

DEBATE

How can we change beliefs? A Bayesian perspective

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Abstract: How can Randomised Controlled Trials (RCTs) change our beliefs? The fact that they do update prior beliefs to different posterior beliefs is explained by Bayesian philosophy.

Crucial points in Bayesian analysis include setting the first prior expectation right and sequential updating of the prior in the light of new evidence. Bayesian analysis depends highly on the evidence included.

RCT evidence can only falsify the placebo hypothesis, it cannot indicate which mechanism of action could be responsible for an intrinsic effect and therefore cannot overturn existing beliefs. Bayesian reasoning could structure further discussion, but subjectivity is an inherent element of this process. In the case of homeopathy the first prior is not a common prior shared by all parties to the debate, but a paradigm, this prevents common updating of beliefs. Only by keeping an open mind towards other paradigms and all possible hypotheses can a low Bayesian prior be elevated to the point of accepting a new paradigm, this is more relevant than Bayesian calculations. *Homeopathy* (2008) 97, 214–219.

Keywords: Bayes theorem; Paradigm; RCT; Meta-analysis; Homeopathy

Introduction

The same set of homeopathy trials, with addition of newer trials has been repeatedly re-analysed. Analyses of the complete set indicate that the effect of homeopathy cannot be exclusively attributed to placebo.^{1,2} Analyses of certain subsets indicate that the placebo hypothesis could still hold.³ Trials of conventional treatments, however, suffer from the same shortcomings. Kleijnen says (about homeopathy): “Based on this evidence we would be ready to accept that homeopathy can be efficacious, if only the mechanism of action were more plausible”.¹ A key argument in this discussion is that the way a homeopathic medicine is manufactured is “an outrage to human reason”.⁴ In other words: Prior beliefs reach a point where they cannot be overthrown. It appears that meta-analysis of Randomised Controlled Trials (RCTs) is only the ultimate and conclusive proof if it proves what was expected! The positive

outcome of Kleijnen’s and Linde’s meta-analyses did not increase believe in homeopathy, but according to the editor of the *Lancet* the outcome of Shang’s analysis meant “the end of homeopathy”.^{4,5} Apparently homeopathy has to produce more or different proof than conventional medicine. Bayesian reasoning is presented to defend this attitude,⁶ but Martin Chaplin stated that such an attitude is unscientific.⁷

Introducing Bayes’ theorem complicates the discussion. First there are prior beliefs which should be discussed and might be questionable. Then there is the process of updating beliefs. The tests that are applied to update beliefs can be interpreted in different ways. Does Bayesian reasoning help us in this discussion? This paper considers beliefs, not truth.

Bayesian reasoning

Bayesian reasoning is essentially based on the mathematical law of conditional probability. In card playing, the condition that one card was drawn changes the probabilities of what the next card will be. There are several rearrangements of the formula of conditional probability

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which constitute the several variants of the Bayesian formula. Intuitively the simplest variant is:

$$\text{Posterior odds} = \text{LR} \times \text{prior odds}^1$$

Bayesian updating of odds or chances can also be used to update our beliefs about truth, or to describe an algorithm of the way we learn. Using formulae seems scientific, but it obscures the subjectivity of gathering data and constituting prior beliefs.

Prior belief

The prevailing dogma is that "Accepting that infinite dilutions work would subvert more than conventional medicine; it wrecks a whole edifice of chemistry and physics".⁸ The underlying conviction seems to be that medicines can only act by molecular interactions. But new developments do indicate the possibility of structural information, for instance: the structure of DNA influences its binding to proteins.^{9,10} The July 2007 issue of *Homeopathy* included several possibilities concerning the structure of water to explain homeopathy.^{7,11}

Prejudice and *reductio ad absurdum* may also influence prior beliefs. Vandenbroucke states: "Microbiologists know for sure that infinite dilutions of an antibiotic will never show any effect on bacterial growth".⁶ In other words: Homeopathic physicians expect the same effect from the homeopathic potency of a conventional medicine as from the original medicine. Of course it would be impossible to take colleagues with such expectations seriously. But the statement is not accompanied by any reference or corroborating data. Which homeopathic physician prescribes homeopathic preparations of antibiotics for infections?

Prior beliefs are updated in the Bayesian process, but the first prior belief has a special position. This first prior belief is very strong, we need to consider how strong and why. It is in fact paradigmatic and might not be susceptible to Bayes' theorem.

