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Study design quality and signalment of dogs used for research published in peer-reviewed journals

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1. Introduction

In daily practice, veterinarians need to include recent knowledge to provide optimal diagnostics and treatments (Haimerl et al. 2013). An important source of new information are scientific articles reporting research results published in peer reviewed journals (Grindlay et al. 2012). However, even in these articles, quality deficiencies have been identified in recent years (Amann 2005;Giuffrida 2014;Arlt 2017;Di Girolamo and Winter 2017). For example, by taking a closer look on the literature on reproduction in dogs it was found that the majority of publications reviewed referred to low evidence levels and did not allow to draw sound conclusions (Arlt et al. 2010). Another study compared the literature on bovine, canine and equine reproduction and confirmed a low quality of many randomised controlled trials (Simoneit et al. 2011). Substantive deficits exist likewise in the reporting of publications on bovine and canine trials as well as in bovine and porcine conference proceedings (Brace et al. 2010;O'connor et al. 2010;Sargeant et al. 2010).
It has been stated that just because a study has been published this doesn't mean it is any good (Dean 2013). In the context of the identified quality deficiencies, the question arises if limitations vary also between veterinary specialities.
One objective of this project was, therefore, to evaluate the quality of studies on dogs related to six different veterinary medicine specialities: cardiology, internal medicine, neurology, orthopaedics, reproduction, and surgery. The quality was assessed with an already validated and published checklist (Arlt et al. 2010).

Another question that arises was what kind of dogs are used in clinical and experimental research. In medical research, dogs have been and still are widely used as testing animals (Balls 2016) although worldwide actual and precise figures are not easy to retrieve because relatively few countries collate and publish research animals statistics (Taylor et al. 2008).
It has been estimated that for experimental or scientific purposes 79.9 million animals, out of which 207.724 were dogs, have been used worldwide in 2015 (Taylor and Alvarez 2019). This was a 36.9 % increase on the equivalent estimated figure for 2005 of 58.3 million animals (Taylor et al. 2008;Taylor and Alvarez 2019). The most widespread use of experimental animals occurs in China, followed by Japan and the United States (Petetta and Ciccocioppo 2021). Around 800.000 laboratory animals were used in 2019 in the US, of which 7 % (= 56.000) were dogs (Speaking of Research 2021). In the EU, from 2017 to 2018 the number of animals used in research decreased by five per cent to around 9 million animals, out of which 0.3 % (= 27.000) were dogs and cats (European Comission 2021). Purpose of research projects on dogs include gaining basic biological knowledge, answering

questions referring to human health by using dogs as models for the development of drugs, diagnostic tests, vaccines and medical devices and questions directly linked to canine physiology or diseases (Rossi et al. 1999). Dogs often are preferred as models for human conditions because they are physiologically and clinically more similar than other species such as mouse (Hytonen et al. 2016), and pet dogs also share the environmental conditions of their owners. It has been stated that the most suitable and utilized breed in clinical trials are Beagles (Andersen 1970). These dogs are commonly kept in kennels in homogenous groups in terms of age, weight, sex and neuter status in research facilities of universities or pharmaceutical companies (Bolman 2022). Beagles are medium size, have a short coat and an even temperament what makes them particularly suitable for medical research in contrast to other breeds. These advantages make it easier to standardise specific and relevant conditions in research settings and the experiment cheaper (Giraud and Hollin 2016).

Especially Beagles often serve as models for research focusing on human health such as toxicology of medications and other (Albert et al. 1994). Research on Beagles has led to various relevant findings for human medicine such as different information about infection with helicobacter pylori (Rossi et al. 1999), or better insights into effects of the frequency of tooth brushing (Tromp et al. 1986).

Depending on the research question, alternatives for the use of research dogs may be the enrolment of client-owned dogs or the retrospective evaluation of medical records. Findings of these approaches might even better represent the heterogeneity of dogs seen in daily practice and better address real clinical conditions. However, depending on the research question, a high heterogeneity regarding breed, age, sex, weight, neuter status, housing, feeding and other parameters in a study population may lead to a significant influence of confounders (Skelly et al. 2012;Sargeant and O'connor 2014). Especially if potential confounders are not considered during the analysis and interpretation of research results, this may lead to biased outcomes and conclusions. There is evidence that sex, weight, age, breed, or neuter status of the dogs which take part in a clinical trial are important when it comes to different conditions and diseases, such as joint disorders (Comerford et al. 2011;Hart et al. 2020), metabolic conditions (Puurunen et al. 2022) and periodontal diseases (Wallis and Holcombe 2020).

The objective of the second study was, therefore, to evaluate what kind of dogs were utilized in clinical and experimental trials. We aimed to assess and compare information about the dogs including breed, sex, age, weight, and neuter status in the context of six different veterinary medicine specialties. In addition, yet, it has not been evaluated to which extent Beagles have been used in veterinary research.

The following questions should be clarified as part of this study:

1.) How is the study design quality of research on dogs published in peer-reviewed journals?

Vet Rec. 2022;*190*:e1382. doi:10.1002/vetr.1382.

2.) Is there a quality difference of research between the six veterinary specialities?

