return on a separate occasion for the hepatitis B immunisation. Defaulting did not seem to be a contributing factor to the sharp drop off of hepatitis B vaccine coverage beyond the first dose. In the 1988 vaccination coverage survey defaulters were few. In addition, clinics can identify them by duplicate road to health cards, and defaulters' homes are visited by clinic sisters. More importantly, hepatitis B vaccine was not always available when children did attend clinics.

In either event the high dropout rate in an otherwise excellent primary health care programme emphasises the difficulties in introducing a new vaccine to routine expanded programme on immunisation programmes and the need to devise strategies to minimise disruption. Previous studies have shown that diphtheria, tetanus, and pertussis, BCG, and hepatitis B vaccines may effectively be administered simultaneously.¹⁷ A tetravalent vaccine for diphtheria, tetanus, pertussis, and hepatitis B, with all four constituents mixed into the same phial, would ensure that hepatitis B vaccine coverage would at least reach that of diphtheria, tetanus, and pertussis.

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Clinical trials of homoeopathy

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Abstract

Objective—To establish whether there is evidence of the efficacy of homoeopathy from controlled trials in humans.

Design—Criteria based meta-analysis. Assessment of the methodological quality of 107 controlled trials in 96 published reports found after an extensive search. Trials were scored using a list of predefined criteria of good methodology, and the outcome of the trials was interpreted in relation to their quality.

Setting—Controlled trials published world wide.

Main outcome measures—Results of the trials with the best methodological quality. Trials of classical homoeopathy and several modern varieties were considered separately.

Results—In 14 trials some form of classical homoeopathy was tested and in 58 trials the same single homoeopathic treatment was given to patients with comparable conventional diagnoses. Combinations of several homoeopathic treatments were tested in 26 trials; isopathy was tested in nine trials. Most trials seemed to be of very low quality, but there were many exceptions. The results showed a positive trend regardless of the quality of the trial or the variety of homoeopathy used. Overall, of the 105 trials with interpretable results, 81 trials indicated positive results whereas in 24 trials no positive effects of homoeopathy were found. The results of the review may be complicated by publication bias, especially in such a controversial subject as homoeopathy.

Conclusions—At the moment the evidence of clinical trials is positive but not sufficient to draw definitive conclusions because most trials are of low methodological quality and because of the unknown role of publication bias. This indicates that there is a legitimate case for further evaluation of homoeopathy, but only by means of well performed trials.

Introduction

A survey of 293 general practitioners in The Netherlands showed that 45% of them think that homoeopathic remedies are efficacious in treating upper respiratory tract infections or hay fever.¹ On the other hand, many doctors do not believe that homoeopathy is an efficacious treatment as it is highly implausible that infinitesimally diluted substances retain their biological effects. It is also often stated that homoeopathy has not been evaluated using modern methods—that is, controlled trials. The first argument may be true, but the second is certainly not true. Reading an article about pollen C30 in hay fever increased our interest in homoeopathy.² We could not believe the positive result (was it coincidence?) and therefore we started to search for further reports. Here we present 107 controlled trials of homoeopathy.

Homoeopathic medicine is a system developed by Samuel Hahnemann from the similia concept: "similia similibus curantur." This implies that a diluted, "potentised" agent, which (when undiluted) in healthy

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individuals induces complaints resembling those of the patient, can be used to cure the patient.

Potentialisation is a combination of dilution and shaking of a substance. A plant—for example, *Arnica montana*—is macerated and dissolved in alcohol. One part of this “mother tincture” is mixed with nine parts (D1 potency) or 99 parts (C1 potency) of 90% alcohol (the concentration of the alcoholic solution may vary between manufacturers) and then vigorously shaken. This process can be repeated many times, resulting in very high dilutions (potencies): D6 means one molecule of the original substance in 10^6 molecules of 90% alcohol; C6 means one molecule in 10^{12} molecules. In potencies of D24 or C12 and higher it is very unlikely that even a single molecule of the mother tincture is present. The idea is, however, that higher potencies work more strongly than lower potencies.

