

# Evidence-based human homeopathy and veterinary homeopathy, and their potential to help overcome the problem of antibiotic resistance – an overview

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## Abstract

The basic principles of homeopathy, and its legal and scientific foundations, are discussed in an overview to address the positions of the World Health Organization (WHO) and the Commission of the European Union (EU) on complementary medicine. According to WHO, the problem of antimicrobial resistance poses a global threat. The EU Commission's current One Health Action Plan requests research into complementary medicine and WHO urges Member States to include complementary medicine in their national health policies.

Regarding external evidence on the general use of human and veterinary homeopathy, evidence level 1a studies are reviewed. Focusing on the external evidence on the use of homeopathy in infections, some evidence level 1a, 1b, 2c studies, and a case report, are described in more detail.

In conclusion, evidence for the effectiveness of human and veterinary homeopathy in general, and in particular, of homeopathic treatment for infections, is available. In particular, individualised homeopathy demonstrates effects at all quality levels according to the Cochrane criteria, even in methodologically high-quality studies. As in most areas of human and veterinary medicine, further good/excellent studies are necessary. In compliance with the principles of homeopathy, further methodologically high-quality trials focusing on the homeopathic treatment of infections are the next logical step. The selection of the *simile* (the individually appropriate homeopathic medicine) by suitably trained homeopathic doctors/veterinarians is essential for the

## Evidenzbasierte Veterinär-/Homöopathie und ihre mögliche Bedeutung für die Bekämpfung der Antibiotikaresistenzproblematik – ein Überblick

Angesichts der globalen Bedrohung durch die Antibiotikaresistenzproblematik gemäss Weltgesundheitsorganisation (WHO) und der Forderung der Kommission der Europäischen Union (EU) im aktuellen One Health Action Plan nach Forschung im Bereich der Komplementärmedizin sowie der Forderung der Weltgesundheitsorganisation, die Komplementärmedizin in die nationalen Gesundheitssysteme zu integrieren, werden überblicksartig die Grundprinzipien der Homöopathie sowie ihre gesetzlichen und wissenschaftlichen Grundlagen erörtert.

Hinsichtlich externer Evidenz zur Human- und Veterinär-Homöopathie im Allgemeinen wird auf Studien der Evidenzstufe 1a eingegangen. Bei Fokussierung auf die externe Evidenz zur Homöopathie bei Infektionen werden auszugswise Studien der Evidenzstufe 1a, 1b, 2c sowie ein Fallbericht näher beschrieben.

Zusammenfassend kann gesagt werden, dass Evidenz für die Wirksamkeit der Human- und Veterinär-Homöopathie im Allgemeinen und im Speziellen bei homöopathischen Behandlungen von Infektionen vorhanden ist. Es sind vor allem für die individualisierte Homöopathie Effekte auf allen Qualitätsstufen nach Cochrane-Kriterien erkennbar, auch in den methodisch hochwertigen Studien, aber wie in der Mehrzahl der Gebiete der Veterinär-/Medizin sind weitere gute/exzellente Studien nötig.

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effectiveness of homeopathy. Implementation of studies at university facilities is a prerequisite for quality assurance. Consequently, further integration of homeopathy at universities is a necessary requirement for the patients' best interests.

**Keywords:** Antimicrobials, antibiotic resistance, evidence, homeopathy, veterinary homeopathy

Unter Einhaltung der Prinzipien der Homöopathie erscheint die Durchführung weiterer methodisch hochwertiger Studien zur homöopathischen Behandlung von Infektionen als der nächste logische Schritt. Für die Wirksamkeit der Homöopathie ist die Auswahl des *Similes* (des individuell passenden homöopathischen Arzneimittels) durch entsprechend ausgebildete homöopathisch behandelnde Ärzte/Tierärzte – für die Qualitätssicherung der Studien deren Durchführung an universitären Einrichtungen Grundvoraussetzung. Folglich ist die bessere Integration der Homöopathie an den Universitäten eine notwendige Forderung im Sinne der Patienten.

**Key words:** Antibiotika, Antibiotikaresistenz, Evidenz, Homöopathie, Veterinär-Homöopathie

## List of abbreviations

AMG	Medicines Act ( <i>Arzneimittelgesetz</i> )
ANOVA	Analysis of Variance
BASG	Austrian Federal Office for Safety in Health Care ( <i>Bundesamt für Sicherheit im Gesundheitswesen</i> )
BfArM	German Federal Institute for Drugs and Medical Devices ( <i>Bundestinstitut für Arzneimittel und Medizinprodukte</i> )
CI	Confidence interval
EASAC	European Academies Science Advisory Council
EBM	Evidence-based medicine
HP	Homeopathic pharmacopoeia
HMG	Federal Act on Medical Products and Medical Devices ( <i>Heilmittelgesetz</i> )
HTA	Health Technology Assessment
KPAV	Regulation on complementary and herbal medicinal products ( <i>Komplementär- und Phytoarzneimittelverordnung</i> )
MESD	Mean effect size difference
NHMRC	National Health and Medical Research Council (Australia)
OR	Odds ratio
ORS	Oxacillin-resistant <i>Staphylococcus</i>
PCT	Pragmatic controlled trial
RCT	Randomised controlled trial
Swissmedic	Swiss Agency for Therapeutic Products
SMD	Standardised mean difference
TAKG	Austrian Veterinary Medicinal Products Control Act ( <i>Tierarzneimittelkontrollgesetz</i> )
TAMV	Swiss Veterinary Medicines Act ( <i>Tierarzneimittelverordnung</i> )
WBF	Swiss Federal Department of Economic Affairs, Education and Research ( <i>Eidgenössisches Departement für Wirtschaft, Bildung und Forschung</i> )
WHO	World Health Organization

## Introduction

The way homeopathy has been represented in the media over the past years suggests a lack of knowledge of integrative medicine (a combination of patient-oriented conventional and complementary medicine). A look across the Atlantic shows how reputable American Universities have handled the phenomenon of 'complementary medicine' over the past 25 years. A sensational publication in 1993 led to the creation of an Office for Alternative Medicine within the National Institute of Health.<sup>22</sup> In 1998, the Office became an independent National Center for Complementary and Alternative Medicine, which was renamed in 2012 the Academic Consortium for Integrative Medicine and Health. Furthermore, in the US complementary medicine is a self-evident part of the curriculum of the top Medical Schools, ranging from Harvard to Stanford, and in the Veterinary Schools. In Europe, with the exception of Switzerland, there is hardly any academic integration and very few public or university funds available for research into complementary medicine.

A descriptive study of dairy farms in Germany, France and Spain, found that homeopathic treatments should be carried out *lege artis*, including follow-up checks and adequate documentation, as for other complementary or conventional medical procedures.<sup>45</sup> An adequate monitoring system could contribute to the testing of the effectiveness of homeopathy, but veterinarians also need to be at least familiar with complementary medical treatment methods in order to be more involved in the treatment process and able to discuss it with farmers.<sup>45</sup> In order to meet this aim, there is a need for veterinarians trained in homeopathy, as required by the American consensus guidelines for an integrative veterinary medicine curriculum in universities.<sup>62</sup>

Switzerland can be cited as a role model for Europe, where the following is required for veterinary medicine

with regard to teaching and research at the university in accordance with Article 10 (i) of the Medical Professions Act: Graduates of the study of veterinary medicine should have adequate knowledge of the methods and therapeutic approaches of complementary medicine, as is required by law for human medicine and dentistry in Article 8 (j).<sup>7</sup>

It is therefore obvious for veterinary, human and dental medicine that, as in Switzerland and the USA, homeopathy as a complementary medicine is taught and actively researched at universities worldwide, for the benefit of patients in the context of integrative veterinary and human medicine and in accordance with the requirement of Article 17 of the Austrian Constitutional Law and of paragraph (§) 2 of the Austrian University Act for 'freedom of science and its teaching'.<sup>5, 10</sup>

As the discussion around homeopathy is controversial and often held at a non-scientific level, this article aims to provide an overview of the basic principles of homeopathy, its legal basis and the current scientific evidence. The null hypothesis is that there is insufficient evidence for university teaching of, and further research into, homeopathy. The alternative hypothesis is that there is sufficient evidence on homeopathy to be able to demand university teaching and high-quality research.