Vet Rec. 2022;*190*:e1382. doi:10.1002/vetr.1382.

3.) What kinds of dogs are used in clinical and experimental research? How is the distribution of sex, breed, neuter status, weight, and age?

Animals. 2022, 12, 1487, doi:10.3390/ani12121487

4.) Is there a difference in signalment of the dogs used for the studies of six veterinary specialities?

Animals. 2022, 12, 1487, doi:10.3390/ani12121487

The results of the studies are given in the two publications, which form the basis for the present cumulative dissertation.

1.1. Evidence-based Veterinary Medicine

Veterinarians are obliged to life-long learning to provide appropriate and up to date diagnostics and treatments. In addition, every year an immense amount of new scientific veterinary information is published. Many authors claim that practitioners should be aware of the latest research findings in order to choose the best examination and treatment options for their patients (Brennan et al. 2020).
The aim of Evidence-based Veterinary Medicine (EVBM) is to base decisions in practice on valid, clinically relevant research data (Evans and O'connor 2007). The definition of Evidence-based Veterinary Medicine used by the Centre of Evidence-based Veterinary Medicine at the University of Nottingham is: ´Evidence-based Veterinary Medicine is the use of the best relevant evidence in conjunction with clinical expertise to make the best possible decision about a veterinary patient. The circumstances of each patient, and the circumstances and values of the owner/carer, must also be considered when making an evidence-based decision´ (Dean 2013).

According to the Evidence-based Veterinary Medicine (EBVM) manifesto launched by the scientific journal Veterinary Record, it is necessary to bring the best available evidence into the consultation room so that particular problems can be better handled by the veterinarian and that clients are better informed about the options they are given (Jarvis 2020).
This is an important part of the shared decision-making (SDM) where the practitioner could either have the role as a guardian, a teacher, or a collaborator. The latter provides information and education about diagnostic and treatment options and makes their professional opinions. It forms the basis for a partnership, where the client actively participates in the decision-making process (Cornell and Kopcha 2007). Relationship-centered care has been identified as being the best practice in veterinary medicine and this kind of SDM communication training should be part of the veterinarian curricula (Janke et al. 2021).

The latest scientific information is usually brought to the veterinarian via scientific journals. Most of the research articles go through a peer-review process in order to ensure the high quality and scientific relevance of the studies published (Arlt 2013).
Nevertheless, it has been claimed that the practitioner has to be able to appraise the evidence and quality (Holmes 2004) because even articles published in peer reviewed scientific journals may be of low quality and prone to bias (Arlt and Heuwieser 2014;Arlt 2016). Due to the packed curriculum of veterinary studies, however, the ability to appraise the quality of studies is hardly trained in many veterinary schools (Janicke et al. 2020). This means that many veterinarians may not be sufficiently aware of possible weaknesses within the scientific literature (Haimerl et al. 2013).
In order to help practitioners to appraise published studies, an online resource has been published: https://learn.rcvsknowledge.org/course/view.php?id=2
This source provides an overview about the concepts of EBVM, appraisal of veterinary literature and implementation of new information into veterinary case management.
For the classification of the different types of information, evidence levels have been defined (Sackett 1997) and a ‘staircase of evidence’ was developed (Fig. 1) (Arlt 2016).
The highest level of Evidence-based Veterinary Medicine are the systematic reviews and meta-analyses, which combine several studies related to the same topic and analyse them as if they were one single study (Kastelic 2006). Usually, these studies are based on a specific question, which is intended to be answered by this approach. For that, meta-analyses and systematic reviews follow rigid literature selection and evaluation protocol, what makes these information generating tools different from `normal´ literature reviews.