Updating of belief

If we use Bayesian reasoning to update beliefs we have to ask ourselves: which belief do we want to update, with which evidence, how and to what extent?

Which belief should be updated? The dogma that there should be chemical molecular interaction cannot be modified by RCTs. Placebo-controlled RCTs measure if the effect is due to placebo or not. If it is not due to placebo any other mechanism of action could be responsible. Of all possible mechanisms for homeopathy molecular interaction seems hardly possible, although Chaplin has discussed some possible specific mechanisms.⁷ Non-specific

mechanisms seem endorsed by the fact that the effect of a homeopathic medicine differs from that of conventional medicines. The effect gradually builds up and is not confined to one diagnosis or organ. How can you accept that the homeopathic medicine cures grief as well as headache and herpes of the lips when you have never 'seen' it?

With which evidence? Fundamental research seems to be required to update beliefs about the necessity of chemical molecular interaction. This important point gets little attention. And the instruments for proving should value the method on its own terms. If you don't acknowledge the '*Natrum muriaticum* personality' as an entity you cannot accept RCT on *Natrum muriaticum* personalities instead of conventional diagnoses.

How? Suppose that we just want to update the placebo hypothesis. Opponents of homeopathy regard Shang's analysis as proof of bias in clinical trials of homeopathy and their belief in the placebo hypothesis increases. But after analysing the data omitted from this meta-analysis one could regard the same analysis (including the subsequently provided data) as either proof of bias in the meta-analysis procedure or, proof of the higher quality of homeopathy trials compared to matched trials of conventional treatments.¹² So, the same data could change beliefs in opposite ways, depending on bias in the analysis and prior belief.

To what extent? The alternative conclusion from the Shang analysis implies less quality bias for homeopathy than for conventional medicine. Should this imply the end of allopathy, as the editor of the *Lancet* concluded for homeopathy? Few people will endorse this conclusion and this indicates that the degree of updating beliefs depends on which prior we choose. For conventional medicine the existing evidence is rightfully considered as prior. For homeopathy apparently a different first prior – based on the theoretical problem – its 'implausibility' is chosen, not the existing evidence from Linde's meta-analysis that led to Shang's hypothesis.

An accepted diagnosis is an accepted method

Consider a refugee with palpitations, flashbacks, headache and insomnia. Nowadays we recognise this combination of symptoms as Post-Traumatic Stress Disorder (PTSD). With psychotherapy we get closer to the source of the disease than with a combination of beta-blockers, painkillers and tranquillisers. But suppose psychotherapy, and therewith the diagnosis PTSD, was not an accepted entity. Then we would require RCT evidence that psychotherapy works better than beta-blockers.

Now consider a '*Natrum muriaticum* person'. His complaints started a year ago after severe grief, he has headaches worse in the sun and problems falling asleep. He also has had recurrent herpes of the lips for 15 years. For the homeopathic physician the '*Natrum muriaticum*' personality is an accepted diagnosis, and he will not be surprised that the herpes is also cured by *Natrum muriaticum*. Others will only accept RCT proof that *Natrum muriaticum*

¹Odds = chance/(1 – chance); in words: the chance that something will happen divided by the chance that it will not happen. Odds = 1 means: chance is fifty-fifty. LR = Likelihood ratio = true positives/false positives.

works for headache. And if it does, they will say "Why should we accept this homeopathic medicine for this indication if we already have painkillers?". This is a circular process: proof that does not measure the surplus value of a method, does not detect the surplus value.

Sequential updating of belief

Bayesian reasoning is not a one step process but should consider all possible evidence for sequential updating of belief. In sequential updating the posterior odds after one piece of evidence serves as prior odds for the following calculation based on new information.

Evidence from RCT could be translated into LR by using the 'minimum Bayes factor' proposed by Goodman.¹³ Rosendaal and Bouter simplified this by assigning one significantly positive RCT a likelihood ratio of 16.¹⁴ Their estimate of the prior that homeopathy 'works' was one in a million; they actually meant 'works in an accepted pharmacological way'. Then they calculate with Bayes' formula that the chance that homeopathy works goes from one in a million to less than one in ten thousand after one RCT. Thus there is still little evidence that homeopathy works. But, as stated before, RCTs are about falsifying the placebo hypothesis, not about the chemical interaction hypothesis. Another objection is that theoretical priors are not used in conventional medicine. Priors should be elicited from experts in the field of practice¹⁵ or the outcome of an existing RCT can be used as the prior.¹⁶

The importance of the first prior, and its subjectivity, influences the beginning of the updating process. Absurd priors meet emotional objections to even starting the updating process. But very low priors especially are strongly influenced by proof using Bayes' formula. If we suppose that the proof of one RCT has LR = 16, sequential updating for eight positive trials proceeds as in Table 1.