## Material & Methods

This narrative review will summarize a.) the basic principles of homeopathy according to The Organon of the Healing Art and current guidelines, b.) the legal provisions applying to homeopathic medicinal products and on the implementation of veterinary homeopathic therapies in Switzerland, Austria and Germany in accordance with current legislation, and c.) Meta-analyses (quantitative and statistical processing of studies, in this case randomized controlled trials (RCTs)) and systematic reviews covering various indications and different homeopathic methodologies, corresponding to a literature and database search up until August 2019 (pubmed.gov, cam-quest.org/de, carstens-stiftung.de/databases, Google Scholar, doctoral theses) with the following search strategy: «(homeopath\* OR homeopath\*)» summarized by article type «meta-analysis» and «systematic review». <sup>43, 75</sup> Then, the first and second reports of the Australian National Health and Medical Research Council (NHMRC) from 2012 and 2015 and the statement by the European Academies Science Advisory Council (EASAC) from 2017 were examined in more detail.<sup>18, 65, 25</sup> The main topic is the importance of homeopathy for addressing the problem of antibiotic resistance, as shown by examples of the most rep-

resentative meta-analyses, systematic reviews, RCTs, studies on health services research and a case report according to the literature and database search mentioned up to August 2019, with the following search strategy: «((homeopath\*[Title/Abstract]) AND (antibiotic\*[Title/Abstract]))», «((homeopath\*[Title/Abstract]) AND (antimicrobial\*[Title/Abstract]) NOT (antibiot\*[Title/Abstract]))», «((homeopath\*[Title/Abstract]) AND (infection\*[Title/Abstract]))», «((homeopath\*[Title/Abstract]) AND (respiratory[Title/Abstract]))», «((homeopath\*[Title/Abstract]) AND (mastitis[Title/Abstract]))», «(complementary\*[Title/Abstract]) AND (antibiotic\*[Title/Abstract]))», or quick search for diseases, «infections» or indication «acute childhood diarrhea», «acute cystitis», «acute diarrhoeal disorders, diarrhea», «acute diarrhoeal disorders, diarrhoea», «acute febrile infections», «acute febrile infections», «acute fevers», «acute respiratory and ear complaints», «acute respiratory infections», «acute rhinitis», «acute rhinopharyngitis», «acute sinusitis» and «homeopathy AND infections». <sup>91</sup>

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## Results

### Individualised, so-called classical homeopathy or single-substance homeopathy

Individualised, so-called classical homeopathy or single-substance homeopathy is a medical system developed by the German physician Dr. Samuel Hahnemann (1755-1843). The treatment is based on the law of similars – *Similia similibus curentur*, or 'Let like be cured by like'. In standardized homeopathic pathogenetic trials, the administration of a homeopathic medicine to healthy individuals induces symptoms, which can be cured in sick individuals by this same homeopathic medicine. The patient's individual symptoms lead to the *simile*, i.e., the homeopathic medicine, the symptoms of which, generated in healthy individuals, best reflect the patient's symptoms.<sup>43, 75</sup> Homeopathic medicinal products are produced in a standardized manner in accordance with the regulations of the European Pharmacopoeia or of the Homeopathic Pharmacopoeia (HP).<sup>80, 37</sup>

### Non-individualised, so-called clinical homeopathy

In the case of non-individualised, so-called clinical homeopathy, one or more homeopathic medicines are administered according to the indications. In complex homeopathy, so-called 'complexes', containing several homeopathic medicinal products, are used in an indication-related or organotropic manner. Such homeopathic medicinal products are produced in a standardized manner in accordance with the regulations of the European Pharmacopoeia or of the Homeopathic Pharmacopoeia (HP).<sup>80, 37</sup>

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## Legal foundations of veterinary homeopathy

### Definition of homeopathic medicinal products

In Switzerland, homeopathic medicinal products are defined in the Heilmittelgesetz or Federal Act on Medical Products and Medical Devices (HMG) under Article 4, Paragraph 1.<sup>6</sup> According to the Austrian and German Arzneimittelgesetz or Medicines Act (AMG), homeopathic medicinal products are also considered medicinal products and are defined as such under §1 (10) and §4 (26) of the AMG.<sup>9,31</sup> According to the Komplementär- und Phytoarzneimittelverordnung or Regulation on complementary and herbal medicinal products (KPAV), single-substance homeopathic medicinal products are 100% identical in terms of production, quality and application, regardless of whether they are used in animals or humans.<sup>82</sup>

### Process for marketing homeopathic medicinal products

In Switzerland, the marketing of homeopathic medicinal products is regulated by the HMG and the KPAV.<sup>6, 82</sup> In the EU, the registration of homeopathic medicinal products without indication and the authorisation of homeopathic medicinal products with an indication are laid down in EU Directive 2001/83 (Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use) and in the AMG.<sup>20, 9, 31</sup>

### Implementation of veterinary homeopathic therapies

The EU Regulation on veterinary medicinal products (Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EG) comes into force on 28.1.2022 and stipulates that the legal regulation of the implementation of veterinary homeopathic therapies continues to take place at a national level.<sup>84</sup> In Switzerland, the use of homeopathic medicinal products in animals is regulated by the Tierarzneimittelverordnung or Veterinary Medicines Act (TAMV), in Austria by the Tierarzneimittelkontrollgesetz or Veterinary Medicinal Products Control Act (TAKG) and in Germany by the AMG.<sup>86, 11, 31</sup> In Switzerland, homeopathic medicinal products may also be rededicated if a medicinal product is approved for the indication or target species to be treated, according to Article 6, Paragraph 3.<sup>86</sup> In Austria, § 4 (6) and § 4b (3) of the TAKG allow the use of homeopathic medicinal products without indication that are registered for humans, regardless of the cascade regulation.<sup>11</sup> In Germany, this is made possible by Paragraph 56 (2) of the AMG.<sup>31</sup>

### Regulations for organic production

The Swiss Ordinance on Organic Farming and Labelling of Organically Produced Products and Foodstuffs cle-

arly states: «The use of veterinary medicinal products in organic stock farming shall comply with the following principles: Phytotherapeutic products (e.g. plant extracts, excluding antibiotics, or plant essences), homeopathic products (e.g. plant, animal and mineral substances) and trace elements and products laid down by the Federal Department of Economics, Education and Research (WBF) shall be used in preference to chemically-synthesised allopathic veterinary medicinal products or antibiotics, provided that their therapeutic effect is shown by experience to be effective for the species of animal and the condition for which the treatment is intended.»<sup>85</sup> The EU Organic Farming Regulation (Regulation (EU) 2018/848 of the European Parliament and of the Council of 30 May 2018 on organic production and labelling of organic products and repealing Council Regulation (EC) No. 834/2007) continues to make the same statement as the Swiss Organic Farming Regulation, even after revision.<sup>83</sup>

