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Recommendations for Designing, Conducting and Reporting Clinical Observational Studies in Homeopathic Veterinary Medicine

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Abstract

Background Clinical observational studies are an important methodological approach in human and veterinary research, examining and describing treatment experience with good external validity. There are currently few observational studies in the field of homeopathic veterinary medicine.

Aim The aim of the study was to develop recommendations for designing, conducting and reporting observational studies in homeopathic veterinary medicine.

Materials and Methods A literature review was performed using various search strategies for identifying guidelines and checklist tools relevant for observational studies, veterinary research and homeopathy. Useful guidelines were selected. Prior recommendations for designing and conducting observational studies in human homeopathic medicine were supplemented with recommendations for homeopathic veterinary medicine that were evaluated by an expert panel.

Results The veterinary extension of the Strengthening the Reporting of Observational Studies in Epidemiology – Veterinary (STROBE-Vet) statement was identified as a useful tool to improve the reporting quality of observational studies, and it has been supplemented here with additional recommendations that are applicable to homeopathy. STROBE-Vet is complemented in the literature by several reports, checklists and guidelines on veterinary medicine in general, such as the Checklist for One Health Epidemiological Reporting of Evidence (COHERE) and the Animal Health Surveillance Reporting Guidelines (AHSURED). Identified items that related to laboratory animal research were excluded as non-relevant to our study.

Keywords
- clinical observational studies
- homeopathic veterinary medicine
- guidelines
- recommendations

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Conclusion Clinical observational studies are an important methodological approach, having currently unrealized potential in the field of homeopathic veterinary medicine. With relatively minor adjustments, the practical guidelines and checklists available to researchers in designing, conducting and reporting observational studies in human homeopathic medicine have been adapted for homeopathic veterinary medicine, for which high quality can be assured by implementing recommendations such as those in STROBE-Vet. With the emergence of the One Health concept, the COHERE checklist can be viewed with growing significance.

Introduction

A common methodological approach in conventional veterinary medicine, a clinical observational study may help define a research question in a natural setting without any experimental intervention.[1] Examples include describing the natural history of disease, investigating treatments or other interventions over time, and assessing risk of harm. Until now, guidelines and recommendations for clinical observational studies in homeopathy have only been produced for studies in humans.[2] This article was initiated to meet the need for corresponding guidelines regarding observational research in veterinary homeopathy.

The three classical types of observational design in epidemiological research are cohort (prospective or retrospective), cross-sectional, and case-control studies.[3,4] A cohort study is a particular form of longitudinal observation in which a group of animals sharing some similarity, such as a treatment or diagnosis, has been exposed to a putative causal factor and followed over time.[2–7] In a comparative (or parallel) cohort study a group of animals is compared with one or more other group(s).[2–7] In a cross-sectional study, data collected at one given point in time are analyzed across a sample population or a pre-defined subset is analyzed.[2–7] Case-control studies are retrospective: animals with the outcome of interest – e.g., an existing health problem ("cases") – are matched with a control group of animals not exhibiting the respective condition/disease but are otherwise similar ("controls").[2–7] Cohort and cross-sectional studies in most cases must be large and they are therefore expensive. Case–control studies are an easier and less expensive possibility to gather useful information from relatively few subjects: they are an appropriate design for investigations with rare outcomes or diseases with long latency periods.[5] In-depth information about cohort, cross-sectional and case–control studies can be found in diverse sources.[2–7]

There is a longstanding debate within conventional research, as well as within complementary and integrative medicine research, on whether experimental designs or observational designs are better for investigating treatment effects.[2,8] The conclusion arises that each research design comprises different aims, strengths and limitations[2,8–12] and therefore both are needed. Teut et al have provided a good overview of the advantages of observational studies.[2] Observational studies provide "real-world" data and involve no change to the regular ongoing clinical care of a patient. They allow description and examination of treatment options, and they are usually less costly to realize than experimental trials. In most observational studies, there are no or only a few predefined inclusion and exclusion criteria. Longer examination periods, which are often necessary, for example in the treatment of chronic diseases, are possible and affordable, since costs are much lower as compared with randomized controlled trials (RCTs).

Observational studies may provide valuable data on whether investigations using experimental designs are justified. The most important limitation of observational studies is that they do not provide information on whether a health change is uniquely due to the treatment or due to other extraneous factors – which can only be investigated using controlled experimental designs. In other words, observational studies do not investigate the efficacy of a specific intervention (efficacy being defined as "the extent to which a specific intervention, procedure, regimen or service produces a beneficial result under ideal conditions").[13] Efficacy may be best investigated within an explanatory study design such as an RCT using placebo as control. However, observational studies can explore effectiveness (defined as "the extent to which a specific intervention, procedure, regimen or service, when deployed in the usual circumstances of living and practice, does what it is intended to do for a specified population").[13] Comparative effectiveness is most thoroughly investigated using a pragmatic RCT design, such as by comparing two different interventions, or by examining adjunctive treatment versus usual care.