We see that 7 trials suffice to bring belief from one in a million to nearly 100%! The combined LR of seven studies is 16⁷ = 268,435. In reality beliefs will not change to this extent, but this is not due to statistical uncertainty. We become increasingly aware of limitations and bias of RCTs and, after a positive RCT we could introduce the alternative hypothesis that the RCT was biased.

Comparing hypotheses

Bayesian reasoning is not only used for updating beliefs, but also for comparing alternative hypotheses. For this purpose, another variant of the Bayesian formula is used:

$$P(H_i|E) = \frac{P(H \cap E)}{P(E)} = \frac{P(E|H_i) \times P(H_i)}{\sum_{\text{all hypotheses}} P(E|H_i) \times P(H_i)}$$

where H_i is a certain hypothesis (i) and E is the evidence. In words: the probability of Hypothesis i , given evidence E , is the probability of evidence E , given Hypothesis i , times the probability of Hypothesis i , divided by the sum (for all possible hypotheses i) of the probabilities of the evidence, given each hypothesis, multiplied by the probability of each hypothesis.

Table 1 Sequential updating of belief; the posterior chance from evidence no. 1 becomes the prior chance for evidence no. 2, etceteras

RCT number	Prior-chance	Posterior-chance	LR+
1	0.000001	0.000016	16
2	0.000016	0.000256	16
3	0.000256	0.004079	16
4	0.004079	0.061505	16
5	0.061505	0.511856	16
6	0.511856	0.943748	16
7	0.943748	0.996289	16
8	0.996289	0.999767	16

Woodworth illustrates the comparison of hypotheses by the trial of OJ Simpson (OJS).¹⁷ OJS's ex-wife was murdered and DNA material was found at the scene of the crime that was very probably OJS'. The argument of the defence, however, was that this DNA evidence could have been planted there. So there are three hypotheses: (1) The DNA belongs to OJS, (2) the DNA belongs to someone else, and (3) the DNA was planted (see Table 2).

The outcome of the Bayesian comparison of hypotheses in OJS' case was that the existing evidence mostly supported the hypothesis that the evidence was planted ($P=0.94$). Adding the hypothesis that the DNA was planted reduces the probability of OJS's guilt to 0.06. This example is just for illustration. The reader who is puzzled after these calculations is probably in the same position as the members of the jury in the actual OJS trial. In fact the Bayesian calculations compensate for the over-estimation of DNA evidence. Leave out the calculations and common sense remains. The real questions is: do the judge and jury accept the possibility that the police planted the evidence? Bayesian reasoning can be very complex and dependent on presenting (and accepting) all hypotheses and all evidence.

The parallel in the homeopathy debate is that the real issue is not 'is the evidence strong enough?', but 'can the evidence be trusted?'. In 1991 (Kleijnen *et al.*) the conclusion was that "a conventional method would have been acknowledged with this amount of evidence".² Then a new hypothesis to undermine this conclusion came up: publication bias. In 1997 (Linde *et al.*) the publication hypothesis was falsified and the quality bias hypothesis came up.^{1,18} The next objection might be that one cannot assess study quality from a publication, or difficulties in interpreting meta-analysis, e.g. because of heterogeneity.

Table 2 The probabilities of different hypotheses, updated by the same DNA evidence

Hypothesis, H	Prior, P(H)	Likelihood, P(E H)	Joint, P(H ∩ E)	Posterior, P(H E)
H ₁ : OJS	6.25 × 10 ⁻⁸	1	6.3 × 10 ⁻⁸	0.06
H ₂ : other	≈ 1	0.588 × 10 ⁻⁸	≈ 0.6 × 10 ⁻⁸	0.00
H ₃ : planted	≈ 10 ⁻⁶	1	≈ 100 × 10 ⁻⁸	0.94
		P(E)	≈ 106.9 × 10 ⁻⁸	

Source: Woodworth.

The comparison of hypotheses in medicine is complicated by the influence of editors and peer reviewers of medical journals. Peer review and selection of papers is a subjective process. Decisions are again influenced by the first prior, the paradigm. Who will be the judge and jury in the case of homeopathy and can they be impartial enough to accept all relevant evidence?

