopathy is nothing more than a placebo effect. If that is the case, then homeopathy should have similar outcomes to placebo, sometimes better, sometimes worse. However, in two-third of all studies analysed, homeopathy is more effective than placebo, in less than 10% worse than placebo and comparable in the remaining cases. The only other arguments against homeopathy is the possibility of deceit or errors made in research. Errors are made in biomedical research, homeopathic or conventional. But the question is if errors occur more in homeopathic than conventional studies?

Trends

If we are not certain about something, we look for trends. For example, cloudy weather means a higher chance of rain. A comparable trend in biomedicine is that the effect of treatment decreases as the quality of research improves. This is observed in both conventional and homeopathic research.⁸ But is this trend

stronger in homeopathy than in conventional medical science? The Swiss researchers assumed that the trend towards a negative outcome for homeopathy would be increased with increasing quality of studies. They evaluated all studies and found the opposite. Then they divided their studies by diagnosis and found the same. For acute upper respiratory tract infections homeopathy proved to work whichever way you look at it. Finally they came up with a combination of eight studies which did show the desired trend, but nobody is allowed to know which studies they are!

Lack of clarity

The more you read *The Lancet* paper the more you doubt it. It is really strange that it does not clarify which eight studies were chosen to observe the claimed trend. That is scientific misbehaviour in itself and it gets worse if the criticism from the PEK commission mentioned above is concealed.

But then a graphic is portrayed that should show what they really have done (Figure 2).

This top graph used a similar method to analyse the quality of the study as Linde (Figure 1) (vertical axis), but in contrast to the Linde graph, the strength of the

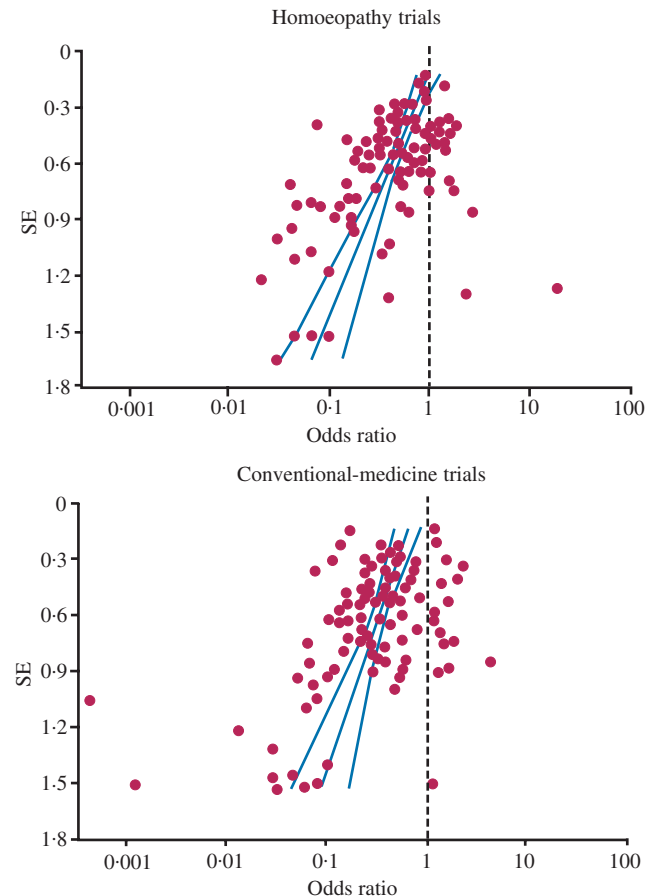


Figure 2.

effect increases to the left. A striking contrast with Linde's graph is the presence of just a few dots in the lower part. This picture does not correspond to the general expectation and observation of comparable pictures that studies of low quality (lower part of the graph) are usually more numerous than studies with better quality. Perhaps, studies have been omitted. This is strange because they studied whether omitting studies caused bias or not. The publication shows that they excluded about 50 of 155 studies, 43 on the basis of not providing sufficient information and inability to identify a matching trial of conventional medicine. This is where subjectivity may play a role. If we look at the list of analysed studies, it is notable that four studies with positive result have been left out but were ranked very well in previous analyses.⁹⁻¹²

What effect does the removal of dots in the lower part of the graph have in this picture? Three hypothetical lines are shown. The central line indicates that studies of low quality give more positive results (bottom left) and studies of high quality give less positive results (upper right). The upper right section of the line indicates the trend on which the conclusion is based. Add a few dots to the lower right and upper left and the line will be more vertical and the trend disappears. By adding the four dots of the above-mentioned good quality studies⁹⁻¹² to the above left of the picture, the trend becomes more positive. The lower graph depicts conventional studies and its slope is more vertical, ie the effect decreases with increasing study size. However, in the text the authors state the opposite, i.e. that for homeopathic studies the trend that the effect decreases with improved quality is (not significantly) less than for conventional studies. Thus, the graphs suggest the desired conclusion, but the data in the text demonstrate the opposite.