### Summary of the legal foundations of veterinary homeopathy

Homeopathic medicinal products without indication, called single-substance homeopathic medicinal products according to KPAV, are available for the primary homeopathic treatment of animals, according to the TAMV (Switzerland), TAKG (Austria) and AMG (Germany).<sup>82, 86, 11, 31</sup> This meets the requirements of the Swiss and EU organic farming regulations for primary homeopathic treatment, assures a free choice of therapy and fulfils a desire of the population that animals are treated homeopathically.<sup>85, 83</sup>

## Literature review on evidence-based homeopathy

### Modern evidence-based medicine

By definition, modern evidence-based medicine (EBM) is based on three pillars: the clinical experience of doctors and veterinarians, the values and wishes of clients and patients and the current state of scientific research.<sup>74</sup> Homeopathy is based on all three pillars of evidence-based medicine: First, the internal evidence comprises the following: a.) Doctors and veterinarians with additional training in homeopathy who collect, document and publish positive clinical experiences in their practice; b.) standardized homeopathic pathogenetic trials on healthy individuals; and c.) numerous homeopathic *materia medica* such as those by Vermeulen, which document the clinically verified symptoms of the homeopathic medicines and are based on publications from the last 200 years.<sup>14, 43, 87</sup> Secondly, as far as patient preference is concerned, homeopathy, as in many other countries, is desired by the population in Switzerland, Austria and Germany. In May 2009, 67% of the Swiss

population voted “yes” to the new constitutional article on the consideration of complementary medicine in application, research and teaching, which resulted in 2015 in the inclusion of complementary medicine in the Medical Professions Act and led, in 2017, following a Federal Council decision, to the definitive inclusion of complementary medicine in the basic health insurance in Switzerland.<sup>24</sup> According to current figures, 97% of Swiss paediatricians are asked about complementary medical treatment methods and most often (35%) refer to specialists who work in homeopathy.<sup>39</sup> According to recent market research, 56% of Germans have experience of homeopathy and 71% of Austrians use homeopathy.<sup>44, 78</sup> Thirdly, with regard to external evidence, it should be recalled that regarding the effectiveness of homeopathy, there are several thousand studies on human and veterinary homeopathy, including studies of evidence classes 1a and 1b, as well as methodologically high-quality studies. The levels of evidence are shown in Table 1.

### Particularity of classical (= individualised) homeopathy

The following particularity of classical (= individualised) homeopathy needs to be explained to understand why, below, evidence on both human and veterinary homeopathy will be discussed: homeopathic medicines without indication are 100% identical in terms of production, quality and application principles, regardless of whether they are used in animals or humans. If the *simile* principle is followed that classical (= individualised) homeopathic therapy is based on the individual and not on the indication, and if homeopathy is effective for one or more indications, it would seem logical that its effectiveness in other indications can be concluded.

### Level of evidence 1a studies in homeopathy in humans

As an introduction, mention should be made of the Health Technology Assessment (HTA) report which was commissioned by the Swiss Federal Office of Public Health in order to be able to make informed decisions about whether homeopathy should be included in the list of services offered by the statutory health insurance companies.<sup>3</sup> The main findings of the Swiss HTA report are as follows: evidence from laboratory tests and clinical studies shows that homeopathy is effective and, in the way it is practised in Switzerland, inexpensive and safe. 20 of 22 systematic reviews of clinical studies showed a positive trend in favour of homeopathy. The clearest evidence of effectiveness was found in upper respiratory tract infections and allergic diseases. 29 studies were identified, including 24 with positive results.<sup>3</sup>

According to our literature and database research, six comprehensive meta-analyses were carried out up to 2014

Levels of Evidence - Classification by therapy / prevention / aetiology / harm according to the Centre for Evidence-Based Medicine, Oxford	
1a	Systematic reviews (with homogeneity) of randomized controlled trials
1b	Individual randomized controlled trials (with narrow confidence interval)
1c	All or none
2a	Systematic reviews (with homogeneity) of cohort studies
2b	Individual cohort study including low quality randomized controlled trials (e.g. <80% follow-up)
2c	«Outcomes» Research; ecological studies
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case-series (and poor quality cohort and case-control studies)
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research or «first principles»

**Table 1:** Levels of Evidence, Oxford Centre for Evidence-based Medicine, produced by Bob Phillips, Chris Ball, Dave Sackett, Doug Badenoch, Sharon Straus, Brian Haynes, Martin Dawes since November 1998. Updated by Jeremy Howick March 2009. <https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/>

in the field of human homeopathy, which take various indications into account. Five meta-analyses came to the conclusion that the effectiveness of homeopathic therapy differs from placebo, but that further methodologically high-quality research is required in order to be able to draw final conclusions.<sup>47, 48, 49, 19, 56</sup> Only in one meta-analysis, that of 2005, did the authors conclude that homeopathy has no effectiveness beyond that of placebo.<sup>77</sup> It should be noted that in the meta-analysis of 2005, the inclusion and exclusion criteria were subsequently modified, which changed the assessment from positive to negative.<sup>30</sup> The following table shows how many studies were excluded from the respective analysis and whether individualised or non-individualised homeopathy was examined (Table 2).

Also to be mentioned are the following three publications, which were not published in any peer-reviewed journal: the second (2015) and first (written in 2012, published in 2019) Australian NHMRC Report and the EASAC Statement (2017).<sup>65, 18, 25</sup>

Whereas the first Australian NHMRC Report, which was initially concealed, gave a positive evaluation for homeopathy in at least five indications (including upper respiratory tract infections and otitis media – with relevance for antibiotic resistance), the second NHMRC Report published in 2015 reported a negative result.<sup>18, 65</sup> The 2017 EASAC statement, which, out of the six aforementioned reviews with meta-analysis, only took into consideration the one from 2005 and the second Australian NHMRC Report and hence also skipped the meta-analysis from 2014, without providing reasons for doing so, also came to a negative conclusion.<sup>25, 47, 48, 49,</sup>

**Table 2:** Results of the literature and database search covering 1991 to 2014: Six reviews with meta-analysis of various indications including the first and second Australian NHMRC Report (2012/2019; 2015) and the EASAC Statement (2017)

Publication	Year	Level of Evidence	Peer-reviewed journal	Inclusion and exclusion criteria: described in the section Material and Methods of the individual publications	Studies excluded from analysis	Homeopathic methodology		Valuation
						individualized	non-individualized	
Kleijnen et al	1991	1a: syst. review + meta-analysis	BMJ	of 107 studies, 105 were considered	2%	X	X	+
Linde et al	1997	1a: syst. review + meta-analysis	Lancet	of 119 studies, 89 were considered	25%	X	X	+
Linde et al	1999	1a: syst. review + meta-analysis	J Clin Epidemiol	of 89 studies, 10 were considered	89%	X	X	+
Sucherat et al	2000	1a: syst. review + meta-analysis	Eur J Clin Pharmacol	of 118 studies, 17 were considered	86%	X	X	+
Shang et al	2005	1a: syst. review + meta-analysis	Lancet	of 165 studies, 110 were considered <b>not</b> described in methodology: subsequent reduction from 110 to 8 studies	33%	X	X	+
Mathie et al	2014	1a: syst. review + meta-analysis	Syst Rev	of 32 studies, 22 were considered	31%	X		+
Second Australian NHMRC Report	2015	1a: syst. review	No	of 176 studies, 5 were considered <b>i.a. at least 150 study participants &amp; Jadad score 5/5</b> <b>(Criteria deliberately chosen in this way? Not used in any other systematic review.)</b>	<b>97%</b>	X	X	-
EASAC Statement	2017	5: Expert opinion	No	<b>No definition of inclusion/exclusion criteria, no systematic review.</b> Based on Shang et al; 2005 & Second Australian NHMRC report 2015, among others	<b>93 / 97%</b>	X	X	-
First Australian NHMRC Report	2019 (2012)	1a: Draft syst. review of 2012	No	of 166 studies, 40 were considered	76%	X	X	+