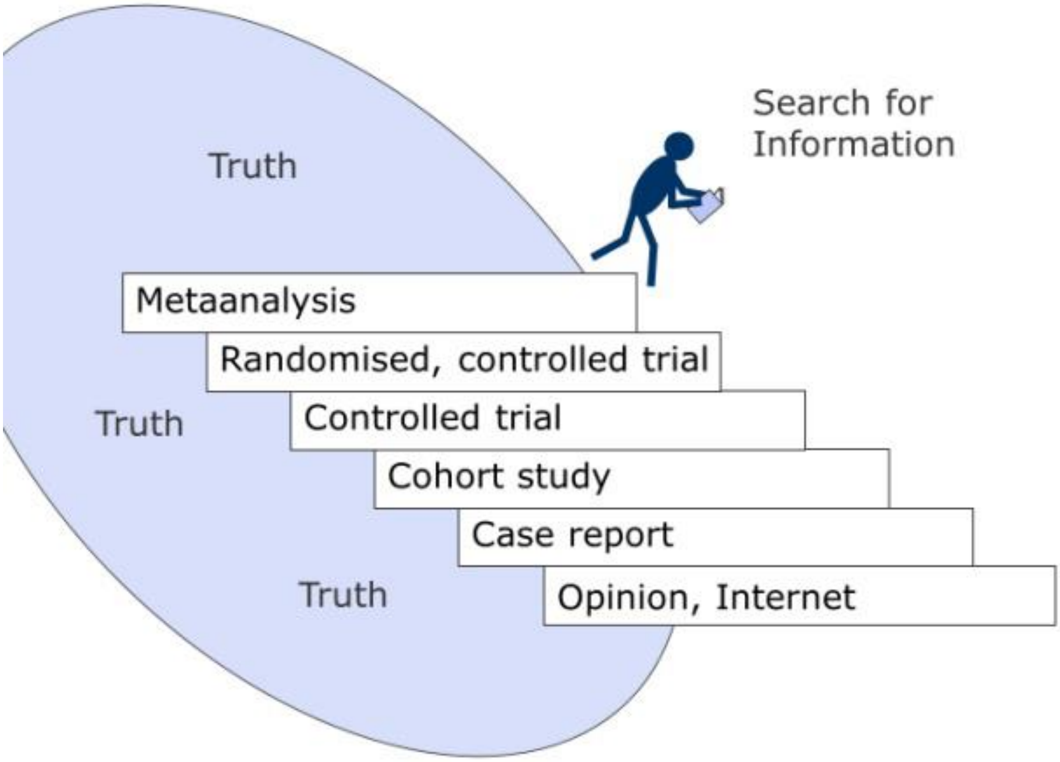

Fig. 1 - Staircase of Evidence (Arlt 2016)

Interventional studies such as the randomized controlled trial (RCT) as gold standard in clinical research (Arlt 2017) can be divided into experimental laboratory studies or clinical trials (Kastelic 2006). The experimental veterinary research usually takes place in a controlled research environment. The dogs used for this approach are mainly purpose bred animals from licensed breeders. Clinical veterinary researches are studies carried out in a natural environment with a naturally occurring disease and in normal veterinary practice, outside a research laboratory and its controls. The dogs can be companion dogs with owners of the public and a variety of breeds, signalments and reproductive capacity.
Unfortunately there is a lower proportion of randomized articles in veterinary medicine compared with the human medical literature, which needs to be improved (Simoneit 2012;Di Girolamo and Meursinge Reynders 2016). Furthermore, are there more likely RCT’s published with a positive outcome if they have pharmaceutical industry funding or involvement (Wareham et al. 2017). In addition, it has been shown that these studies are published faster than studies without positive outcomes or without funding. This phenomenon is referred to as publication bias. It was also stated that manuscripts from Asia were five times more likely to be rejected by editors for publication than other countries, independent from the gender (Edwards et al. 2018).
The observational studies consist of three different study types which are based on

observations, there are no controls. The cohort study follows a specific population which was exposed to a putative causal and compares the result with another population which was not (Kastelic 2006). The cross-sectional survey uses a sample of the whole population and creates two groups to compare at a single time point (Dean 2013). In a case-control study animals with a certain disease or exposure are compared to a matching control group without the disease.

Descriptive studies with the second lowest level of Evidence-based Veterinary Medicine are cases-series and case reports, followed by opinions. They are belonging to the weakest level of evidence and pure descriptions of a group of animals (Dean 2013). These sources of knowledge are considered to have a high risk of bias.

According to these classifications meta-analyses and randomised controlled trials (RCTs) are the sources of information that have the lowest risk of bias. Well-conducted meta-analyses can help practitioners by providing overall conclusions after statistically summarising the results of different randomised, controlled studies focussing on a specific clinical problem.

Next to the levels of evidence, other aspects need to be considered for appraisal of the quality of research papers. These aspects include, for example, the number of experimental animals or samples used, the appropriateness of statistical methods, the handling of missing data and the objectiveness of the discussion (Simoneit et al. 2011).

When using the principles of Evidence-based Medicine, the following five steps presented by (Sackett 1997) should be taken into account.

1. Identify a clinical problem and express it as an answerable question.
   Use for this question the so-called PICO principles. The different parts of the well formulated question stand for P for `patient´, I for `Intervention´, C for ´Control´, O for ´Outcome´ (Vandeweerd et al. 2012).
2. Search for the best evidence to answer the question.
3. Critically appraise the evidence for validity and clinical relevance with the staircase of Evidence.
4. Integrate this appraisal with clinical experience to formulate the best decision for the clinical problem.
5. Evaluate the practitioner’s performance by relating clinical decisions to the best available evidence.

The skills to appraise the quality of a study needs to be learned (Dean 2013). Although the awareness of EBVM is increasing and specific training methods for veterinary students were presented (Arlt and Heuwieser 2011), they are still needed and should be integrated into the veterinarian curriculum. There are three main reasons for including this in the curricula, these

are the societal need for research capacity within health care professionals, the support of career development and employability and last but not least are these skills important for the clinical professional life (Janicke et al. 2020).
In a study about the perception of EVBM in 2011, between 25.2 % and 76.5 % of the participants, which were vets in the US, responded that they were not familiar with common EBVM-related terms (Mckenzie 2011). Similar results gave a survey from 2013, where only 52.1 % of the participating German vets attributed themselves a high ability to evaluate the quality of literature found (Haimerl et al. 2013).
An international group was formed in order to implement educational approaches that will inspire future researchers and produce evidence-based practitioners (Janicke et al. 2020).
To support a more systematic appraisal literature evaluation, checklists for the different study types have been published (Young and Solomon 2009).

