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Homeopathy
in the prevention of
upper respiratory tract
infections in children



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Abbreviations and definitions

CAM	Complementary and alternative medicine
CI	Confidence interval
OTC	Over the counter (e.g. medicines bought for self-treatment)
RCT	Randomised controlled trial
SD	Standard deviation
URTI	Upper respiratory tract infections

Conventional medicine: The prevailing practice of contemporary western medicine.

Effectiveness: A measure of the extent to which a health care intervention fulfils its objectives.

Efficacy: A measure of to which extent a specific intervention produces a beneficial result under ideal conditions. Ideally, efficacy is based on the result of a randomised controlled trial.

Ultramolecular: Diluted to an extent where there theoretically is very unlikely that any molecules are left of the original substance.

Purpose of the thesis

The research presented in this thesis, has two fundaments:

1. The findings in a survey of 1097 patients visiting 80 different homeopaths in Norway (Steinsbekk 2003). The survey revealed that it had been a nearly threefold increase in the proportion of children among patients visiting homeopaths over 15 years. It also revealed that the most frequent reason for encounter among these children were respiratory and skin problems.
2. The need for research based on the “real world” use of homeopathy that (Linde 1997);
 - a. increases the knowledge about those patients that actually visits homeopaths and
 - b. investigates the effectiveness¹ of homeopathic care and efficacy² of homeopathic medicine for conditions and patient groups that frequently are treated by homeopaths.

The main research questions therefore became:

- Why do parents take their children to homeopaths?
- What is the effectiveness of homeopathic care in prevention of upper respiratory tract infections in children?
- What is the efficacy of self-treatment with self-selected homeopathic medicines in prevention of upper respiratory tract infections in children?

The operational aims of the thesis is presented on page 33

¹ Effectiveness is a measure of the extent to which a health care intervention fulfils its objectives (Last 2001).

² Efficacy is a measure of to which extent a specific intervention produces a beneficial result under ideal conditions. Ideally efficacy is based on the result of a randomised controlled trial (Last 2001).

The homeopathic context

A popular saying is that homeopaths treat the patient, not the disease. What is meant is that homeopaths use the individual characteristics of the patient in their classification system and in deciding which homeopathic medicine to prescribe. Because of this, patients can get different homeopathic medicines when they have the same health problem (conventional diagnosis).

This is reflected in two main deviations from what is usually seen in a “traditional” randomised controlled trial where the aim is to investigate the efficacy of a specific drug in the treatment of a specific disease (conventional diagnosis). The deviations are that in the studies presented in this thesis, there is more than one drug and more than one diagnosis.

The thesis at a glance

What is known

- Homeopathy is the most frequently used form of complementary and alternative medicine (CAM) in Norway.
- There have been homeopaths practicing in Norway for more than 130 years.
- Reason for encounter in homeopathic practice is similar to general practice with exception of cardio vascular complaints.
- The proportion of children among patients visiting homeopaths in Norway has increased from 10% in 1985 to 26% in 1998.
- There are no studies that has explored why parents take their children to homeopaths.
- During the last year, Norwegian children aged four with frequent colds and otitis media visited physicians ten times more frequently than other children.
- Children with upper respiratory tract infections (URTI) are frequent antibiotic users.
- The most frequent reason for visiting a homeopath in Norway among children is skin and respiratory complaints.
- There are very few studies evaluating the effectiveness of individualised homeopathic care for URTI in children.
- Homeopathic medicines are bought over the counter for self-treatment most frequently for respiratory complaints.
- There are no study on whether patients can select the same homeopathic medicine as a trained homeopath would prescribe.
- There is a controversy over whether ultramolecular³ homeopathic medicines can have any effect.
- There are no randomised controlled studies showing a statistical significant specific efficacy of homeopathic medicine in children with URTI, although there is a trend for an effect.

³ Ultramolecular means that it is diluted to an extent where there theoretically is very unlikely that any molecules are left of the original substance (Swayne 2000).

What does this thesis add

- Experiences of conventional medical treatment of the child can led the parents to take their child to a homeopath because the parents
 - do not want to give the medication prescribed by the doctor;
 - they want treatment while waiting for a problem to be assessed;
 - they do not want to continue to use the prescribed medication;
 - they stop taking conventional medication due to side effects;
 - or
 - they are not offered any treatment by the medical doctor.
- Parents would consult a medical doctor if they felt insecure about the health conditions of the child and would visit a homeopath when they felt that seriousness of the condition was clarified.
- Parents choose homeopathy either because they have been recommended it from relatives and friends or because they have personal experience from using it.
- There are parents who take their child to homeopaths despite not understanding or having belief in whether ultramolecular homeopathic medicines can have effects.
- By using simplified constitutional indications for the homeopathic medicines *Calcarea carb*, *Pulsatilla* and *Sulphur*; parents were able to choose the same as homeopaths prescribed for 55% (95% confidence interval 43%-67%) of the children.
- There was a clinical relevant effect of individualised homeopathic care in the prevention of upper respiratory tract infections in children.
- There was no effect over placebo of self-treatment with one of three self-selected ultramolecular homeopathic medicines for prevention of upper respiratory tract infections in children.

List of papers

Paper I

Steinsbekk A, Bentzen N, Brien S. Why do parents take their children to homeopaths? - A qualitative study. Submitted.

Paper II

Steinsbekk A, Fønnebø V, Lewith G, Bentzen N. Homeopathic care for the prevention of upper respiratory tract infections in children. - A pragmatic randomized controlled trial comparing individualised homeopathic care and waiting list controls. Submitted.

Paper III

Steinsbekk A, Bentzen N, Fønnebø V, Lewith G. The use of simplified constitutional indications for self-prescription of homeopathic medicine. *Complement Ther Med* 2004;12(2-3):112-117.

Paper IV

Steinsbekk, Aslak, Bentzen, Niels, Fønnebø, Vinjar & Lewith, George. Self treatment with one of three self selected, ultramolecular homeopathic medicines for the prevention of upper respiratory tract infections in children. A double-blind randomized placebo controlled trial. *British Journal of Clinical Pharmacology* 2005; 0 (0), -.doi: 10.1111/j.1365-2125.2005.02336.x
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General introduction

Overview of homeopathy in Norway

In 1827 homeopathy was described in the Norwegian medical journal “Eyr” by one of the central persons of modern medicine in Norway, Fredrik Holst (Holst 1827). A book in Norwegian on homeopathy was published by “A Norwegian homeopath” in 1870 (En norsk homeopat 1880) (the reference is the second edition). Another book was published in 1893 (Ohm 1893) and in the same decade an international conference on homeopathy was held in Christiania (now Oslo), the capital of Norway. The association organising only homeopaths in Norway today, Norwegian Homeopathic Association (NHL), was established in 1930.

The first homeopathic school was established in 1975 in Oslo and the second in 1987 also in Oslo. By spring 2004, nearly 700 students have graduated from these schools. None of the schools is officially accredited. The studies are part time and the duration is at least five years. This includes both medical and homeopathic subjects. Norwegians, who wanted to take a homeopathic education before the schools were established, had to study abroad.

Homeopathy is not a part of the official health system and is regulated under the “Law of alternative therapies” (Befring 2004). This law makes it legal for every citizen to treat patients as long as they don’t harm them. Anyone can call himself or herself a homeopath without any control of whether or not they have a training in homeopathy.

Norwegian Homeopathic Association has nearly 430 members who all have completed an approved homeopathic education. Nearly $\frac{1}{4}$ of the members are authorised health personnel as well, mostly nurses. There are few medical doctors who are fully trained in homeopathy, and the vast majority of homeopathic prescribing is by homeopaths who are not medical doctors. Among Norwegian

medical doctors, one in five hundred practiced homeopathy in 1993 (Aasland 1997).

