



# Efficacy of homeopathy in livestock according to peer-reviewed publications from 1981 to 2014

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**Homeopathy is widely used in livestock, especially in order to reduce the use of antibiotics, although it is often seen as controversial. A comprehensive literature review has been conducted to assess the efficacy of homeopathy in cattle, pigs and poultry. Only peer-reviewed publications dealing with homeopathic remedies, which could possibly replace or prevent the use of antibiotics in the case of infective diseases or growth promotion in livestock were included. Search results revealed a total number of 52 trials performed within 48 publications fulfilling the predefined criteria. Twenty-eight trials were in favour of homeopathy, with 26 trials showing a significantly higher efficacy in comparison to a control group, whereas 22 showed no medicinal effect. Cure rates for the treatments with antibiotics, homeopathy or placebo varied to a high degree, while the remedy used did not seem to make a big difference. Looking at all the studies, no study was repeated under comparable conditions. Consequently, the use of homeopathy currently cannot claim to have sufficient prognostic validity where efficacy is concerned. When striving for high therapeutic success in treatment, the potential of homeopathy in replacing or reducing antibiotics can only be validated if evidence of efficacy is confirmed by randomised controlled trials under modified conditions.**

WITHIN the scientific community and veterinary practice, the use of homeopathy in food-producing animals is highly controversial. However, there is evidence that homeopathic remedies are widely used in these animals (Hovi 2001, ECCH 2007, IMPRO 2015). For organic agriculture, the use of homeopathy is even promoted. According to the European Commission Regulation (EC No 889/2008, Article 24[2]) (European Commission 2008) on organic agriculture, homeopathic and other products should be used in preference to chemically synthesised allopathic veterinary treatment, provided that the resultant therapy is effective for the species of animal and the condition for which the treatment is intended.

In the case of infectious bacterial diseases, antimicrobial drugs have been used in livestock production for decades as the first and often only effective option for individual or group treatment. Nowadays, the use of antibiotics in food-producing animals is often unpopular among consumers (Midan Marketing 2014, Mintel Group 2015, Niamh 2015). 'Antibiotic-free' or 'raised without antibiotics' labelled products are enjoying increased popularity in both Europe and the USA. This development is fuelled by, among others, mis- and overuse of antibiotics in human and animal medicine, which has promoted the development of resistant strains of bacteria worldwide (Laxminarayan and others 2013). Correspondingly, many farmers and veterinarians see homeopathy as an alternative for treating diseases in

farm animals and thus reducing the consumption of antibiotics.

Homeopathy was introduced by Samuel Hahnemann as early as 1796 and claims as a method to treat diseases with dilute remedies that cause the same symptoms undiluted in healthy individuals as the disease does (simile principle). Those symptoms are seen as very specific and individual, resulting in the requirement for a detailed diagnostic procedure where not only the symptoms and cause of the disease are considered, but also the patient's behaviour, constitution and conditions that may cause aggravation or amelioration of symptoms, to find the corresponding remedy for each patient (Hahnemann 1869).

Reviews on the efficacy of homeopathy in people have found that the success of homeopathic treatment in general cannot be completely due to placebo effects, but studies have provided insufficient evidence that homeopathy is efficacious (Linde and others 1997). In fact, the quality of the methodologies used was low (Linde and others 2001) and the bias high in homeopathic trials on people. At the same time, there is weak evidence for the particular effectiveness of homeopathy as compared to conventional treatment (Shang and others 2005). Up until now, only a few scientific publications have reviewed the efficacy of homeopathy in animals (Kowalski 1989, Hektoen 2005, Rijnberk and Ramey 2007, Ruegg 2008), revealing diverse results. Previously, a review and meta-analysis of randomised placebo-controlled trials in veterinary homeopathy with a special focus on medical conditions were published by Mathie and Clausen (2014, 2015). Due to the low number and quality of studies available, particularly regarding the risk of bias, they found very limited evidence for distinguishable differences between homeopathy and placebo in clinical interventions, demanding the need for new and higher quality research in veterinary homeopathy. For food-producing animals, there has been no review of peer-reviewed publications conducted on the efficacy of homeopathy. The aim of this review was therefore to systematically evaluate the existing knowledge on the efficacy of homeopathic remedies used for the prevention or treatment of diseases in livestock that are usually treated with antimicrobials by considering more scientific, peer-reviewed publications

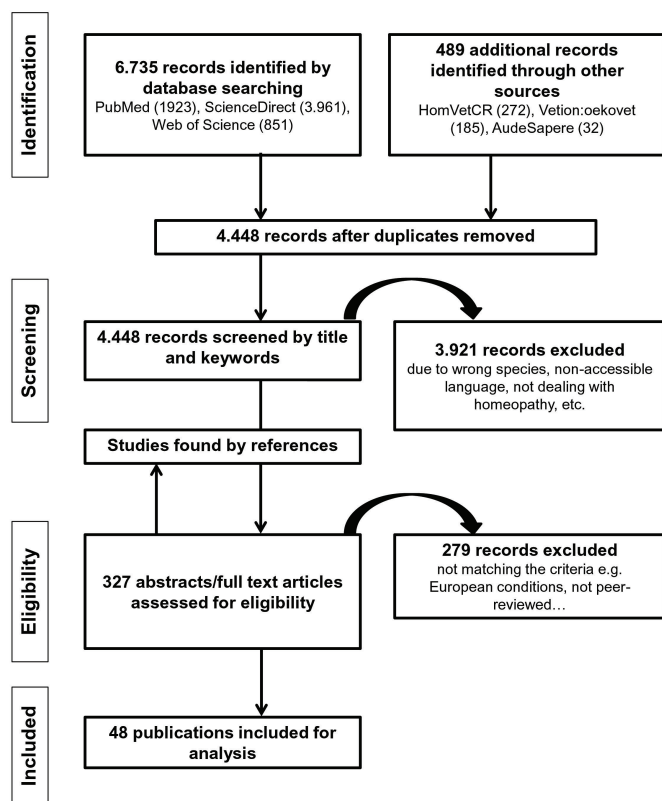
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**FIG 1: Search process for publications based on the PRISMA guidelines**

(including doctoral thesis) and a comprehensive timeframe from 1981 to 2014. Within the analysis, additional information on trial conditions, remedies used and treated species were taken into account.

## Methods

The search for scientific publications was carried out in the following databases: PubMed, ScienceDirect and Web of Science. Specific databases on veterinary homeopathy were available at HomVetCR (Carstens-Stiftung) (2016), Vetion:oekovet.de (2016) or AudeSapere (2016) and also taken into account. Further publications were found by relying on the reference list of considered studies. The searches were performed in February 2014 and updated up to the end of June 2016. The search terms were defined according to the PICOS approach (Moher and others 2009):

- Population: 'livestock' OR 'dairy' OR 'cows' OR 'cattle' OR 'bovine' OR 'heifer' OR 'calves' OR 'pigs' OR 'sows' OR 'piglets' OR 'poultry' OR 'swine' OR 'porcine' OR 'turkeys' OR 'broiler/s' OR 'chicken' OR 'hen/s'
- Intervention: 'homeopathy' OR 'veterinary homeopathy' OR 'homeopathic' OR 'dilution' OR 'complementary veterinary medicine' OR 'isopathy' OR 'nosodes'
- Comparison: 'prevention' OR 'prophylaxis' OR 'metaphylaxis' OR 'treatment/s' OR 'therapy' OR 'comparison'
- Outcome: 'efficacy' OR 'effectiveness' OR 'effect/s' OR 'efficiency'
- Setting: 'clinical trial' OR 'review' OR 'trial/s' OR 'study/ies'.

Only publications in peer-reviewed scientific journals and doctoral theses were taken into account. The studies considered addressed the efficacy of homeopathic drugs in cattle, pigs or poultry in production diseases under European or comparable conditions (in respect to housing, breeds, intensive farming). Included in the evaluation were only studies dealing with homeopathic remedies, which could possibly replace or prevent the use of antibiotics in the case of infective production diseases or growth promotion. The time frame of publications considered was from 1981 to 2014. Accessible languages were English and German. The main reasons for excluding publications were: that no peer-review was performed (conference abstracts, journals without

peer-review), trials only dealt with companion animals, and/or trials that dealt with diseases that were not infectious, eg, hormonal-treated fertility disorders.

The search and filtering process (Fig 1) was performed by the same person following the PRISMA guidelines (Liberati and others 2009). The following information was extracted from each study according to a predefined protocol (available from the authors): author, publication year and source, research body, species/group, farming system, purpose of application, disease in focus, exclusion criteria, diagnostic method and person diagnosing, remedy used (as well as origin [producer]), ingredients and potency of the remedy, method of administration, study design and control groups, methods of measurement, possible risk of bias and outcome of the study. Publications including more than one clinical trial were regarded as separate studies for the purpose of the evaluation and comparison of data.

In medicine, efficacy indicates the capacity for beneficial change (or therapeutic effect) of a given intervention (eg, a drug). When talking in terms of efficacy vs effectiveness, effectiveness relates to how well a treatment works in the practice of medicine, as opposed to efficacy, which measures how well treatment works in clinical trials or laboratory studies (Thaul 2012).

This review classified homeopathic treatment as efficacious when the homeopathic remedy presented a statistically significant improvement in comparison to a placebo, a conventionally treated or an untreated group of farm animals. If the impact of a homeopathic treatment did not differ significantly to that from a placebo or an untreated group, or was worse, nil efficacy was reported. Results were classified as 'inconclusive', when the level of efficacy did not differ significantly between the homeopathic group and the group employing antibiotics (without a further control group as placebo or untreated), when the values of particular parameters improved while others deteriorated or when the authors did not provide a clear result. To assess the possible influence of single dichotomous factors on reporting efficacy of homeopathy in a trial, a sensitivity analysis was performed, expressing the effect size as odds ratio (OR) with 95 per cent confidence interval and P values calculated according to Sheskin (2004).

## Results

From the 4448 publications found, 48 publications were identified, which met the given criteria (Fig 1). These publications featured 52 individual clinical trials (including 34 trials with cattle, 12 with pigs and six with poultry). One publication included three separate clinical trials (Day 1986), and two publications each included two clinical trials (Schütte 1991,1994).

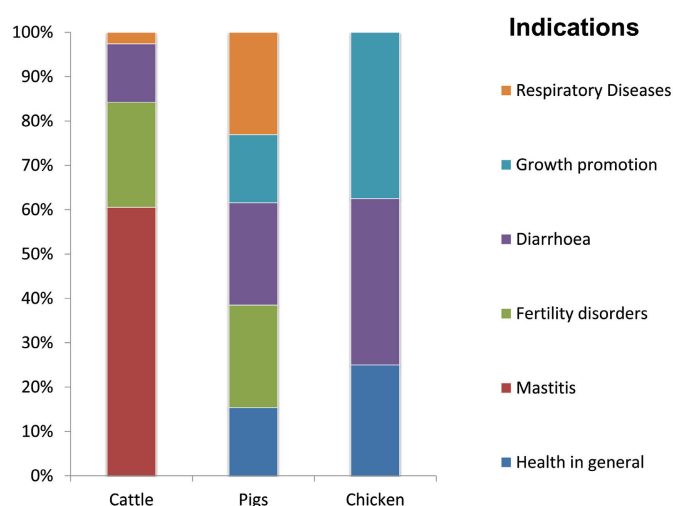
The 33 scientific papers were primarily published in homeopathic journals (eg, *Homeopathy*, *British Homeopathic Journal*, *International Journal of High Dilution Research*, *Alternative Therapies in Health and Medicine*, *Zeitschrift für Ganzheitliche Tiermedizin*), and only a few were found in veterinary journals (eg, *Veterinary Record*, *Journal of Dairy Science*, *Journal of Animal Science*, *Berliner und Münchener Tierärztliche Wochenschrift*, *Transboundary and Emerging Diseases*). Fifteen doctoral theses on homeopathy in livestock were available, having originated from veterinary or agricultural universities. The greater part of the studies were published between the years 2003 and 2014 (n=25). It seems fewer studies were published before, with 14 publications in the time period 1981 until 1991 and nine publications between 1992 and 2002.