Observational studies tend to have greater external validity than experimental studies (external validity: the extent to which the study results can be generalized to the population that the sample is meant to represent), while they have less internal validity (the extent to which the observed treatment effects can be attributed to the differences in treatment, with minimum confounding factors).[14]

Different kinds of studies provide a range of useful information for decision makers. For example, a pilot observational study may explore the feasibility of an intervention, preceding and justifying a subsequent experimental study. On the other hand, the outcomes of an experimental study may be further explored in a subsequent observational (post-marketing surveillance) study to check the usefulness and safety of the experimental treatment in daily practice (i.e., in a "real-world" setting).

There are unique challenges for conducting and designing studies in homeopathic veterinary research. If conducting

methodologically high-quality studies on individualized homeopathy, certain homeopathic principles should be accommodated – for example, the strategy used to select the simile (the individually appropriate homeopathic medicinal product). In epidemic diseases in farm animals, a single homeopathic medicinal product as "genus epidemicus" may be considered (Gaertner et al, submitted for publication), requiring a different approach. During the last two decades, different guidelines, statements and tools have been developed and published to enhance the quality of main study types and the transparency of health research. These guidelines and statements can be found on the *equator network* website (https://www.equator-network.org/).

In 2018, the Scientific Society for Homeopathy (WissHom, Köthen, Germany) started a project to develop guidelines and recommendations for high quality research in homeopathy. Publications are published at the WissHom website (www.wisshom.de). An article about observational studies in homeopathic human medicine was published in August 2020,[2] and one about homeopathic case reports in February 2022.[15] Further articles about systematic reviews (SRs), meta-analyses (MAs), RCTs and basic research are in preparation. The articles for SR/MAs, RCTs and case reports can be applied to both human and veterinary homeopathic medicine. This article focuses on clinical observational studies in homeopathic veterinary medicine.

Literature Background

To date, hardly any observational studies have been published in homeopathic veterinary medicine. A rudimentary search using the search terms "((observational[Title]) OR (outcome[Title]) OR (cohort[Title]) OR (case–control*[Title]) OR (cross-sectional*[Title])) AND ((homeopath*[Title]) OR (homoeopath*[Title]))" found 91 results (July 17, 2022). Two independent researchers then scanned the results for homeopathic veterinary medicine. Only one result was found when the search was restricted to title: a prospective uncontrolled observational pilot study.[16] More results (768 articles in total) were found by searching the abstract for observational*, cohort*, cross-sectional*, case–control* "(((observational) OR (outcome) OR (cohort) OR (case–control*) OR (cross-sectional*)) AND ((homeopath*[Title]) OR (homoeopath*[Title])))": for example Maeschli et al (descriptive observational study), Stevens et al (retrospective cohort study), Orjales et al, and Keller et al (cross-sectional studies).[17–20] However, the majority of the articles report neither observational nor veterinary studies.

There is a potential for designing, conducting, and reporting clinical observational studies in homeopathic veterinary medicine to provide useful information for stakeholders.

Aim and Objective

The aim of this article is to provide recommendations for designing, conducting and reporting clinical observational studies in homeopathic veterinary medicine, with a view to enhancing the quality of future publications.

Materials and Methods

In May 2020 we conducted a first exhaustive literature review, using various search strategies to identify all guidelines and tools relevant and valid for observational studies, veterinary research and homeopathy (search 1: (reporting guideline[All Fields] OR reporting guidelines[All Fields]) AND ("veterinary"[Subheading] OR "veterinary"[All Fields]); search 2: reporting AND guideline* AND veterinary; search 3: design* AND guideline* AND veterinar*; search 4: conduct* AND guideline* AND veterinar*; search 5: (guideline*[MeSH Terms]) AND (veterinar*[MeSH Terms]); search 6: (guideline*[MeSH Terms] AND guideline*[Title/Abstract]) AND (veterinar*[MeSH Terms] AND veterinar*[Title/Abstract]) on https://pubmed.ncbi.nlm.nih.gov/advanced/. One combined advanced search, limited to the years 2005 to 2020, was performed in addition to the former six searches. Sets of results from all seven searches were used:

Search number, Query, Sort By, Filters, Search Details, Results (hits):

1, guideline*[MeSH Terms], guideline*[MeSH Terms], 176,209.
2, guideline*[Title/Abstract], guideline*[Title/Abstract], 346,602.
3, #1 OR #2, guideline*[MeSH Terms] OR guideline*[Title/Abstract], 446,678.
4, veterinar*[MeSH Terms], veterinar*[MeSH Terms], 29,506.
5, veterinar*[Title/Abstract], veterinar*[Title/Abstract], 51,716.
6, #4 OR #5, veterinar*[MeSH Terms] OR veterinar*[Title/Abstract], 67,024.
7, #3 AND #6, (guideline*[MeSH Terms] OR guideline*[Title/Abstract]) AND (veterinar*[MeSH Terms] OR veterinar*[Title/Abstract]), 1,965.
8, #3 AND #6, from 2005 - 2020, (guideline*[MeSH Terms] OR guideline*[Title/Abstract]) AND (veterinar*[MeSH Terms] OR veterinar*[Title/Abstract]), 1,479.