Various comparisons were made between homeopathic studies and comparable conventional studies. The homeopathic studies proved to be of better quality in several respects, for example:

- 19% of the homeopathic studies were of good quality, with conventional studies 8%.
- Heterogeneity was significantly lower in homeopathy than in conventional research ($p = 0.011$), therefore the error this study explicitly searched for occurs more frequently in conventional studies.

An attempt was made to demonstrate that studies of homeopathy are dubious because of bad quality and larger heterogeneity than conventional studies, but the opposite proved to be true. The decrease of the effect with increasing study quality was 24% lower in conventional studies. However, from these data it cannot be concluded that homeopathy is better as this number did not reach statistical significance. But the researchers claim to have proved the opposite based on a selection of eight out of 110 which cannot be checked.

Phantoms

Nobody believes that you can make an amputated leg grow with a medicine. Let us call research that cannot have a positive outcome a phantom. Phantom research does not mean that medicines in general do not work, but that the outcome indication is a phantom. Studies into such phantoms are nevertheless done though they are less obvious. In conventional medicine research preliminary analyses are done and phantoms eliminated. In homeopathy such preliminary analysis is hardly possible. Thus it can happen, for instance, that research is conducted on homeopathy for the prevention of influenza. In day-to-day practice homeopathy is not used for this indication, it is quite possible that this is a phantom and that homeopathy does not work in prevention of influenza.

There are many other possible causes for absence of positive results. In a study of homeopathy on asthma an inappropriate outcome measure was used.¹³ According to this instrument the situation of the patients before treatment was so good that no further improvement could be expected from treatment. Phantoms and studies with methodological shortcomings give false negative outcomes. The authors of the paper excluded 30% of the available studies, but not on the rationale of false negative studies.

Fictitious conclusion

It is therefore possible to find good quality studies with a negative result. But this does not mean that the method does not work. Neither does the discovery of a trend in some studies mean that this trend is present in all studies. One might just as well say that the lack of effect of antidepressants implies that conventional biomedicine in general is not effective. The authors of the paper have found two groups of studies of which they state make a possible comparison between homeopathy and regular medicine. Of one group, we know that it concerns eight researches of homeopathy on acute upper bronchial infections. Analysis of this group shows that the result do not decline with increasing quality of the studies. Scientifically, this is a spectacular conclusion. Previous analyses show that evidence for homeopathy can measure up to evidence for conventional medicine. One was based on the lack of proof for any single indication; the other, that with increasing quality, the evidence would become weaker. Both objections have been cleared.

From an opponent of homeopathy such as Egger, one might expect that he wants to avoid this conclusion. A second group of eight studies has been found, which can be boxed together. Neither are the criteria and the identity of the studies clearly given, nor is the reader allowed to see what has been done with these studies. Nevertheless, the conclusion drawn from these studies has been generalized to all homeopathy.

Table 1

Example	Non-responder rate		Number of subjects needed		
	Verum (%)	Placebo (%)	Per group	Odds ratio	SE log OR
I	40	50	400	0.67	0.14
II	30	50	100	0.43	0.30
II	20	50	40	0.25	0.51

By circular reasoning, it is concluded that the evidence for homeopathy in upper respiratory infections is no longer valid either.

It is incredible that the Editors of a leading medical journal as *The Lancet* accepts that the most vital data of a study are kept a secret. The authors have apparently concealed the fact of the criticisms of the PEK programme management.¹⁴ According to the PEK management there is a heterogeneous group of disorders and treatment. This fact in itself leads to the reported results. The PEK report includes Table 1.

When a strong effect is expected fewer patients are necessary. In example III in the table above, for example, in the verum group only 20% do not respond to the treatment against 50% in the placebo group. It is for all three examples very improbable that the odds ratio could be one (which means no specific effect). The proposition of the ISPM that larger patient numbers stand for better research is incorrect. The PEK management stated clearly that this secret group of eight researches should not be pooled. With this in mind it is clear that the whole base of the reasoning and the final conclusion is incorrect.