In most of the studies (54 per cent), the production method was not specified. The remaining studies were defined as either conventional (33 per cent, particularly pig and poultry farms) or as organic (6 per cent, exclusively dairy farms). Seven per cent of the studies had looked at both farming systems.

The main purpose of applying homeopathic remedies in clinical trials was prevention of disease (quoted in a total of 30 studies, including six studies aiming for good general health or growth promotion). Furthermore, 18 studies referred to the therapeutic treatment of diseases, while four studies focused on metaphylactic treatment (medication administered before the onset of clinical signs in the herd).

## Indication

The reason for using homeopathic remedies to treat disease was different for each species (Fig 2). In studies dealing with cattle, treatment



**FIG 2: Distribution of the indications in relation to the use of homeopathy**

was for mastitis or fertility disorders in dairy cows. Calves were only treated for the indications diarrhoea and pneumonia. The studies on pigs ranged between fertility disorders, especially mastitis-metritis-agalactia syndrome (MMA) in sows, respiratory infections and diarrhoea in piglets, and growth promotion and general health in fattening pigs. In the case of poultry, the main indication for using homeopathy was growth promotion or the treatment of diarrhoea.

Studies which included more than one treatment indication were counted per indication. Nearly all animals treated with remedies had become sick through natural infection. An artificial infection was only induced in two studies on chickens: Velkers and others (2005) induced an *Escherichia coli*-infection in the chickens on day 8 and Berchieri and others (2006) challenged chickens on the day 17 after birth with a broth culture of *Salmonella* Enteritidis.

### Exclusion criteria

Nineteen of 52 studies defined criteria for the exclusion of animals from trial participation or gave reasons for exclusion of animals during the trial. Animals were primarily excluded for showing systemic clinical signs (eg, fever, loss of appetite) or severe organ damage, which affects the ability of an animal's immune system to react to a stimulus, as well as the presence of additional diseases or any further medication being taken at the time of the study, missing data or because the animals died or were sold prematurely.

### Diagnostic procedure

In the various studies diagnostic procedures to evaluate the amelioration or deterioration of health or performance and to measure the effect of the applied remedy were quite heterogeneous. The diagnostic methods were divided into four groups:

1. Direct tests (DT): eg, laboratory tests for detection of the pathogen in milk, faeces, blood, and so on.
2. Indirect tests (IT): eg, California mastitis test or conductivity milk test, rectal palpation of the uterus, general blood parameters, and so on.
3. Clinical signs (CS): eg, optical assessment of milk for clots, observation of clinical signs such as alterations in faeces consistency, coughing, and so on.
4. Measurements (M): eg, body temperature, body weight, milk yield, and so on.

In more than half of the trials, two ( $n=22$ ) or more parameters ( $n=9$ ) were considered when diagnosing diseases or the possible effects of using remedies. The most frequently undertaken diagnostic test was the recording of clinical signs, followed by direct tests. Indirect tests, often available as on-site tests, and additional measurements were performed to a lesser degree (Fig 3). An individualised homeopathic diag-

nostic procedure enclosing the choice of an appropriate (and often different) homeopathic remedy for the individual was performed in five trials (Seifert 1987, Hektoen and others 2004, Werner and others 2010) with two of them limiting the selection of possible remedies ((Sonnenwald 1986, Williamson and Lacy-Hulbert 2014). The question of who had diagnosed a disease or observed a clinical sign remained unanswered in 22 of 52 studies. In 13 studies, homeopathic expertise was provided by a veterinarian, trained or experienced in homeopathy or accompanied by a trained homeopath (Hektoen and others 2004) or supervised by an external veterinarian experienced in homeopathy (Werner and others 2010). In 11 trials, a veterinarian diagnosed the clinical signs, in three trials the farmer decided whether the animal improved or not, in one case the diagnosis was made by the veterinarian and farmer together in another, an immunologist and in a further trial an automated milking system gave the diagnosis.

### Remedies

In general, two types of homeopathic remedies were available: remedies including only one active ingredient in the initial tincture (used for classic or individualised homeopathy) and remedies combining two or more active ingredients in the initial tincture (used for complex homeopathy). Fifty-six per cent of the studies saw complex remedies (with combined ingredients) being employed and 34 per cent of the studies saw classic single remedies being used. In the remaining studies (10 per cent), the type of homeopathic remedy was not revealed or was impossible to differentiate (eg, parallel use of single and complex remedies). The producers of the applied remedies were not listed in 30 per cent of the studies. In the other cases, the companies Heel (15 per cent) and DHU (13 per cent) were most often listed as producers of remedies, followed by other small producing companies or local pharmacies (42 per cent). The homeopathic dilutions or potencies of the applied drugs were either high ( $n=21$  trials) from D60 (respectively C30, a 1: 10-60 dilution) to D400 (respectively C200, a 1: 10-400 dilution) or low potencies ( $n=21$ ) from D1 (a 1:10 dilution) to D24 (a 1:10-24 dilution), where the letter 'D' stands for decimal dilution steps and 'C' for centesimal dilution steps. In six studies, the potency was not mentioned. Four studies considered both high and low potencies (Tiefenthaler 1990, Vohla 1991, Knierim 1992, Egan 1995). The ingredients used in the studies were of herbal, mineral or animal origin. Nosodes, a specific type of homeopathic preparations often called 'homeopathic vaccines' were made up either from the pathogen or from products of the disease (eg, pus, sputum) and used in nine trials.

### Methods of administration

The means of administration differed depending on whether individuals or groups of animals were treated. For groups, the administration was solely oral (by drinking water or mineral salt). For individuals, the drugs were usually administered orally or infrequently via subcutaneous or intramuscular injection, topical (eg, vulval spray or udder cream) or by intramammary injection.

### Study design

The 'evidence-based medicine' approach is premised upon the current knowledge level based on clinical studies and scientific publications, which confirm or invalidate the efficacy of a certain measure or remedy (Panesar and others 2010). In single clinical trials, double-blind randomised-controlled trials (RCTs) are regarded as the 'gold standard' for proving the empiric evidence of efficacy of a remedy tested (European Medicines Agency [EMA] 2001, Kaptchuk 2001). With this in mind, the structures of the selected trials were examined with respect to their ability to measure the efficacy of homeopathy on the level of evidence-based medicine.

Seventy-nine per cent of the single clinical trials were RCTs ( $n=41$ ). The remaining studies were either non-randomised controlled trials, eg, parallel groups ( $n=6$ ) or observational trials without a control group ( $n=5$ ). The RCTs ( $n=41$ ) could be divided into 21 non-blind trials, nine single-blind trials and 11 double-blind trials. 'Single-blind' means that the patient is not aware of the true nature of the drug applied. In the case of animals, a single-blind experiment means that the person administering the drug is not aware of the true nature of the applied drug or the ingredients. Double-blind trials include a 'blinding' of both the user and

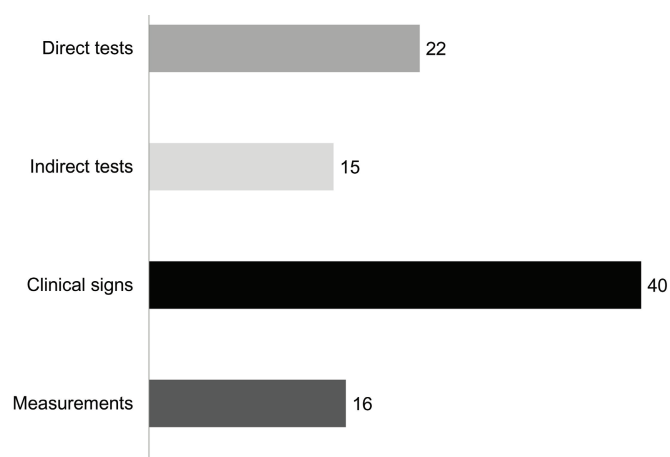


FIG 3: Quality of diagnostic measures

the sample assessor (Schulz and Grimes 2002). The blinding aims to eliminate effects such as observation bias and wishful thinking, which could occur if the samples are evaluated by someone who already knows the group's organisational and treatment methods.

Control groups (eg, an untreated group, placebo group or antibiotic-treated group) were also included in this evaluation. More than half of the trials (65 per cent) had a study design with only one control group, 17 per cent included two control groups and four studies compared the experimental group with three control groups. The five observational studies did not use any control or parallel group at all. Out of all 64 control groups, 42 per cent were treated with a placebo, 31 per cent with antibiotics, 10 per cent with a different conventional treatment (eg, teat sealers or a local disinfectant) or a combined treatment (eg, antibiotic combined with a placebo or a homeopathic remedy) and only 17 per cent included an untreated group.

### Efficacy

In total, 54 per cent (n=28) of the trials were able to confirm the efficacy of the homeopathic remedy administered, while 42 per cent (n=22) found no benefit compared with the placebo or untreated group. Four per cent (n=2) had inconclusive results. When considering a single species (Table 1) only homeopathic studies dealing with pigs were found to be frequently efficacious, while studies with cattle or poultry were seen to have a similar distribution of efficacious and non-efficacious treatment.

Trials demonstrating the efficacy of the homeopathic remedy were published mainly in scientific journals (21 out of 28 positive trials), as well as studies with a negative outcome (14 out of 22 negative). In journals focussing on alternative treatments, 15 of 18 trials reported that the homeopathic remedy tested was effective (odds ratio [OR] 3.75, 95 per cent confidence interval [CI] 0.63 to 22.04, P=0.14), while in journals with a broader focus on veterinary medicine, 12 out of 18 trials found the homeopathic treatment was ineffective (OR 0.27, 95 per cent CI 0.05 to 1.57). Results described in a doctoral thesis on homeopathic remedies were nearly evenly distributed between non-efficacious (n=8) and efficacious (n=7), apart from one thesis which revealed inconclusive results.