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<sup>19, 56, 77, 65</sup> It is debatable whether the second Australian NHMRC Report, without peer review, using rather unconventionally elected, non-EBM-conforming inclusion criteria, and the EASAC statement, without peer review and selective references, should have been classified as complying with EBM criteria.<sup>65, 25</sup>

To assess the study quality of meta-analyses of RCTs, the internal validity of randomized controlled studies is evaluated. In the various meta-analyses listed above, different instruments were used for this purpose: the (now outdated) Jadad Score and a separate scale for assessing internal validity.<sup>47, 48, 49, 19</sup> In the 2005 review with meta-analysis, study quality was assessed using criteria similar to the Jadad score. In the review with meta-analysis by Mathie et al. from 2014, as well as in the later ones from 2017, 2018 and 2019 – these are not included in the table, but are briefly discussed below – modern Cochrane tools were used, supplemented with a differentiated classification of bias categories (to assess the risk of bias).<sup>77, 56, 58, 59, 57</sup>

The review programme by Mathie et al. from 2014, 2017, 2018 and 2019 differs significantly from earlier systematic reviews.<sup>56, 58, 59, 57</sup> All four reviews with meta-analysis also cover different medical indications, but a distinction is made according to homeopathic methodology (individualised or non-individualised) and according to comparison group (placebo or other than placebo). The 2014 review, including meta-analysis, found effectiveness for individualised homeopathy compared to placebo.<sup>56</sup> It was shown that the homeopathic medicines prescribed in the context of individualised homeopathy have small, specific treatment effects. For the three highest quality studies, there was also a statistically significant effect for homeopathy (OR= 1.53 for n= 22, (95% confidence interval (CI)= 1.22–1.91), OR= 1.98 for n= 3 (CI= 1.16–3.38)).<sup>56</sup> Such effect sizes correspond e.g. to those of fluoxetine for the therapy of severe depression, which is indispensable in clinical practice.<sup>56</sup> The 2018 review with meta-analysis examined RCTs of individualised homeopathy compared to other than placebo, i.e. compared to no treatment, to other treatment or as a complementary form of therapy.<sup>59</sup> Homeopathy as a complementary therapy showed statistical significance (pooled standardized mean difference (SMD)= -0.26; CI= -0.47--0.05).<sup>59</sup> The results of these two systematic reviews with meta-analysis indicate the effectiveness of individualised homeopathy.<sup>56, 59</sup> Non-individualised homeopathy was compared with placebo in the 2017 review with meta-analysis (54 RCTs) and found a statistically significant difference between the two groups (SMD= -0.33; CI= -0.44--0.21). However, 28 of these studies were assessed as having 'high risk of bias' and evaluation of the subset of the three most reliable papers did not confirm the significant result.<sup>58</sup>

Furthermore regarding non-individualised homeopathy, the 2019 systematic review with meta-analysis (17 studies, three of which were evaluable) comparing with other than placebo, showed a small, non-significant effect (SMD= 0.08; p= 0.46) for the three equivalence or non-inferiority studies.<sup>57</sup>

## Literature review of evidence-based veterinary homeopathy

According to our literature and database search, there are two systematic reviews (2014 and 2015) and one meta-analysis (2015) for veterinary homeopathy, covering various indications.<sup>53, 55, 54</sup> One review (2014) and the meta-analysis showed evidence for the effectiveness of veterinary homeopathy compared to placebo.<sup>53, 54</sup> The other review (2015) examined evidence from RCTs that were controlled with conventional medications; however, the study quality in this review was too low to give a meaningful answer.<sup>55</sup> The single meta-analysis shows evidence for the effectiveness of veterinary homeopathy compared to placebo (p= 0.01 for n= 15, pooled OR= 1.69 (CI= 1.12–2.56), p= 0.02 for n= 2, pooled OR= 2.62 (CI= 1.13–6.05)).<sup>54</sup>

## A selection of the literature as representative as possible of the contribution of homeopathy to solving the problem of antibiotic resistance

The list of studies of levels of evidence 1a, 1b and 2c on the importance of human and veterinary homeopathy for the treatment of infections (Table 3) is only a small excerpt from the existing literature. The aim was to make a selection that was as representative as possible; only studies with levels of evidence 1a, 1b and 2c are included.

The results of experimental studies with both methodological strengths and weaknesses indicate the effectiveness of homeopathy in infections; furthermore, data from health services research examining the everyday suitability of homeopathy show the potential for a significant reduction in the use of antibiotics through homeopathic treatment. The following overview (table 3) shows in which studies homeopathic principles were followed.

## Regarding the four studies of level of evidence 1a and 1b on the homeopathic treatment of infections in animals

While the conclusions differ, the results of the 2016 review on the effectiveness of homeopathy in infectious diseases in farm animals correspond to those of the re-

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views of 2014 and 2015 (which are described in the literature review section on evidence-based veterinary homeopathy). They highlight the need for more methodologically high-quality studies in order to be able to draw firm conclusions and make any clinical recommendations.<sup>21, 53, 55</sup>

In the 2019 review, 32 studies on mastitis in cows were examined (date range 1982 to 2016) and a quality score was introduced, assessing for the first time homeopathic methodology. The eight studies with the highest quality concluded homeopathy to be effective.<sup>93</sup> This review reached the further conclusion that the suitable homeopathic medicine, the *simile*, must be individually selected for the individual treatment/prophylaxis. Also, a study in mastitis in cows caused by udder-pathogenic bacteria showed that, together with appropriate preventive measures and drying-off management, homeopathy enabled up to a 75% reduction in the use of antibiotics.<sup>93, 63</sup>

The 2010 double-blinded RCT investigating piglets afflicted by diarrhoea caused by *Escherichia coli* (*E. coli*) showed that significantly fewer piglets developed diarrhoea in the homeopathic group compared to placebo ( $p < 0.0001$  at individual animal level;  $p = 0.0024$  at group level; linear model).<sup>12</sup> In addition, the severity of the disease appeared to be lower and in the case of diarrhoea, its duration appeared to be shorter.<sup>12</sup> In the 2015 meta-analysis on veterinary homeopathy and the reviews on veterinary homeopathy of 2014 and 2016, the study was classified as being of high methodological quality.<sup>53, 54, 21</sup>

In the RCT of 2018 regarding homeopathic alternatives to antibiotics for mastitis in cows, the authors underline a number of conditions in the conclusion, such as the need for good homeopathic practice according to classic homeopathic principles for successful therapy (not least because of certain weaknesses in their own study). They also point out the need for regular controls, a combined treatment with conventional medicine and homeopathy for mastitis caused by particular bacteria, and an initial homeopathic treatment until the results of the sensitivity testing are known.<sup>46</sup>

#### Regarding the four studies of level of evidence 1a and 1b on the homeopathic treatment of infections in humans

The meta-analysis of 2003 on the individualised homeopathic treatment of childhood diarrhoea showed a significant reduction in the duration of the disease in 242 children aged six months to five years old in three double-blinded RCTs (Mean Effect Size Difference (MESD) = 0.66 days,  $p = 0.008$ , CI = 0.16–1.15).<sup>42</sup>