Evidence-based Veterinary Medicine should continue to change and improve, how veterinarians can provide the best available care to clients and patients (Schmidt 2007).

2. Research papers

2.1. Study design quality of research on dogs published in peer-reviewed journals

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Vet Record

ORIGINAL RESEARCH

Study design quality of research on dogs published in peer-reviewed journals

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Abstract

Background: In the past it has been criticised that only a low proportion of well-designed and well-reported studies in some medical specialities is available. The objective of this study was to systematically evaluate the quality of literature about canine medicine published in peer-reviewed journals in relation to six specific veterinary medicine specialities.

Methods: A literature search was conducted and 25 studies per speciality were selected. The quality of the articles (n = 150) published between 2007 and 2019 was evaluated with a validated checklist.

Results: In articles related to all specialities, deficits were found, such as not adequate number of animals in 60.0% of the studies. In 88.0%, information about housing and feeding of the dogs were not specified. In 69.4% of the prospective clinical studies, an ethical approval was reported, and written informed consent of the owners was obtained in 46.2%.

Conclusions: The findings revealed extensive deficits in the design and reporting of studies in canine medicine. The demand for improvement is obvious and should be addressed by authors, reviewers and journal editors in the future. Our results underline that practitioners should critically appraise the quality of literature before implementing information into practice.

KEYWORDS
evidence-based veterinary medicine, literature quality, veterinary specialities

INTRODUCTION

Every year an immense amount of new scientific veterinary information is published. Many authors claim that practitioners should be aware of the latest research findings in order to choose the best examination and treatment options of their patients.[1] According to the evidence-based veterinary medicine (EBVM) manifesto launched by Vet Record, it is necessary to bring the best available evidence into the consultation room so that particular problems can be better handled by the veterinarian and that clients are better informed about the options they are given.[2] The latest scientific information is usually brought to the veterinarian via scientific journals. Most of the research articles go through a peer-review process in order to ensure the high quality and scientific relevance of the studies published.[3]

Nevertheless, it has been claimed that the practitioner has to be able to appraise the evidence and quality[4] because articles in scientific journals may be of low quality and prone to bias.[5,6] Due to the packed curriculum of veterinary studies, however, the ability to appraise the quality of studies is hardly trained in many veterinary schools.[7] This means that many veterinarians may not be sufficiently aware of possible weaknesses within the scientific literature.[8]

In order to help practitioners to appraise published studies, an online resource has been published: https://learn.rcvsknowledge.org/course/view.php?id=2

For the classification of the different types of information, evidence levels were defined[9] and a 'staircase of evidence' was developed.[6] Meta-analyses and randomised controlled trials (RCTs) are the sources of information that have the lowest risk of bias. Well-conducted meta-analyses can help practitioners by providing overall conclusions after statistically summarising the results of different randomised, controlled studies focussing on a specific clinical problem. Sadly, in veterinary medicine, only a few meta-analyses have been published to date.[10] Opposed to that is information belonging to the weakest level of evidence; for example, expert opinions or single case reports. These sources of knowledge are considered to have a high risk of bias.

Next to the levels of evidence, other aspects need to be taken into account for appraisal of the quality of research papers. These aspects include, for example, the number of experimental animals or samples used, the appropriateness of statistical methods, the handling of missing data and the objectiveness of the discussion.[11] To support a more systematic appraisal literature evaluation, checklists have been published.[12]

Quality deficiencies in veterinary literature have been identified in peer-reviewed veterinary journals in recent years.[13–16] For example, by taking a closer look on the literature on reproduction in dogs, Arlt et al.[17] found that the majority of publications reviewed referred to low evidence levels and did not draw sound conclusions. Simoneit et al.[11] compared the literature on bovine, canine and equine reproduction and confirmed a low quality of many RCTs. Substantive deficits exist likewise in the reporting of publications on bovine and canine trials as well as in bovine and porcine conference proceedings.[18–20]

In the context of the identified quality deficiencies, the question arises if limitations vary between veterinary specialities.

The objective of this project was, therefore, to evaluate the quality of studies on dogs related to six different veterinary medicine specialities: cardiology, internal medicine, neurology, orthopaedics, reproduction and surgery. The quality was assessed with a validated checklist published by Arlt et al.[17]

MATERIAL AND METHODS

A literature search in the databases PubMed (www.pubmed.gov) and CAB Abstracts (www.cabdirect.org/) was conducted on 31 October 2020.

The following search keywords were used: Clinical trial AND dogs AND speciality. For each search procedure *speciality* was replaced by cardiology, internal medicine, neurology, orthopaedics, reproduction and surgery. Terms were connected with the Boolean operator 'AND'. The obtained bibliographic records were transferred into six lists using Endnote (Alphasoft GmbH, Frankfurt am Main, Germany).

The publications found for cardiology were 2981 (PubMed) and 88 (CAB Abstracts), internal medicine 7730 (PubMed) and 906 (CAB Abstracts), neurology 953 (PubMed) and 106 (CAB Abstracts), orthopaedics 523 (PubMed) and 507 (CAB Abstracts), reproduction 6403 (PubMed) and 525 (CAB Abstracts) and for surgery 7698 and (PubMed) 5192 (CAB Abstracts). The search lists were merged together, and duplicates were deleted.

