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DEBATE

Bayesian homeopathy: talking normal again

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Homeopathy has a communication problem: important homeopathic concepts are not understood by conventional colleagues. Homeopathic terminology seems to be comprehensible only after practical experience of homeopathy. The main problem lies in different handling of diagnosis. In conventional medicine diagnosis is the starting point for randomised controlled trials to determine the effect of treatment. In homeopathy diagnosis is combined with other symptoms and personal traits of the patient to guide treatment and predict response. Broadening our scope to include diagnostic as well as treatment research opens the possibility of multi factorial reasoning. Adopting Bayesian methodology opens the possibility of investigating homeopathy in everyday practice and of describing some aspects of homeopathy in conventional terms. *Homeopathy* (2007) **96,** 120–124.

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Introduction

Homeopathy has a communication problem. An important problem is that of incommensurability of terminology; we often use a different language from conventional colleagues. We talk of 'remedy picture' instead of diagnosis. We value peculiar symptoms highly while conventional doctors ignore them. In our secret language we refer to Hahnemann's aphorism 153 (referring to peculiar symptoms) to indicate why a certain medicine was prescribed. We use an unusual term, 'pathognomonic' to indicate that symptoms typical of a disease are unimportant, the opposite to conventional medicine.[1] Our alternative language is necessary to express something that is missing in conventional medicine, but it creates problems when trying to communicate with conventional colleagues. How can we convince others that we must prescribe on 'remedy picture' rather than diagnosis when we can offer nothing but experience to support this assertion? It would be easier if we used a common language. And in fact such a language has existed for nearly two and a half centuries, and has recently regained importance in conventional medicine.[2,3] This language is based on mathematical theory of conditional probability. The theologian and mathematician Thomas Bayes (Fig. 1) developed this theory to describe how knowledge increases following experience.[4] If we describe our method in Bayesian terminology we can again communicate with our conventional colleagues.

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Bayes' theorem

The basic idea of Bayesian methodology is that new heuristic evidence changes the probability of a hypothesis (an heuristic is a replicable method or approach in learning, discovery, or problem-solving). The odds of a hypothesis before the new evidence (prior odds) are multiplied by the likelihood ratio (LR) of the new evidence to obtain the new odds (posterior odds) of the hypothesis. Posterior odds = LR × prior odds. We are accustomed to probability or chance rather than odds, but chance can be converted to odds and vice versa as follows:

$$\text{Odds} = \text{chance}/(1 - \text{chance}),$$

$$\text{Chance} = \text{odds}/(1 + \text{odds}).$$

The likelihood ratio of heuristic evidence is calculated using a 2 × 2 table (Table 1). Here the heuristic evidence is about the likelihood of the presence of an illness after a diagnostic test.

Figure 1 The Reverend Thomas Bayes (1702–1761).

Table 1 2 × 2 Table showing relation between the results of diagnostic tests and the presence of illness

	Illness present	*Illness absent*	*Total*
Test positive	*a*	*b*	*a* + *b*
Test negative	*c*	*d*	*c* + *d*
	a + *c*	*b* + *d*	*a* + *b* + *c* + *d*

The likelihood ratio of a positive test is calculated as follows:

$$LR(+) = (a/(a+c))/(b/(b+d)),$$

or in words, LR is the occurrence of a positive test in the population with the disease divided by the occurrence of the positive test in the population without the disease. LR is assessed in diagnostic research and combines the sensitivity and specificity of a test in a single value. For example diagnostic ultrasonography for appendicitis.[5] The LR of a positive test is: LR = (76/(76 + 24))/(10/(90 + 10)) = 7.6 (Table 2).

The practical value of Bayes' theorem is that we can see the positive outcome of a test from a clinical perspective: one positive test is not enough to be certain of a diagnosis, but it increases the likelihood. The degree of certainty about a diagnosis depends on what is already known. Suppose that we rely totally on ultrasonography and perform ultrasonography on every patient with abdominal pain in general practice. The occurrence of appendicitis in general practice in patients with abdominal pain is about 2%, so the odds are 2/98.[6] After a positive ultrasonography the odds become 7.6 × 2/98, a probability of 7.12%. The

Table 2 2 × 2 Table showing relation between the results of ultrasonography and the presence of appendicitis, derived from Horton et al[5]

	Appendicitis present	*Appendicitis absent*	
US positive	76	10	86
US negative	24	90	114
	100	100	200

decision to operate the patient should not be taken on such a low probability. But actual practice is different because a doctor has already examined the patient before referral for ultrasound. After examination by a doctor the chance that a patient with abdominal pain referred for ultrasound has appendicitis rises to about 50%, the odds are 1. In such patients, referred for ultrasound by a doctor, the odds of appendicitis after a positive ultrasonography are 7.6, the probability 88.3%. The doctor has done a good job using his clinical diagnostic skills.