In the review of 2005, the subgroup analysis of eight RCTs on acute respiratory tract infections showed effectiveness (OR = 0.36, CI = 0.26–0.5), regardless of the

quality of the studies.<sup>77</sup>

The review of 2018, which examined the effectiveness and safety of homeopathy versus placebo or conventional therapy in children between 0 and 16 years of age with acute respiratory tract infections, showed a negative outcome for homeopathy.<sup>36</sup> This example shows, once again, how inclusion and exclusion criteria can lead to contrary results in two systematic reviews for certain indications (in this case, acute infections of the respiratory tract). In the review of 2018, the study population was restricted to children, so that the negative result in terms of effectiveness was only based on two RCTs of homeopathic therapy, as shown in a study in 2019.<sup>36, 73</sup>

The effectiveness of homeopathic medicines in people with sepsis was studied in 2005.<sup>29</sup> Seventy patients with severe sepsis received a homeopathic medicine or placebo in addition to standard therapy as part of a double-blinded RCT carried out in the intensive care unit.<sup>29</sup> On day 180, the survival rate in the homeopathically treated group was statistically significantly higher than in the placebo group ( $p = 0.043$ ; Kruskal-Wallis test). The results could also be confirmed after an intention-to-treat evaluation ( $p = 0.0248$ ; Chi square test).<sup>29</sup>

Finally, it should be noted that the 2006 Swiss HTA report on homeopathy identified 29 studies of various designs in 5,062 patients with infections of the upper respiratory tract/allergy and described an overall positive result for homeopathy. Six of the seven controlled studies showed equivalence with conventional therapy; eight of the 16 placebo-controlled studies showed significance for homeopathy.<sup>3</sup>

#### Regarding the three studies of level of evidence 2c on the homeopathic treatment of infections in humans

The international, multicentric cohort study of 2007 compared homeopathic and conventional therapy for acute respiratory tract and ear diseases in primary care in 1,577 patients and showed no inferiority of the homeopathic treatment method in terms of complete recovery or significant improvement after 14 days (86.9% vs. 86.0%;  $p = 0.0003$ ; Chi-square test, Fisher's exact test, Wilcoxon's rank sum test). A statistically significant earlier onset of improvement within the first seven days of treatment was observed, both in children ( $p = 0.0488$ ; Chi-square test, Fisher's exact test, Wilcoxon's rank sum test) and adults ( $p = 0.0001$ ; chi-square test, Fisher's exact test, Wilcoxon's rank sum test) as well as a lower rate of side effects in adults ( $p = 0.0032$ ; chi-square test, Fisher's exact test, Wilcoxon's rank sum test).<sup>34</sup>

The prospective, controlled observational study of 2014 showed that patients who opted for a doctor with additional training in homeopathy for the treatment of in-



Table 3: A selection of the literature as representative as possible of the contribution of homeopathy to the problem of antibiotic resistance

Publication	Year	Level of Evidence	Peer-reviewed journal	Investigated indication / Question / Population	Observation of homeopathic principles	Result
Doehring et al.	2016	syst. review	Vet Rec	Infectious diseases Livestock	Yes*	-**
Zeise et al.	2019	syst. review	Open Agricult	Mastitis Dairy cows	Yes	+
Camerlink et al.	2010	RCT	Homeopathy	<i>E.coli</i> /diarrhoea Piglets	Yes***	+
Keller et al.	2018	RCT	Vet Rec	Mastitis Dairy cows	No	-
Jacobs et al.	2003	Meta-analysis of 3 RCTs	Pediatr Infect Dis	Diarrhoea Children	Yes	+
Shang et al.	2005	syst. review + meta-analysis	Lancet	Acute respiratory tract infections Humans	Yes*	+
Hawke et al.	2018	syst. review	Cochrane Database Syst Rev	Respiratory tract infections Children	Yes	-
Frass et al.	2005	RCT	Homeopathy	Sepsis Humans	Yes	+
Haidvogel et al.	2007	Observational study	BMC Complem Altern M	Respiratory tract and ear infections Humans	Yes*	+
Grimaldi-Bensouda et al.	2014	Observational study	PLoS One	Upper respiratory tract infections Humans	Yes*	+
Van der Werf et al.	2016	Observational study	BMJ	Antibiotic consumption GP practices Humans	Yes*	+
Orjales et al.	2016	Observational study	Homeopathy	Large animal practice treatment number Dairy cows	Yes*	+
Stevens et al.	2016	Observational study	J Dairy Sci	Large animal practice antibiotic use Dairy cows	Yes*	+
Maeschli et al.	2019	Observational study	Complement Med Res	Large animal practice antibiotic use Livestock	Yes*	+

\*in a part of the included studies/veterinarians/doctors,

\*\*Conclusion contradicts that of the meta-analysis and of the reviews of 2014 and 2015,<sup>53,54</sup>

\*\*\*prophylactic use

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fections of the upper respiratory tract, were prescribed significantly fewer antibiotics (OR= 0.43; CI= 0.27–0.68; n= 518) and antipyretic/anti-inflammatory medicines (OR= 0.53; CI= 0.38–0.76) with the same effectiveness of the therapies (OR= 1.16; CI= 0.9–3.2) and fewer side effects.<sup>32</sup>

In 2016, the number of antibiotics prescribed by general practitioners with and without complementary medicine training was compared in the UK. Results showed that doctors with additional training have a significantly lower prescription rate of antibiotics (RR= 0.78; CI= 0.64–0.97).<sup>81</sup>

### Regarding the three studies of level of evidence 2c on the homeopathic treatment of infections in animals

In the study of 2016 (number of treatments) in organic dairy farms that had their animals treated with homeopathy, the number of treatments required was 0.13 per animal per year, compared to 0.54 in farms that had their animals treated exclusively conventionally.<sup>67</sup> A noteworthy side result of the study was that 83% of the farmers were satisfied with the effectiveness of homeopathy.<sup>67</sup>

In the observational study of 2016 (antibiotic use) it was shown that dairy farms that treated mastitis homeopathically, used selective drying-off therapy and participated in a herd health management programme supervised by a veterinarian, had lower antibiotic use than those where this was not applied ( $p \leq 0.05$ ; multivariable linear regression analysis).<sup>79</sup>

The current observational study of 2019 was able to show that in the course of the Kometian project in Switzerland, which involved complementary medical, predominantly homeopathic therapy, the antibiotic treatment incidence on farms was significantly decreased ( $p < 0.001$ ; Wilcoxon signed rank test), down from 27 treatments per 100 animals to 18 in the first year.<sup>51</sup>

### Case report

Finally, a case report on the possibilities of individualised homeopathy as a successful therapeutic approach to antibiotic resistance should be cited: the case report documents the course of a wound healing disorder in a four-year-old trotter gelding, associated with antibiotic-resistant bacteria. The patient failed to respond to antibiotic therapy based on gentamicin (6.6 mg/kg/q24h iv, Gentavan®, Vana GmbH, Vienna, Austria) and penicillin (30,000 IU/kg/q6h iv, penicillin G-sodium®, Sandoz GmbH, Kundl, Tyrol, Austria) for 12 days followed by oral administration of sulfadiazine sodium

and trimethoprim (15 mg/kg/q24h, po, Equibactin®, Produlab Pharma BV, Raamsdonksveer, the Netherlands).<sup>91</sup> A bacteriological examination of a deep wound swab and sensitivity testing revealed Oxacillin-resistant *Staphylococcus haemolyticus* and *Actinobacillus equuli*, 14 days after the start of therapy.<sup>91</sup>