The use of homeopathy in Norway

Homeopathy is the most frequently used form of complementary and alternative medicine (CAM) in Norway (Norges Offentlige Utredninger 1998). In 1997, thirty-seven percent of the population over 18 years had been to a homeopath during their lifetime. The proportion was 33% in 1994 (Opinion 1994). Both these surveys are cross sectional telephone surveys with 1000 randomly selected participants who were 18 years and older.

The national health surveys conducted by Statistics Norway have included a question on visits to homeopaths. In 1975 one in two thousand (0,05%) of the Norwegian population had seen a homeopath during the last 14 days (Statistisk sentralbyrå 1977). This proportion increased to one in four hundred (0,25%) in 1985 (Statistisk sentralbyrå 1987). More recent figures are not available for 14-day periods, but almost one in fifty (1,83%) of the Norwegian population had visited a homeopath during the last 12 months in 1995 (Statistisk sentralbyrå 1997). Due to the different timeframe in the questions, these figures cannot tell whether there has been an increase in the proportion of Norwegians who visits a homeopath. All these studies were carried out through personal interviews with more than 10.000 people of all age groups.

The proportion of Norwegian medical doctors who had been treated with homeopathy themselves were four percent in 1993 (Aasland 1997) and seven percent in 1995 (Pedersen 1996).

The most recent survey was done in 2001 and was a cross sectional telephone survey with 1 000 randomly selected participants who were 18 years and older (Opinion 2001). They found that seven percent of the population had used homeopathy (the question this time was not on visits) during the last twelve months and that 72%

of the population had at least some confidence in homeopathy. By comparison a survey published in 1977 found that half of the Norwegian population had confidence in homeopathy (Bruusgaard 1977).

The total number of users is likely to be higher than the telephone surveys shows, as the telephone surveys only include those who were 18 years and older. In a survey from 1985 of patients visiting homeopaths, 10% of the patients were below the age of 10 (Lærum 1985), and the proportion increased to 26% in 1998 (Steinsbekk 2003).

Who visits homeopaths in Norway?

There have been some studies into the characteristics of patients visiting homeopaths in Norway (Christie 1991; Lærum 1985; Røisland 1983; Steinsbekk 2003; Straumsheim 1991; Straumsheim 1992a; Straumsheim 1992b).

In 1983 a study of 301 patients in a single homeopathic practice in a small Norwegian town was published as a student thesis (Røisland 1983). It found that the most frequent reasons for encounter were muscle/skeleton complaints followed by neurological and psychological complaints. Fifty-four percent of the patients had complaints that had lasted for more than five years. Sixty-four percent of the patients were women, and children under ten years of age constituted five percent of the patients.

A survey from 1985 including 1 070 patients visiting 54 different homeopaths found that the average patient was a woman in her thirties with higher education (Lærum 1985). The proportion of health personnel was higher among the patients than in the population. The main reason for encounter was musculoskeletal, digestive, psychological, skin and respiratory complaints. Forty-three percent of the patients had had their complaints for more than five years. The main reason for visiting a homeopath was fear of side effects or no effects from conventional treatment, dissatisfaction

with conventional treatment or that they had tried “everything else”. Most of the patients had heard about homeopathy from friends and relatives.

A survey from 1991 with 13 homeopaths and 431 patients found that women counted for 71% of all patients and that the proportion of patients under 10 years of age was 17% (Straumsheim 1992a). The main reason for encounter was respiratory, skin, psychological and musculoskeletal complaints. This study also included an evaluation of the outcome (Straumsheim 1992b) and it was preceded by a smaller study with 200 patients (Straumsheim 1991).

A book published in 1991 was based on several studies describing CAM users and most of these patients had visited homeopaths (Christie 1991). There were more females than males, the patients more frequently had higher education but all socioeconomic groups were represented and nearly all patients had been to a medical doctor before they sought a CAM practitioner.

The most recent survey was done with 1 097 patients visiting 80 different homeopaths (Steinsbekk 2003). Almost half of the patients had used prescription drugs provided by a medical doctor the previous month for the same complaints they presented to the homeopath. The patients sought homeopathy most often because of respiratory and skin complaints. Four of the five most common reasons for encounter in homeopathic practice in 1998 were also found among the five commonest reasons for consultations in general practice (Rokstad 1997). One in four patients visiting homeopaths in 1998 were children between 0 and 9 years of age.

Research on homeopathy in Norway

The first published study on the clinical effect of homeopathic treatment in Norway was a pilot study on prevention of lower urinary tract infections (Straumsheim 1990). Subsequently there have been published articles from randomised controlled trials on individualized homeopathic treatment of migraine (Straumsheim

2000), individualized homeopathic treatment of trauma after tooth extraction (Lokken 1995), standardized treatment with Arnica for muscle soreness (Tveiten 1991; Tveiten 1992; Tveiten 1998; Tveiten 2003) and isopathic⁴ treatment of birch allergy with homeopathic medicines made of birch pollen (Aabel 2000b; Aabel 2000a).

There have also been some homeopathic provings⁵, one of which is published internationally (Bruset 1995). There have also been some master thesis at Norwegian universities focusing on various aspects of homeopathy (Arnes 1994; Braathen 1998; Evang 2003; Folden 1997; Heggland 2000; Lunde 1995).

⁴ Isopathy is the use of medicines derived from the causative agent of the disease itself, e.g. Pollens to treat hayfever (Swayne 2000).

⁵ Proving is a trial testing substances on healthy volunteers (Swayne 2000).

What is homeopathy?

Homeopathy is a method of medical practice based on the principle of similarity (or similia principle, *similia similibus curentur*). The hypothesis is that substances capable of causing symptoms in healthy subjects can be used as medicines to treat people who are ill with similar patterns of symptoms.

Although Hippocrates and others have written about the idea of curing ‘like with like’, it was formally systematised by the German physician Samuel Hahnemann (1755-1843). The story is that Hahnemann translated an herbal text from English to German, which said that Cinchona bark (*China officinalis*) cured malaria because it was bitter. He decided to try this himself, and took repeated doses. He experienced symptoms similar to malaria and hypothesised the similia principle based on this.

One example of the similia principle is the reactions usually seen when peeling an onion: It causes tears and burning sensations in the eyes. This is similar to symptoms of hayfever, and based on the similia principle a homeopathic medicine made from onion is considered by the homeopath for patients with hayfever. A similar example from conventional medicine is to desensitise patients against the allergen they react to by injecting small doses of the same allergen. Vaccination is also used as an exemplification of the similia principle.

To explore the effect different substances have on humans, and thereby find their indications, homeopaths have done so-called provings continually for 200 years. In a proving a substance is administered to healthy persons and all reactions, both physical and psychological are recorded carefully. This information is found in homeopathic materia medicas, which are collections of the total sum of symptoms different substances have provoked in humans. The homeopathic practitioner should ideally match the complete status of symptoms of a patient with the recorded symptoms in the material medica for over two thousand different homeopathic medicines.

The vital force or life force is a central feature of homeopathy (Bell 2004a). It is a metaphysical concept of the energy that animates (breaths life into) the organism, but in homeopathy it is seen as the self-regulating properties of the body. Homeopathic medicines are believed to induce a process of reorganisation of functions by stimulating the self-regulating properties of the body (Bell 2004a).

Hahnemann held that in principle, the real cause of a disease could not be explained in total. This was due to the intricate mechanisms of action together with the activity of the regulating properties of the body (Hahnemann 1978) (paragraph 6 and 7). Therefore, his view was to take the symptoms and signs of the disease as they appear in the patient and treat the patients according to this by applying the similia principle. Homeopaths pay most attention to the symptoms that is not typical for the disease as such, but rather to the symptoms that are unique for the patient. This explains why homeopaths emphasise the individual features of the patient and not the conventional diagnosis.

Homeopathic medicines

Homeopathic medicines, in the European Union legally called “homeopathic medicinal products”, consist of medicines with a botanical, chemical, mineral, or zoological origin. Original substances have undergone a homeopathic manufacturing process called potentisation which is a process of serial dilution and succussion⁶ (Schmidt 2003). Homeopathic medicines are used in both dilutions where there still are traces of the original substances, and in dilutions where there theoretically is very unlikely that any molecules are left of the original substance.