Practical experience

Beliefs are also updated by practical experience, but here we must be more aware of the influence of chance than with RCT. In this case we use probability densities to update beliefs to indicate the credible interval. Probability densities are updated by essentially the same formula. A full discussion of probability densities is beyond the scope of this paper. Figures 1 and 2 show such densities, the peaks correspond with point estimates. The densities express all statistically possible values.

An example: It is unlikely that a nine months old baby with cyanosis and dyspnoea becomes less dyspnoeic and cyanotic within 5 min after administering a supposed placebo. Such an experience will update belief that this medicine is not a placebo a little bit. If we perform Bayesian analysis with a low prior expectation of 5% that the medicine could work our beliefs after one such experience are updated to 8%. This is graphically displayed in Figure 1. The peak of the posterior curves shifts a bit towards a higher probability, but the probability distribution is very similar.

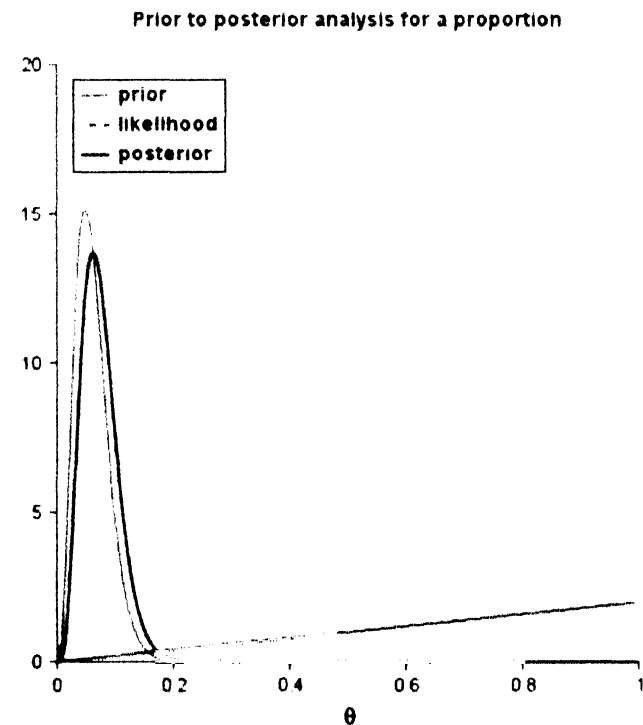


Figure 1 Updating probability distribution (θ) of beliefs after one positive experience (likelihood). Prior belief is 5%, posterior belief becomes 8%, but the posterior distribution is nearly the same. The line presenting the likelihood is not correctly drawn by the program. Graph made using LearnBayes (British Open University).

When doctors are asked why they practice homeopathy they usually give examples of cases with comparable discrepancy between expectation and outcome, especially concerning chronic and recurrent complaints where conventional medicine failed. Memory is unreliable and we tend to remember successful cases better than failures, but we disregard this here for clarity. Suppose experience of 100 cases with a prior expectation of 5% placebo recovery and, say, 60% successes in reality, the posterior density function lies much nearer the observed distribution (likelihood) (Figure 2), our belief that the medicine worked is updated to nearly 40% and the posterior probability distribution does not overlap with the prior probability distribution. This could mean several things: either a placebo can do more than expected, or 'stronger' placebos are possible, or the medicine is not a placebo. Pragmatic considerations, like broadening therapeutic possibilities, can influence the willingness to accept alternative hypotheses. After a number of cases one will also see the surplus value of the method.

Synthesis

This is just a rough indication of how evidence could be evaluated according to Bayes' philosophy. Sequential updating and comparing of hypotheses should consider all kinds of information, like:

- Possible bias in homeopathy and in conventional trials.
- Other forms of scientific evidence, like outcome studies and fundamental research.