We assigned an individual number to every article. From each list 50 articles were selected with a random number generator (https://rechneronline.de/zufallszahlen/).

Specific inclusion and exclusion criteria for articles were defined before the literature search was conducted. Publications had to be in English or German language and published between and including 2007 and 2019.

Case reports or case series with a number of animals lower than $n < 10$, opinions or clinical experiences and abstracts with less than 500 words were excluded.

Availability of the articles via internet or the veterinary libraries of Berlin, Hannover, Gießen, Leipzig or Munich was necessary for inclusion of the articles into the study. Papers which were not available and could not be obtained via inter-lending were excluded.

Studies or case reports without statistical analysis and studies on other species such as humans, cats or other were excluded. In addition, in vitro studies were not included.

Studies were defined as interventional studies if the researchers applied interventions in a retrospective or prospective manner. The definition of observational studies comprised cross-sectional, cohort or case control studies and case reports (with $n > 10$), in which the investigator did not act upon study participants, but instead observed natural relationships between factors and outcomes.[21]

The number of articles which met the inclusion criteria from the initial randomly selected 50 articles per speciality were 28 for cardiology, 26 for internal medicine, 29 for neurology, 28 for orthopaedics, 30 for reproduction and 27 publications for surgery. For further article selection and analysis of the data, the software SPPS (Version 25.0; SPSS Inc., Munich, Germany) was used. For the second randomisation, SPSS 'Random sample of cases' function was used to obtain the final 25 studies per speciality.

From these final 150 articles, 134 articles were accessed via online databases, nine papers were retrieved in the veterinary library of the University of Berlin and two articles were obtained via inter-lending from other libraries.

The assessment of the articles using the checklist (Appendix 1) was trained in a pretest with 10 articles by three investigators. The results were compared, and the classification was standardised where necessary. Only single assessment results varied among the three investigators, variation was in no case more than one grading point. As repeatability of classification conducted by the three independent investigators was substantial, only one investigator continued with the assessment.

For evaluation of the literature, a slightly modified version of the checklist developed in 2010 by Arlt et al.[17] was used. The checklist assesses the parameters 'material and methodology', 'study design', 'statistics', 'presentation and information content', 'practical applicability' and 'conclusions', whether the data are sufficient to draw sound conclusions.

One modification was that the option of choosing 'neutral' was not available for this study. The answer categories are a scale from 'strongly agree', 'agree' to 'disagree' or 'strongly disagree' or 'not determined'.

Furthermore, the authors agreed on strict assessment patterns: if no information regarding a specific item of the checklist was given in the article, the parameter was set 'disagree'. If information for a

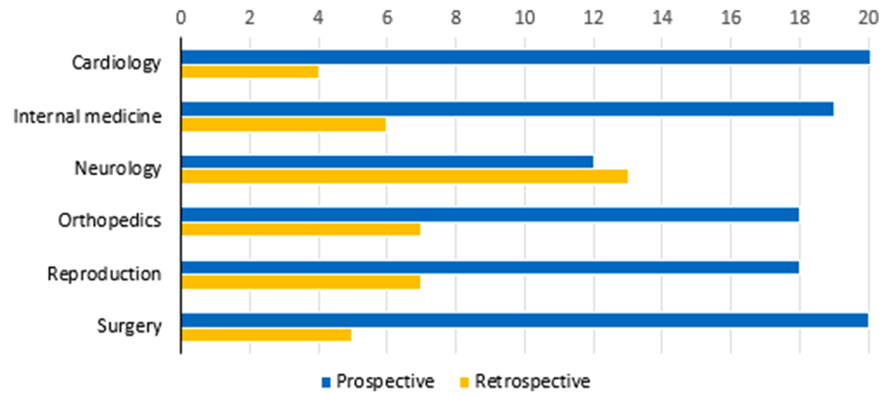

FIGURE 1 Number of articles per veterinary speciality with a prospective versus retrospective approach ($n = 150$)

specific parameter was given partly, for example if age or breed of the dogs was given for some but not all animals, this item was also categorised as 'disagree'. Only if the information of the checklist parameter was given for all dogs used in the study, the answer was set 'agree'.

In addition to the items of the checklist, the ownership of the dogs used for the trials was documented. Every prospective study was checked for information on owners' consent and if an ethics committee approved the study.

Statistical analysis

All statistical analyses were conducted in IBM SPSS for Windows (Version 24.0; SPSS Inc.). Categorical data were presented descriptively as raw numbers and percentages. To identify differences between the specialities, the non-parametric Mann–Whitney *U*-test was used as indicated by the distribution. Statistical significance was set at $p < 0.05$.

RESULTS

General information about the papers

The selected 150 articles were published in 62 different journals, 108 (72.0%) were prospective and 42 (28.0%) were retrospective. Taking a closer look at the specialities, cardiology had the highest proportion of prospective articles ($n = 20$ articles, 80.0%) and neurology the most retrospective studies ($n = 13$ articles, 52.0%, $p < 0.05$) (Figure 1).