TABLE 1: Number of trials and outcome regarding the efficacy of the homeopathic remedy applied

Species	Number of trials	Efficacy	Inconclusive results	No efficacy
Cattle	34	15	1	18
Pigs	12	9	1	2
Poultry	6	4	0	2
Summary	52	28	2	22

TABLE 2: Cure rates for therapeutic use of different remedies

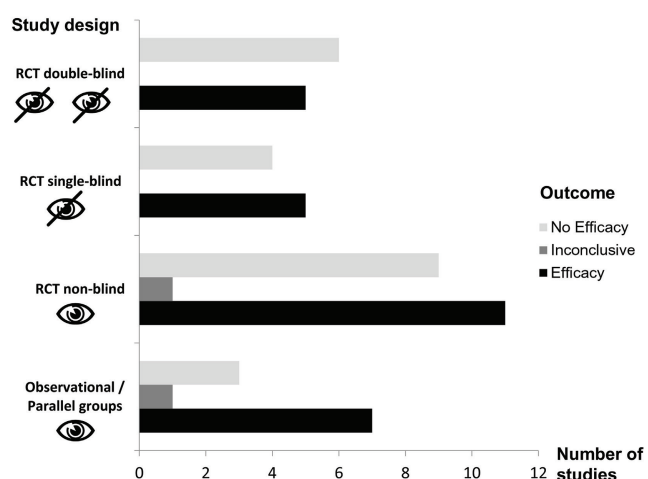
Species	Indication	Recovery effect with			Author (year)
		Homeopathy	Allopathy	Placebo	
Cows	Mastitis	34% <sup>a</sup> 18% <sup>d</sup>	26% <sup>a</sup> 24% <sup>d</sup>		Sonnenwald (1986)
Cows	Mastitis	34% <sup>a</sup> 18% <sup>d</sup>	26% <sup>a</sup> 24% <sup>d</sup>		Merck and others (1989)
Cows	Mastitis	33% <sup>a,o</sup> 80% <sup>a,p</sup>	67% <sup>a,o</sup> 50% <sup>a,p</sup>		Tiefenthaler (1990)
Cows	Mastitis	19% <sup>a</sup> 47% <sup>e</sup> 29% <sup>f</sup>	20% <sup>a</sup> 45% <sup>e</sup> 35% <sup>f</sup>	6% <sup>a</sup> 56% <sup>e</sup> 13% <sup>f</sup>	Hektoen and others (2004)
Cows	Mastitis	47% <sup>b</sup> 31% <sup>c</sup>	24% <sup>b</sup> 24% <sup>c</sup>	30% <sup>b</sup> 4% <sup>c</sup>	Werner and others (2010)
Cows	Mastitis	5% <sup>a,g</sup> 10% <sup>a,h</sup>	17% <sup>a,g</sup> 65% <sup>a,h</sup>		Walkenhorst (2006)
Cows	Mastitis	63% <sup>e</sup> 36% <sup>n</sup>	95% <sup>e</sup> 74% <sup>n</sup>		Williamson and Lacy-Hulbert (2014)
Calves	Diarrhoea	83% <sup>i</sup>		80% <sup>i</sup>	Kayne and Rafferty (1994)
Calves	Diarrhoea	69-77% <sup>l,m</sup>		69% <sup>m</sup>	Hornig (2014)
Sows	MMA	61% <sup>m</sup>	35% <sup>m</sup>		Seifert (1987)

<sup>a</sup> Full recovery = no pathological findings of milk and udder and negative cyto-bacteriological results of milk samples  
<sup>b</sup> Full recovery = no pathological findings of milk and udder with negative bacteriological results of milk samples on first day of disease  
<sup>c</sup> Full recovery = no pathological findings of milk and udder with positive bacteriological results of milk samples on first day of disease  
<sup>d</sup> Clinical recovery = no pathological findings of milk and udder and with positive bacteriological or/and positive cytological results of milk samples  
<sup>e</sup> Clinical recovery = no pathological findings of milk and udder  
<sup>f</sup> Bacteriological recovery = negative bacteriological result of milk samples after treatment and negative California mastitis test  
<sup>g</sup> Cows with clinical mastitis at minimum one udder quarter  
<sup>h</sup> Cows without clinical signs, but positive bacteriological result of milk samples at minimum one udder  
<sup>i</sup> Range of results due to the use of different homeopathic remedies  
<sup>l</sup> Clinical recovery = change from watery to pasty faeces; animals treated by homeopathy recovered one day earlier  
<sup>m</sup> Clinical recovery  
<sup>n</sup> Bacteriological recovery = negative bacteriological result of milk samples after treatment  
<sup>o</sup> Test group = cows with acute mastitis with disturbed general condition  
<sup>p</sup> Test group = cows with acute mastitis without disturbed general condition  
 MMA Mastitis-metritis-agalactia syndrome

### Treatment success

In order to provide information on cure rates, 18 out of 52 clinical trials which administered homeopathy exclusively for therapeutic reasons were further analysed. Only 10 of these trials gave information on cure rates (Table 2), while eight trials did not define cure rates at all. Instead, the effectiveness of the homeopathic remedy was evaluated on the basis of other criteria, for example, number of recurring treatments, mortality, duration of diarrhoea, fertility parameters, milk yield, and so on.

A wide range of different criteria for defining recovery or cure was found, for example, in case of mastitis: 'full recovery' with or without cyto-bacteriological recovery, or 'clinical recovery' with or without cyto-bacteriological recovery, or only 'bacteriological recovery', and so on. This made comparison and interpretation of the results more difficult. Correspondingly, the different cure rates could not all be compared directly to one another. Overall, the cure rates in the seven studies focusing on mastitis ranged from 5 per cent to 80 per cent for a treatment with homeopathic remedies, from 17 per cent to 95 per cent when using a conventional remedy (predominantly antibiotics),



**FIG 4: Study design and result for efficacy of homeopathy in the studies**

and from 4 per cent to 56 per cent for the administration of a placebo. In two studies, the results comparing homeopathic remedies with a placebo for diarrhoea in calves seemed to be the same. The results for MMA in sows favoured homeopathy compared to allopathy.

### Efficacy and remedy

When the outcomes of the trials were compared with the type of remedy used (single or complex remedies), no differences were found. Remedies with low potencies (D1 to D12) showed the same results as homeopathic treatments with high potencies (more than D24) as far as efficacy was concerned (OR 1, 95 per cent CI 0.28 to 3.54, P=1) and did not depend on the purpose of use (prevention, treatment, metaphylaxis) nor the indication (eg, mastitis, diarrhoea), species or the performance of an individualised treatment procedure.

### Study design and risk of bias

Fig 4 shows the results of the studies evaluated with a focus on the study designs. The double-blind RCTs reported efficacy (n=5) of the homeopathic treatment almost as often as they reported lack of efficacy of it (n=6). Single-blind RCTs and non-blind RCTs on homeopathy had a tendency to be efficacious. Observational trials or parallel groups (without randomisation) were most likely to present evidence of efficacy.

All trials were also analysed for a possible risk of bias, which incorporated both study design and study conduct (Table 3). Studies were regarded as having a 'low' risk of bias when: they included a randomisation, a control group, blinding of the people directly involved in their administration and evaluation, the absence of selective reporting and other shortcomings within the trial, and no direct or indirect funding of the study by the producer of the conventional or homeopathic remedy. Only 13 studies displayed a low or unclear risk of bias. Shortcomings and risk for selective reporting or bias were found in 39 trials to various degrees. Some studies only considered a very small number of animals (eg, 10 to 40 animals) in the trial. Therefore, conclusions drawn could only be very limited. Often, studies were financially supported, eg, by the producer of the homeopathic or conventional remedy (full funding or free provision of remedies), which might have influenced the results (n=12). In one trial, all of the researchers worked for the supplier of the homeopathic remedy, which certainly entailed a conflict of interests (Aubry and others 2013). However, studies with such vested interests reported efficacy of homeopathy less often than studies with no overt vested interest (OR 0.87, 95 per cent CI 0.23 to 3.37, P=0.84 vs OR 1.15, 95 per cent CI 0.30 to 4.42). Further shortcomings were that the origin, contents or potencies of remedies were not presented (n=10), compromising any attempt to repeat a trial. In trials where antibiotics were used as a control, the antimicrobial substance was often chosen without considering guidelines for prudent use or existing knowledge about resistance characteristics of the pathogen in focus, eg, penicillin treatment for *E coli*-infection (Coelho and others 2009). One study also mentioned the exclusion of certain homeopathic remedies and their test results because they were not positive (Berchieri and others 2006). The intake of the homeopathic remedy was not easy to define, eg, as the administration was via concentrate or water troughs. Further

**TABLE 3: Risk of bias**

Authors (year)	Randomised	Control	Blinding	Free from vested interest	Free of other shortcomings	Risk of bias
Boerms (1981)	Y	AB	N	N	Potency unknown	High
Frerking and Romansky-Rieken (1981)	Y	AB, COM	N	U	N	High
Day (1984)	N	U	N	U	Intake unsure, some sows did not receive the full course of medication due to closeness to farrowing, only 20 animals considered	High
Day (1986) - trial 1	N	U	N	U	Uneven distribution of animals	High
Day (1986) - trial 2	Y	P	Y	U	Intake of medication unsure	Low
Day (1986) - trial 3	N	U	N	U	Uneven distribution of cows, missing information on remedy	High
Sonnenwald (1986)	Y	AB	N	U	Groups not completely randomised (grazing cows and farmer intervention)	High
Seifert (1987)	Y	CON	N	N	U	High
Stopes and Woodward (1990)	N	N	N	U	U	High
Drösemeier (1989)	Y	AB, P	Y	N	N	High
Merck and others (1989)	N	AB	N	U	Different times for follow-up checks	High
Erbe (1990)	Y	P	N	U	Uneven distribution, only 42 animals considered	High
Tiefenthaler (1990)	Y	AB, COM	N	U	Only 41 animals considered	High
Wirth (1990)	Y	P	N	U	Uneven distribution, 42 animals considered	High
Schütte (1991) - trial 1	Y	AB, P	N	U	U	High
Schütte (1991) - trial 2	Y	P	N	U	U	High
Vohla (1991)	N	P, U	Y	U	U	High

TABLE 3: Risk of bias (continued)

Authors (year)	Randomised	Control	Blinding	Free from vested interest	Free of other shortcomings	Risk of bias
Knierim (1992)	Y	P	Y	U	Only 30 animals considered	Low
Kayne and Rafferty (1994)	Y	P	Y	U	20 animals considered	Low
Schütte (1994) - trial 1	Y	P	Y	U	U	Low
Schütte (1994) - trial 2	Y	P	Y	U	U	Low
Egan (1995)	N	N	N	U	15 animals considered	High
Searcy and others (1995)	Y	P	N	U	26 animals considered	High
Guajardo-Bernal and others (1996)	Y	P	Y	U	Only 10 animals considered	High
Sandoval and others (1998)	Y	AB	N	U	U	High
Albrecht and Schütte (1999)	Y	P, AB	N	N	U	High
Hümmelchen (1999)	Y	P	Y	N	U	High
Verdier and others (2003)	Y	P	Y	U	U	Low
Garbe (2003)	Y	AB, P, COM	Y	N	U	High
Schütte (2003)	N	N	N	U	U	High
Hektoen and others (2004)	Y	P, AB	Y	U	Unknown potency	Low
Schlecht (2004)	Y	P	Y	N	39 animals considered	High
Holmes and others (2005)	Y	P	Y	U	U	Low
Velkers and others (2005)	Y	U, AB	N	U	U	High
Berchieri and others (2006)	N	U	N	U	Selective reporting (exclusion of ineffective remedies tested)	High
Walkenhorst (2006)	Y	AB	N	N	U	High
Enbergs and Sensen (2007)	Y	CON	N	U	U	High
Soto and others (2008)	Y	U, P	N	U	Uneven distributed initial weight	High
Amalcaburio and others (2009)	Y	U	N	U	U	High
Arlt and others (2009)	Y	P	Y	N	U	High
Coelho and others (2009)	Y	AB	Y	U	46 animals considered, AB known to be resistant to pathogen in trial	High
Camerlink and others (2010)	Y	P	Y	U	U	Low
Klocke and others (2010)	Y	U, CON	N	N	U	High
Werner and others (2010)	Y	P, AB	Y	U	U	Low
Da Silva and others (2011)	N	N	N	U	Remedy data missing	High
Hadipour and others (2011)	Y	AB	N	U	Potency unknown	High
Kiarazm (2011)	Y	P	Y	U	Potency unknown	Low
Wagenaar and others (2011)	Y	U, CON	N	U	Remedy data missing	High
Sato and others (2012)	Y	P	Y	U	U	Low
Aubry and others (2013)	N	N	N	N	Researcher worked for supplier	High
Hornig (2014)	Y	P	Y	U	U	Low
Williamson and Lacy-Hulbert (2014)	Y	AB	N	U	U	High

AB Antibiotics, COM Combined treatment of homeopathy and antibiotics, CON Conventional treatment including antibiotics, N No, P Placebo, U Untreated, Y Yes

risks found were: groups were not evenly distributed, measures were not scientifically valid, eg, subjective or very indirect measures for improvement or cure, homeopathy was only tested in combination with antimicrobials or no control (placebo/untreated) was considered. Altogether, studies with a high possible risk of bias were more prone to report efficacy of homeopathy than studies with a low risk of bias (OR 1.71, 95 per cent CI 0.48 to 6.11, P=0.41 vs OR 0.58, 95 per cent CI 0.16 to 2.09).