Avogadro's number (6.023×10^{23}) gives the theoretical limit for when there no longer is any molecule left of the original substance. Homeopathic medicines that during the manufacturing process are diluted beyond this limit are termed ultramolecular.

⁶ Succussion is vigorous shaking with impact or “elastic collision” (Swayne 2000).

Overview of homeopathic research

The following chapter is an overview with examples of published research on homeopathy. It is not a systematic review, but it aims at giving an overview of the main research that has been carried out in areas that relates to the areas studied in this thesis. This structure is based on a strategy for research development proposed by the National Research Centre on Complementary and Alternative Medicine (NAFKAM) at the University of Tromsø, Norway (Fønnebø 2003).

The choice of research method is dependent on the question for which an answer is sought. The type of question will vary according to ones place in society:

- From a governmental/regulatory view, it is of interest to know to what extent the therapy is used in society (Giannelli 2004) and the likelihood of patients being harmed by using it. In other words, a request for a description of the use of the therapy and the safety aspects.
- For the patients the central question is if the therapy, as it is given in real life, is helping the patient to recover health or reduce symptoms. The focus is on the everyday effectiveness of the therapy.
- The scientific communities want to understand which part of the therapy that has an effect and what the mechanisms of action are.

Table 1 presents these questions with examples of research methods that can be used to answer them.

Table 1. Strategy for research development with examples of research questions and methodology.

	Question	Research method
Description	What is the prevalence of use of the treatment? Who uses the treatment, why and for which conditions? What are the costs?	Descriptive studies. Cross sectional surveys. Qualitative studies.
Safety	Is the treatment as it is delivered safe for the patients?	Surveillance. Cohort. Case control. Observational studies
System-/ treatment effectiveness	How do the patients experience the effect of the treatment as it is given in everyday practice? What is the effectiveness of the treatment compared to conventional care for a group of patients.	Outcome/observational/ documentation studies. Pragmatic randomised clinical trials. Controlled clinical trials.
Component efficacy	What is the effect of the intervention? The intervention can e.g. be the medicine or the consultation	Randomised clinical trials. Meta analysis.
Mechanism of action	What are the biological/-physical mechanisms?	Basic research. Laboratory research.

Description: The use of homeopathy in the Western World

Homeopathy is one of the most commonly used form of CAM in the Western World (Harris 2000). In the European Union, three out of four citizens know about homeopathy and of these 29% use it for their own health care (Commission of the European Communities 1997). The figures are lower in USA (Eisenberg 1998), and the number vary between the Nordic countries with the lowest number of users in Denmark (Launsø 1996).

The characteristics of patients visiting homeopathic practitioners are described in multi centre studies done in different countries (Anelli 2002; Becker-Witt 2004; Goldstein 1998; Jacobs 1998; Jansen 1995; Lee 2000; Swayne 1989; Trichard 2003b; Van Wassenhoven 2004). There are also some studies from single practices (Colin 2000; Jain 2003; Neville-Smith 1999; Sevar 2000; Slade 2004; Treuherz 2000; Ward 1995), and from homeopathic hospitals (Clover 2000; Richardson 2001). The main features are that most of the users are females (typically 65%-70% of all patients) and patients who suffer from chronic complaints. Most patients have tried conventional treatment before they consult the homeopath. The main reason for encounter is respiratory, psychological, skin and neurological complaints.

Homeopathic medicines are, in some countries, frequently bought over the counter (OTC) for self-treatment (Borneman 2001; Eisenberg 1998; Kayne 1999; Reid 2002; Thomas 2001). In England 1,2% of the population had visited a homeopathic practitioner during the last year in 1998 and 8,6% of the population had used homeopathic OTC medicines (Thomas 2001). In 1997, 3,4% of the population in USA had used homeopathy during the last year (Eisenberg 1998). Of these, 17% had been to a homeopathic practitioner.

The proportion of children among patients visiting homeopathic practitioners seems to be generally high. In USA in 1992, 24% of

the patients in homeopathic practice were under 15 years compared to 17% for conventional medicine (Jacobs 1998). In Netherlands 24% were under 11 years in 1992 (Jansen 1995), in Germany 24% were under 16 years in 1999 (Becker-Witt 2004) and in France 15% were between 2 and 7 years in 2000 (Trichard 2003b).

There are no studies exploring why parents take their children to homeopaths, but there are some surveys on why parents use CAM for their children (Fong 2002; Loman 2003; Menniti-Ippolito 2002; Sanders 2003; Spiegelblatt 1994). The reasons are word-of-mouth-recommendations, fear of side effects from drugs, that the child suffered from chronic medical problems that weren't improved by conventional medical treatment, general dissatisfaction with conventional medicine and a more personalised attention in alternative medicine.

The cost effectiveness of homeopathic care is explored in some outcome studies where especially the reduction in conventional drug use is in focus (Becker-Witt 2003a; Frei 2001a; Frenkel 2002; Guthlin 2004; Jain 2003; Slade 2004; Trichard 2003a; van Haselen 1999; Van Wassenhoven 2004).

Safety/adverse effects

An international multi centre study of patients visiting homeopathically trained medical doctors, found that 8% of the patients who received homeopathic treatment reported adverse effects⁷ compared to 23% for those receiving conventional treatment (Riley 2001). A German study found that there were more adverse effects from homeopathic treatment (7%) than from acupuncture (5%) (Guthlin 2004).

A feature of homeopathy often mentioned is the initial or therapeutic

⁷ Adverse effect is an undesirable or unwanted consequence of a preventive, diagnostic or therapeutic procedure (Last 2001).

tic aggravation, which is a temporary worsening of the symptoms that can occur after the intake of a homeopathic medicine (Swayne 2000). An international multi centre study with 1 025 patients found that 2.7% of the patients experienced adverse effects, 7.8% significant aggravation and 25.4% slight aggravation at the beginning of the homeopathic treatment (Anelli 2002). 40% of all patients in this study remembered to having been informed of the possibility of an aggravation.

A review of the literature on adverse effects from homeopathic treatment concluded: “Homeopathic medicines in high dilutions, prescribed by trained professionals, are probably safe and unlikely to provoke severe adverse reactions” (Dantas 2000).

Effectiveness of homeopathic care

In all effectiveness studies, there is no way of knowing what constitutes the observed effect, e.g. if it is the intervention or contextual effects. If there are no controls, an observed effect can be due to improvement over time as well. On the other hand, such studies can give information about the extent to which a health care intervention fulfils its objectives and is therefore valuable.

There are a number of studies on the effectiveness of homeopathic care. One type is observational or outcome studies on the effectiveness of homeopathic care in sub groups of patients. The examples are homeopathic care for hyperactive children (Frei 2001b), patients with hot flushes (Clover 2002), patients with atopic and allergic disorders (Frenkel 2002), male infertility (Gerhar 2002), patients with headache (Muscari-Tomaioli 2001) and patients with respiratory complaints (Riley 2001).

Another type is observational or outcome studies that look at the overall effectiveness in the whole patient population regardless of complaint. There are some studies from single practice and hospitals suggesting that 60-80 percent of the patients report an improvement after homeopathic care (Clover 2000; Richardson

2001; Sevar 2000; Slade 2004; Treuherz 2000). Two multi centre studies have found equal results to this (Attena 2000; Van Wassenhoven 2004).

Some observational and randomised pragmatic studies have compared homeopathic care to conventional care or treatment for; any presented complaint (Becker-Witt 2003a), for patients with respiratory and ear complaints (Riley 2001) and children with glue ear (Harrison 1999), recurrent acute rhinopharyngitis (Trichard 2003a) and otitis media (Friese 1997). These studies have found that homeopathic care have equal or significant better outcome compared to conventional care.

Most of these studies are rather simple observational studies without controls. They are all open (not blinded) and they cannot be used to say anything about a specific effect of homeopathic medicines.