Because of the secrecy we do not know if there are phantoms among the eight studies. But looking at patient numbers it is likely that the prophylactic action of homeopathy on influenza has been examined. In three studies, 1595, 1270 and 501 patients were included. But these may be phantom outcomes.

Diversionsary tactics

From the arguments discussed above, the conclusion must be drawn that *The Lancet* meta-analysis does not meet the minimum criteria for publication in biomedicine journals. The question remains why *The Lancet* published anyway. We can only speculate: one reason may be to counteract the upcoming publication of a report on Homeopathy of the World Health Organisation. The draft version of this report, which had been circulated for comment, comes to the conclusion that homeopathic treatment is effective and that further research is warranted.

The meta-analysis published in *The Lancet* was only a small part of the PEK program. Other studies that formed part of the PEK program showed that homeopathic treatment is cheaper than conventional treatment, and that patients treated with homeopathy

show greater improvement, experienced less side effects and hospitalization.

The Swiss authorities did not welcome these positive outcomes for homeopathy. A preliminary report of the PEK commission with the recommendation that homeopathy should remain part of the Swiss health insurance was omitted after political pressure. The Swiss homeopathic doctors wanted to publish the positive data of the PEK program but were forbidden to do so. The economist on the project was fired and his data were withdrawn. The Swiss homeopathic doctors have the economic evaluation that the PEK committee was not willing to publish.¹⁵ These figures show that homeopathic treatment can reduce the costs of medical treatment considerably.

Conclusion

Earlier analysis investigating the specific effects of homeopathy has shown that existing evidence for efficacy of homeopathy can compete with evidence for conventional medicine. From *The Lancet* paper it can be concluded that the placebo-controlled clinical trials on homeopathy are of higher quality and less heterogeneous than otherwise comparable conventional studies. In addition, the decrease in effect size with increasing quality of the studies is less for homeopathy than for conventional medicine. A third conclusion that can be drawn from the paper is that homeopathy is effective for upper respiratory tract infections. There is now evidence that homeopathy is more than a placebo effect: the hypothesis that all swans are white can be falsified, as soon as the first black swan is found.

The results published in *The Lancet* are biased and tried to draw a different conclusion. The graphs are not congruent with the conclusion drawn from them. The eight studies on which the conclusions were based are not identified, and the criticisms of the PEK commission are not mentioned or taken into account. According to the commission the heterogeneity in the sub-analysis of eight studies is due to the heterogeneity of the selection of the studies.

The editors of *The Lancet* have made a serious mistake by accepting the paper for publication as the readers are not able to follow the argumentation that lead to the conclusions. The statement of the editors in the same edition of *The Lancet* that this publication

should mean the end of homeopathy is biased, and the paper proves the opposite.

For more than 15 years now, the discussion and research on homeopathy has been directed towards proving that it is nothing more than a placebo effect. However, all the arguments and analysis that have come up fail, and question the efficacy of conventional medicine just as much.

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Open letter to the Editor of *The Lancet* from the Swiss Association of Homoeopathic Physicians (SVHA)

The study on homoeopathy by Shang *et al*¹ from the Department of Social and Preventative Medicine, University of Berne, Prof Egger, published in *The Lancet* on the 27/8/2005, has been part of the Swiss Complementary Medicine' Evaluation Programme (PEK). For the last 2 years the authors have been stating in the media that homoeopathic effects are placebo effects, but have withheld the basis of their statement until this year. We do not consider this procedure as very fair. Professor Egger invited us to make our criticism of his study public in a formal 'Letter to the Editor'. However, our letter was not accepted for publication. We therefore decided to make our comments public in the form of this open letter.

The meta-analysis of homoeopathy by Aijing Shang *et al*, formed part of the Swiss 'Complementary

Medicine Evaluation Programme' (PEK). The meta-analysis compares 110 homoeopathic and 110 matched trials of allopathy.

The meta-analysis may be statistically correct. But its validity and practical significance can be seen at a glance: not one single qualified homoeopath would ever treat one single patient in clinical practice as presented in any of the 110 analysed trials! The study cannot give the slightest evidence against homoeopathy because it does not measure real individual (classical) homoeopathy. It confounds real homoeopathic practice with distorted study forms violating even basic homoeopathic rules. The correct selection of the homoeopathic remedy almost entirely depends upon the totality of individual symptoms and signs whereas most homoeopathic RCT's use