Analysing the countries of the affiliation of the authors revealed that 30 different countries were represented in total. The majority of authors ($n = 39$ articles, 26.0%) belonged to institutions in the US, followed by the UK ($n = 17$ articles, 11.3%), Germany, Switzerland and China (each $n = 8$ articles, 5.3%).

Considering the study design, 91 of 150 appraised publications were classified as interventional studies (60.7%) and 59 were observational studies (39.3%, Figure 2). The most interventional studies were found in surgery, with 19 articles. The most observational studies ($n = 15$) were published in the field of neurology ($p < 0.05$).

The results of the evaluation of materials and methodology of the 150 studies revealed that the objective was given for most of the studies (98.6%) (Figure 3a). When it comes to the housing of the animals used in the clinical studies, it was described in 12.0% of the 150 articles (Figure 3b). The housing of the dogs was more often documented for dogs which were not client owned but bred or kept as experimental animals.

When it comes to the specification of the inclusion criteria of the dogs, most authors of articles on internal medicine, neurology and surgery documented them. However, in 11 (44.0%) articles on cardiology and nine (36.0%) on orthopaedics and reproduction, respectively, inclusion criteria were not specified (Figure 3c).

Demographics of the sample population

In 98 (65.3%) articles, the breeds of the dogs used in the study were documented. The proportion of articles including complete breed information was highest in neurology (80.0%), cardiology and surgery (each 76.0%) (Figure 3d).

In 25 (16.6%) out of 150 studies, the age of all dogs was given (Figure 3e). More specifically, in none of the articles on reproduction the age of all enrolled dogs was specified, while the highest proportion of articles including age information was found in studies on surgery ($n = 8$, 32.0%, $p < 0.05$).

Study size of the evaluated literature

The number of the animals used for the study was given in most of the articles of all different specialities. For two studies, one on reproduction and one on orthopaedics, the authors did not specify the number of enrolled animals. The median sample size for all included studies was 31 dogs (Q1: 16; Q3: 64). For the different specialities, the median sample size was mostly homogenous (Table 1).

For 90 (60.0%) of the 150 articles, the number of animals should be considered not adequate (Figure 4a). The sample size was predominantly too small in neurology ('strongly disagree' and 'disagree': 19 studies) and the most adequate in reproduction trials ('strongly agree' and 'agree': 13 studies, $p < 0.05$). A power

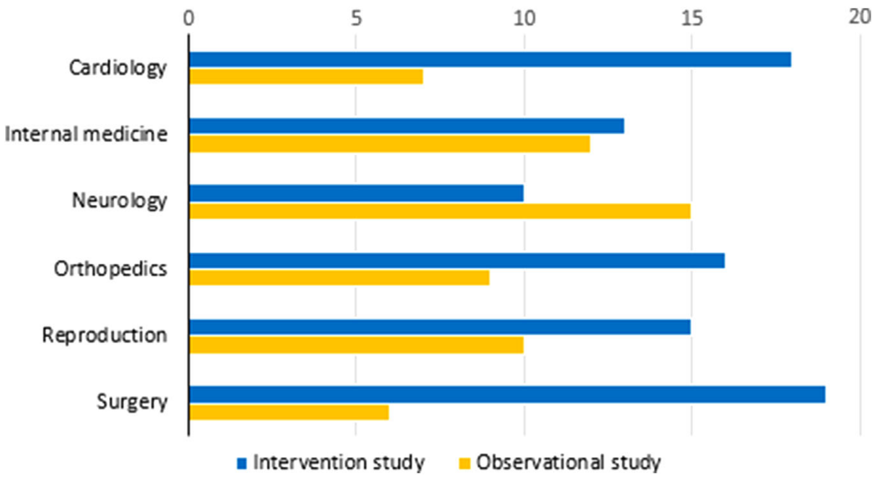

FIGURE 2 Number of articles per veterinary speciality with an interventional versus observational approach ($n = 150$)

TABLE 1 Median sample size and quartile (Q1/Q3) of 25 studies per veterinary speciality (six) and total ($n = 150$)

Speciality	Median sample size	Quartile Q1	Quartile Q3
Cardiology	32	22	207
Internal medicine	31	14	53
Neurology	33	15	56
Orthopaedics	36	19	95
Reproduction	35	18	74
Surgery	25	16	40
Total	31	16	64

calculation in order to determine the sample size of a clinical study was documented for less than 45.0% of the articles.

Statistical analysis

For the adequacy of statistical analysis of the studies three main items were reviewed, which were the description of statistics, the number of animals and information about handling of missing data (Figure 4).

In total, the description of the statistics was adequate and comprehensible in 95.3% of the articles. In cardiology, internal medicine and surgery two articles were identified that did not fulfil the criteria (Figure 4b). Although p-values were given, there was no information on applied statistical tests.

When it comes to the handling of missing data, in 48% of the studies potential missing data were described. For the specialities surgery and internal medicine authors of 15 articles each (60.0%) referred to missing data, while for orthopaedics and reproduction this was true in eight articles (each 32.0%, $p < 0.05$) (Figure 4c).