Component effect

Component effect – meta analysis of clinical trials on homeopathic medicines vs. placebo

The main body of clinical research on the efficacy of homeopathic medicines has been done in placebo-controlled studies. There have been two meta analysis pooling studies on heterogenic clinical conditions and heterogenic homeopathic interventions together to calculate the overall efficacy of homeopathic medicines compared to placebo (Cucherat 2000; Linde 1997). Both these meta analysis have found an effect of homeopathic medicine over placebo, but this effect is weakened for the best methodological studies. Such pooling of heterogeneous data has to be treated cautiously, as they might mask important differences between studies.

Component effect – laboratory research on homeopathic medicines

There are probably more published papers on laboratory research

on homeopathic medicines than there are controlled clinical studies. The Carsten stiftung in Essen, Germany have a database that now includes over 800 publications that report on over 1 000 different studies (Albrecht 2002).

The only meta analysis in this area was published in 1994 (Linde 1994a). It included 135 studies on the protective effects of what was called serial agitated dilutions (SADs) of toxin preparations. They found that the average percent protection of SADs over controls was 19.7 (95%CI 6.2-33.2). Some of the studies meet quality and comparability criteria for meta-analysis. These were divided into five comparable groups suitable for meta analysis and four of these five meta analysis showed significant effects from SAD preparations over controls.

A systematic review of published experiments on homeopathic preparations (potencies) that target physical properties found 36 studies (Becker-Witt 2003b). They concluded that most of the studies had serious methodological flaws, preventing any meaningful conclusion.

A laboratory model that study the action of histamine dilutions on basophil activation have been repeated in some studies and in independent laboratories (Belon 2004) and the methodology has been developed further by others (Lorenz 2003). These studies report that they have found an effect on basophil activation of histamine that is homeopathically diluted beyond 10^{-23} (ultramolecular).

Component effect – reviews of clinical trials on homeopathic medicines for specific conditions

A comment from the authors of the first large review of clinical trials in homeopathy illustrates a frequent reaction to claims that homeopathic medicines have an effect (Kleijnen 1991): "The amount of positive evidence even among the best studies came as a surprise to us. Based on this evidence we would readily accept that homeopathy can be efficacious, if only the mechanism of action

were more plausible”. They concluded based on a review of 105 studies that “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.”.

A systematic review of systematic reviews of clinical studies in homeopathy done by the NHS Centre for Reviews and Disseminations, University of York, UK, found eight such studies (NHS centre for reviews and disseminations 2002). They concluded: ”There is currently insufficient evidence of effectiveness to recommend homeopathy as treatment for any specific condition”.

A critical overview of homeopathy published in 2003 concluded (Jonas 2003): “There is also evidence from randomized, controlled trials that homeopathy may be effective for the treatment of influenza, allergies, postoperative ileus, and childhood diarrhoea. Evidence suggests that homeopathy is ineffective for migraine, delayed-onset muscle soreness, and influenza prevention. There is a lack of conclusive evidence on the effectiveness of homeopathy for most conditions.”.

All these reviews base their conclusions on including studies with heterogenic homeopathic interventions together.

Mechanism of action

There is no established model for the mechanism of action of homeopathy. This concerns both how the similia principle works and the action of ultramolecular homeopathic medicines.

It is claimed that the similia principle is used, although not acknowledged, in conventional medicine (Eskinazi 1999). The article gives e.g. examples of conventional drugs where the same dose can induce opposite effects in different physiologic states (i.e. digoxin can induce or aggravate arrhythmia as well as control it). There is a systematic research program on the similia principle

(van Wijk 1997b). The concepts of self-defence and self-recovery are central with respect to application of the similia principle in this research: “At the cellular level, self-defence and recovery largely depend on the availability of proteins with a cell-protective function”. They have found that “agents (stressors) which shows a higher degree of resemblance in cellular response when applied in high doses also show a higher degree in stimulation of development of survival capacity when applied in low doses” (van Wijk 1997a).

There are a number of theories on the mechanism of action for ultramolecular homeopathic medicines (Bellavite 2002; Schulte 1998). One often cited is the theory of the “memory of the water”. Other theories build on complexity theory including non-linearity, self-organisation and dynamicity (Bellavite 2003; Hyland 2002), and quantum mechanics and entanglement (Milgrom 2003; Walach 2003). There are also research into possible biomarkers for the action of ultramoleculare homeopathic medicines in patients (Bell 2004b; Bell 2004c).

The methodological quality of homeopathic clinical trials

As is evident from the previous overview and the conclusion in systematic reviews, there have been many studies on homeopathy with poor methodology (Cucherat 2000; Linde 1997; Mathie 2003). Studies with better methodological quality tend to yield lower effect size of homeopathic medicines compared to placebo, but there were no linear relationship between quality and effect size (Linde 1999). It has been stated that homeopathic research is clearly in its infancy (Jonas 2001). A guideline for enhancing the quality of clinical and laboratory homeopathic studies was published in 1994 focusing on both methodology and how to describe the homeopathic intervention (Linde 1994b).

An investigation of methodological quality of RCTs in CAM found that homeopathic trials scored better than acupuncture trials and worse than trials on herbal medicine (Linde 2001). The mean quality score for the CAM trials were about the same as the score for two reviews of trials of conventional medicine using the same methodology to assess the quality (Moher 1996; Moher 1998). For the trials on homeopathy, less studies were randomised and less studies had details on dropouts and withdrawals (Linde 2001).

A comprehensive systematic review of the quality of homeopathic clinical trial was published in 2001 (Jonas 2001). The main problem areas were found to be with external validity (small sample, few multi centres). Compared to a sample of high quality conventional clinical trials, the methodological quality of homeopathic trials was not so good, but the internal validity quality score were similar.

If a methodological topic was not described in a publication, even if it was applied in the trial, the quality score would be affected. Aspects like this might introduce some bias into the nature of the reported methodological shortcomings. Nevertheless, new clinical trials on homeopathy have to pay attention to the methodological

issues raised above. The finding that homeopathic clinical trials have low sample size and there are few multi centre studies (Jonas 2001), suggest that there is a funding problem as larger multi centre trials are more expensive. Another aspect is the lack of research infrastructure. Homeopathy is mainly taught, practiced and researched outside established institutions like universities, research centres and national health services. This places a limitation on the available economical resources and the access to highly qualified and experienced researchers.

Upper respiratory tract infections

The term URTI is a separate diagnosis (Wonca International Classification Committee 1998) while at the same time commonly being used as a generic name for all infections in ear/nose/throat. Most upper respiratory tract infections are viral (Wald 1991), and may lead to complications as otitis media, tonsillitis and sinusitis. Over 50% of episodes of otitis media occur during an episode of common cold (Antonia 2002). Based on the result of a pragmatic randomised controlled trial comparing prescription with antibiotic to delayed prescription of antibiotics for children with acute otitis media, it was concluded that for children that are not very unwell systemically, delayed prescription of antibiotics is acceptable (Little 2001c). In children with otitis media without fever and/or vomiting, antibiotic treatment has little benefit on distress and night disturbance on day three after seeing a medical doctor (Little 2002).

The clinical course of viral URTI is described as lasting more than seven days for 50% of children (Butler 2003). A quarter of the children are still ill after ten days.

A Norwegian population based cross sectional study among four and five years old children found that nearly half of all children had two episodes or more of common colds, one in ten had acute otitis media and 7% tonsillopharyngitis during a twelve months period (Kvaerner 2000). Another Norwegian population study found that during the last year, four year old children with URTI visited physicians ten times more frequently than other children (Wefring 2001). URTI is the most frequent reason for a drug prescription including antibiotics in general practice in Norway (Straand 1998).

Homeopathic treatment of URTI

There have been a number of studies on the effect of homeopathic care and homeopathic medicines for the treatment of URTI (Linde 1997). Only a few studies have looked at children with URTI.