An additional search was performed at the www.equator-network.org website. Search terms were "observational studies" and ("animals" or "veterinary").

Subsequently, we supplemented the recommendations for observational studies in homeopathic human medicine by Teut et al[2] with recommendations for homeopathic veterinary medicine and evaluated these recommendations in an expert panel.

Results

Results of the literature search. The sets of results from the six literature searches were as follows: Search 1 resulted in 47 articles, including those on the STROBE-Vet (**St**rengthening the **R**eporting of **Ob**servational Studies in **E**pidemiology – **Vet**erinary) statement.[1] Search 2 resulted in 216 articles, including COHERE (**C**hecklist for **O**ne **H**ealth **E**pidemiological

Reporting of **E**vidence).[21] Search 3 resulted in 615 articles, search 4 resulted in 456 articles, search 5 resulted in 96 articles and search 6 resulted in 20 articles, which included further guidelines on observational studies as well as on other study types. All six literature searches resulted in a total of 1,450 (47+216+615+456+96+20) articles.

Two independent reviewers screened for the usefulness of these 1,450 articles and also the 1,479 articles obtained through the combined advanced search for the years 2005 to 2020. The *equator* website search revealed four guidelines: STROBE-Vet,[1] **Sta**ndards for **R**eporting of **D**iagnostic Accuracy studies that use **B**ayesian **L**atent **C**lass **M**odels (STARD-BLCM),[22] COHERE[21] and a Utstein-style guideline.[23] The literature searches found no other guidelines on observational studies in veterinary medicine. However, searches found several clinical guidelines such as RECOVER[24] and CURATIVE,[25] several older guidelines that are now integrated in STROBE-Vet,[1] one guideline on surveillance design for descriptive observational studies, named AHSURED,[26] and a study design synopsis for observational study design in equine research.[7] In addition to items on veterinary medicine, our search found non-relevant articles related to research in laboratory animals, such as ARRIVE,[27] MINPEPA[28] and PREPARE,[29] which are not discussed further here.

Guidelines and Tools for Veterinary Medicine – Designing and Conducting Observational Studies

Questions and recommendations to enable researchers to design and conduct high-quality observational studies in homeopathic veterinary medicine were extracted from the identified texts and synthesized. To summarize, most recommendations for designing, conducting and reporting clinical observational homeopathic studies in humans are relevant also for veterinary medicine. One of the most important differences between observational studies in human and veterinary homeopathy is that large numbers of farm animals can be treated with homeopathy under standardised circumstances, and hence special consideration of potential confounding factors such as management changes is needed. Additionally, disease-specific and general outcome measures may be different for veterinary medicine. These are presented in ►**Table 1**.[30–35]

Guidelines and Tools for Veterinary Medicine – Reporting Observational Studies

Our literature search identified two principal sets of guidelines that have been developed by international research groups to support the reporting of observational studies in veterinary (as well as human) medicine and thus to help increase study quality:

STROBE-Vet Statement

This is the most important guideline for reporting observational studies.[1,36] The original STROBE statement, for human medicine,[37,38] was elaborated between 2004 and 2007 by an international group of methodologists, researchers and journal editors, revised by a larger group of STROBE contributors, and published in 2007. The STROBE-Vet Guidelines were developed for reporting on studies related to animal health, animal production, and animal welfare or food safety.[1,36] They were elaborated in a consensus meeting of experts in 2014. A central tool of the STROBE statement for strengthening the reporting of observational studies is a checklist that was modified and extended to address issues particular to veterinary medicine; importantly, the STROBE-Vet checklist also retains the original wordings related to human medicine. It can be found at: https://www.equator-network.org/reporting-guidelines/strobe-vet-statement/.

We have supplemented the STROBE-Vet Guideline with recommendations for *homeopathic* veterinary medicine in ►**Table 2**. In doing so, our expert panel recognized that this could be achieved most effectively by basing the recommendations firmly on those already published for observational studies in homeopathic human medicine[2]: to explain why homeopathy is being investigated; to describe the rationale for comparators/control groups; to describe the medical setting and the qualification and experience of the included homeopathic providers; to define how to classify and report adverse events, adverse drug reactions and homeopathic aggravations; to report treatment adherence; and to describe the homeopathy patient sample (and comparator group, if any), the types of homeopathy used, the homeopathy-related analysis strategies applied, the homeopathic medicinal products prescribed, the concomitant therapies and co-therapies, and the number and duration of consultations and follow-ups. For homeopathic veterinary medicine, special consideration of potential confounding factors, such as management changes, is needed.