The diagnosis of appendicitis, like many others, cannot be based on a single test. A number of tests have to be performed to get enough reasonable certainty about a diagnosis. For the general practitioner seeing a patient with abdominal pain, the prior chance of appendicitis is 1%. After anamnesis and physical examination the posterior chance is 50%. After referral for ultrasound the prior chance is 50% and after ultrasonography the posterior chance is 88.3%. The increasing probability after adding new information is an essential feature of Bayes' theorem.

Diagnosis and therapy: different research

Science in medicine is often identified with randomised controlled trials (RCT), but RCTs cannot answer all questions. Research divides the medical process in two: before and after diagnosis. In researching the diagnostic part (before diagnosis) we assess the probability that a diagnosis is correct if the assessed diagnostic test (or symptom) is present or positive. The research question in the second part (after diagnosis) is quite different: does the effect of the therapy differ from placebo or from that of another treatment? This does not mean that the treatment effect is certain in each patient, we do not know how certain an effect is for a given patient, even if the effect is statistically 'proven' in a group of patients. From a scientific point of view, RCTs are highly valued because they give the most reliable answer about the specificity of the effect of the medicine.

But from the patient's point of view, the RCT gives a surrogate outcome; it does not indicate an individual's chances of cure. Figure 2 shows why. The effect of a medicine is the end of a chain of procedures and depends, among other things, on a correct diagnosis. Even if the diagnosis is correct and the therapy is effective according to RCT evidence an individual does not know his chances of cure or benefit.

Other variables, such as co-morbidity, may influence the result. To know chances of cure or benefit we have to measure the whole chain of procedures between complaints and cure. In how many cases does a 'positive chain' (positive diagnosis + proven treatment) lead to a cure or not? We could make a 2 × 2 table of this process (Table 3).

This is the same procedure as in diagnostic research. It gives the patient a more practical answer; will I get cure or benefit if the diagnosis is correct and the treatment effective? But in scientific terms the answer is more difficult to handle. Which variables influence effect? The influence of a number of variables has to be assessed and some of them may be poorly defined.[7] For patients with the same diagnosis several variables may differ, leading to different chance of cure or benefit. This could be addressed by Bayesian research. But the outcome (cure/benefit) may also be poorly defined, often there is no gold standard.[8]

Effect modification

Experience in homeopathic practice tells us that prescribing on diagnosis alone is rarely effective. The chances of cure/benefit increase if other indications for a homeopathic medicine are added. The problem in homeopathy is the similar to that in the diagnosis of appendicitis: a reliable outcome cannot be based on one fact. Homeopathic prescribing can be described as a Bayesian procedure that can be assessed the same way as diagnostic instruments. The outcome is a probability, not a yes or no statement about effectiveness. In homeopathy the diagnosis can be used, but has the same (or less) value as other symptoms. The research question in homeopathy is: How likely is cure when given symptom(s) (or diagnosis) are present? This influence of different variables on outcome of therapy is known in epidemiology as 'effect modification'; the presence of different variables influences the chances of cure. See Figure 3.

This knowledge enables us to communicate about homeopathic prescribing in 'normal' language. Traditionally we refer to the 'remedy picture' matching the 'patient picture'. But in Bayesian terms we can describe our reasoning as in the following hypothetical example:

- The prior chance that *Rhus toxicodendron* will cure a patient with a rheumatic complaint, if prescribed without any further information is 5%.
- The LR for 'amelioration by motion' and *Rhus-t* = 6. This modifies the posterior chance to 25% if this symptom is present.
- If the patient also has a desire for cold milk (LR = 5). This second symptom modifies the posterior chance to 45%.
- If the symptoms aggravate in wet weather (LR = 3). This third symptom modifies the posterior chance of a favourable response to 75%.

There are reasons to expect that this line of thinking will become more important in conventional medicine. The present monocausal concept of disease stems from the 'microbiological' revolution of the last 150 years. But there is a new revolution going on, genomics and proteomics. Pharmacogenetics is based on genomics and tells us that there is a genetic predisposition for reactions to medicines and that disease is usually a multifactorial causal process.[9] The presence of a specific genetic makeup (genotype) influences chances of cure. Homeopathy works with phenotype, the expression of genotype. In our hypothetical example the symptoms 'amelioration by motion', 'desire for cold milk' and 'aggravation from wet weather' could be regarded as the phenotypical expressions of the genotype of this patient modifying the chance of success with *Rhus toxicodendron*.