### Species-specific results Studies on cattle

Altogether, 34 trials on cattle matched the selection criteria (Table 4). The main focus (85 per cent) was on dairy cows (n=29), the other studies dealt with calves (n=5). Homeopathy was proved efficacious in 15 studies, but no evidence was found in 18 studies and inconclusive results were returned for one of them. Five out of eight studies performing double-blind RCTs reported no homeopathic efficacy,

TABLE 4: Publications on cattle

Authors (year)	Species	Indication	Study design	Diagnostic measure	Effect of homeopathy?
Boerms (1981)	Calves	Pneumonia / diarrhoea treatment	RCT non-blind	CS	IR: only vague improvement, no sign, differences between AB and HOM group
Frerking and Romansky-Rieken (1981)	Calves	Diarrhoea treatment	RCT non-blind	CS	No: repeated treatments necessary, more deaths, also no effect in combination with antibiotics
Day (1986) – trial 1	Dairy cows	Postpartum disorders prevention	RCT non-blind	CS	Yes: no dead calf compared to untreated group (7 deaths). 2 of 7 cows (HOM) required assistance during birth and 18 of 18 in untreated. Fewer cases of mastitis/metritis in HOM (0/4) compared to untreated (9/10)
Day (1986) – trial 2	Dairy cows	Mastitis prevention	RCT non-blind	CS	Yes: mastitis cases decreased (at high infection risk). Mastitis increased in untreated 'low risk' group
Day (1986) – trial 3	Dairy cows	Mastitis prevention	RCT single-blind	CS	Yes: lower mastitis incidence compared to P
Sonnenwald (1986)	Dairy cows	Mastitis (acute) Individualised treatment	RCT non-blind	DT/IT/CS	IR: no significant difference between HOM and AB treatments. <i>Streptococcus</i> : better result with AB. Gram-negative bacteria: HOM more effective than AB
Stopes and Woodward (1990)	Dairy cows	Mastitis prevention	Observational	CS	No: no preventive effect
Merck and others (1989)	Dairy cows	Mastitis treatment	Observational	CS	Yes: good healing rates especially for <i>E coli</i> infections
Erbe (1990)	Dairy cows	Retained placenta / endometritis metaphylaxis	RCT non-blind	IT/CS	Yes: occurrence of endometritis and retained placenta significantly reduced compared to P
Tiefenthaler (1990)	Dairy cows	Mastitis treatment	RCT non-blind	DT/IT	No: no differences between HOM group, AB group and COM
Wirth (1990)	Dairy cows	Retained placenta / endometritis metaphylaxis	RCT non-blind	IT/CS	Yes: occurrence of endometritis and retained placenta significantly reduced compared to P
Vohla (1991)	Dairy cows	Puerperal diseases & calf health (prevention)	Observational	CS	No: no differences to U and P
Knierim (1992)	Dairy cows	Parturition and puerperal disorders (prevention)	RCT double-blind	IT/CS/M	No: no influence compared to P
Schütte (1994) – trial 1	Dairy cows	Mastitis metaphylaxis	RCT single-blind	M	No: no difference between P and HOM
Schütte (1994) – trial 2	Dairy cows	Retained placenta (prevention)	RCT single-blind	CS	No: no difference between a P and HOM
Egan (1995)	Dairy cows	Subclinical mastitis treatment	Observational	DT/IT	No: no response, mastitis even deteriorated.
Searcy and others (1995)	Dairy cows	Subclinical mastitis metaphylaxis	RCT non-blind	IT/M	Yes: 4.5 times less subclinical mastitis than in P group
Hümmelchen (1999)	Dairy cows	Postpartum disorders (prevention)	RCT non-blind	DT/IT/CS/M	Yes: better development than P for birth, placenta retention, occurrence of mastitis other infections
Garbe (2003)	Dairy cows	Mastitis metaphylaxis	RCT double-blind	DT/IT/CS	No: no prophylactic or therapeutic effect in comparison with AB dry off or P
Verdier and others (2003)	Calves	Diarrhoea treatment	RCT double-blind	CS/M	No: no difference in comparison to P
Hektoen and others (2004)	Dairy cows	Clinical mastitis individualised treatment	RCT double-blind	CS	No: no efficacy beyond P or AB group. AB also comparably poor in effectiveness
Schlecht (2004)	Dairy cows	Udder health (prevention)	RCT single-blind	DT/IT	Yes: improved health parameter compared to P
Holmes and others (2005)	Dairy cows	Mastitis prevention	RCT single-blind	IT	No: no significant differences between HOM and P on any sample day
Walkenhorst (2006)	Dairy cows	Clinical and subclinical mastitis treatment	RCT non-blind	DT/IT/CS	No: no effect, only comparable with self-healing rates. AB in all cases more effective
Enbergs and Sensen (2007)	Dairy cows	Chronic endometritis treatment	Observational	IT/M	Yes: culling and conception rate improved, shorter interval until pregnancy, lower insemination index, higher first-service pregnancy rate. Comparable to hormone treatment, less effective than CON intrauterine treatment
Arlt and others (2009)	Dairy cows	Endometritis prevention	RCT double-blind	DT/IT	No: not effective in prevention or in enhancing reproductive performance
Klocke and others (2010)	Dairy cows	Mastitis prevention (at drying off)	RCT non-blind	DT/IT/CS	Yes: lower SCC and 'normal milk secretion' compared to U, but worse than teat sealer
Werner and others (2010)	Dairy cows	Mastitis individualised treatment	RCT single-blind	DT/CS	Yes: positive over P group with mastitis, no difference to AB treatment after 4 and 8 weeks
Kiarazm and others (2011)	Dairy cows	Subclinical mastitis treatment	RCT single-blind	DT/IT	Yes: SCC and bacterial detection were significantly lower in HOM than P group after treatment (day 21 and 28)

TABLE 4: Publications on cattle (continued)

Authors (year)	Species	Indication	Study design	Diagnostic measure	Effect of homeopathy?
Wagenaar and others (2011)	Dairy cows	Mastitis metaphylaxis	Observational	DT/IT	No: no improvement compared with U group
Aubry and others (2013)	Dairy cows	Early subclinical mastitis treatment	Observational	IT/M	Yes: significant reduction of electrical conductivity and increased milk yield 4 to 7 days after treatment
Hornig (2014)	Calves	Diarrhoea treatment	RCT double-blind	CS/M	No: No significant difference compared to P for all chosen parameters
Williamson and Lacy-Hulbert (2014)	Dairy cows	Mastitis individualised treatment	RCT non-blind	CS	No: curing rate of antibiotics was significantly higher (no P or U group)

AB Antibiotics, COM Combined treatment of homeopathy and antibiotics, CON Conventional treatment including antibiotics, CS Clinical signs, DT Direct test, HOM Homeopathy, IR Inconclusive results, IT Indirect test, M Measurements, P Placebo, RCT Randomised controlled trial, SCC Somatic cell count, U Untreated

while three demonstrated efficacy (Day 1986, Hümmelchen 1999, Schlecht 2004).

Twenty studies dealt exclusively with udder health, including prevention or treatment of acute or subclinical mastitis, drying off (Schütte 1994, Klocke 2010) or udder health in general (Schlecht 2004). Apart from mastitis, fertility disorders, especially around the parturition such as retained placenta and endometritis, were addressed in nine studies. Remarkably, almost all studies on fertility disorders used homeopathy exclusively for prevention and not for therapeutic treatment. Only Enbergs and Sensen (2007) examined the use of two different homeopathic complex remedies to treat chronic endometritis, yielding a positive result. Wirth (1990) and Erbe (1990) applied different metaphylactic homeopathic remedies to their experimental groups to reduce retained placenta and endo-

metritis, both with a positive outcome.

When only taking into account studies on dairy cows, 14 out of 29 publications were able to prove efficacy of the homeopathic remedy, while in the same number of studies no benefit of homeopathy was shown. One of the studies failed to show a clear result: Sonnenwald (1986) struggled with undefined results comparing homeopathic and antibiotic treatment for acute mastitis. The homeopathic treatment showed better results for Gram-negative mastitis-causing bacteria and antibiotics were more effective for Gram-positive *Streptococcus* subspecies.

Four of the five studies on calves dealt exclusively with the treatment of diarrhoea (Frerking and Romansky-Rieken 1981, Kayne and Rafferty 1994, Verdier and others 2003, Hornig 2014). Of these studies, only Kayne and Rafferty (1994) reported the sin-

TABLE 5: Publications on pigs

Authors (year)	Species	Indication	Study design	Diagnostic measure	Effect of homeopathy?
Day (1984)	Sows	Stillbirth prevention	Observational	M	Yes: number of stillbirths decreased significantly compared to an untreated group
Seifert (1987)	Sows	MMA individualised treatment	RCT non-blind	CS/M	Yes: less treatments needed to recover compared to allopathy. Average treatment duration was slightly shorter. Higher litter weight and lower piglet mortality
Drösemeier (1989)	Sows	MMA prevention	RCT double-blind	DT/CS/M	No: no difference on MMA infection rate compared to P or AB group
Schütte (1991) - trial 1	Pigs	Respiratory tract diseases prevention	RCT non-blind	CS	Yes: HOM mix over 10 days lessens the sickness rate (18.1 per cent) in comparison to placebo (24.3 per cent), more effective than subtherapeutic AB dose (19.1 per cent) but less than therapeutic AB dose (10.4 to 8.3 per cent)
Schütte (1991) - trial 2	Pigs	Respiratory tract diseases prevention	RCT non-blind	CS	Yes: HOM remedy had a significantly lower infection rate (17.7 per cent) than P (24.3 per cent) within a 5-day treatment double dosed
Guajardo-Bernal and others (1996)	Sows	Growth promotion	RCT single-blind	M	No: no difference in birth weight of litters compared to P
Albrecht and Schütte (1999)	Piglets	General and respiratory disease metaphylaxis	Observational	CS	Yes: significantly effective when compared with the P and routine low-dose AB for reduction of disease and prevention of respiratory diseases, but not better than a therapeutic dose of AB
Schütte (2003)	Pigs	Health in general	Observational	CS/M	Yes: AB use could be reduced by 60 per cent (over 3 years) on participating farms
Soto and others (2008)	Piglets	Post-weaning diarrhoea and weight loss prevention	RCT non-blind	M	IR: piglets treated with HOM had less weight loss as control group and less but not significant different to P. No statistical difference between food consumption or diarrhoea
Coelho and others (2009)	Piglets	<i>E coli</i> diarrhoea prevention	RCT double-blind	CS/M	Yes: highest weight gain and significant reduction of diarrhoea compared to AB control (but medical agent of AB is known to have high resistance to <i>E coli</i> )
Camerlink and others (2010)	Piglets	<i>E coli</i> diarrhoea prevention	RCT single-blind	DT/CS	Yes: less transmission and duration of disease shorter and less diarrhoea than in P group
Da Silva and others (2011)	Pigs	Growth promotion	Observational	M	IR: last of six measurements was higher, but at slaughter no significant weight differences found. Lack of a control group (and only five pigs per group)

AB Antibiotics, COM Combined treatment of homeopathy and antibiotics, CON Conventional treatment including antibiotics, CS Clinical signs, DT Direct test, HOM Homeopathy, IR Inconclusive results, IT Indirect test, M Measurements, P Placebo, RCT Randomised controlled trial, U Untreated



gle homeopathic drug *Arsenicum album* 30C as efficacious, resulting in recovery one day faster in the homeopathically treated calves than in the placebo group. Boerms (1981) tested the effectiveness of the classic homeopathic remedy *Echinacea* in combination with standard allopathic remedies for treating pneumonia and enteritis in calves. This was trialled in comparison with 'pure' standard antibiotic treatment without significant differences in cure rates compared to *Echinacea*.