The STROBE-Vet checklist[1,36] advises veterinary researchers to indicate why the study is being conducted, and to ensure that the level of organization is clear and considered. This is because observational studies in veterinary medicine often deal with repeated measures (in an individual animal or a herd) or involve animals maintained in groups, which lead to statistical non-independence. Among variables for hypothesis-driven studies, the STROBE-Vet checklist recommends a description of the putative causal factor underlying the treatment or diagnosis. The checklist also includes recommendations on describing the development, validation and administration of any questionnaire used to collect data and the efforts made to assess the accuracy of those data, along with statements concerning transparency (funding, authors' roles, quality standards, any conflict of interests, ethical approval).

Checklist for One Health Epidemiological Reporting of Evidence (COHERE)

"*One Health* is defined as the intersection and integration of knowledge regarding humans, animals, and the environment"; however, with an expanding scientific literature on the topic, "there is considerable heterogeneity of approach and quality of reporting in One Health studies".[21] COHERE was developed by an international expert group whose representation included "human medicine, veterinary medicine, public health, allied professionals, clinical laboratory science, epidemiology, the social sciences, ecohealth and environmental health".[21] The

Table 1 Practical recommendations to design and conduct observational studies in veterinary homeopathy

Item	Description
Aims and objectives	What exactly is your research question? What setting do you want to describe? Take some time to write down your aims and research questions.
Background information	Find out how other researchers have investigated your field of interest and what they have found out. A systematic review on your topic would be a possible first step, which helps you to understand your research field and later on helps you to design your observational study and discuss results. You may also contact experts in this field very early to include their knowledge and expertise. Based on the background information, is it necessary to change your research questions?
Design	Is an observational study the appropriate design for your research question? If you are aiming to investigate the efficacy of a drug, you will need an RCT design instead. If an observational design is appropriate, which study design will best fit your research questions? Do you need a control group? Do you already have good data available and could use these for a retrospective case-control design? Or do you plan to investigate prospectively with a cohort or comparative cohort study design? Would a "snapshot" perspective derived from a cross-sectional study design be an option?
Patients	Which setting, group of *animals* or sample do you want to investigate? In observational studies, your sample should *comprise animals being treated in "real-world" circumstances*. Therefore, try to minimize inclusion and exclusion criteria. How do you get access to your *animals*? For prospective studies: Would *pet owners or farmers* be willing to participate in your study? For retrospective studies: are you authorized to use and analyze the data, and in which way? Do you get access to the necessary data? Find out about data protection rules and regulations being relevant to your research question and data.
Therapy and setting	What is the therapy/*intervention* and the setting you are observing in your sample? Please observe and describe it. In retrospective studies, you may study a (random) small sample of medical records to determine if the documentation includes the necessary information you are looking for.
Control/Comparator	When using a control group (also from the "real world"), is this group/sample appropriate? *Potential confounders need to be identified and considered.* If necessary, you may include a small field study and observe the control in an authentic medical setting. As for *Therapy and setting* above, in retrospective studies you may study a (random) small sample of medical records to determine if the documentation includes the necessary information.
Medication	To organize your study and the data collection, consider in advance which type of medication is used in your research sample/setting. For homeopathy there are many possibilities, such as individualized, classical, constitutional, clinical, standardized, single constituent or complex (multi-constituent), and isopathy. Also think about dose, potency, frequency/repetition – similarly for a comparator group, if applicable.
Outcomes	For prospective studies, identify potential outcomes that fit your sample and reflect your research questions. Start with identifying outcomes in past studies and reflect on how appropriate those would be for your study. Take some time to take qualitative interviews with *pet owners or farmers* from your sample to determine about perceived outcomes that matter to them. You may also interview other clinical or research experts in your field. Another possibility for finding better outcomes is focus groups. A focus group is a form of qualitative research: a small but relevant group of *pet owners or farmers* and/or experts is studied in guided or open discussions about the potential and relevant outcomes which can be expected from a larger population. This may help you to find out more about the changes perceived under your therapeutic setting and how to measure them. When choosing outcomes, try to include validated outcome measures as much as possible. Outcomes usually include disease-specific measures (such as, *in veterinary medicine, a body condition score for dogs*[30], *the HeLP (hemangiosarcoma likelihood prediction model) score for dogs with spontaneous hemo-abdomen*[31]). With general measures, it is possible to observe general changes across different types of disease conditions and patients. Examples of general outcome measures used *in veterinary medicine are: Helsinki chronic pain index (HCPI)*[32]*; Quality of life assessment (QLA)*[33]*; visual analog scale for pain (VAS pain); locomotion (VAS loc)*[34]. In retrospective outcome studies, your random sample of medical records will enable you to get an overview of documented outcomes and quality of documentation before planning in more detail. Once you have decided upon outcomes, you have to consider using online or paper questionnaires, depending on your budget and logistical possibilities.