At the first homeopathic treatment the wound showed inflammation, oedema, putrid discharge and a seroma. The horse was treated with classical homeopathy. By the second day improvement was already evident as the signs of pain had subsided. Ten days after the start of therapy, the edges of the wound had become soft, there was no pus, no swelling, no oedema or seroma. Five weeks after the start of therapy, the wound was completely closed. The homeopathic medicine Silicea terra was chosen on the basis of the following symptoms: emaciation despite appetite, malnutrition in the past, purulent wound infection with noticeably hardened wound edges. These physical signs of disease combined with the sensitive, cautious character of the animal led to the *simile*, the homeopathic medicine that best reflects both the physical manifestation of the disease and the nature of the patient.<sup>91</sup> The homeopathic medicine Silicea terra C30 was administered: three globules every 24 hours on three consecutive days, per oris. (Silicea terra C30, Homeocur, Retz, Austria). In this case the homeopathic medicine was administered on an individual basis, being one of many homeopathic medicines that can be effective in the treatment of purulent wound healing disorders associated with antibiotic-resistant bacteria. Depending on the individual case, other homeopathic medicines can be used for such a disorder.<sup>91</sup>

### Discussion

In view of the global threat posed by antibiotic resistance, the recommendations of the EU Commission in the current One Health Action Plan for research in the field of complementary medicine, as well as the calls of WHO to integrate complementary medicine into national health care systems, based on basic principles of homeopathy, and its legal and scientific foundations, this narrative review aims to examine the following question: how does the current scientific evidence of homeopathy compare with a) the current reporting by scientific organizations, b) conventional medicine and c) data from RCTs versus data on suitability for everyday use, the so-called Real World Data?<sup>26, 92</sup>

Based on the facts a) that homeopathic medicinal products without indication are 100% identical with regard to production, quality and principles of application, regardless of whether they are used in animals or humans and b) that if the *simile* principle is adhered to and

the proof of effectiveness of individualised homeopathy in one or more indications is available, the logical consequence seems to be that it can be concluded that it is effective in other indications and, c) that the authors of the EASAC statement discuss human and veterinary homeopathy simultaneously in their statement, the discussion of the evidence in human and veterinary homeopathy seems to lay the foundations for a comprehensive presentation of the evidence on homeopathy.

#### a) First and second Australian NHMRC report and EASAC statement

The first Australian NHMRC Report of 2012 showing 'encouraging evidence for the effectiveness of homeopathy' in at least five indications was kept under lock and key and was only published at the end of August 2019 after pressure from an international consortium of scientists, patient associations, and medical and veterinary associations.<sup>18</sup>

A closer examination of the second Australian NHMRC Report published on the NHMRC website in 2015 showed that 176 studies were initially identified. In addition, the NHMRC required a very high level of quality (Jadad score 5/5) and a minimum number of 150 participants for the studies to be considered 'reliable'.<sup>65, 27</sup> This inclusion criterion is surprising, as the sample size calculation depends on the expected difference in the effect size. In addition, it can be assumed that no ethics committee would approve studies in which a certain number of cases is stipulated, especially if fewer study participants would be sufficient due to the sample size calculations. In addition, the NHMRC itself regularly conducts studies with fewer than 150 participants – examples are the NHMRC information paper on the effects of lead on human health, which included studies with participant numbers ranging from 52 to 780, or the clinical guidelines of the NHMRC for management of borderline personality disorders, which included studies with at least 16 patients.<sup>66, 64, 27</sup> Nor does Cochrane (an international network for the improvement of the scientific basis for decisions in the health system) exclude RCTs solely on the basis of the number of study participants.<sup>15</sup> These scientifically unjustifiable inclusion and exclusion criteria of the NHMRC led to the fact that only five studies remained that were regarded as 'reliable' which were all classified as negative with the conclusion that there is no «reliable» evidence of effectiveness of homeopathy for any indication.<sup>65</sup> It seems that other, non-scientific reasons, led to this negative reporting. Only the second Australian NHMRC report received a lot of media attention, as did the EASAC statement from 2017.

Regarding the statement of EASAC 'Homeopathic products and practices: assessing the evidence and ensuring

consistency in regulating medical claims in the EU', the following points should be emphasized:<sup>25</sup> In the introduction, the authors declare that the aim of the statement is to reinforce criticism of health and scientific arguments made against homeopathic medicinal products.<sup>25, 27</sup> It can be concluded that objective reporting was not the aim. EASAC's criticism is also directed against the current EU law on homeopathic medicinal products, EU Directive 2001/83.<sup>25, 27</sup> A recent jurisprudence paper shows that the medicinal safety demanded by EASAC has already been met by EU Directive 2001/83.<sup>88</sup> The information on the websites of the Swiss Agency for Therapeutic Products (Swissmedic), the Austrian Federal Office for Safety in Health Care (BASG) and the German Federal Institute for Drugs and Medical Devices (BfArM) are good examples of how EU law is implemented accordingly.<sup>76, 4, 8</sup> EASAC's approach to explain the successful practical application of homeopathic medicines by the placebo effect, and to simply summarise the results achieved in clinical studies as 'poor study design (...) or publication bias' falls short of the mark. By definition, placebo effects include all positive psychological and physical reactions that are not due to the specific effectiveness of a treatment, but to its psychosocial context.<sup>90</sup> Particularly in view of the successes of veterinary homeopathy, where the person administering the medicine in many cases does not come into direct contact with the animal, e.g. when administering homeopathic medicines via the drinking water - common practice in farm animal practice - the statement, the effectiveness of homeopathy is based on the consideration for the patient is not tenable. In addition, EASAC did not examine the studies summarized in the statement in detail.<sup>25</sup> It can be stated that the review with meta-analysis of 2014 and the criticisms of the review of 2005 were not taken into account in the EASAC statement.<sup>56, 30, 50, 77, 25</sup> The review with meta-analysis of 2014, which could have been included in the EASAC statement as the most current at the time and only included studies on individualised (= classical) homeopathy, in contrast to the previously published reviews, showed a chance of the effectiveness of homeopathic medicines with individualised use, which is 1.5 to 2 times higher than placebo.<sup>56</sup> Of the previously published reviews with meta-analysis, only the negative result of the one of 2005 is based solely on studies with non-individualised homeopathy. The sensitivity analysis carried out in the meta-analysis of 2014 confirms the positive result, while a sensitivity analysis of the meta-analysis of 2005 later performed by other authors could not confirm the negative result; the authors themselves did not carry out a sensitivity analysis.<sup>56, 77, 50</sup> In addition, in the meta-analysis of 2005, there were not 110 homeopathic and 110 matched (i.e. matching in criteria such as indication) conventional studies evaluated as indicated, but only six conventional studies in

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indirect comparison to eight homeopathy studies. This subsequent modification of the inclusion and exclusion criteria changed the evaluation from positive to negative.<sup>30</sup> Overall, 93% of the studies were excluded. Reasons for the exclusion (also of further methodologically high-quality scientific work of level of evidence 1a) were not given in the EASAC statement.<sup>25, 47, 48, 49, 19, 56</sup> The EASAC statement focuses mainly on the second Australian NHMRC Report and the review of 2005.<sup>25, 65, 77</sup> The 2010 House of Commons Science and Technology Committee Report «Evidence check 2: Homeopathy» was also mentioned.<sup>38</sup> This report was also politically motivated and after being signed by only four members of the committee, was promptly rejected after a «House of Commons Early Day Motion» signed by 70 members of parliament (MPs).<sup>38, 27</sup> The question, whether the second Australian NHMRC report, with its lack of peer review, very unusually and deliberately chosen, non-EBM-compliant inclusion criteria, and the EASAC statement, with its lack of peer review and selective references, are appropriately rated with EBM criteria can therefore be answered with 'No'.<sup>65, 25</sup>