Ethical approval and owners consent

The evaluation of the prospective studies regarding an ethical approval revealed no differences between the specialities. For 71.4% of cardiology studies, 73.7% of internal medicine studies, 75.0% of neurology studies, 77.8% of orthopaedic studies, 62.1% of reproduction studies and for 64% of surgery studies an ethical approval was documented.

The results of the assessment for ownership information and information about informed consent of the owners led to four potential outcomes (Figure 5). Either the dogs were experimental animals owned by the research institutions, the origin of the dogs was not described, an informed consent was given by the owners or informed consent for privately owned dogs was not documented. For research in the field of cardiology in 11 of the articles (44.0%) experimental animals were used. The written consent was best documented in articles on internal medicine with 10 articles (52.6%) and neurology with nine articles (75.0%, $p < 0.05$). There were two articles in surgery and two in reproduction in which the origin of the dogs was not documented.

DISCUSSION

Veterinarians need to apply the best available evidence and inform their clients based on the latest research findings. In that regard, practitioners have to read and appraise the evidence and quality of articles published in scientific journals. The use of invalid or biased information may lead to misleading diagnoses or treatment failures.

Studies which identify limitations of recently published studies may be helpful in terms of pointing out factors which should be focused on when reading scientific articles. In addition, they may help to improve planning and reporting studies.

This project evaluated with the help of an approved but slightly modified checklist the quality of 150 studies belonging to six different veterinary medicine specialities. The six specialities were chosen because of their clinical relevance and relevance in the veterinary curricula. It has to be noted that no international uniform definitions for the specialities exist and that they may overlap considerably. In addition, some authors see the term 'internal medicine' as a superordinate

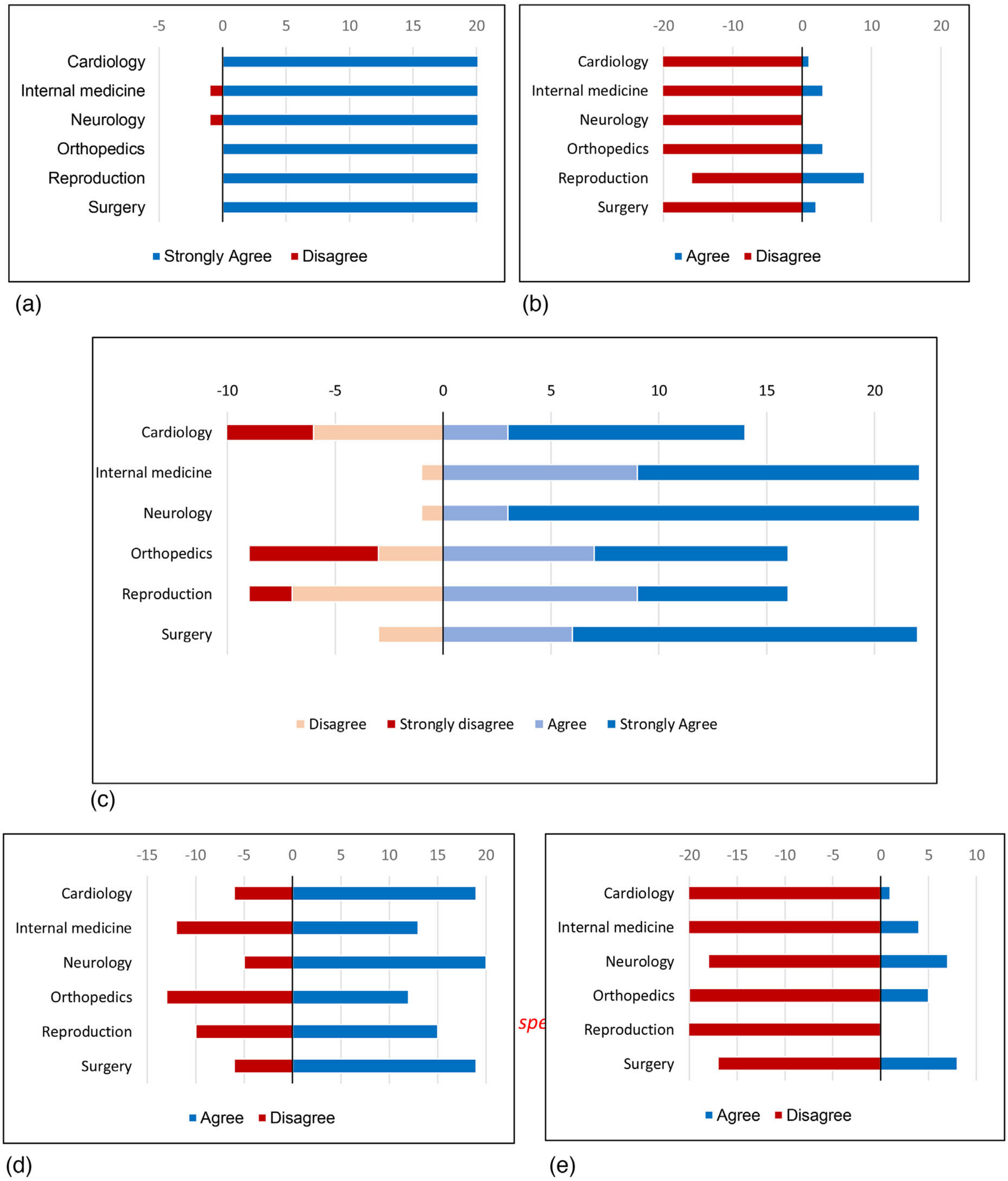

FIGURE 3 Critical appraisal of the material and methodology statements (a–e) of 150 veterinary studies within the six veterinary specialities (each 25 studies) via approved checklist and agree/disagree scale: (a) the objective of the study is presented; (b) housing information about the animals is given; (c) inclusion criteria about the animals is given; (d) breed of the animals is given; (e) the age of the animals is given