Table 1 (*Continued*)

Item	Description
Statistics	Try to include an experienced statistician or biometrician as early as possible. This will help you to avoid mistakes, improve quality and lessen the burden of your work. The statistician will also assist and guide your team in building up a database for your outcome data documentation. The typical work of a statistician includes reflecting on design and methods, calculating a sample size (if necessary), writing down the statistical information and the statistical analysis plan for your study protocol, assisting in establishing a database for your data, analyzing and discussing your data, and assisting in your publication.
Budget and funding	The budget you may use for your research is a crucial resource. Please reflect early on how much money you have for your study. Also calculate how much unpaid help you may receive: many studies in homeopathy have been realized with low budgets and much unpaid help. However, funding and resources help to increase the quality of your research. Consider applying for funding or a grant with your study idea and protocol.
Team	Consider early what kind of expertise you may need and what kind of expertise and service you may have to recruit and pay for.
Study protocol	Draft your study protocol and be sure to improve your draft by receiving critical reviews from peers and experts. Whilst it is not mandatory for observational studies, before including patients or data it is worth registering your study protocol online *if possible, e.g., in the Veterinary Clinical Trials Network*[35]. Most peer-reviewed journals want to check your manuscripts with your registered study protocols. *Check to find if your country has a national study registry.*
Data and quality management	Consider using a quality- and data-management system/plan. Pre-defined guidelines and standard operating procedures help to improve the quality of your research.
Ethics and legal situation	Find out which ethics board is responsible for dealing with your study protocol: *e.g., from the university you are collaborating with, or a national college of veterinarians*. If formal ethics consideration is required, prepare and submit the necessary documents and await the board's approval. Find out about the legal situation regarding your planned study and follow the laws and regulations.
Others	Before conducting a large (and possibly expensive) observational study it may be beneficial to realize a small-scale pilot study as a first step to test your approach and learn from any mistakes.

Source: Adapted from Teut et al,[2] and supplemented by our expert panel with the permission of the original authors.
Note: Supplements related to veterinary medicine are *underlined/italicized*.

aims of the COHERE standards are, on the one hand, to improve the quality of reporting of observational or interventional epidemiological One Health studies and, on the other hand, to "promote the concept that One Health studies should integrate knowledge from these three domains" of human, animal and environmental health. Due to equal integration of these three domains in a publication that would be classified as a One Health study, the COHERE expert review group recommend that the Methods section of such a paper should include a detailed description of interactions/relationships among human, animal and environmental samples, as well as information concerning measurement and analysis.[21] Further to this, the review group emphasizes that the Results section should contain a detailed description of comparative statistics, qualitative comparisons or integrated analyses among human, animal and environmental variables, highlighting the potential lack of independence or group effects that may impact statistical inference. Finally, the Discussion section should contain a detailed description of discordance in acquisition, analysis or interpretation of data among the three domains (e.g., species-specific differences that may impact results). The COHERE standards can be found at: https://www.equator-network.org/reporting-guidelines/cohere/.

Further Reports, Checklists, and Guidelines in Veterinary Medicine

On the website www.equator-network.org, further reports for specific issues in veterinary medicine can be found, such as Utstein-style guidelines on uniform reporting of in-hospital cardiopulmonary resuscitation in dogs and cats,[23] proposed definitions and criteria for reporting time frame, outcome and complications for clinical orthopaedic studies in veterinary medicine[39], and STARD-BLCM.[22]

Additionally, reporting guidelines for animal health surveillance (**A**nimal **H**ealth **Su**rveillance **Re**porting Gui**d**elines, AHSURED) were identified, consisting of a 40-item, 11-section checklist for descriptive observational studies,[26] available at https://github.com/SVA-SE/AHSURED/wiki and a synopsis on observational study design in equine research.[7] AHSURED recommends a description of the background terminology, component characteristics, the target population, the test protocol, the study design, the sampling strategy, the results and their interpretation, as well as comments on the timeliness of the work.[26] All items are covered in a useful checklist with a detailed item description and information on the objective-specific relevance of these items for the surveillance in question: freedom from disease, case

Table 2 STROBE Statement—checklist and STROBE-Vet Statement—checklist of items that should be included in reports of observational studies (cohort, case-control and cross-sectional studies), with additional recommendations for homeopathy studies