### Studies on pigs

Twelve studies on pigs were identified (Table 5). Nine trials found the homeopathic remedy to be effective, two could not prove the tested remedy to be efficacious and one had inconclusive results. The various outcomes seemed not to be related to the study design. Observational trials and open RCTs, as well as single- or double-blind RCTs, were performed with either efficacy or no efficacy or inconclusive results for the applied homeopathic remedy reported.

The age of the animals varied considerably between the trials evaluated: five trials were performed with sows, four trials with mainly fattening pigs and three with piglets. The reasons listed for application of homeopathic remedies were predominantly prevention (n=10). Three studies addressed fertility disorders in sows (Day 1984, Seifert 1987, Drösemeier 1989), three dealt with respiratory infections (Schütte 1991 [two trials], Albrecht and Schütte 1999) and three with diarrhoea (Soto and others 2008, Coelho and others 2009, Camerlink and others 2010), while two focused on growth promotion (Guajardo-Bernal and others 1996, Da Silva and others 2011) and one simply aimed for a good general health (Schütte 2003). The three disease complexes mentioned are among the most common reasons for the use of antibiotics on pig farms in practice (Christensen and others 1995, Petersen and others 2008). The prevention or treatment of fertility disorders (in particular stillbirth and MMA) with homeopathic remedies was effective in two out of three trials in sows. It should be noted that the trials that were efficacious were either a parallel group trial (Day 1984) or a non-blind RCT (Seifert 1987), while the one study that failed to yield evidence of efficacy of preventing MMA in sows was a double-blind RCT (Drösemeier 1989).

In a study on respiratory disease and general state of health, homeopathy was significantly more effective than low dosage antibiotics or a placebo for fattening pigs, but was less effective than a high dosage antibiotic metaphylaxis (Albrecht and Schütte 1999). In the earlier non-blind trial of Schütte (1991), a metaphylactic treatment with two different homeopathic complex remedies yielded a significantly higher efficacy compared with a placebo depending on the duration of treatment, but was not as efficacious as an antibiotic treatment.

Two of the studies dealt with growth promotion: Guajardo-Bernal

and others (1996) administered a very high dilution (C201) of sulfur to pregnant sows and examined the weight and performance of the new born piglets in a single-blind RCT. It found no significant difference in the birth weights and the further development of the piglets in comparison with a placebo group. In an observational trial, Da Silva and others (2011) treated the pigs directly with a complex remedy in two different treatment schemes aiming for growth promotion. The weight recorded differed between the groups within the study period, but as there was no control group, no clear outcome could be concluded. Studies by Soto and others (2008), Coelho and others (2009) and Camerlink and others (2010) aimed to prevent diarrhoea in piglets. Coelho and others (2009) and Camerlink and others (2010) performed a double and single blind RCT, respectively. Both studies yielded a positive result for efficacy of homeopathy in comparison to a control group treated with an antibiotic or placebo. Soto and others (2008) showed that homeopathically treated piglets lost less weight compared to an untreated control or placebo group, but the difference between the placebo and homeopathy groups was not significant. The only study evaluating the influence of homeopathy on general health in pigs measured by clinical signs, gravity and length of illness, therapeutic results and antibiotic consumption (Schütte 2003) showed that the consumption of antimicrobials on the participating farms could be reduced by 60 per cent (over three years) when homeopathy was used.

### Studies on poultry

Only six studies were found dealing with homeopathic treatment in poultry production and they were performed exclusively on chickens (Table 6). Efficacy of homeopathic treatment was proven in four studies out of the six.

In three trials, homeopathy was administered to treat diarrhoea caused by *Salmonella* (Sandoval and others 1998, Berchieri and others 2006) or *E coli*-infection (Velkers and others 2005). The remaining three studies looked at growth promotion (Amalcaburio and others 2009, Hadipour and others 2011, Sato and others 2012), and one study combined this with observations on improved immune reactivity (Sato and others 2012). The four studies where homeopathic treatment was effective were performed as observational (Sandoval and others 1998), non-blind RCTs (Berchieri and others 2006, Hadipour and others 2011) and a double-blind RCT (Sato and others 2012). Berchieri and others (2006) induced an infection to test the preventive effect of a *Salmonella* nosode and found a significant lower faecal excretion of *Salmonella* Enteritis when compared with an untreated group. Hadipour and others (2011) compared the growth promoting effects of a combined homeopathic remedy with undefined potency to a group treated with a standard regime of antibiot-

TABLE 6: Publications on poultry

Authors (year)	Species	Indication	Study design	Diagnostic measure	Effect of homeopathy?
Sandoval and others (1998)	Chicken	Salmonellosis treatment	RCT non-blind	DT/CS	Yes: efficacy not significantly different to AB group
Velkers and others (2005)	Chicken	<i>E coli</i> diarrhoea prevention	Observational	DT/CS/M	No: no difference compared to U control
Berchieri and others (2006)	Chicken	Salmonellosis (induced) prevention	RCT non-blind	DT	Yes: faecal excretion of <i>Salmonella enteritidis</i> significantly lower than in untreated control
Amalcaburio and others (2009)	Chicken	Growth promotion	RCT non-blind	DT/M	No: no difference in growth speed or final weight compared to an untreated control
Hadipour and others (2011)	Chicken	Growth promotion	RCT non-blind	DT/CS/M	Yes: higher growth rate, final weight and food conversion ratio compared to CON treatment (AB and vaccines)
Sato and others (2012)	Chicken	Growth promotion and immune system improvement.	RCT double-blind	DT/CS/M	Yes: less mortality, increased productivity, a higher viability and a possible shunt to B lymphocyte activity and higher weight gain (only for females) than in U control

AB Antibiotics, CON Conventional treatment including antibiotics, CS Clinical Signs, DT Direct Test, IT Indirect Test, M Measurements, RCT Randomised controlled trial, U Untreated

ics and vaccines. They found a 5 per cent lower mortality and significantly higher weight gain in the homeopathic experimental group. Sato and others (2012) performed a double-blind RCT with chickens and noted that the group with *Thymulin* in a D5 (1:10<sup>-5</sup>) dilution benefitted from an immune stimulating and growth-promoting effect, compared to an untreated group.

The two studies with a negative outcome were an observational study (Velkers and others 2005) and a non-blind RCT (Amalcaburio and others 2009). One of them used high dilutions (C12 or C30) of a combined homeopathic remedy in comparison to an untreated control (Amalcaburio and others 2009). The other study administered three different combinations of homeopathic drugs combined with an *E coli* nosode, all in a high dilution (C30, C200), with no effect compared to the untreated or antibiotic-treated control groups (Velkers and others 2005).

### Heterogeneity among the trials

A classic comparison of the individual clinical trials within a systematic review according to the principles of evidence-based medicine was not possible. These principles involve randomisation, blinding and several clinical trials performed on the same species, disease and remedy to be evaluated in a systematic way. A large heterogeneity among all clinical trials was found. Differences emerged in various areas:

- **Patients.** The patients included in the trials differed with respect to species. Differences within species were in relation to: age of farm animals, performance level, resilience, and thus different individual abilities to respond to pharmaceutical active ingredients.
- **Remedy.** The remedies used in the trials differed with respect to ingredients in classic and combined homeopathic remedies, high and low dilutions (potencies), administration method, pharmaceutically active ingredients (not standardised). Remedies were administered in different ways for various indications in order to achieve preventive, metaphylactic, therapeutic, growth-promoting or immune system stimulating effects.
- **Context.** The trials were performed in different contexts, distinguished among others by: diseases, pathogens, means of infection (naturally occurring or artificially induced), farm animals' living conditions regarding hygiene standards, feeding regimen and treatment procedures. In 54 per cent of the studies, the living conditions were not described.
- **Expertise:** Diagnostic procedures in the trials were performed by people who differed considerably in education, expertise and knowledge of treatment strategies. Choice of remedy and means of measuring the therapeutic effect of the homeopathic remedy applied differed between trials. This was also the case regarding assessment of therapeutic effects (eg, visual improvement in milk) compared to an objective analysis (eg, complete clinical examinations accompanied by external laboratory tests) (Fig 3).

Within the studies considered, the use of the same remedy administered to the same species with a comparable medical indication was not repeated. Thus, the results lack any reproducibility.

### Discussion

Taking into account the long existence of homeopathy and use in livestock production, only a comparatively small number of scientific studies focussing on the efficacy of homeopathy have been conducted so far. Four publications summarised a limited number of trials with different search criteria while considering various species, including livestock. Three of them evaluated the efficacy of homeopathy as poor or insufficient; one of the reports did not come to a clear result due to limitations in scientific quality of studies available:

- Kowalski (1989) evaluated homeopathic treatment in veterinary literature for a doctoral thesis and found that homeopathy had certain effects, but only one homeopathic trial seemed to have been efficacious. Fourteen controlled, clinical trials (not including experimental trials on single animals and general treatises on remedy pictures) were assessed. Ten of the 14 trials considered cattle or pigs, while the rest dealt with cats, dogs or horses.
- Hektoen (2005) took into account three single clinical trials and the publication of Kowalski (1989) to evaluate the efficacy of homeopathy in animals. The remaining sources covered broader literature

and conference proceedings or grey literature on the topic 'homeopathy and placebo effect', predominantly considering human medicine. The resulting article did not emerge with a clear decision on the efficacy of homeopathy, because of the poor quality of the available studies.

- Rijnberk and Ramey (2007) considered 10 publications from human medicine, for example, homeopathy reviews, while only four clinical trials including animals (three on cattle, one on dogs) were considered. They published a report on the lack of effectiveness of veterinary homeopathy pointing out among other things the existence of no significant differences of homeopathic remedies and placebos when compared in studies.
- Ruegg (2008) compared different treatment strategies of mastitis and its efficacy. Four publications (Egan 1998, Hektoen and others 2004, Holmes and others 2005, Rijnberk and Ramey 2007) were considered and concluded that efficacy data for veterinary homeopathy appear to be almost completely lacking.

In comparison to the reports previously published, dealing with the effectiveness of homeopathy in animals, the current review encompasses a much higher number of studies. One reason is the fact that much time has passed between the first review by Kowalski (1989) and today. Apart from publications in peer-reviewed journals, the current review also included doctoral theses in German. This reflects the situation in German-speaking countries, where (for unknown reasons) homeopathy is more frequently used than in other countries (Kayne 2006, Mathie and others 2012, Albrecht 2013, Allensbach Institute for Public Opinion Research 2014). In their characterisation of research literature on veterinary homeopathy in preparation of following publications, Mathie and others (2012) did not define doctoral thesis as peer-reviewed as was done in this review. Due to the extended literature search using multiple sources, it can be assumed that nearly all peer-reviewed articles on homeopathy in livestock matching the search criteria were considered. Thus, the current review can claim to be the most comprehensive review on homeopathy in farm animals so far.