Using the similia principle the classical homoeopath tries to find a substance that fits the patient's complaints as much as possible. Unusual symptoms that do not fit the symptom complexes recognised by conventional medicine may be considered even more important than the regular symptoms. This is why homoeopathy is a highly individualised treatment, resulting in different treatments for patients who would receive an identical treatment in conventional medicine. In modern homoeopathy combinations of several or many homoeopathic substances are often used, especially in over the counter preparations. The classical homoeopath will never use this polypharmacy. Also, according to classical homoeopathy a similia must be used and not a potentiation of the causal agent (for example, pollen in hay fever or lead in lead poisoning), which is called isopathy. Phytotherapy is the administration of herbs or low potencies of herbs (D2 or so). These preparations may still have pharmacological effects, and therefore it is sometimes difficult to demarcate phytotherapy from modern homoeopathy, the fundamental difference being the applied low dose toxicology principle in homoeopathy. This description of homoeopathy indicates that it is not just another therapy but a distinct outlook in medicine, and several interpretations have developed, often contradictory to one another.

For this review we searched exhaustively for published reports to investigate the clinical evidence of the efficacy of homoeopathy, regardless of its (to us) implausibility. The positive and negative evidence was weighed against the methodological quality of the research.

Materials and methods

Trials were eligible if parallel index and control groups were included. Crossover designs were also eligible, but controlled studies in animal models were excluded.

Experiments were found by various strategies: a computer search (MEDLINE online 1966-90; key-word homoeopathy); checking references extensively, in articles on clinical research and in textbooks^{4,5}; checking the proceedings of conferences of homoeopathy; checking the contents of several journals of homoeopathy; personal communication with researchers; writing to and visiting major manufacturers of homoeopathic preparations; and visiting several libraries specialising in homoeopathy. This process of collection took place over a period of more than three years. Trials published in any language were eligible, without restrictions.

Classical homoeopathy uses individual diagnoses and treatments. From a homogeneous group given diagnoses in conventional medicine the patients suitable for homoeopathic treatment can be selected. This results in acceptable participants from both regular

and homoeopathic points of view. Individual treatment is prescribed, and then the patients are randomly allocated to homoeopathic or placebo treatment. If necessary, the prescription may be changed in the course of time and, of course, patients who started on placebo stay on placebo.⁶

When the same homoeopathic drug or combination of homoeopathic drugs is given to all patients with a comparable regular diagnosis, trial methodology is the same as in regular medicine. This also goes for trials testing isopathy.

Because the effects of most homoeopathic treatments are meant to last for longer periods, the interpretation of crossover trials is complicated by carryover effects. The analysis will be very difficult, and consequently parallel experiments are preferable.

To explore the possibility that an increasing likelihood of bias (an increasing number of methodological shortcomings) is reflected in the results of the trials, criteria for a methodological assessment of the experiments were established. We put much weight on the number of participants. In most indications for homoeopathic treatment subjective symptoms are the main outcome phenomenon. Substantial improvements of patients in the control group can be expected, and fairly large groups, which are comparable at baseline for prognostic factors, are needed for valid assessment of the efficacy. In trials with limited numbers of participants one cannot be confident that randomisation will equally divide known and unknown confounders over the experimental and control groups. As well, publication bias may be less likely for experiments with large numbers of participants: the effort and costs entailed will increase the likelihood that a paper is submitted for publication. Thus a main argument for our emphasis on relatively large numbers of participants was not the likelihood of type II error, which also depends on the estimated size of the effect, but mainly our worry about incomparability at baseline of the groups and the likelihood of publication bias.

Other major criteria for methodological soundness were randomisation and double blindness. When prognostic factors of the illness, other than the intervention under study, are insufficiently known, random allocation to the contrasted treatments is useful to ensure a comparable prognosis. Double blindness is important for keeping the intervention exactly the same in the contrasted groups except for the homoeopathic treatment, and for an unbiased assessment of the effects. This is especially important if it concerns the relief of subjective symptoms, as is often the case in homoeopathic treatment.

Starting from a maximum score of 100 points, we divided these among seven methodological criteria.

(1) *Patient characteristics adequately described: 10 points*—Description of the symptoms and, if appropriate, of their duration and severity.

(2) *Number of patients analysed: 30 points*—One hundred or more patients per group analysed=30 points, 50-99 patients per group=20 points, and 25-49 patients per group=10 points. A crossover trial with 70 participants (35 given active treatment and 35 given placebo in each period) would score 10 points. In trials assessing the prophylactic effects of homoeopathy the number of patients with the outcome phenomenon was used.