	Item no.	Recommendation STROBE	Additional recommendation for homeopathy studies	Recommendation STROBE-Vet
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract		(a) Indicate that the study was an observational study and, if applicable, use a common study design term
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found		(b) Indicate why the study was conducted, the design, the results, the limitations and the relevance of the findings
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Explain why homeopathy is investigated in your study	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any pre-specified hypotheses		(a) State specific objectives, including any primary or secondary pre-specified hypotheses or their absence
				(b) Ensure that the level of organization is clear for each objective and hypothesis[a]
Methods				
Study design	4	Present key elements of study design early in the paper	Describe the rationale of comparators/control groups	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up and data collection	Describe the medical setting, e.g., primary *veterinary* care, hospital, university or private (also in control group) Describe the qualifications and experience of included homeopathic care providers (and providers in control groups)	(a) Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up and data collection
				(b) If applicable, include information at each level of organization
Participants[b]	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants.		(a) Describe the eligibility criteria for the owners/farmers and for the animals, at each relevant level of organization
				(b) Describe the sources and methods of selection for the owners/farmers and for the animals, at each relevant level of organization
				(c) Describe the method of follow-up
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed cases. *Case-control study*—For matched studies, give matching criteria and the number of controls per case		(d) For matched studies, describe matching criteria and the number of matched individuals per subject (e.g., number of controls per case)

Table 2 (*Continued*)

	Item no.	Recommendation STROBE	Additional recommendation for homeopathy studies	Recommendation STROBE-Vet
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers. Give diagnostic criteria, if applicable	Define in advance how to classify adverse events, adverse drug reactions and homeopathic aggravations	(a) Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers. If applicable, give diagnostic criteria
				(b) Describe the level of organization at which each variable was measured
				(c) For hypothesis-driven studies, the putative causal structure among variables should be described (a diagram is strongly encouraged)
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		(a) For each variable of interest, give sources of data and details of methods of assessment (measurement). If applicable, describe comparability of assessment methods among groups and over time
				(b) If a questionnaire was used to collect data, describe its development, validation and administration
				(c) Describe whether or not individuals involved in data collection were blinded, when applicable
				(d) Describe any efforts to assess the accuracy of the data (including methods used for "data cleaning" in primary research, or methods used for validating secondary data)
Bias	9	Describe any efforts to address potential sources of bias		Describe any efforts to address potential sources of bias due to confounding, selection or information bias
Study size	10	Explain how the study size was arrived at		(a) Describe how the study size was arrived at for each relevant level of organization
				(b) Describe how non-independence of measurements was incorporated into sample size considerations, if applicable
				(c) If a formal sample size calculation was used, describe the parameters, assumptions and methods that were used, including a justification for the effect size selected
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding		(a) Describe all statistical methods for each objective, at a level of detail sufficient for a knowledgeable reader to replicate the methods. Include a description of the approaches to variable selection, control of confounding, and

(*Continued*)

Table 2 (*Continued*)

	Item no.	Recommendation STROBE	Additional recommendation for homeopathy studies	Recommendation STROBE-Vet
				methods used to control for non-independence of observations
		(*b*) Describe any methods used to examine sub-groups and interactions		(b) Describe the rationale for examining sub-groups and interactions and the methods used
		(*c*) Explain how missing data were addressed		(c) Explain how missing data were addressed
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed. *Case-control study*—If applicable, explain how matching of cases and controls was addressed. *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy.		(d) If applicable, describe the analytical approach to loss to follow-up, matching, complex sampling and multiplicity of analyses
		(*e*) Describe any sensitivity analyses		(e) Describe any methods used to assess the robustness of the analyses (e.g., sensitivity analyses or quantitative bias assessment)
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed		(a) Report the numbers of owners/farmers and animals at each stage of study and at each relevant level of organization – for example, numbers eligible, included in the study, completing follow-up and analyzed
		(b) Give reasons for non-participation at each stage		(b) Give reasons for non-participation at each stage and at each relevant level of organization
		(c) Consider use of a flow diagram		(c) Consider use of a flow diagram and/or a diagram of the organizational structure
Descriptive data on exposures and potential confounders	14*	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	Describe the homeopathic patient (and control) sample. Report types of homeopathy used: individualized, formula, isopathy, mixed conventional + homeopathy (and therapies used in control groups). If possible, report on homeopathic analysis strategies applied (types of repertorization). Report homeopathic medicinal products prescribed (frequencies, potencies, dosages, timing, form of medication, manufacturer), conventional medications prescribed (frequencies, dosages), and others (also in control). Also report on prescription criteria or treatment concepts being applied. Describe concomitant therapies and co-therapies and *other potential confounding factors: e.g. management changes* (also in any comparator group).	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders by group and level of organization, if applicable

Table 2 (*Continued*)