Comparing the previous reports (Kowalski 1989, Hektoen 2005, Rijnberk and Ramey 2007, Ruegg 2008) with this review's findings, only a very small number of trials on animals were considered and the selection criteria were either unclear or not even stated. These facts may have caused the authors to be biased in their reporting of the results.

Contrary to the summary reports of the previous authors, Clausen and others (2013) and Mathie and Clausen (2014, 2015) published three articles exclusively on randomised placebo-controlled trials in veterinary medicine built upon each other. The main focus was on medical conditions, for example, randomisation, risk of bias according to Cochrane's evidence-based medicine principles, individualised/non-individualised treatments, and so on, to assess whether homeopathic interventions are distinguishable from corresponding treatments with placebo. They found two trials of 18 (2014) and 15 (2015), respectively with reliable evidence, free from vested interest precluding general conclusions about the efficacy of homeopathy and very limited evidence for differences between homeopathy and placebo within placebo-controlled RCTs. The authors saw a need for a higher quality research on veterinary homeopathy.

Homeopathic trials performed as a single-blind or non-blind RCT, parallel groups or an observational trial (Fig 4) tended to be more frequently efficacious than a double-blind RCT, indicating that positive outcomes may partly be due to a bias caused by a conscious or unconscious preference for a certain treatment. The biggest proportion of the trials (79 per cent) were RCTs – a high quality level according to the principles of evidence-based medicine and regarded as the standard for a remedy's clinical proof of efficacy by the scientific community (van Sluijs 2005). This may lead to the general conclusion that homeopathic remedies are able to support the healing process under certain conditions. However, the evidence-based medicine method is also prone to errors (eg, by a narrow scope of considered studies) producing misleading conclusions or results claiming efficacy where there might be none (Weymayr 2013).

A critical point in the current methods of performing trials on efficacy is that they are conducted under standardised conditions and do

not consider the situation animals actually experience on farms. The focus is mainly on the remedy without particular focus on the interactions between animals and their living conditions, and their ability to react to a certain pathogen. The variability of the living conditions and of the pre-existing situations on farms are not considered either, for instance, regarding the appropriateness of diagnostics to determine the most suitable remedy or treatment procedure. Thus, a certain remedy which proved efficacious in a scientific trial may not be effective under farm conditions.

No differences concerning the outcome were found in relation to the means of publication in scientific journals or as doctoral theses. The number of non-peer-reviewed publications found was more than double the number of peer-reviewed journals. Similar results were found by Clausen and others (2013), who evaluated all studies, collected by the HomVetCR database on veterinary homeopathy, focusing on the content of placebo-controlled trials. The peer-reviewed studies were more often published in journals dedicated to homeopathy or alternative therapies than in journals on veterinary medicine in general. It can be assumed that journals which focus on complementary and alternative therapies like homeopathy are rather more likely to receive articles dealing with this therapy. There is an increased risk for publication bias; for example, reports with positive results for a tested method or remedy are usually more likely to be published than those with negative results (Arlt and Heuwieser 2010). In this evaluation, articles published in journals focussing on alternative treatments were much more likely to present an efficacy (positive publication bias) while it was vice versa for articles in journals focussing more on conventional therapies (negative publication bias) but failed to provide statistically significant differences (OR 3.75, 95 per cent CI 0.63 to 22.04,  $P=0.14$ ).

Comparing the reasons why homeopathic remedies were used, positive results tended to occur more often for a preventive use ( $n=16$  of 28) than for a therapeutic ( $n=8$  of 28) or a metaphylactic use ( $n=4$  of 28). Remarkably, when strictly following the simile-rules ('like cures like') of homeopathic treatment, a preventive effect is difficult to achieve because a complete homeopathic clinical picture is lacking and so is the matching remedy picture. The results of the trials contradict this principle, but may be an unspecific reaction of the immune system to the stimulus (the remedy). A different case might be the special form of homeopathic remedy called 'nosode', manufactured using a sample of diseased matter as a basis (usually from a certain animal in the herd to be treated), highly diluted and mainly used for prevention. The dilution process reduces the amount of infective pathogens to almost zero but could possibly induce unspecific humoral immunity.

The most objective and scientific way to assess the outcome of treating a diseased animal is to perform a direct test (eg, on the presence or absence of the pathogens responsible) and this is best performed by an official laboratory. Starting from this basis, the treatment assessment methods can be listed as follows: direct test > indirect test performed onsite > clinical signs > measurements. The list starts with the most scientific methods and ends with the least scientific ones. The person performing the diagnostic procedures may well have judgement, which varies according to education and experience. The complexity of factors which results in a cure and the performance of different diagnostic measures might distort the resultant efficacy of a remedy applied. Expertise is a prerequisite in finding the appropriate remedy and helps inform any ongoing adaptations of the treatment when necessary. However, when any factors present which cause disease are left undiscovered and are not instantly removed, animals may still remain ill. If farm animals are kept under living conditions where their immune systems are under strain or exhausted, neither conventional nor alternative remedies will be able to provide a sufficient cure rate.

While conventional medication focuses primarily on the indication, homeopathy addresses the individual reactions and symptoms arising in the first place. Correspondingly, to an extent the conventional approach acts in a context-invariant way whereas the homeopathic approach considers the context, particularly observing how animals behave in a specific situation. Thus, an assessment of the effectiveness of homeopathic medication should not exclude the context in which these remedies are employed.

When compared in the same trial, there were differences in the therapeutic effect homeopathy and the placebo had. This ranged between 0 per cent and 27 per cent (Werner and others 2010, Hornig 2014). Sometimes relatively small and insignificant differences were found between the homeopathic remedy and the placebo groups in clinical trials. This raises the question whether the effects of homeopathy are comparable to a placebo effect. Nevertheless, 12 trials were performed above a dilution of 1:10<sup>24</sup> and showed a positive outcome for the efficacy of the homeopathic remedy administered in relation to a control treatment. The efficacy of a placebo generally corresponds to the function of self-healing forces of the body without the influence of an active substance. Therefore, a comparison of homeopathy with a placebo and an untreated group aids the distinction between the effect a placebo has and the self-healing effect. When aiming to find an alternative to an existing medicine, it is necessary to undertake trials with the above remedy, the proposed alternative and a placebo group in order to come up with valid results (European Medicines Agency 2001). This ensures that animals receive the most effective therapy possible.

In order to be considered as an alternative to antimicrobials in cases of bacterial infections, homeopathic remedies ought to be at least as effective. In 18 studies, a homeopathic treatment was compared with an antimicrobial treatment. In several cases, the efficacy of the chosen homeopathic remedy was higher than the conventional treatment with antimicrobials. Differences between the cure rate of homeopathic and antibiotic treatment in a trial ranged between 2 per cent (Hektoen and others 2004) and 30 per cent (Tiefenthaler 1990) in favour of homeopathy. However, a comparable amount of trials reported homeopathic remedies as having poorer cure rates compared with the conventional treatment, with differences ranging between 1 per cent to 55 per cent in the same trial (Hektoen and others 2004, Walkenhorst 2006). In other studies, no significant differences could be found in the cure between the experimental group treated with homeopathy and an antibiotic control group (Boerms 1981, Tiefenthaler 1990, Sandoval and others 1998). Furthermore, it has to be considered that in most trials no sensitivity tests on the bacterial resistance patterns of the bacteria responsible were performed before choosing the antimicrobial for treatment. Performing a sensitivity test in the trials might have led to altering the drug selected, thus causing the antimicrobial tested to be more effective overall.

When taking the total number of studies into account, not even one study was repeated under comparable conditions. Consequently, the existing conditions, which enable a systematic review to be carried out completely are not given. The current evidence of studies providing evidence in favour of homeopathy lacks reproducibility and therefore cannot claim to have sufficient prognostic validity. No general conclusions can be drawn as to whether a homeopathic remedy shown to be significantly more effective than a control treatment in a specific context is also effective in a different context or under different conditions (as the previous trial describes). It cannot be concluded whether it is better, worse or ineffective.

The efficacy of a remedy cannot be reduced to the concentration of pharmaceutically active ingredients alone and cannot be isolated from the context in which it is used. It is the result of complex interactions of various factors which include, among others: the individual's immune strength and capacity to react to stimuli, the degree the main and any secondary causes are eliminated, an adequate diagnosis and an appropriate treatment (no matter of the kind), and, last but not least, the farm animals' living conditions, especially in relation to nutrient supply and hygiene conditions.

In practice, homeopathy may well not be applied according to a certain standard in diagnostic, treatment and education due, among other reasons, to the different level of homeopathic education of farmers and veterinarians. However, it is also questionable whether conventional medicine (eg, antibiotics) is always used according to the guidelines on the prudent use of antibiotics in veterinary medicine in farm practice as the Federation of Veterinarians of Europe (2014) recommend. Various publications indicate that farmers rarely instigate diagnostic tests to detect the pathogen responsible (Ouweltjes and others 2008, Doehring and Sundrum 2013).

## Conclusions

In a considerable number of studies, a significant higher efficacy was recorded for homeopathic remedies than for a control group. Therefore, the potential medical efficacy of homeopathy under certain conditions cannot be ruled out. However, this does not necessarily imply that homeopathic remedies are effective under different conditions. This is especially true for the context-sensitive treatment strategy of homeopathy, which considers (beside clinical signs and the pathogen responsible) behaviour, constitution and conditions in which the animal is living in. The review revealed that all studies included were conducted under very specific conditions, but no trial was repeated in a comparable manner. Thus, the previous studies cannot be generalised and have to be regarded as single-case studies. The first priority when medically treating animals should always be to apply the most effective treatment or remedy and thus prevent unnecessary suffering of the animal, if only for the reasons of animal welfare. Due to the unknown level of effectiveness of on-farm homeopathy, this can only be achieved by the appropriate control and monitoring of treatment success in farm practice. Due to a lack of prognostic validity, replacing or reducing antibiotics with homeopathy currently cannot be recommended unless evidence of efficacy is reproduced by RCTs and proven in various farm practice conditions.