(3) *Randomisation: 20 points*—Twenty points if the method of randomisation was described and correct, 10 points if the method was not described or if some form of pseudorandomisation was applied. If there were fewer than 25 participants per group, half the score was given unless there was prestratification (matching) on relevant items and a table showing comparable baseline characteristics.⁷

(4) *Intervention well described: 5 points*—Adminis-

tration (doses, duration) and origin (method of manufacture) of homeopathic preparations.

(5) *Double blinding: 20 points*—Twenty points if the placebo was described as indistinguishable, 10 points if double blinding was only mentioned.

(6) *Effect measurement relevant and well described: 10 points*—Measurement of the effect must be sensible and reproducible. Five points each for relevance and adequate description.

(7) *Presentation of the results in such a manner that the analysis can be checked by the reader: 5 points*—Depending on measurement of the effect, at least the mean(s) and standard deviation, standard error, or confidence interval in each group must be mentioned, or the number of patients with a certain outcome (for example, if rates or proportions were used).

Sometimes only part of the score was given if the description was unclear, or if only some of several interventions, measurements of outcome, or data presentations met the criteria. In the second criterion we chose to use the number of patients analysed instead of the number randomised because in many publications drop outs were not accounted for. Often the number of patients admitted was not even mentioned. In the seventh criterion we did not demand confidence intervals for the comparisons between groups because then virtually no trials would score the criterion, with only a few exceptions.^{2 8 9}

All articles were scored by at least two of us, and differences, which were mainly caused by reading errors or by unclear descriptions in the publications, were resolved by discussions. Most of these differences occurred in patient characteristics and descriptions of measurement of the effect; in these cases the relevance and sensibility had to be judged. The largest difference was 13 points.

Assessment of articles using these criteria provides a score that gives an indication of the methodological quality of each trial. This quality is an important factor in weighing the conclusions of different trials and, of course, on the impact on the reader's opinion of all the evidence presented. We have selected well established methodological criteria,¹⁰ and our assessment can be checked by the reader (table I).

Results

Table I shows some methodological characteristics of the better trials (those scoring 55 points or more).^{2 8 11-31} Some good studies have been reported, but overall the methodological quality was disappoint-

ing. Patient characteristics were described adequately in 56 trials. More than half of the publications (63) were of trials in which fewer than 25 patients per group were treated. Sixty eight trials were randomised, but only 17 described the method of randomisation. The intervention was adequately or reasonably well described in 80 trials. Seventy five were double blind, but the placebo was described as indistinguishable in only 31 trials. In 67 publications the effect measurement was judged to have been sensible and well described. Sufficient data for the reader to check the analysis were given in 65 trials.

It is difficult to compare the quality of trials that score more or less the same, and in the lower range the results of all studies may be seriously biased because of several methodological shortcomings. Consequently, we present in detail the results of only the best trials (those scoring 60 points or more) (table II).^{2 11-24}

In 14 experiments some form of classical homeopathy was tested.^{22 32-44} Only one of these scored more than 60 points. In a randomised double blind trial Brigo gave one or sometimes two of eight chosen drugs (belladonna, gelsemium, ignatia, cyclamen, lachesis, natrium muriaticum, silicea, or sulphur in a C30 potency) to 30 patients with migraine headache; 30 controls received a placebo. After four months the patients treated with homeopathy fared much better than the controls on severity of attacks: on a 10 cm visual analogue scale the severity changed from 9.1 to 2.9 in the homeopathic group and from 8.4 to 7.8 in the control group. Similar differences were found for the frequency and the duration of the attacks.²²

In about half of the controlled trials (58 studies) the same single homeopathic treatment was given to a group of patients with comparable conventional diagnoses. Combinations of homeopathic treatments (polypharmacy) were tested in 26 studies, and isopathy in nine. Only one trial compared dilutions with potencies (a positive trend was found in favour of the potency)¹³ and in a few trials different potencies or different homeopathic substances were compared with each other.^{12 15 24 66 79}

Twenty eight trials were published before 1980, 38 in the period 1980-4 and 41 from 1985 onwards. Forty two trials were published in English, 34 in German, 30 in French, one in Italian, and one in Portuguese. Several trials were published in more than one language (for example, Italian and French); in those cases we chose the reference of the most comprehensive and most easily obtainable publication.