	Item no.	Recommendation STROBE	Additional recommendation for homeopathy studies	Recommendation STROBE-Vet
			Describe number and duration of consultations and follow-ups (also in any comparator group).	
		(b) Indicate number of participants with missing data for each variable of interest		(b) Indicate number of participants with missing data for each variable of interest and at all relevant levels of organization
		(c) *Cohort study*—Summarise follow-up time (e.g., average and total amount)		(c) Summarise follow-up time (e.g., average and total amount), if appropriate to the study design
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Report adverse events, adverse drug reactions and homeopathic aggravations Report on treatment adherence (optional, if assessed)	(a) Report outcomes as appropriate for the study design and summarise at all relevant levels of organisation
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		(b) For proportions and rates, report the numerator and denominator
		Cross-sectional study—Report numbers of outcome events or summary measures		(c) For continuous outcomes, report the number of observations and a measure of variability
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included		(a) Give unadjusted estimates and, if applicable, adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders and interactions were adjusted. Report all relevant parameters that were part of the model
		(*b*) Report category boundaries when continuous variables were categorized		(b) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g., analyses of sub-groups and interactions, and sensitivity analyses		Report other analyses done, such as sensitivity/robustness analysis and analysis of sub-groups
Discussion				
Key results	18	Summarize key results with reference to study objectives		Summarize key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		Discuss strengths and limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results, considering objectives,		Give a cautious overall interpretation of results, considering objectives, limitations,

(*Continued*)

Table 2 (*Continued*)

	Item no.	Recommendation STROBE	Additional recommendation for homeopathy studies	Recommendation STROBE-Vet
		limitations, multiplicity of analyses, results from similar studies, and other relevant evidence		multiplicity of analyses, results from similar studies and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results		Discuss the generalisability (external validity) of the study results
Other information				
Transparency	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		(a) Funding – Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based
				(b) Conflict of interests – Describe any conflict of interests, or lack thereof, for each author
				(c) Describe the authors' roles – provision of authors' declarations of transparency is recommended
				(d) Ethical approval – Include information on ethical approval for use of animal and human subjects
				(e) Quality standards – Describe any quality standards used in the conduct of the research

Source: The additional recommendations for homeopathy studies have been adapted for veterinary medicine *(underlined, italicized)*, with permission from Teut et al[2].

[a]Level of organization recognizes that observational studies in veterinary research often deal with repeated measures (within an animal or herd) or animals that are maintained in groups (such as in pens); thus, the observations are not statistically independent. This non-independence has profound implications for the design, analysis and results of these studies.

[b]The word 'participant' is used in the STROBE statement. However, for the veterinary version, it is understood that 'participant' should be addressed for both the animal owner/farmer and for the animals themselves.

*Give such information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

detection, prevalence estimation, and early detection.[26] In addition to the recommendations on reporting clinical observational studies provided by the STROBE-Vet statement, the synopsis on observational study design in equine research gives several practical examples of "Dos and Don'ts" when designing, conducting and reporting such studies.

The www.equator-network.org website also contains the more general report, *Writing for Publication in Veterinary Medicine. A Practical Guide for Researchers and Clinicians.* This online material has been "designed to help residents, graduate students, and early-career faculty in veterinary medicine gain independence and confidence in writing and publishing scientific articles".[40] It can be downloaded at: https://www.equator-network.org/reporting-guidelines/writing-for-publication-in-veterinary-medicine-a-practical-guide-for-researchers-and-clinicians/.

Guidelines not Specific to Veterinary Medicine

Relevant guidelines and statements are described in detail by Teut et al[2]:

The **Re**porting of Studies **C**onducted using **O**bservational **R**outinely Collected Health **D**ata (RECORD) statement was created as an extension to STROBE.[41]

The **G**ood **R**ese**a**rch for **C**omparative **E**ffectiveness (GRACE) checklist contains a set of key principles to assess the quality of observational studies in comparative effectiveness research.[42]

The **E**uropean **N**etwork of **Ce**ntres for **P**harmacoepidemiology and **P**harmacovigilance (ENCePP) offers a free web resource, *Guide on Methodological Standards in Pharmacoepidemiology*: http://www.encepp.eu/standards_and_guidances/methodologicalGuide.shtml.

Other resources (also for other than observational studies):

The **T**ransparent **R**eporting of **E**valuations with **N**on-randomized **D**esigns (TREND) guidelines "emphasize the reporting of theories used and descriptions of intervention and comparison conditions, research design, and methods of adjusting for possible biases in evaluation studies that use non-randomized designs".[43]

Guidelines for Homeopathy not Specific for Veterinary Medicine

Reporting **D**ata on **Ho**meopathic **T**reatments (RedHot) is a supplement to CONSORT and is principally a guide for reporting RCTs. It includes a checklist for reporting data on

homeopathic treatments. Its authors emphasized, however, that it was intended to be useful also for clinical observational studies.[44] The RedHot checklist contains many of the points that are listed in STROBE (►**Table 2**) and includes, for example, reporting details of the study's rationale, its prior evidence base, the medications used (pharmacopoeia, dilution method, and trade name), the clinical setting, the patients' clinical history, the number of homeopathic practitioners and their current schools or styles of homeopathy, as well as any control or co-interventions (duration, frequency, and intended effect).