A prospective observational outcome study on 230 children with acute otitis media was performed at a paediatric clinic in Switzerland (Frei 2001a). 28% of these patients started with antibiotics after having been treated homeopathically for 12 hours. The authors compared their result to that of placebo from another study and calculated that the individual homeopathic treatment was 2.4 times faster than placebo in controlling pain.

In France, the outcome of homeopathic vs. conventional care for 499 children with rhinopharyngitis (common cold) was investigated in a prospective non-randomised observational comparison study only published as conference proceedings (Trichard 2003a). There were significantly fewer episodes of acute rhinopharyngitis in the homeopathic care group (2.77 episodes) compared to conventional care (3.83 episodes) during six months. The quality of life outcome also showed significant results in favour of homeopathic care.

A prospective non-randomised observational study in Germany compared homeopathic care by a homeopathic ENT specialist (103 children) with conventional care by four conventional ENT specialists (28 children) for children with acute otitis media (Friese 1997). They found a trend for faster resolution of pain (median 2 vs. 3 days, $p=0.119$) and fewer recurrences in children (29% vs. 43% with recurrences) in the homeopathic care group.

In England the effect of homeopathic care and conventional care for glue ear in 33 children was studied in an open randomised comparison trial (Harrison 1999). They found that significantly more children with glue ear progressed to a normal tympanogram (75% vs. 31%, $p=0.015$). There was a trend for more children to

have improved hearing (64% vs. 56%) in the homeopathy group after one year.

A double blind placebo controlled trial was conducted in the Netherlands investigating the efficacy of individually prescribed homeopathic medicines vs. placebo in prevention of URTI in 175 children (de Lange de Klerk 1994). For the main outcome mean daily symptom score over one year, there was a difference of 0.41 ($p=0.06$) in favour of homeopathic medicine compared to placebo. The authors questioned the clinical value of this.

In USA a preliminary double blind placebo controlled trial investigated the efficacy of individually prescribed homeopathic medicines vs. placebo for acute otitis media in 75 children (Jacobs 2001). They found that after five days 19% of those receiving homeopathic medicines had treatment failure (pain and/or fever) and 31% in the placebo group ($p=0.39$). This difference increased during the next weeks.

Based on this it seems to be an effect of homeopathic care and a non-significant tendency for a specific effect of homeopathic medicines. However, as the studies are on different conditions, it is not possible to draw any definite conclusions.

Operational aims of the studies

This thesis is about why parents take their children to homeopaths and the effect of homeopathic treatment in prevention of upper respiratory tract infections (URTI) in children. Four different studies with the following aims were undertaken:

To explore in depth through qualitative interviews specific issues as to why parents take their children to homeopaths. (Paper I)

To investigate whether individualised homeopathic care is effective in the prevention of URTI in children over a 12 week period. (Paper II)

To develop simplified constitutional indications for three homeopathic medicines to enable parents of children with recurrent episodes of URTI to choose homeopathic medicine for their child, and to evaluate if these choices match the prescriptions of trained homeopaths. (Paper III)

To investigate whether self-treatment with self-selected homeopathic medicines is more efficacious than placebo in preventing URTI in children over a 12 week period without any interference by a homeopath. (Paper IV)

Why do parents take their children to homeopaths? - a qualitative study

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Abstract

Objectives:

To investigate why parents take their children to homeopaths.

Method:

Purposive sampling to recruit nine parents who had been to a homeopath with their child for the first time the last three months. The parents were interviewed in depth using a semi structured interview guide.

Results:

Experiences with conventional medical treatment of the child led the parents to take their child to a homeopath: The parents did not want to give the medication prescribed by the doctor; they wanted treatment while waiting for a problem to be assessed; they did not want to continue to use the prescribed medication; they stopped taking conventional medication due to side effect; or they were not offered any treatment by the medical doctor. The parents would consult a medical doctor if they felt insecure about the health conditions of the child and would visit a homeopath when they felt that situation was clarified.

Conclusion:

Parents in this study would consult a medical doctor before seeing the homeopath, mainly because they feel uncertain and want a medical doctor to examine the child. Due to various experiences with the medical encounter or treatment together with recommendations or personal experience leads the parents to take their child to a homeopath.

**Homeopathic care for
the prevention of upper respiratory
tract infections in children.
- A pragmatic randomized controlled trial
comparing individualised homeopathic
care and waiting list controls.**

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trial, Prevention, Upper respiratory tract infection.

Summary

Background and objective: Children under ten constitute 26% of patients visiting homeopaths in Norway. This study investigates whether individualised treatment by homeopaths is effective in preventing childhood upper respiratory tract infection (URTI).

Design: Open, pragmatic, randomised, parallel group trial with waiting list group as control.

Patients: 169 children below the age of 10, recruited by post from children previously diagnosed with URTI.

Interventions: Children were randomly assigned to receive either pragmatic homeopathic care from one of five homeopaths, or to a waiting list control using self-selected conventional health care.

Main outcome measure: The outcome relates to the prevention of new episodes of URTI measured with median total symptom score over 12 weeks.

Result: There was a significant difference in the predefined main outcome in favour of homeopathic care (24, 95% confidence interval 11.4-35.6) compared to the control group (44, CI 32.1-60.8) ($p=0.026$). The difference in median number of days with URTI symptoms was statistically significant with 8 days (CI 4-11.6) in the homeopathic care group and 13 days (CI 9.1-15) in the control group ($p=0.006$). There was no statistical difference in the use of conventional medication or care between the two groups.

Conclusion: In this study there was a clinical relevant effect of individualised homeopathic care in the prevention of URTI in children. The study gives no data on the specific effect of homeopathic medicines.



ELSEVIER

The use of simplified constitutional indications for self-prescription of homeopathic medicine[☆]

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KEYWORDS

Homeopathy;
Self-prescription;
Self-treatment;
Norway;
Child;
Upper respiratory tract

Summary

Objectives: To develop simplified constitutional indications for homeopathic medicines so that parents of children with recurrent upper respiratory tract infection (URTI) could choose homeopathic medicines for their children more “accurately”, and to subsequently evaluate if these choices match the prescriptions of trained homeopaths.

Design and setting: To initially select the most commonly used homeopathic medicines for URTI, data from a survey of 1097 patients visiting 80 different Norwegian homeopaths were used. A simplified constitutional indication was then developed for the three homeopathic medicines most frequently prescribed for recurrent URTI and otitis media. The constitutional indications were developed by a group of five homeopaths and were then sent to 20 homeopaths for further evaluation. To evaluate the parents’ choice of homeopathic medicines compared to the prescription by trained homeopaths, a group of 11 randomly selected homeopaths were asked to participate. They recruited parents of 70 child patients.

Result: By using simplified constitutional indications for the three most commonly prescribed remedies, *Calcarea carb*, *Pulsatilla* and *Sulphur*, parents were able to choose the same homeopathic medicine as homeopaths’ prescribed for 55% (95% CI 43–67) of children with URTI. There was excellent agreement between parents’ choice and homeopaths’ prescription for the three medicines (Kappa of 0.77, $p < 0.001$).

Conclusion: Simplified constitutional indications can be used to improve the quality of the choice of homeopathic medicines purchased over the counter (OTC) for self-treatment.

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Introduction

Patients can initiate treatment with homeopathic medicines either by going to a homeopath or by buying the homeopathic medicine over the counter

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Self treatment with one of three self selected, ultramolecular homeopathic medicines for the prevention of upper respiratory tract infections in children. A double-blind randomized placebo controlled trial

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Keywords

Calcarea carb, children, homeopathy, prevention, *Pulsatilla*, randomized controlled trial, self treatment, *sulphur*, upper respiratory tract infection

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Aims

Homeopathic medicines are frequently purchased over the counter (OTC). Respiratory complaints are the most frequent reason for such purchases. Children with upper respiratory tract infection (URTI) are frequent users of homeopathy. This study investigates the effect of self treatment with one of three self selected ultramolecular homeopathic medicines for the prevention of childhood URTI.