According to conventional diagnoses, several groups

TABLE I—Scoring of methodological characteristics of clinical trials of homeopathy

	Characteristics of patients (max = 10)	Number analysed (max = 30)	Randomisation (max = 20)	Intervention (max = 5)	Double blinding (max = 20)	Measurement of effect (max = 10)	Presentation of data (max = 5)	Total score (max = 100)
GRECHO 1989 ^{11 12}	10	30	10	5	20	10	5	90
Reilly <i>et al</i> 1986 ²	10	20	20	5	20	10	5	90
Ferley <i>et al</i> 1989 ⁹	10	30	10	5	20	8	5	88
Wiesnauer <i>et al</i> 1985 ¹⁴	5	20	20	5	20	10	5	85
Arnal-Laserre 1986 ¹⁴	10	10	20	5	20	10	5	80
Wiesnauer and Gaus 1986 ¹⁵	10	20	10	5	20	10	5	80
Zell <i>et al</i> 1988 ¹⁶	10	10	20	5	20	10	5	80
Valero (Raphanus sativus) 1981 ¹⁷	10	20	20	5	10	10	5	80
Aulagnier 1985 ¹⁸	10	30	10	5	10	10	0	75
Wiesnauer <i>et al</i> 1983 ¹⁴	5	10	20	5	20	10	5	75
Bordes and Dorfman 1986 ²⁰	10	10	10	5	20	10	5	70
Valero (Pyrogenium) 1981 ¹⁷	10	10	20	5	10	10	5	70
Ferley <i>et al</i> 1987 ²¹	8	10	10	5	20	10	5	68
Brigo 1987 ²²	10	10	20	3	10	10	5	68
Maiwald <i>et al</i> 1988 ²³	10	20	15	5	0	10	5	65
Wiesnauer <i>et al</i> 1989 ²⁴	5	10	10	5	20	10	0	60
Bignamini <i>et al</i> 1987 ²⁵	10	0	10	3	20	10	5	58
Chevrel <i>et al</i> 1984 ²⁶	10	10	10	3	10	10	5	58
Gassinger <i>et al</i> 1981 ²⁷	10	10	20	3	0	10	5	58
Ritter 1966 ²⁸	5	20	10	3	10	5	5	58
Wiesnauer and Gaus 1987 ²⁹	10	0	10	5	20	10	3	58
Lewith <i>et al</i> 1989 ³⁰	10	0	5	5	20	10	5	55
Savage 1977 ³¹	10	0	5	5	20	10	5	55