In conclusion, we suggest that it was not scientific honesty, but a fundamental rejection of homeopathy – in view of the perceived lack of plausibility regarding the active principles of homeopathy – that led to the reports and statements discussed. Nevertheless, the evidence determined and published according to the usual scientific criteria speaks in favour of the effectiveness of homeopathy.<sup>61, 73</sup>

#### b) In comparison with the external evidence of conventional medicine, the following should be noted

A 2007 review of Cochrane reviews of predominantly conventional therapies revealed that 96% of all systematic reviews call for more methodologically high-quality research.<sup>23</sup> 49% of these publications present results that do not allow any conclusions to be drawn about the benefit/harmfulness of the examined intervention. According to this review, 7% of all medical procedures are actually harmful.<sup>23</sup> Only 1.38% of conventional therapies are definitely effective, 43% are classed as effective, but the studies show methodological deficiencies. Based on the results of the meta-analyses of 2014, 2017, 2018, 2019, homeopathy should be classified provisionally in the group of therapies (conventional 44%: 1.38% plus 43%), which are effective but need further research.<sup>56, 58, 59, 57, 23</sup>

#### c 1) Demands for further methodologically high-quality homeopathic studies

The prerequisite for carrying out methodologically high-quality studies on individualised homeopathy is that the principles of homeopathy are taken into ac-

count, since the selection of the *simile* is decisive for the effectiveness of the homeopathic treatment, because only an application *lege artis* can be effective for the respective patient. If the individually appropriate homeopathic medicine, the *simile*, is not selected by appropriately trained and experienced homeopathic doctors/veterinarians according to the basic homeopathic principles, it is unlikely that the desired effectiveness will follow. In a study from 2008 it was shown that, for the successful application of individualised homeopathy, the basic principles – i.e., individualised selection of a homeopathic medicine tested on a healthy individual according to the principle of similarity – must be taken into account.<sup>70</sup> In this sense, it is appropriate to cite the underlying additional training of the respective authors in publications on homeopathy.

The limit of the present study is the narrative nature of the review, it is not a systematic review. However, there are already sufficient systematic reviews of human medical homeopathy in existence (current review programme 2014, 2017, 2018 and 2019).<sup>56, 58, 59, 57</sup> A systematic review for veterinary homeopathy is currently not feasible due to two missing prerequisites: a) First, in 2016, the model validity of RCTs on individualised homeopathy was examined.<sup>60</sup> This model would have to be adapted to the RCTs on individualised veterinary homeopathy before carrying out a corresponding systematic review and meta-analysis on individualised veterinary homeopathy, encompassing various indications; b) secondly, there is a lack of a large number of methodologically high-quality RCTs carried out in accordance with the principles of homeopathy and the guidelines for randomized controlled studies.<sup>89</sup> Indeed, these can only be carried out at university institutions with the availability of public, independent research funds. The classic double-blind RCT is designed for a specific experimentally created examination situation: testing a medicine for a specific indication. If this experimental approach, which has been used with some success for research in conventional medicine, is adapted to homeopathic research, there are some further challenges – in addition to those of the RCTs in conventional medicine with regard to the transferability of the results to everyday practice. In homeopathic research, which follows an individualised methodology, due to the iterative procedure of finding homeopathic medicines and the different assessment of the course and the success of the therapy (e.g., first improvement of the general condition, only then improvement of the local pathology), further considerations must be taken into account. The points mentioned make it difficult to carry out RCTs in homeopathy, but do not make them impossible. As a simple model, diarrhoea due to *E. coli* in piglets is in principle well-suited to examining the effectiveness of homeopathic medicine using an RCT.<sup>12</sup> On the other hand, the

importance of health care research in the form of pragmatic controlled studies (PCTs) should be emphasized for assessing the suitability of homeopathic and conventional medicines for everyday use.<sup>69</sup> Regardless of the question of RCT or PCT, in studies other than placebo-controlled studies, it is of course generally important to ensure that homeopathic therapy is compared with state-of-the-art therapy.

### c 2) Conclusion on the literature review of evidence-based homeopathy and on the most representative selection of literature on the contribution of homeopathy to the problem of antibiotic resistance: human and veterinary medicine

Five of the six meta-analyses on various indications up to 2014 came to the conclusion that the effectiveness of homeopathic therapy differs from that of placebo. Only the systematic review with meta-analysis of 2005 as well as the second Australian NHMRC report and the EASAC statement – the inadequacies of which were discussed above – showed no effectiveness of homeopathy. In contrast, in the review program from 2014, 2017, 2018, and 2019 out of a total of 131 original articles 13 RCTs with minimal risk of bias were identified.<sup>56, 58, 59, 57</sup> Ten of these RCTs tested homeopathy in comparison to placebo and resulted in a mean OR of 1.68 (CI= 1.25–2.24;  $p < 0.001$ ), i.e. a statistical significance for the effectiveness of homeopathy compared with placebo. Five of the 13 RCTs with minimal risk of bias also showed high reliable evidence.<sup>2, 40, 41, 16, 68</sup> For individualised homeopathy in particular, effects are recognizable at all quality levels according to Cochrane criteria, also in the methodologically high-quality studies. However, as in the majority of the fields of human and veterinary medicine, further high-quality studies are also necessary in human and veterinary homeopathy. As for veterinary homeopathy, the review of 2014 and the meta-analysis of 2015 showed evidence of the effectiveness of veterinary homeopathy compared to placebo.

Regarding the results of the veterinary review of 2016, in which the authors conclude that, ‘... the use of homeopathy as an alternative to the use of antibiotics cannot be recommended as long as the evidence of effectiveness is not reproduced via RCTs...’, it should be specified that – also due to the prohibition of identical studies by the Animal Experiments Act – not the requirement for a replication, but for further methodologically high-quality studies should be the basis for clinical recommendations.<sup>21</sup> In addition, it should be taken into account that the cited recommendation of the authors of the review of 2016, which they relativize as described above, is not based on a meta-analysis, but only on a review of relevant literature.<sup>21</sup> The same findings apply to the 2017 review of non-antimicrobial treatments for mastitis in

cows.<sup>28</sup> In addition, studies that include prophylactic use were excluded from this review. In summary, it can be stated that all authors identified the need for further methodologically high-quality studies and the single meta-analysis shows evidence for the effectiveness of veterinary homeopathy compared to placebo ( $p = 0.01$  for  $n = 15$ , pooled OR= 1.69 (CI= 1.12–2.56),  $p = 0.02$  for  $n = 2$ , pooled OR= 2.62 (CI= 1.13–6.05)).<sup>54</sup>

The list of studies on the importance of veterinary homeopathy for the treatment of infections does not claim to be exhaustive. For every homeopathic treatment – as with every antibiotic therapy – it must be made clear that an optimization of husbandry, management and feeding is crucial for sustainable therapeutic success. The human homeopathic studies mentioned are also merely the most representative selection. Evidence of the effectiveness of homeopathy in treating infections is sufficient to justify further research in this field. A Cochrane review on the effectiveness of antibiotic therapy for the indication of acute respiratory tract infections in children shows a negative result yet the majority of antibiotics are generally prescribed in the indication of acute infections of the respiratory tract in humans. In this context, further studies in the field of homeopathy are absolutely essential.<sup>73</sup>

In addition to the results of studies to prove the effectiveness of homeopathy in infections, data from health services research, so-called ‘real world data’, clearly show the potential for a significant reduction in the use of antibiotics through homeopathic treatments. This is also the result of a narrative review of 2019, which examined the potential of complementary medicine with regard to a reduction of use of antibiotics. The review emphasizes the need for further research in order to be able to present more methodologically high-quality evidence on (cost) effectiveness;<sup>1</sup> a legitimate claim in view of the global threat posed by antibiotic resistance. In this specific area, further university studies are necessary in cooperation with homeopathic doctors and veterinarians, a requirement that is also supported by the published figures from 2018, of 50% unfounded or improper antibiotic use in veterinary medicine and supported by the 2019 reported 33,000 deaths in human medicine in the EU caused by infections with antibiotic-resistant bacteria.<sup>52, 13</sup> Further literature references that could not be included in this review due to lack of space are available from the first author.