Methods

A double-blind randomized parallel group placebo controlled trial was carried out in 251 children below the age of 10 years, recruited by post from those previously diagnosed with URTI when attending a casualty department. The children were randomly assigned to receive either placebo or ultramolecular homeopathic medicines in C-30 potency (diluted 10⁻⁶⁰) administered twice weekly for 12 weeks. Parents chose the medicine based on simplified constitutional indications for the three medicines most frequently prescribed by Norwegian homeopaths for this group of patients. The main outcome measure relates to the prevention of new episodes of URTI measured with median total symptom score over 12 weeks.

Results

There was no difference in the predefined primary outcome between the two groups ($P = 0.733$). Median URTI scores over 12 weeks in the homeopathic medicine group were 26.0 (95% confidence interval (CI) 16.3, 43.7) and for placebo 25.0 (95% CI 14.2, 38.4). There was no statistical difference between the two groups in median number of days with URTI symptoms or in the use of conventional medication/care.

Conclusions

In this study there was no effect over placebo for self treatment with one of three self selected, ultramolecular homeopathic medicines in preventing childhood URTI. This can be due to the lack of effect of the highly diluted homeopathic medicines or the process of selection and type of medicines.

General discussion

Methodological considerations of the intervention trials

The main methodological issues are discussed in the papers, and in the following, some of these are elaborated upon and given a more detailed discussion.

Recruitment and trial periods

The two intervention trials (study II and IV) recruited patients simultaneously. It was sent invitation to 1 937 patients who had attended the casualty department at the university hospital in Trondheim between September 2002 and December 2003. Of these, 395 (20,5%) returned the signed informed consent form. In addition, 86 patients were recruited by folders distributed to local child health centres in November 2002 (n=29) and an advertisement in the local newspaper in January 2004 (n=57). Of these 481 children, 420 returned the baseline questionnaire and were randomised.

The trials took place simultaneously in two periods; September 2002 to June 2003 (n=161) January to June 2004 (n=259). Those patients attending the casualty department between August 2002 and January 2003 participated in the first part and those participating in the second part attended the casualty department between February and December 2003.

Characteristics of the participants/generalisability

An important aspect of the generalisability of the results from the intervention trials is whether the participants are similar to the population (all children with URTI in Trondheim). The inclusion criteria should ensure the inclusion of children that consult the health

service for URTI. This group was expected to be the largest group of children needing medical care, as documented in the Norwegian population study which showed that during the last year, four year old children with frequent colds and otitis media visited physicians ten times more frequent than other children (Wefring 2001).

As a group, the participating children cannot be said to have been very bothered with URTI. The average child, who was three years old, had “only” had two ear infections and two throat infections during his/her lifetime. Among Norwegian four year olds, one in three have had an episode or more of otitis media and nearly one in three have had four or more episodes of colds during the last year (Wefring 2001). The participating children therefore probably belong to the population of children who have some complaints but who are not very troubled.

Whether the participants are representative for patients with URTI visiting homeopaths is another question. There are no data from homeopathic practice in Norway that can be used to compare the participants in the trials to the “usual” patients in homeopathic care. Based on the impression of the homeopaths in the homeopathic care trial, the participants seemed to be less ill and they failed to attend their scheduled consultations more frequently than their usual patients do. As a speculation, this could indicate that in everyday life homeopaths are for the larger part visited by the more ill children since patients have to pay all expenses themselves when they consult a homeopath. In the trials, the costs of the consultation and the study medication were covered. This was also emphasised in the recruitment material.

It can be expected that those participating in a homeopathic trial do so because they are believers in homeopathy/CAM. The parents to the participating child patients were asked about this in the baseline questionnaire. Nearly 40% reported to have confidence in homeopathy, a further 60% were “neutral” and the rest (2.5%) had no confidence. In 2001 52% of the Norwegian adult population said that homeopathy should be part of the national health service

(Opinion 2001). Although these figures are not directly related, they suggest that the parents of the children in this project did not differ largely from the adult population with regard to their view on homeopathy.

Withdrawal after randomisation but before start of the study

If there are many withdrawals, the result of the study might be compromised if there are more withdrawals in one group as this might indicate that the withdrawals are treatment related (Altman 1991). Further more the whole study might be compromised as the whole process of statistical inference from sample to population fails if the sample is not representative. In high quality clinical trials on homeopathy that has reported on this, the average dropout rate was 17% (Jonas 2001).

As is evident in the tables with baseline characteristics of the children in paper II (table 2) and IV (table 3), the randomisation ensured a balanced distribution of the participants in the two trials. In the intervention trials, 84% (142/169, paper II) and 79% (199/251, paper IV) of those randomised were included in the final analysis. There was no data on those not analysed as they did not start the study after randomisation or did not return any data. It was accounted for the reason for not starting the study for about half of the patients that were not in the analysis (figure 1 in paper II and IV). The main reason was practical issues like being too busy to find time to participate.

The number of patients who did not start in the study was almost the same in each group, indicating that the results from study II and IV are valid. Those not starting the study were compared to the reminders in each groups and there was no significant difference between them for the baseline characteristics. This indicates that the sample included in the final analysis is as close to the population as the original sample is.

Replacement of missing data for those starting the study

If the number of participants with missing data is small and equal in each group in a clinical trial, the common approach is to omit all such patients (Altman 1991). One possible approach to ensure that this is sensible is to assign the most optimistic and pessimistic outcome to patients with missing data. If these analyses gives similar results, and these results are similar to an analysis without those missing, then the data from those missing can be omitted.

In the intervention trials it was pre-planned (stated in the protocol) that missing data should be replaced with the average of the recorded values carried forward. By doing this, it was found that the participants with missing data for part of the study tended to do worse, although not statistically significant, than those without missing data. As the number of patients with missing data for part of the studies were comparable (study IV) or higher for the homeopathic care group (study II), there was no reason to change the planned handling of missing data.

Diagnostics of URTI

It was left to the parents to decide if their child was ill and whether it involved the ear/nose/throat. This is in line with a homeopathic approach, but does not facilitate the criteria for a conventional medical diagnosis. The term URTI might therefore be misleading if it is looked upon as a single diagnosis (Wonca International Classification Committee 1998). It might be argued that the most appropriate term for the condition investigated would be children with complaints in ear/nose/throat and not URTI. Nevertheless, as the term URTI is frequently used as a generic name for all ear/nose/throat infections, the use of the term in this studies seems appropriate.

Outcome measurement

Only one measurement approach was used for the outcomes (mono method bias). It was the parents of the patients that completed the diaries, meaning that all results are based on self-reporting from someone other than the patient (proxy). This was intended because the aim was to measure the effect on how the parents judged the condition of their child. Due to the prospective design, that the trial studied the effect on prevention and the definition of URTI used (see above), it would be of little value to include a before/after evaluation by an independent observer.

The main outcome measure, the symptom diary used on days when the parents judged their child to be ill with URTI complaints, could reach a score on 11 each day. The median scores in the studies were about 3 for each day when the parents judged their child to be ill with URTI. The reason for using the symptom score as the main outcome was that it was expected to give higher variability than number of days with URTI and thereby be a more sensitive measure. In a future study with this outcome, it might be considered if a more detailed scoring could be used, e.g. a four (Jacobs 2000) or seven (Watson 2001) point Likert scale. This would further increase the variability and thereby the sensitivity to measure changes.

It was decided to set the study time to three months after consultations with other homeopaths as well as for practical purposes. This could be viewed as too short a period to measure prevention of URTI. By including children with a URTI diagnosis from a medical doctor, the anticipation was that these would be more prone to get new episodes of URTI. The sample size was calculated based on fifteen days with URTI in the untreated group. The median days with URTI was thirteen and the median number of episodes was two in the standard care group not receiving any “study” intervention. This indicates that the study time was reasonable, but could in hindsight have been prolonged to four months.

The homeopathic intervention

The homeopathic prescribing is frequently based on the characteristics of the patients. Therefore the intervention cannot be standardised as long as the inclusion criteria is a conventional medical diagnosis. As is evident from study III, it is possible to mirror homeopaths prescription without involving the homeopath. But as study II shows, a homeopath would have used many more different homeopathic medicines in the treatment of this patient group than the three medicines in study IV.