Eighty four controlled trials scored <55 points.^{32 33 104}

TABLE II—Characteristics and results of best trials

	Score for methodology (max=100)	Indication (No of patients/No of controls)	Intervention	Results (No of patients/No of controls)
Polypharmacy:				
Ferley <i>et al</i> 1989 ⁹	88	Treatment of influenza (237/241)	Anas barbariae hepatis, cordis extractum C200 v placebo	Recovery rate within 48 hours (17.1%/10.3%)
Arnal-Laserre 1986 ¹⁴	80	Duration of delivery (53/40)	Actea racemosa C5, arnica C5, caulophyllum C5, gelsemium C5, pulsatilla C5 v placebo	Duration of delivery: (5.1/8.5 hours); "dystocie" [problems with dilatation] (11.3%/40%)
Zell <i>et al</i> 1988 ¹⁶	80	Ankle sprains (33/36)	D2-D6 combination of 14 substances v placebo	No of patients without pain after 10 days: (28/13)
Aulagnier 1985 ¹⁸	75	Bowel movements after abdominal operation (100/100)	Opium C9, raphanus C9, arnica C9 v placebo	Days until first flatus (2.5/3.2); days until first faeces (4.0/4.9)
Bordes and Dorfman 1986 ²⁰	70	Dry cough (30/30)	C3 combination of 10 substances v placebo	Very good or good result after 1 week (20/8)
Ferley <i>et al</i> 1987 ²¹	68	Prevention and treatment of influenza (588/594)	D1-D6 combination of 10 substances v placebo	Incidence (6.5%/7.2%); duration of symptoms (7.0/6.8 days)
Maiwald <i>et al</i> 1988 ²³	65	Influenza (88/82)	Aconitum D4, bryonia D4, lachesis D12, eupatorium perfoliatum D3, phosphorus D5 v acetyl salicylic acid 1500 mg days 1-4, 500 mg days 5-10	Positive result within 4 days (29%/23%)
Wiesenauer <i>et al</i> 1989 ²⁴	60	Sinusitis (45, 38, 35/34)	(1) Luffa operculata D4, kalium bichromicum D4, cinnabaris D3 (2) Kalium bichromicum D4, cinnabaris D3 (3) Luffa operculata D4; v (4) placebo	Combination score of 6 symptoms (no difference between the 4 groups)
Same formula in all patients:				
GRECHO 1989 ^{11, 12}	90	Bowel movements after abdominal operation (4 groups of 150)	(1) Opium C15 (2) Opium C15, raphanus C5 v (3) Placebo (4) No treatment	Time until first faeces: (1) 96 hours (2) 99 hours (3) 94 hours (4) 95 hours Similar results for first peristaltic sounds and first flatus
Wiesenauer and Gaus 1985 ¹¹	85	Pollinosis (50/55, 59)	(1) Galphimia glauca D6 v (2) Galphimia glauca dilution 10 ⁻⁶ (3) Placebo	Improvement of nasal symptoms after 2, 4 weeks: (1) 60%, 78% (2) 40%, 51% (3) 41%, 58% Similar results for ocular symptoms
Valero 1981 ¹⁷	80	Postoperative infections (54/74)	Raphanus C7 v placebo	No of patients with infection (15/20)
Valero 1981 ¹⁷	70	Bowel movements after abdominal operation (43/37)	Pyrogenium C7 v placebo	Time until first flatus (53.3/58.6 hours)
Wiesenauer <i>et al</i> 1983 ¹⁹	75	Pollinosis (41/45)	(1) Galphimia glauca D4 v (2) Placebo	Improvement of symptoms after 2, 4 weeks: (1) 83%, 81% (2) 47%, 57%
Comparison of several homoeopathic treatments:				
Wiesenauer and Gaus 1986 ¹⁵	80	Pollinosis (62, 56, 54, 63)	Galphimia glauca (1) C2 (2) C4 (3) D4 (4) LM4	Improvement of nasal symptoms after 2, 4 weeks: (1) 67%, 83% (2) 71%, 79% (3) 67%, 82% (4) 69%, 85% Improvement of ocular symptoms after 2, 4 weeks: (1) 64%, 83% (2) 73%, 88% (3) 65%, 82% (4) 76%, 89%
Isopathy:				
Reilly <i>et al</i> 1986 ²	90	Pollinosis (74/70)	Pollen C30 v placebo	Change in 100 mm visual analogue scale symptom score after 5 weeks (-17.2 mm/-2.6 mm)
Classical homoeopathy:				
Brigo 1987 ²²	68	Migraine (30/30)	8 possible homoeopathic remedies C30 v placebo	Change in 10 cm visual analogue scale symptom score after 4 months (-6.2 cm/-0.6 cm). Similar results for frequency and duration of attacks

of indications emerged: diseases of the respiratory system (19 trials on respiratory infections, five trials on hay fever, and one on asthma); gastrointestinal complaints (seven trials); and pain from several sources (27 trials, of which six were of rheumatological diseases). Table III presents the outcome of all 107 trials. In 42 we thought that insufficient data were given to check the authors' interpretation of the outcome(s). Consequently the results reflect not our conclusions but the inference made by the authors of the publications, who to us seem sometimes to be a little overoptimistic. In most cases, however, a positive result indicates that there was a statistically significant difference in the main outcome(s) between the contrasted groups, whereas a negative result means that no significant difference was found ($p>0.05$). We could not pool the results statistically because of the heterogeneity of the studies.

The evidence is to a large extent positive: of the better studies 15 trials showed positive results whereas in seven trials no positive effect could be detected (in one trial only homoeopathic treatments were compared with each other). The trials with a methodological score below 55 points showed an even clearer trend: in most publications positive results were reported (66 positive, 17 negative). Overall, of the 105 trials with interpretable results, 81 indicated positive results whereas in 24 trials no positive effects of homoeopathy were found compared with (mostly) placebo controls. In the two other trials only homoeopathic treatments were compared to each other.