## Conclusion

The current national laws (Switzerland, Austria, Germany) and the EU legislation guarantee the quality and safety of homeopathic medicinal products as well as the

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safety of homeopathic therapies carried out *lege artis*.<sup>6, 8, 9, 11, 20, 31, 71, 82, 83, 84</sup> Evidence for the effectiveness of human and veterinary homeopathy in general, and in particular in the treatment of infections, has been sufficiently proven to justify further research in this area. Five of the six meta-analyses on various indications up to 2014 (table 2) came to the conclusion that the effectiveness of homeopathic therapy differs from that of placebo.<sup>47, 48, 49, 19, 56</sup> Only the systematic review with meta-analysis of 2005 and the second Australian NHMRC report, and the EASAC statement (all of which excluded over 90% of the studies from the analysis), claimed that homeopathy had no effect beyond placebo.<sup>77, 65, 25</sup> A review of 2013 already confirmed that more than 90% of all studies had to be excluded in order to be able to conclude that homeopathy is not effective.<sup>33</sup> Effects on all quality levels according to Cochrane criteria are recognizable, especially for individualised homeopathy, even in the methodologically high-quality studies. Obvious non-scientific interests have consequently led to misinformation about homeopathy.<sup>61</sup> In addition to studies to demonstrate the effectiveness of homeopathy in infections, data from health care research, so-called ‘real world data’, show the potential for a significant reduction in the use of antibiotics through homeopathic treatments (table 3). Not least because of the global threat posed by the problem of antibiotic resistance, both human homeopathy and veterinary homeopathy urgently need further methodologically high-quality studies. For the quality assurance of further studies, their implementation at university facilities is a prerequisite, which can only be made possible through the integration of complementary medicine including homeopathy at the universities. This necessary consequence and requirement in the interests of the patient is already expressed in the American consensus guidelines for an integrative veterinary medicine curriculum and is legally anchored in Switzerland by the Medical Professions Act for university teaching and research.<sup>62, 7</sup>

## Conflict of interest

All authors are practising doctors or veterinarians with additional training in homeopathy in addition to their scientific work and have no financial or economic conflicts of interest to declare.

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## L'homéopathie et l'homéopathie vétérinaire fondées sur les faits et leur potentiel pour aider à surmonter le problème de la résistance aux antimicrobiens – un aperçu

Les principes de base de l'homéopathie et ses fondements juridiques et scientifiques sont discutés dans cette revue pour répondre aux positions de l'Organisation mondiale de la santé (OMS) et de la commission de l'Union européenne (UE) sur la médecine complémentaire. Selon l'OMS, le problème de la résistance aux antimicrobiens constitue une menace mondiale. Le plan d'action One Health actuel de la Commission européenne demande des recherches en médecine complémentaire et l'OMS exhorte les États membres à inclure la médecine complémentaire dans leurs politiques nationales de santé.

En ce qui concerne les preuves externes sur l'utilisation générale de l'homéopathie humaine et vétérinaire, des études de niveau de preuve 1a sont passées en revue. En se concentrant sur les preuves externes de l'utilisation de l'homéopathie dans les infections, certaines études de niveau de preuve 1a, 1b, 2c et un rapport de cas sont décrits plus en détail.

En conclusion, des preuves de l'efficacité de l'homéopathie humaine et vétérinaire en général et en particulier du traitement homéopathique des infections, sont disponibles. L'homéopathie individualisée démontre en particulier des effets à tous les niveaux de qualité selon les critères Cochrane, même dans des études de haute qualité méthodologique. Comme dans la plupart des domaines de la médecine et de la médecine vétérinaires, d'autres bonnes voire excellentes études sont nécessaires.

Conformément aux principes de l'homéopathie, d'autres essais de haute qualité méthodologique axés sur le traitement homéopathique des infections sont la prochaine étape logique. La sélection des *simile* (médicament homéopathique adapté individuellement) par des médecins/vétérinaires homéopathes dûment formés est essentielle pour l'efficacité de l'homéopathie. La mise en œuvre d'études dans les établissements universitaires est une condition préalable à l'assurance qualité. Par conséquent, une intégration plus poussée de l'homéopathie dans les universités est une condition nécessaire dans l'intérêt des patients.

**Mots clés:** Antibiotiques, résistance aux antibiotiques, preuves, homéopathie, homéopathie vétérinaire

## Evidenze basate sull'omeopatia veterinaria e il suo potenziale significato nell'affrontare il problema della resistenza agli antibiotici – una panoramica

In considerazione della minaccia globale rappresentata dal problema della resistenza agli antibiotici secondo l'Organizzazione Mondiale della Sanità (OMS) e della richiesta della Commissione dell'Unione Europea (UE) nell'attuale One Health Action Plan per la ricerca nel campo della medicina complementare, nonché della richiesta dell'Organizzazione Mondiale della Sanità di integrare la medicina complementare nei sistemi sanitari nazionali, i principi fondamentali dell'omeopatia e le sue basi giuridiche e scientifiche vengono discussi in questa panoramica. Per quanto riguarda le evidenze esterne sull'omeopatia umana e veterinaria in generale, verranno discussi gli studi al livello di prova 1a. Con particolare riguardo alle prove esterne sull'omeopatia per le infezioni, vengono descritti più dettagliatamente gli studi delle prove di livello 1a, 1b, 2c e in un caso di studio.

In sintesi, si può dire che ci sono prove dell'efficacia dell'omeopatia umana e veterinaria in generale e soprattutto nei trattamenti omeopatici delle infezioni. Ci sono prove di omeopatia individualizzata a tutti i livelli di qualità basati sui criteri di Cochrane, anche in studi metodologicamente di alta qualità, ma come nella maggior parte dei campi della medicina veterinaria e umana, sono necessari altri studi di buona/eccellente qualità.

Nel rispetto dei principi dell'omeopatia, il passo logico successivo è quello di effettuare ulteriori studi di alta qualità metodologica sul trattamento omeopatico delle infezioni. La scelta delle similitudini (il farmaco omeopatico adattato alle esigenze individuali) da parte di medici/veterinari omeopatici adeguatamente formati è un requisito fondamentale per l'efficacia dell'omeopatia. Inoltre, la realizzazione di studi presso le università è un requisito necessario per la garanzia della qualità. Di conseguenza, una migliore integrazione dell'omeopatia nelle università è un requisito indispensabile nell'interesse dei pazienti.

**Parole chiave:** antibiotici, resistenza agli antibiotici, evidenze, omeopatia, omeopatia veterinaria

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Evidence-based human homeopathy and veterinary homeopathy, and their potential to help overcome the problem of antibiotic resistance – an overview  
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