The causal relation between genotype and effect is more apparent than between phenotype and effect, but a causal relation between genotype and phenotype is

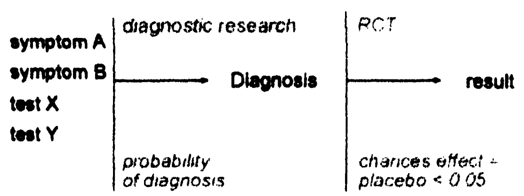

Figure 2 From symptom to result via diagnosis.

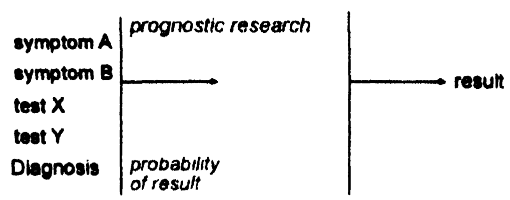

Figure 3 From symptoms directly to result.

Table 3 2 × 2 Table showing relation between the results of the medical process and its outcome

	Cure	No cure	
Diagnosis positive+effect proven	*a*	*b*	*a* + *b*
Diagnosis and/or effect negative	*c*	*d*	*c* + *d*
	a + *c*	*b* + *d*	*a* + *b* + *c* + *d*

plausible. In Bayesian methodology plausibility is not so important; the presence of a symptom predicts result if there is a statistical relation between symptom and result. For clarity, I have simplified the diagnostic/prognostic process by assuming that the different symptoms are independent. In reality the various elements (symptoms) may be interrelated. The elements give indications, but for the final diagnosis or choice of the homeopathic medicine qualitative interpretations are indispensable.

Peculiar symptoms

In aphorism 153 of the Organon Hahnemann stated that peculiar symptoms are the most important indications for homeopathic medicines. Peculiar means that the prevalence of the symptom is very low in the general population, but the symptom is more common in the population who will respond to a particular medicine. Suppose that symptom A occurs in only 50 of 10 000 patients, but in half of the population cured by medicine X. The 2 × 2 table is shown in Table 4. The LR of symptom A is (25/50)/(25/9950) = 199: a prior chance of 5% rises to 91.3% posterior chance if the symptom is present. So Hahnemann's observation can be translated into Bayesian terms: Peculiar symptoms have high LRs.

Pathognomonic symptoms

A 'pathognomonic symptom' is a symptom that is diagnostic of a particular disease. Kent taught that pathognomonic symptoms give little information. This translates into Bayesian terms as follows: if we know that the patient has a particular disease, then symptoms typical of that disease do not increase the chance that a medicine will work, even if the symptom is typical of that medicine. For instance, suppose that the symptom 'amelioration by motion' occurs in 70% of all patients with rheumatoid arthritis, and in 70% of all patients who respond to *Rhus tox* (See Table 5).

Table 4 Hypothetical 2 × 2 table for a peculiar symptom

	Cure by medicine X	Rest	
Symptom A positive	25	25	50
Symptom A negative	25	9925	9950
	50	9950	10 000

Table 5 2 × 2 Table: the hypothetical influence of the symptom 'amelioration by motion' on benefit from Rhus toxicodendron in a population with rheumatoid arthritis

	Cure by Rhus-t.	Remainder	
Motion ameliorates positive	70	630	700
Motion ameliorates negative	30	270	300
	100	900	1000

In this case the 'remainder-population' is the rheumatoid arthritis population not responding to *Rhus toxicodendron*. For this population LR of 'amelioration by motion' is 1: the presence of this symptom does not increase the likelihood of response to *Rhus tox*. At first sight this seems contra-intuitive, we know from practical experience that the symptom 'amelioration from motion' is an indication for *Rhus toxicodendron*. But the situation here is not 'normal practice', not even in a rheumatologist's practice, but it is typical for RCTs, where one diagnosis is investigated.

The diagnosis rheumatoid arthritis and the symptom 'amelioration from motion' are not independent. The symptom 'amelioration from motion' is caused by the illness rheumatoid arthritis. The translation of 'if symptom A is pathognomonic for disease X, it is not important' is 'if symptom A is not independent of disease X, it is not important'.

Conclusion

Homeopathic physicians learn empirically to apply certain rules which are not so strange as they appear at first sight. In selecting medicines they use similar techniques as in clinical diagnostics. With Bayesian methodology we can use more normal language to explain important aspects of homeopathy. For instance:

- *The similia rule*: Chances of effect of a homeopathic medicine are modified by phenotypical features of the patient similar to those of a medicine and increase as more similar symptoms are present.
- *Aphorism 153 of the Organon*: Unusual symptoms often have high LRs and are therefore strong indications for medicines that are relatively often linked to those symptoms.
- *Pathognomonic symptoms*: If two properties of the same patient are not independent the combined value is less than if they were independent.

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