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## References

- ALBRECHT, H. (2013) The situation of complementary medicine in Germany. *Forschende Komplementärmedizin* **20**, 73-77
- ALBRECHT, H. & SCHÜTTE, A. (1999) Homeopathy versus antibiotics in metaphylaxis of infectious diseases: a clinical study in pig fattening and its significance to consumers. *Alternative Therapies in Health and Medicine* **5**, 64-68
- ALLENSBACH INSTITUTE FOR PUBLIC OPINION RESEARCH (2014) Homöopathische Arzneimittel 2014-Bekanntheit, Verwendung und Image. [Homeopathic remedies 2014 - Awareness, use and image]. [www.homeopathie-tv.com/wp-content/uploads/2015/08/Ergebnisse\\_Allensbach\\_deSombre\\_170dpi.pdf](http://www.homeopathie-tv.com/wp-content/uploads/2015/08/Ergebnisse_Allensbach_deSombre_170dpi.pdf). Accessed November 25, 2016
- AMALCABURIO, R., FILHO, L., HONORATO, L. A. & MENEZES, N. A. (2009) Homeopathic remedies in a semi-intensive alternative system of broiler production. *International Journal of High Dilution Research* **8**, 33-39
- ARLT, S. & HEUWIESER, W. (2010) Evidence-based complementary and alternative veterinary medicine—a contradiction in terms? *Berliner und Münchener tierärztliche Wochenschrift* **123**, 377-384
- ARLT, S., PADBERG, W., DRILLICH, M. & HEUWIESER, W. (2009) Efficacy of homeopathic remedies as prophylaxis of bovine endometritis. *Journal of Dairy Science* **92**, 4945-4953
- AUBRY, E., ISSAUTIER, M. N., CHAMPOMIER, D. & TERZAN, L. (2013) Early udder inflammation in dairy cows treated by a homeopathic medicine (Dolisovet): a prospective observational pilot study. *Homeopathy* **102**, 139-144
- AUDESAPER (2014) Veterinary and aquaculture. now: initiative to promote research in homeopathy. <http://researchinhomeopathy.org/database/veterinary/>. Accessed November 14, 2016
- BERCHIERI, A., Jr, TURCO, W. C., PAIVA, J. B., OLIVEIRA, G. H. & STERZO, E. V. (2006) Evaluation of isopathic treatment of *Salmonella enteritidis* in poultry. *Homeopathy* **95**, 94-97
- BOERMS, E. (1981) Untersuchungen über die Wirksamkeit von *Echinacin R* als einmalige subkutan verabreichte Zusatztherapie bei Erkrankungen junger Kälber. [Investigations on the efficacy of *Echinacin R* as additional single subcutaneous therapy administered in diseases of young calves]. PhD thesis, University of Veterinary Medicine Hanover, Germany
- CAMERLINK, I., ELLINGER, L., BAKKER, E. J. & LANTINGA, E. A. (2010) Homeopathy as replacement to antibiotics in the case of *Escherichia coli* diarrhoea in neonatal piglets. *Homeopathy* **99**, 57-62
- CHRISTENSEN, G., VRAA-ANDERSEN, L. & MOUSING, J. (1995) Causes of mortality among sows in Danish pig herds. *Veterinary Record* **137**, 395-399
- CLAUSEN, J., ALBRECHT, H. & MATHIE, R. T. (2013) Veterinary clinical research database for homeopathy: placebo-controlled trials. *Complementary Therapies in Medicine* **21**, 115-120
- COELHO, C., SOTO, F., VUADEN, E., MELVILLE, P., OLIVEIRA, F. & BENITES, N. (2009) Evaluation of preventive homeopathic treatment against colibacillosis in swine production. *International Journal of High Dilution Research* **8**, 183-190
- DA SILVA, S. L. M., ARCANJO, A. H. M., PINTO, L. D. R., ROSA, G. P. & SOUZA, G. H. de (2011) Gain of mass between two profiles of treatments to pigs with self-organizing factors. *International Journal of High Dilution Research* **10**, 271-282
- DAY, C. (1984) Control of stillbirths in pigs using homeopathy. *Veterinary Record* **114**, 216
- DAY, C. (1986) Clinical trials in bovine mastitis: use of nosodes for prevention. *British Homeopathic Journal* **75**, 11-14
- DOEHRING, C. & SUNDRUM, A. (2013) Diagnosis of mastitis in Germany. [Mastitisdiagnostik in Deutschland]. Bundesinstitut für Risikobewertung, p 91
- DROSEMEIER, C. (1989) Einsatz von *Lachesis compositum* bei Zuchtsauen zur Prophylaxe des MMA-Komplexes [Administration of *Lachesis compositum* in breeding sows for prevention of mastitis-metritis-agalactia complex]. PhD thesis, University of Veterinary Medicine Hanover, Germany
- EGAN, J. (1995) Evaluation of a homeopathic treatment for subclinical mastitis. *Veterinary Record* **137**, 48
- EGAN, J. (1998) Homeopathic mastitis control: a study on the uptake and efficacy of products in the Republic of Ireland. *Axient Institute for Animal Health*, pp 22-28
- ENBERGS, H. & SENSEN, B. (2007) Zur Effizienz homöopathischer Behandlungen chronischer Endometritiden von Milchkühen [Efficacy of homeopathic treatments of chronic endometritis in dairy cows]. *Der Praktische Tierarzt* **88**, 534-543
- ERBE, U. (1990) Metaphylaxe puerperaler Störungen beim Rind, insbesondere Retentio secundinarum und Endometritis, durch Anwendung von Puerperal [Metaphylactic treatment puerperal disorders in dairy cows, especially with retained placenta and endometritis, by use of 'Puerperal']. PhD thesis, University of Veterinary Medicine Hanover, Germany
- ECCH (2007) The homeopathic treatment of animals in Europe: a report on the situation in 15 countries. [www.homeopathy-ecch.org/content/view/full/26143/](http://www.homeopathy-ecch.org/content/view/full/26143/). Accessed November 14, 2016
- EUROPEAN COMMISSION (2008) Commission Regulation (EC) No 889/2008 laying down detailed rules for the implementation of Council Regulation (EC) No. 834/2007 on organic production and labelling of organic products with regard to organic production, labelling and control. European Commission
- EMA (2001) Points to consider on missing data. CPMP/EWP/1776/99. [www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/09/WC500003641.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003641.pdf). Accessed November 14, 2016
- FEDERATION OF VETERINARIANS OF EUROPE (2014) Antibiotic Resistance and Prudent use of antibiotics in veterinary medicine. [www.fve.org/news/publications/pdf/antibioen.pdf](http://www.fve.org/news/publications/pdf/antibioen.pdf). Accessed November 14, 2016
- FRERKING, H. & ROMANSKY-RIEKEN, M-E. (1981) Erfahrungen mit Dysenteral bei Durchfallerkrankungen junger Kälber [Experiences with Dysenteral in diarrhea of young calves]. *Der Praktische Tierarzt* **63**, 17-18
- GARBÉ, S. (2003) Untersuchungen zur Verbesserung der Eutergesundheit bei Milchkühen unter besonderer Berücksichtigung des Einsatzes von Homöopathika [Investigation of the effect of homeopathic treatment on the improvement of udder health in dairy cows]. PhD thesis, Free University of Berlin, Germany
- GUJARDO-BERNAL, G., SEARCY-BERNAL, R. & SOTO-AVILA, J. (1996) Growth-promoting effect of sulphur 201c in pigs. *British Homeopathic Journal* **85**, 15-16
- HADIPOUR, M. M., HABIBI, G. H., GHORASHINEJAD, A., OLYAIE, A. & TORIKI, M. (2011) Evaluation of the homeopathic remedies medication on commercial broiler chickens performance. *Journal of Animal and Veterinary Advances* **10**, 2102-2105
- HAHNEMANN, S. (1796) Versuch über ein neues Princip zur Auffindung der Heilkräfte der Arzneisubstanzen, nebst einigen Blicken auf die bisherigen. [Trial on a new principle to find healing power of medical substances along with a few glances at the present]. *Hufelands Journal der practischen Arzneykunde* **2**, 391-439, 465-561
- HAHNEMANN, S. (1869) *Organon of Homeopathic Medicine*. 4th edn. Ed W. M. Radde
- HEKTOEN, L. (2005) Review of the current involvement of homeopathy in veterinary practice and research. *Veterinary Record* **157**, 224-229
- HEKTOEN, L., LARSEN, S., ØDEGAARD, S. A. & LØKEN, T. (2004) Comparison of homeopathy, placebo and antibiotic treatment of clinical mastitis in dairy cows – methodological issues and results from a randomized-clinical trial. *Journal of Veterinary Medicine A* **51**, 439-446
- HOLMES, M. A., COCKCROFT, P. D., BOOTH, C. E. & HEATH, M. F. (2005) Controlled clinical trial of the effect of a homeopathic nosode on the somatic cell counts in the milk of clinically normal dairy cows. *Veterinary Record* **156**, 565-567
- HOMVETCR (2016) Veterinary clinical research: database in homeopathy. [www.carstens-stiftung.de/clinresvet/suche.php](http://www.carstens-stiftung.de/clinresvet/suche.php). Accessed November 15, 2016
- HORNIG, V. (2014) Effekte peroral applizierter Homöopathika auf den klinischen Verlauf von neonatalen Diarrhoeen beim Kalb: eine prospektive, doppelt geblindete Feldstudie [Homeopathic use in cases of neonatal diarrhea in calves: a double blind randomised clinical trial]. PhD thesis, University of Veterinary Medicine Hanover, Germany
- HOVI, M. (2001) Alternative therapy use on UK organic farms: constraints and pitfalls. Proceedings of the Fifth NAHWOA Workshop. Rødding, Denmark, November 11 to 13, 2001. pp 7-13
- HÜMMELCHEN, M. (1999) Untersuchungen über die Prophylaxe von Stoffwechselstörungen mit *Coenzyme compositum* ad us. vet. sowie über eine Lebertherapie mit *Carduus compositum* ad us. vet. bei Milchkühen im peripartalen Zeitraum anhand klinisch-chemischer Parameter [Investigations on the prevention of metabolic disorders with *coenzyme compositum* ad us. vet. as well as a liver treatment with *carduus compositum* ad us. vet. in dairy cows in the peripartal period on the basis of clinical chemistry parameters]. PhD thesis, University of Giessen, Germany
- IMPRO (2015) Impact matrix analysis and cost-benefit calculations to improve managementpractices regarding health status in organic dairy farming. [www.impro-dairy.eu](http://www.impro-dairy.eu). Accessed November 14, 2016
- KAPTCHUK, T. J. (2001) The double-blind, randomized, placebo-controlled trial: gold standard or golden calf? *Journal of Clinical Epidemiology* **54**, 541-549
- KAYNE, S. (2006) The development of homeopathy around the world. In *Homeopathic*