The homeopaths prescription in study II differs somewhat from that of Norwegian homeopath as described in study III. Forty percent of the patients in study II were prescribed *Calcarea carb* compared to 30% among Norwegian homeopaths. In Study IV 40% of the parents self-selected this medicine and this proportion would probably be lower if they had to choose between more homeopathic medicines.

One possible way of conducting a trial so that the homeopathic medicine can be standardised, is to have an inclusion criteria that states that only patients matching the indication for a homeopathic medicine are to be included. This has e.g. been done in a study on fibromyalgia where only patients matching the homeopathic medicine *Rhus tox* was included (Fisher 1989). The problem with this approach is that many patients have to be screened, making the recruitment job very large and giving the study limited external validity.

Discussion of results

Why do parents take their children to homeopaths?

Study I explored why parents take their children to homeopaths. It was found that they mainly do so after having been to a medical doctor and not getting the help they wanted. The reasons found for deciding to go to a homeopath, are mostly similar to the findings in the surveys of why parents uses CAM for their children (Fong 2002; Loman 2003; Menniti-Ippolito 2002; Sanders 2003; Spiegelblatt 1994).

Homeopathy seems to be used as a sort of self-selected second line service. This raises the question of whether there is something that homeopaths “give” the patients that they do not get in the medical encounter. Patients request communication, partnership, and health promotion from general practitioners (Little 2001a; Little 2001b).

It might be that due to their focus on the patients and not the disease, homeopaths have a built in advantage with respect to being patient centred. As long as the focus is on the patient, it is likely that the patients feel that the homeopath takes an interest. This leads to the hypothesis that the a priori view on health and disease might account for the degree of patients centeredness: If one sees the disease as an entity that lives its’ own life, then the focus becomes the disease itself. If on the other hand disease is seen as dependent on the patient and his/hers situation, then the focus becomes the patient.

It would be interesting to study which factors in the medical encounter that might influence whether patients goes on to consult a homeopath/CAM practitioner or not. This could give data that indicate areas for improvement in the medical encounter.

Effectiveness of homeopathic care on children with URTI

In study II it was found that there was a significant and relevant difference in favour of homeopathic care compared to self-selected standard care in the prevention of URTI in children in a three month period. This is in line with others pragmatic randomised (Harrison 1999) and non-randomised/observational studies (Frei 2001a; Friese 1997; Trichard 2003a) on URTI in children. The clinical conditions and settings vary between all these studies, preventing a direct comparison.

Although there is very little research, the result suggests that homeopathic care can be of help for children with both acute and more chronic URT complaints. It also suggests that homeopathic care can be used as both a preventive and acute treatment for these patients.

It is suggested in paper II that the increase in the proportion of children among patients consulting homeopaths might be due to a lay knowledge about beneficial effect of homeopathic care. This suggestion is strengthened by the findings in study I that parents take their children to homeopaths after recommendations from relatives and friends or based on having a positive experience themselves.

As already mentioned, studies on effectiveness cannot give information about any specific effects. Still patients seem to rely on this sort of information in deciding which treatment modality to use (study I).

In the special case of homeopathy, this is even more intriguing because of the implausibility of an effect of ultramolecular homeopathic medicines: “The problem with homeopathy is not that there is no explanation for its possible action. If there is no explanation for the action of an agent, one might still give it the benefit of the doubt under certain conditions. The problem with homeopathy is that the “infinite dilutions” of the agents used cannot possibly produce any effect” (Vandenbroucke 1997). There is a

considerable gap between this view and relying on anecdotic stories or evidence of effectiveness as patients seems to do.

Efficacy of homeopathic medicines on children with URTI

In study IV there was no statistical significant difference between self-treatment with self-selected ultramolecular homeopathic medicines compared to placebo. The two other double blind placebo controlled studies on children with URTI (de Lange de Klerk 1994; Jacobs 2001), have found a non-significant tendency for a specific effect of homeopathic medicines. Both these studies used experienced homeopaths to prescribe homeopathic medicines for the patients.

Study IV has an innovative design as the intervention mirrors the prescribing of homeopaths without exposing the patients to a homeopath. This design should make it possible to reduce the contextual influences of the homeopath – patient interaction. This interaction might raise the non-specific effects and thereby require larger numbers of study participants to find a specific effect of an intervention.

As the post sample-size calculation based on the results from the sub-analysis shows (see discussion, paper IV), 5 000 participants would have to be included to find a significant specific effect of ultramolecular homeopathic medicines using this design. This indicates that if there is a specific effect of ultramolecular homeopathic medicines, it is little feasible to use this design to investigate it using children with URTI as subjects. Although it is possible to do studies of this size, it has never been a homeopathic study that large (Linde 1997), probably due to economic constraints and a lack of research infrastructure.

It is frequently claimed that the effect of ultramolecular homeopathic medicines are equal to placebo (Ernst 2002). The results from study IV support this claim.

A scenario

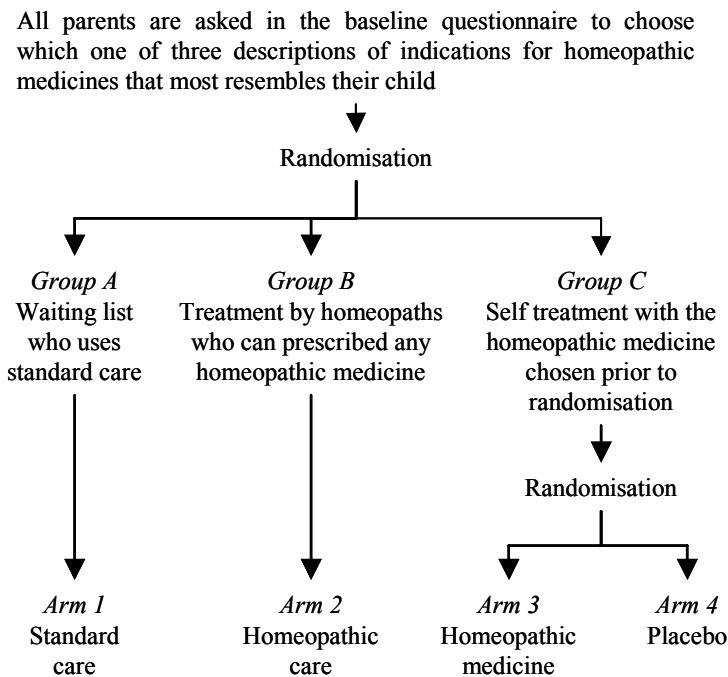
With the relatively large proportion of children with URTI among patients consulting homeopaths, there is a need for further studies investigating both the effectiveness of homeopathic care and the specific efficacy of homeopathic medicines. Nevertheless, for the sake of arguments, imagine that homeopathic care is beneficial and homeopathic medicines equals placebo. What should be the consequences if this scenario was real? Should homeopathic medicines be banned (or at least the public be advised against visiting homeopaths) because the medicines is without effect? Or should one encourage the use of homeopathic care since it is beneficial even when using medicines that gives no effect over placebo?

These questions are probably capable of dividing between opponents and supporters of homeopathy, who will answer according to their own belief. Nevertheless, what it illustrates is the difficulties in practical utilisation of scientific evidence. It is sufficient to look at the long history of reactions against homeopathy from conventional medical bodies (Jonas 2003), to substantiate this. It seems fair to suggest that the answer to the questions above requires a political or ideological clarification/solution more than a scientific one.

Perspectives for the future

There is still a great need for research into what constitutes, if any, the effect of homeopathy as such. It is obvious that there are many aspects that have to be researched, e.g. the effect of the homeopathic medicines, the effect of the interaction between the practitioner and the patients, the effect of having to pay for the service out of ones own pocket and the effect of longer consultations. One starting point is to do studies that separate the patient-homeopath interaction (clinical process) from the specific effects of the homeopathic medicines (Jonas 2001). This would require trials with several arms that make it possible to compare these. A protocol for such a study with five arms has recently been published (Brien 2004).