Discussion

These recommendations are described to improve quality of observational studies in homeopathic veterinary medicine by providing guidance for researchers designing, conducting and reporting clinical observational studies in veterinary homeopathy. A close connection with previously published recommendations for improving the quality of observational studies in *human* medicine is reflected in this review.[2] These recommendations and checklists can also be useful for editors, peer reviewers, and readers of published observational studies.

The aim of guidelines recommended by STROBE, STROBE-Vet, COHERE, AHSURED, RedHot, and this article is to enable their application to the broad range of observational studies in human and/or veterinary medicine, including studies in which the aim is to describe disease occurrence and effects of treatments, and exploratory studies used to generate hypotheses.[1,21,26,36,37,44]

►**Table 1** contains practical recommendations to design and conduct an observational study in homeopathic veterinary medicine, but it is not an exhaustive list. Depending on the particular observational study design, not all aspects have to be considered and not all mentioned aspects (like a One Health context or focus on surveillance systems) may be important. For the latter two, aspects of COHERE or AHSURED may be considered.[2,21,26]

In ►**Table 2**, the items in the STROBE-Vet extension correspond to the items in the original STROBE statement, and both follow the typical order of sections within a scientific manuscript. All relevant checklist items need to be addressed within the paper. One of the most important differences between human and veterinary homeopathic observational studies is that large numbers of farm animals can be treated with homeopathy under standardized circumstances; potential management changes also need to be considered carefully. Apart from that, we propose that most recommendations for designing, conducting and reporting clinical observational homeopathic studies in humans are also relevant to veterinary medicine. We would add that, to assure compliance with homeopathic principles, it is essential that homeopathic veterinarians as well as researchers experienced in veterinary research are included in the research team.

Further specific reports, checklists and guidelines in veterinary medicine might be useful, such as guidelines on uniform reporting of in-hospital cardiopulmonary resuscitation in dogs and cats,[23] the proposed definitions and criteria for reporting time frame, outcome and complications for clinical orthopaedic studies in veterinary medicine,[39] STARD-BLCM,[22] the reporting guidelines for animal health surveillance (AHSURED), and the practical advice on observational study design in equine research.[7]

The COHERE checklist deserves particular attention, given the emerging consensus regarding the inter-linked importance of humans, animals and the environment within the concept of One Health.[21]

The STROBE-Vet guidelines are not intended to be prescriptive, but they focus on the clarity of *reporting*. Nor are they intended to be used as a tool to assess research design or execution quality: indeed, this would be considered misuse of the STROBE statement.[1] Quality assessment tools include GRACE[42] (for observational studies[45–47]), and AMSTAR 2,[48] RELEVANT,[49] ROBINS-I[50] and CATHIS 2.0[51] (for meta-analyses and SRs).

The STROBE-Vet Statement represents the consensus of a group of experts,[1] but it was created without conducting an SR of the published literature.[1,36] Therefore it is possible that selection bias has influenced its recommendations.[1,36] We stress that all these recommendations should be seen as evolving advice. We welcome comments and suggestions for further refinement and revision.

Conclusion

Clinical observational studies are an important methodological approach, with as-yet unrealized potential in the field of homeopathic veterinary medicine. The STROBE-Vet, COHERE, AHSURED and RedHot guidelines, together with the recommendations presented in this article, enable their application to the broad range of observational studies in this medical discipline. In the recommendations identified for homeopathic observational studies, we found much more overlap than difference in their application to veterinary compared with human patients: arguably the most important difference is that large numbers of farm animals can be treated with homeopathy under standardized circumstances, and potential management changes need to be considered carefully. The COHERE checklist deserves particular consideration, given the growing emergence of the concept of One Health, within which future clinical observational studies in homeopathy can contribute to the evidence for effectiveness and cost-effectiveness of integrative health approaches among humans, animals and their environment. High quality in such studies can be assured by consideration of the above-mentioned guidelines and checklists.

Highlights

- Clinical observational studies represent an important methodological design in medical research, investigating humans and/or animals in a natural environment without an experimental intervention.
- We provide an overview of guidelines and tools (e.g., STROBE, STROBE-Vet, COHERE, AHSURED, RedHot) that

should be considered when designing, conducting and reporting observational studies in homeopathic veterinary medicine.
- Pre-existing published statements, guidelines and checklists were supplemented with recommendations for designing, conducting and reporting observational studies in homeopathic veterinary medicine to help ensure their high quality in future publications.
- Aided by COHERE standards, One Health-related clinical observational studies in homeopathy can make future contributions to evidence in integrative health.

Authors' Contributions

P.W., M.F., P.F., C.K.-L., and S.U.-Z. made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work. They drafted the article or revised it critically for important intellectual content. They did the final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of Interest

Besides their work as researchers, all authors except S.U.-Z. practice homeopathy as either veterinarians or physicians.

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