Discussion

In the methods section we indicated that it is possible to perform trials on the efficacy of homoeo-

have selected well established criteria. The reader could apply different weights to the criteria to see whether substantial changes would occur in our methodological ranking, but we think that this will not be the case.

Double blinding, even if the placebo is described as indistinguishable, has to be checked by asking the patients in which group they believe that they were during the trial. Blindness must be checked early in the trial, before the treatment is expected to take effect, because positive effects would break the code. It is easy to state that a trial was double blind, but patients have many ways to break the code. This might explain small differences in favour of homoeopathy. Double blinding was not checked in any trial of homoeopathy.

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*Comparison of homoeopathic treatments.

Although the number of trials is impressive, many questions remain. Virtually no evidence exists about the correct choice of the remedy and the potency to be used (different potencies or homoeopathic substances should be compared in controlled trials). Hahnemann's principles have been brought into practice in innumerable ways, as is indicated by the differences among the trials presented here. The process of producing preparations (the percentage of alcohol in the solution, the number of times that the substance must be shaken during potentiation, etc) and their composition (especially when herbs are used) differ greatly among manufacturers. Also, there is no plausible explanation of the mechanisms through which homoeopathy would act. Substances that contain only the solvent can have no pharmacological actions according to our present knowledge of physics and chemistry. If a homoeopath is asked his or her opinion about these mechanisms, the most likely reply is "I do not know." In practice, if a treatment works knowledge of the mechanisms of action is not necessary, and numerous examples from regular medicine can be cited in which the mechanisms are hardly understood or not at all. However, to assume that an infinitesimally diluted substance in an alcoholic solution has pharmacological effects would mean that essential concepts of modern physics would have to be dismissed.

An important problem in reviewing the literature is publication bias. Especially with a controversial subject such as homoeopathy, several problems may exist. More trials with positive results might have been submitted and accepted by "alternative" journals, whereas small trials with negative results might not have been submitted or might have been rejected. On the other hand trials with positive results might have been rejected and negative trials more readily accepted by "regular" journals. About one third of the trials were published in each of regular journals, alternative journals, and by other means of communication (proceedings, reports, dissertations, books). No relation between the result and the place of publication was seen. Negative results were reported in alternative journals 12 times, in regular journals seven times, and in other publications five times. When talking to authors of trials we identified at least six trials for which no manuscript had been submitted for publication. It is difficult to discover the true reasons for failure to submit an article for publication, but we think that the (possibly negative) results may have been an important factor in these cases.

Nevertheless, much evidence is available. We tried to decrease the effects of publication bias by extensively checking every possible source for publications or reports of trials. We wrote to many researchers and also visited several of them to learn whether there were any unpublished trials and to get further details of the published ones. We used strict criteria to select the best trials and based our main conclusions on the results of these. The amount of positive evidence even among the best studies came as a surprise to us. Based on this evidence we would be ready to accept that homoeopathy can be efficacious, if only the mechanism of action were more plausible. The way in which the belief of people changes after the presentation of empirical evidence depends on their prior beliefs and on the quality of the evidence.^{105 106} Critical people who did not believe in the efficacy of homoeopathy before reading the evidence presented here probably will still not be convinced; people who were more ambivalent in advance will perhaps have a more optimistic view now, whereas people who already believed in the efficacy of homoeopathy might at this moment be almost certain that homoeopathy works.

A trial of very high quality was that of the Groupe de Recherches et d'Essais Cliniques en Homéopathie,

initiated by the French Ministry for Social Affairs and performed by a group consisting of regular and homoeopathic researchers.^{11 12} After the earlier publication of several trials in which homoeopathy was shown to decrease the time to recovery of bowel movements after abdominal surgery, this hypothesis was retested in a rigorous trial comparing four groups of 150 patients (two groups were treated with opium C15 and raphanus C5, one group with indistinguishable placebo, and one group was not treated). No differences at all were found. Will more of such trials for other indications show the same results and refute the existing evidence?