- Pharmacy: Theory and Practice. Ed S. Kayne. Elsevier. pp 59-78
- KAYNE, S. & RAFFERTY, A. (1994) The use of *Arsenicum album* 30c to complement conventional treatment of neonatal diarrhoea ('scours') in calves. *British Homeopathic Journal* **83**, 202–204
- KIARAZM, M., TAJIK, P. & NAVA, H. G. (2011) Assessment of the effect of homeopathic nosodes in subclinical bovine mastitis. *Annals of Biological Research* **2**, 552–562
- KLOCKE, P., IVEMEYER, S., BUTLER, G., MAESCHLI, A. & HEIL, F. (2010) A randomized controlled trial to compare the use of homeopathy and internal teat sealers for the prevention of mastitis in organically farmed dairy cows during the dry period and 100 days post-calving. *Homeopathy* **99**, 90–98
- KNIERIM, U. (1992) Versuche zur Prophylaxe von Geburts- und Puerperalstörungen bei der Milchkuh mit *Lachesis compositum* R in Verbindung mit *Caulophyllum D30* und *Arnika D4* [Investigations on the prophylaxis of parturition and puerperium disorders of dairy cows by application of *Lachesis compositum* R combined with *Caulophyllum D30* and *Arnika D4*]. PhD thesis, University of Veterinary Medicine Hannover, Germany
- KOWALSKI, M. (1989) Homöopathische Arzneimittelanwendung in der veterinärmedizinischen Literatur: Eine Diskussion der bisher publizierten Wirksamkeitsnachweise. [Use of homeopathy in veterinary literature]. PhD thesis, Free University of Berlin, Germany
- LAXMINARAYAN, R., DUSE, A., WATTAL, C., ZAIDI, A. K. M., WERTHEIM, H. F. L., SUMPRADIT, N. AND OTHERS (2013) Antibiotic resistance – the need for global solutions. *The Lancet Infectious Diseases* **13**, 1057–1098
- LIBERATI, A., ALTMAN, D. G., TETZLAFF, J., MULROW, C., GÖTZSCHE, P. C., IOANNIDIS, J. P. A. AND OTHERS (2009) The PRISMA Statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions. Explanation and elaboration. *BMJ* doi: 10.1136/bmj.b2700
- LINDE, K., CLAUDIUS, N., RAMIREZ, G., MELCHART, D., EITEL, E., HEDGES, L. V. & JONAS, W. B. (1997) Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. *The Lancet* **350**, 834–843
- LINDE, K., JONAS, W. B., MELCHART, D. & WILLICH, S. (2001) The methodological quality of randomized controlled trials of homeopathy, herbal medicines and acupuncture. *International Journal of Epidemiology* **30**, 526–531
- MATHIE, R. T. & CLAUSEN, J. (2014) Veterinary homeopathy: systematic review of medical conditions studied by randomised placebo-controlled trials. *Veterinary Record* **175**, 373–381
- MATHIE, R. T. & CLAUSEN, J. (2015) Veterinary homeopathy: meta-analysis of randomised placebo-controlled trials. *Homeopathy* **104**, 3–8
- MATHIE, R. T., HACKE, D. & CLAUSEN, J. (2012) Randomised controlled trials of veterinary homeopathy: characterising the peer-reviewed research literature for systematic review. *Homeopathy* **101**, 196–203
- MERCK, C. C., SONNENWALD, B. M. & RALIWAGE, H. (1989) Untersuchungen über den Einsatz homöopathischer Arzneimittel zur Behandlung akuter Mastitiden beim Rind [Studies on the use of homeopathic medicines for the treatment of acute mastitis in cows]. *Berliner und Münchener tierärztliche Wochenschrift* **102**, 266–272
- MIDAN MARKETING (2014) Antibiotics and growth hormones: the consumers mindset. <http://midanmarketing.com/consumers-case/antibiotics-and-growth-hormones/>. Accessed November 15, 2016
- MINTEL GROUP (2015) Consumers market report research: packaged red meat – US – February, 2015. <http://store.mintel.com/package-red-meat-us-february-2015>. Accessed November 15, 2016
- MOHER, D., LIBERATI, A., TETZLAFF, J., ALTMAN, D. G. & PRISMA GROUP (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Annals of Internal Medicine* **151**, 264–269
- NIAMH, M. (2015) Antibiotic-free – is this the next ethical food label? [www.foodnavigator.com/Market-Trends/Antibiotic-free-Is-this-the-next-ethical-food-label](http://www.foodnavigator.com/Market-Trends/Antibiotic-free-Is-this-the-next-ethical-food-label). Accessed November 15, 2016
- OUWELTJES, W., WINDIG, J. J., JONG, G. DE, LAM, T. J. G. M., NAPEL, J. TEN & HAAS, Y. DE (2008) The use of data from sampling for bacteriology for genetic selection against clinical mastitis. *Journal of Dairy Science* **91**, 4860–4870
- PANESAR, S. S., PHILIPPON, M. J. & BHANDARI, M. (2010) Principles of evidence-based medicine. *Orthopedic Clinics* **41**, 131–138
- PETERSEN, H. H., NIELSEN, E. O., HASSING, A.-G., ERSBOLL, A. K. & NIELSEN, J. P. (2008) Prevalence of clinical signs of disease in Danish finisher pigs. *Veterinary Record* **162**, 377–382
- RIJNBEEK, A. & RAMEY, D. W. (2007) The end of veterinary homeopathy. *Australian Veterinary Journal* **85**, 513–516
- RUEGG, P. L. (2008) Management of mastitis on organic and conventional dairy farms. *Journal of Animal Science* **87**, 43–55
- SANDOVAL, C. H., MORFIN, L. L. & LOPEZ, B. B. (1998) Preliminary research for testing *Baptisia tinctoria* 30c effectiveness against salmonellosis in first and second quality broiler chickens. *British Homeopathic Journal* **87**, 131–134
- SATO, C., LISTAR, V. G. & BONAMIN, L. V. (2012) Development of broiler chickens after treatment with thymulin 5cH: a zoo technical approach. *Homeopathy* **101**, 68–73
- SCHLECHT, S. (2004) Auswirkungen einer prophylaktischen Verabreichung der Präparate *Carduus compositum*, *Coenzym compositum*, *Lachesis compositum* und *Traumeel OP* auf die Eutergesundheit von Milchkuhen [Effects of prophylactic administration of preparations of *Carduus compositum*, *Coenzyme compositum*, *Lachesis compositum* and *Traumeel OP* on udder health of dairy cows]. PhD thesis, Ludwig Maximilian University of Munich, Germany
- SCHULZ, K. F. & GRIMES, D. A. (2002) Blinding in randomised trials: hiding who got what. *The Lancet* **359**, 696–700
- SCHÜTTE, A. (1991) Ein Beitrag zum Thema 'Einstaltungs metaphylaxe in der Schweinemast', Untersuchung über die Verwendung unterschiedlicher allopathischer und homöopathischer Wirkstoffe und Wirkstoffdosierungen zur Verminderung des Erkrankungsrisikos neu aufgestallter Mastschweine unterschiedlicher Herkunft, unter Einbeziehung einer Placebokontrolle mit Berücksichtigung ausgewählter Stallluftparameter [A contribution to the topic 'Housing-in metaphylaxis in fattening pigs', study on the use of different allopathic and homeopathic drugs and dosages for the reduction of risk of disease of new housed-in fattening pigs of different origin, including a placebo control considering selected shelters air parameter]. PhD thesis, Free University of Berlin, Germany
- SCHÜTTE, A. (1994) Ist Forschung in der Veterinärhomöopathie gerechtfertigt? Grundsatzgedanken und eine Zusammenschau über 5 Jahre Forschung zum Thema 'Anwendung der Homöopathie bei Nutztieren' an der Außenstelle der Freien Universität Berlin in Schwarzenbek [Is research in veterinary homeopathy justified?]. *Berliner und Münchener tierärztliche Wochenschrift* **107**, 229–236
- SCHÜTTE, A. (2003) Homöopathie in der Schweinehaltung: Betreuung und Dokumentation der Laienarbeit homöopathischer Arbeitskreise [Homeopathy in pig farming: support and documentation of laity homeopathic working groups]. *Zeitschrift für ganzheitliche Tiermedizin* **17**, 25–28
- SEARCY, R., REYES, O. & GUAJARDO, G. (1995) Control of subclinical bovine mastitis. *British Homeopathic Journal* **84**, 67–70
- SEIFERT, U. (1987) Die Behandlung des Mastitis-Metritis-Agalaktie-MMA Syndroms der Muttersauen mit homöopathischen Arzneimitteln im Vergleich mit einer praxisüblichen allopathischen Therapie. [The treatment of mastitis-metritis-agalactia MMA syndrome of sows with homeopathic medicine compared with a typical allopathic therapy]. PhD thesis, Free University of Berlin, Germany
- SHANG, A., HUWILER-MÜNTENER, K., NARTEY, L., JÜNI, P., DÖRIG, S., STERNE, J. A. C. & OTHERS (2005) Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy. *The Lancet* **366**, 726–732
- SHEKIN, D. (2004) Handbook of Parametric and Nonparametric Statistical Procedures. 3rd edn. Chapman & Hall/CRC
- SONNENWALD, B. M. (1986) Therapie akuter Mastitiden beim Rind unter Anwendung verschiedener homöopathischer Arzneimittel. PhD thesis, Freie Universität Berlin, Germany
- SOTO, E., VUADEN, E. R., COELHO, C. D., BENITES, N. R., BONAMIN, L. V. & DE AZEVEDO, S. S. (2008) A randomized controlled trial of homeopathic treatment of weaned piglets in a commercial swine herd. *Homeopathy* **97**, 202–205
- STOPES, C. & WOODWARD, L. (1990) The use and efficacy of a homeopathic nosode in the prevention of mastitis in dairy herds: a farm survey of practising users. *IFOAM Bulletin for Organic Agriculture* **10**, 6–10
- THAUL, S. (2012) How FDA approves drugs and regulates their safety and effectiveness. <http://fas.org/sfp/crs/misc/R41983.pdf>. Accessed November 15, 2016
- TIEFENTHALER, D. (1990) Der klinische und bakteriologische Euterbefund von homöopathisch und allopathisch therapierten, akuten Mastitiden erkrankten Rindern [Clinical and bacteriological findings of homeopathic and allopathic treated cows suffering from acute mastitis]. PhD thesis, University of Veterinary Medicine Vienna, Austria
- VAN SLUIJS, F. J. (2005) Can homeopathy withstand scientific testing? Proceedings of the DVG-Forum 2. 2005. pp 30–31
- VELKERS, F. C., LOO, A. T., MADIN, F. & VAN ECK, J. (2005) Isopathic and pluralist homeopathic treatment of commercial broilers with experimentally induced colibacillosis. *Research in Veterinary Science* **78**, 77–83
- VERDIER, K. DE, OHAGEN, P. & ALENIUS, S. (2003) No effect of a homeopathic preparation on neonatal calf diarrhoea in a randomised double-blind, placebo-controlled clinical trial. *Acta Veterinaria Scandinavica* **44**, 97–101
- VETION (2016) Vetion:oekovet.de Ökovet bei Vetion. [www.vetion.de/oekovet/publikation/indexpub.htm](http://www.vetion.de/oekovet/publikation/indexpub.htm). Accessed November 16, 2016
- VOHLA, A. (1991) Zur vorbeugenden Anwendung von Sabina in unterschiedlichen Potenzen beim hochtragenden Rind zur Reduktion puerperaler Störungen sowie Erkrankungen der Kälber. [Prophylactic application of Sabina in different potencies to pregnant cows in order to reduce puerperal disorders and new born calf diseases]. PhD thesis, University of Veterinary Medicine Hannover, Germany
- WAGENAAR, J.-P., KLOCKE, P., BUTLER, G., SMOLDERS, G., NIELSEN, J. H., CANEVER, A. & LEIFERT, C. (2011) Effect of production system, alternative treatments and calf rearing system on udder health in organic dairy cows. *NJAS - Wageningen Journal of Life Sciences* **58**, 157–162
- WALKENHORST, M. (2006) Vergleich von homöopathischer und antibiotischer Laktationstherapie zur Behandlung von Mastitiden des Rindes [Comparison of homeopathic and antibiotic treatment of mastitis in lactating dairy cows]. PhD thesis, University of Zürich, Switzerland
- WERNER, C., SOBIRAJ, A. & SUNDRUM, A. (2010) Efficacy of homeopathic and antibiotic treatment strategies in cases of mild and moderate bovine clinical mastitis. *Journal of Dairy Research* **77**, 460–467
- WEYMAYR, C. (2013) Scientabilität – ein Konzept zum Umgang der EbM mit homöopathischen Arzneimitteln [Scientability – a concept for the handling of homeopathic remedies by EbM]. *Zeitschrift für Evidenz, Fortbildung und Qualität im Gesundheitswesen* **107**, 606–610
- WILLIAMSON, J. H. & LACY-HULBERT, S. J. (2014) Lack of efficacy of homeopathic therapy against post-calving clinical mastitis in dairy herds in the Waikato region of New Zealand. *New Zealand Veterinary Journal* **62**, 8–14
- WIRTH, F. (1990) Metaphylaxe puerperaler Erkrankungen beim Rind, insbesondere Retentio secundinarum und Endometritis, durch Anwendung von *Pulsatilla miniplex* [Metaphylactic treatment of puerperal disorders in dairy cows, especially retentio and endometritis by the application of *Pulsatilla miniplex*]. PhD thesis, University of Veterinary Medicine Hannover, Germany