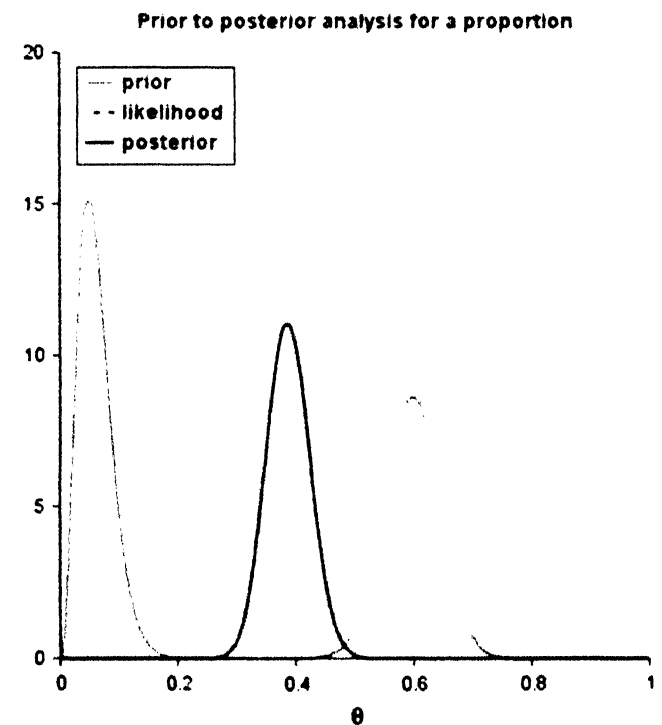


Figure 2 Updating beliefs that a medicine will work after 100 cases with 60% positive outcome. Prior belief is 5%, posterior belief is 37%. The probability distribution shifts towards the likelihood distribution. Graph made using LearnBayes (British Open University).

- Possible mechanisms of action.
- Safety data.
- Experience of patients.
- Experience of homeopathic practitioners.
- The surplus value of the method.

All this information should become available and should be accepted into any overall analysis. We see that the process becomes more and more complicated and the influence of the subjectivity of the first (paradigmatic) prior belief persists through all aspects of this process.

The turning point

A famous example of changing beliefs is provided by one of history's most distinguished homeopaths, JT Kent. The recovery of his wife after a homeopathic medicine turned him from a fierce opponent into an epoch-making homeopathic doctor. Probably many doctors went the same path.

After the above discussion about practical experience it is hard to imagine that one case overturns beliefs completely. Probably there is something else going on. After a shocking event regarding a loved one our fundamental prior beliefs can get out of balance, like Kuhn's crisis on a personal level.¹⁹ After that we may be more susceptible to the opinions of people that we did not take seriously before. We may accept evidence that we did not accept before. We may abandon the first prior, rearrange and re-interpret the evidence and then the process of sequential updating can start.

Discussion

Suppose that we perform all the calculations presented here. Is the problem about proof for homeopathy any clearer after all these formulae and calculations? Probably not; the discussion will just shift towards the admissibility of various kinds of proof and the subjectivity of many parameters that must be estimated. Science is an intrinsically human affair.⁵ It cannot easily overturn our deepest beliefs. Science makes the discussion more and more abstract and we become estranged from reality. Bayesian reasoning could make things worse if we are blind to fundamental flaws in underlying priors and subjectivity in selecting hypotheses and proof.

Whether we look from a Bayesian or a frequentist's perspective, the placebo hypothesis for homeopathy has become less probable with the existing evidence. But there is always a way out, the final step is mistrusting the integrity of the bearer of the unwelcome proof. Kuhn states: "... scientists fail to reject paradigms when faced with anomalies or counterinstances" (p. 78).¹⁹

Apparently the rules for recognition have changed. Originally the RCT was presented as the gold standard. The new hypotheses about publication bias and quality bias proved valid for conventional medicine. The attempts to prove that these two hypotheses were more valid for homeopathy failed. There are other testable hypotheses already proven in conventional medicine, like incomplete reporting and fraud.^{20,21} This kind of bias could also be

present in homeopathy. There is also ghost authorship,²² but this seems unlikely for homeopathy. Should all these hypotheses be tested before recognising homeopathy, while they seem to have no effect on the status of already recognised conventional therapies?

It seems odd that experts in epidemiology acknowledge the results of RCTs, but fail to accept the consequences based on arguments outside their own expertise. Experts in the field they refer to are not so sure about these arguments.^{7,23} It seems fair to use the crossword analogy for science: meta-analysis is just a part of the puzzle.⁸ But what if the dictionary we use to solve the crossword puzzle is incomplete, or if we dismiss certain fields of expertise?

Conclusion

Bayesian analysis of the proof for homeopathy explains why people don't accept proof, but it complicates the discussion unnecessarily. It obscures the real issue: our first prior belief. This paradigmatic first prior belief influences numerous aspects of a large number of decisions that must be made in Bayesian analysis. The first prior belief should be discussed properly and after that, the whole problem might dissolve, because we start looking differently at the existing evidence. Overturning our first prior belief requires a turning point, such as the paradigmatic crisis described by Kuhn, that has not yet been translated into an algorithm, Bayesian or otherwise.

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