The intervention studies in this thesis are more related than it appears from what have previously been written. The grand thought was to design the studies so that it would be possible to explore the issue of the effect of homeopathic care vs. the effect of homeopathic medicines. This was done by integrating the separate investigations (study II and IV) in a four arm design and nearly all aspects of the trials were equal with exception of the intervention. This design has been published in a separate article (Steinsbekk 2004) and is presented in the figure below. In study II arm 1 and 2 were compared and in study IV arm 3 and 4 were compared.



By the time this thesis was submitted, there had not been time to start the analysis comparing all four arms. The plan is to start to do the analysis at the end of 2004/beginning of 2005. This analysis might for the first time give data on the difference between the specific effects of the homeopathic medicines and the contextual effects of the clinical process.

Summary in Norwegian

Hensikten med denne avhandlingen er å undersøke hvorfor foreldre tar sine barn med til homøopat og å undersøke effekten av homøopatisk behandling i forebygging av øvre luftveisinfeksjoner (ØLI) hos barn. Bakgrunnen for de undersøkelsene som er gjort, er at det nesten er en tredobling i andelen barn blant pasienter hos homøopat. Dette utløste spørsmål om hvorfor det er slik. Videre er gjentatte luftveisplager en hovedårsak til at barn oppsøker homøopat. Fordi det er lite forskning på dette temaet ble spørsmålet om effekten av homøopatisk behandling i denne pasientgruppen også utløst. Avhandlingen bygger på fire ulike undersøkelser som er gjennomført mellom august 2002 og juni 2004.

Foreldre til ni barn som nylig hadde vært hos homøopat for første gang ble intervjuet for å undersøke hvorfor foreldre tar sine barn med til homøopat. Alle foreldrene hadde vært hos lege før de kontaktet homøopaten, og det var erfaringer med legebehandlingen som fikk foreldrene til å søke alternativer. Årsakene var at foreldrene 1) ikke ønsket å gi den behandlingen lege foreskrev til barnet, 2) ønsket behandling mens barnet ventet på å bli ferdig utredet, 3) ønsket å avslutte bruken av de medisinene legen hadde foreskrevet for barnet, 4) opplevde at barnet fikk bivirkninger av behandlingen legen hadde gitt og 5) ikke ble tilbudt noen behandling hos legen. Foreldre oppsøker først lege når de er usikre eller bekymret for barnets helsetilstand. De oppsøker homøopat for behandling når dette er avklart. Det er foreldre som oppsøker homøopat med sine barn selv om de ikke forstår eller tror på effekten av homøopatiske medisiner (som kan være svært fortynnet).

Ett hundre og sekstini barn som hadde vært til lege på grunn av en øvre luftveisinfeksjon ble rekruttert til å være med på en undersøkelse av effekten av behandling hos homøopat i forebyggingen av ØLI hos barn. Barna ble tilfeldig fordelt i to grupper. Barna i den ene gruppen fikk time med en gang hos en av fem homøopater som foreskrev homøopatisk behandling på vanlig måte. Den andre gruppen fikk slik behandling etter 3 måneder. Forekomsten av ØLI

var signifikant lavere hos de som fikk behandling hos homøopat med én gang (median 8 dager på tre måneder) sammenlignet med den andre gruppen som brukte standard behandling ved behov mens de ventet (median 13 dager) ($p=0,006$).

Homøopatisk medisin brukes internasjonalt i stor grad til selvbehandling. Man vet ikke om pasientens eget valg av homøopatisk medisin er lik det en homøopat ville foreskrevet. Det ble derfor gjennomført en undersøkelse av om det kan utvikles beskrivelser for indikasjoner for homøopatiske medisiner som gjør at foreldre kan velge samme medisin som en homøopat foreskriver for barn med ØLI. Først ble det funnet fram til tre medisiner, *Calcarea carb*, *Pulsatilla* og *Sulphur* som homøopater i Norge foreskriver til 60% av barn med ØLI. Så ble det utviklet indikasjoner for disse tre medisinene som ble testet ut ved at valgene til 70 foreldre ble sammenlignet med foreskrivingen til 11 homøopater. Foreldrene valgte samme medisin som homøopaten for 55% av barna.

To hundre og femtien barn som hadde vært til lege på grunn av en øvre luftveisinfeksjon ble rekruttert til å være med på en undersøkelse av effekten av en av tre selvvalgte homøopatiske medisiner i forebyggingen av ØLI hos barn. Indikasjonene som ble utviklet ble brukt. Barna ble tilfeldig fordelt til enten å få homøopatisk medisin eller placebo. Det var ingen signifikant forskjell i forekomsten av ØLI mellom de som fikk homøopatisk medisin sammenlignet med de som fikk placebo (median 9 dager på tre måneder i begge grupper) ($p=0,531$).

Summary in English

The aim of this thesis is to explore why parents bring their children to homeopaths and to investigate the effect of homeopathic treatment for prevention of upper respiratory tract infections (URTI) in children. The reason for doing studies on this is that there has been a nearly threefold increase in the proportion of children among patients visiting Norwegian homeopaths. This raised the question of why it is so. Furthermore, recurrent respiratory complaints are a main reason why child patients consult homeopaths. This raised the question of the effect of homeopathic treatment in this patient group, because there is very little research on this. The thesis builds on four different studies conducted between August 2002 and June 2004.

Parents of nine children that recently had been to a homeopath for the first time were interviewed to explore why parents take their children to homeopaths. All parents had been to a medical doctor before consulting the homeopath. It was the experiences with conventional medical treatment that led the parents to look for alternatives. The reasons were that 1) the parents did not want to give the medication prescribed by the doctor, 2) they wanted treatment while waiting for a problem to be assessed, 3) they did not want to continue to use the prescribed medication, 4) they stopped taking conventional medication due to side effects or 5) they were not offered any treatment by the medical doctor. The parents would consult a medical doctor if they felt insecure about the health conditions of the child and would visit a homeopath when they felt that the situation was clarified. There are parents who take their child to homeopaths despite not understanding or having belief in whether ultramolecular homeopathic medicines can have effects.

One hundred and sixty-one children who had been diagnosed with an URTI by a medical doctor were recruited to participate in a trial on the effect of treatment by homeopaths for prevention of URTI in children. The children were randomly allocated to two groups. One group received an appointment immediately with one of five

homeopaths who treated the patients as they do in their everyday practice. The other group (control) got such treatment after three months. The occurrence of URTI judged by the parents were significantly lower among those treated immediately by homeopaths (median 8 days in three months) compared to the control group who used self-selected conventional health care (median 13 days) ($p=0.006$).

Homeopathic medicines are frequently used for self-treatment (over the counter-OTC). It is not known if the choice of the patient is the same, as a homeopath would have prescribed. A study was therefore conducted to explore if there can be developed indications for homeopathic medicines that facilitate that parents can chose the same medicine as a homeopath would prescribe for children with URTI. Firstly, data from a survey was used to find three medicines *Calcarea carb*, *Pulsatilla* and *Sulphur* that accounted for 60% of all prescription made by Norwegian homeopaths for children with URTI. Simplified constitutional indications for these medicines were developed and tested by comparing the choices of 70 parents with the prescription of eleven homeopaths. The parents were able to choose the same homeopathic medicine as homeopaths prescribed for 55% of the children.

Two hundred and fifty-nine children who had been diagnosed with an URTI by a medical doctor were recruited to participate in a trial on the effect of one of three self-selected ultramolecular homeopathic medicines for prevention of URTI in children. The indications developed were used. The children was randomly allocated to receive either ultramolecular homeopathic medicine (C-30) or placebo. There was no difference in the occurrence of URTI judged by the parents among getting ultramolecular homeopathic medicine compared to those getting placebo (median 9 days in three months for both groups) ($p=0.531$).

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