The weight of the presented evidence will probably not be sufficient for most people to decide definitely one way or the other. The question arises, What further evidence would be needed? Investigations in animal or plant models may increase the belief of sceptical people before they have read the evidence from clinical trials, but if no positive results are found homoeopaths may claim that homoeopathy only works in humans. We did not assess the evidence from such investigations; Scofield concluded in 1984 in a comprehensive review article that "despite the great deal of experimental and clinical work there is only little evidence to suggest that homoeopathy is effective. This is because of bad design, execution, reporting or failure to repeat experimental work."¹⁰⁷ If more (well performed) controlled trials in humans are demanded, cooperation between sceptical investigators and homoeopaths is likely to make the trial results more convincing for many readers. The question is how many of such trials would be needed to draw definitive conclusions? The evidence presented in this review would probably be sufficient for establishing homoeopathy as a regular treatment for certain indications. There is no reason to believe that the influence of publication bias, data massage, bad methodology, and so on is much less in conventional medicine, and the financial interests for regular pharmaceutical companies are many times greater. Are the results of randomised double blind trials convincing only if there is a plausible mechanism of action? Are review articles of the clinical evidence only convincing if there is a plausible mechanism of action? Or is this a special case because the mechanisms are unknown or implausible?

In our opinion, additional evidence must consist of a few well performed controlled trials in humans with large numbers of participants under rigorous double blind conditions. The results of the trials published so far, and the large scale on which homoeopathy is brought into practice, makes such efforts legitimate.

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Acute myeloblastic leukaemia — a model for assessing value for money for new treatment programmes

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Abstract

Objective—To measure the effects of changes in treatment of acute myeloblastic leukaemia that may give better value for money.

Design—Retrospective analysis of patients' notes to identify items of management costing money; prospective costing of these items. The Medical Research Council acute myeloblastic leukaemia 9 trial was used to identify the amount and distribution of these costs when either one or two courses of induction treatment were required to obtain complete remission. These findings were then extrapolated to four published international controlled trials using similarly intense treatment and in which the number of courses of treatment required for complete remission was stated, to compare British costs for treatment with idarubicin and daunorubicin, both in combination with cytarabine.

Setting—Leukaemia unit, Royal Marsden Hospital, London.

Subjects—Data on 10 patients receiving intensive induction treatment for acute myeloblastic leukaemia were used to identify 160 items of cost in four broad groups: general (including accommodation), diagnostic, supportive treatment, and cytotoxic chemotherapy. One newly treated patient was prospectively assessed over one month, including a time and motion study, to cost these items; then costs for 268 patients from the MRC trial receiving moderate induction chemotherapy including daunorubicin were assessed, and costs for treatment of 522 patients in the four international studies comparing daunorubicin with idarubicin were analysed.

Main outcome measures—Cost effectiveness was measured as the overall cost to obtain complete remission in untreated patients with acute myeloblastic leukaemia after treatment with idarubicin or daunorubicin.

Results—The 160 costed items were measured for

their sensitivity in varying the total cost of treatment, this being assessed within Britain in other district general and private hospitals to measure the extremes of cost of these items. Overall, idarubicin, although more expensive, showed a substantial saving (£1477 per patient) in total hospital costs, more than offsetting the increased cost (£607) of the new treatment, an overall saving of £870 per patient (5%).

Conclusion—Approaches modelling cost effectiveness may be an essential part of planning new programmes of treatment in the future. This method can be used to estimate the cost effectiveness of the treatments in different environments and countries where costs may vary widely.

Introduction

After the publication of the government's white paper *Working for Patients* there has been widespread debate on the economic aspects of health care policy. Although in a broad economic analysis total costs and benefits for the whole national economy and for individual patients should be considered, at present only costs and effectiveness within the NHS can be assessed, and it is these that this paper considers.

Improvements in survival of patients treated for acute myeloblastic leukaemia have resulted primarily from the development of more intensive treatment regimens, improved supportive care, and marrow transplantation.¹ The standard initial treatment for induction of remission of acute myeloblastic leukaemia is one or two courses of a combination of an anthracycline (for example, daunorubicin) and cytarabine. Both drugs have been available for many years and are fairly inexpensive. If we use as the end point patients who achieve complete remission (are well and have no detectable disease) on one relatively expensive course of treatment then this may cost less overall and be more cost effective than patients attaining remission in two cheaper courses but requiring extra time in hospital.

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