and general term, which may encompass fields such as endocrinology, neurology, cardiology, oncology, infectious and immune-mediated diseases.[22] The definition of fields as speciality or sub-speciality and their relevance may depend on the local conditions and can differ therefore considerably. For this project, neurology and cardiology were defined to be separate specialities.

It is noteworthy that most prospective studies were found in surgery and cardiology. This might be due to the better standardisation possibilities of the patients or different research approaches within these specialities. Another hypothesis could be that pharmaceutical companies are more willing to fund prospective trials in specific specialities. In comparison with human medicine, veterinary medicine has been historically allotted less funding[23] but it should be assessed in future research projects if funding really varies between veterinary specialities.

The high proportion of retrospective neurology studies might be due to the more reviewing character of the best-practice treatment for known diseases

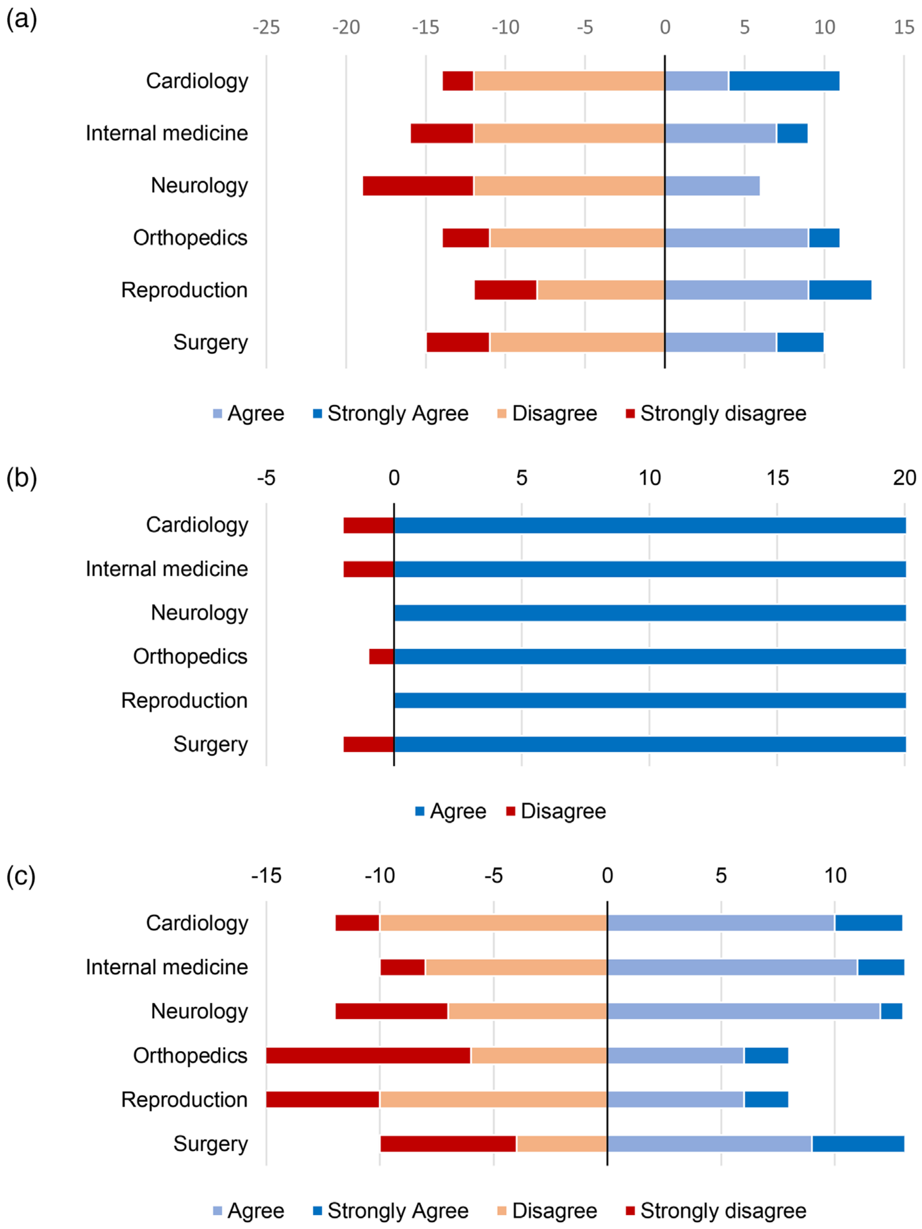

FIGURE 4 Outcome of statistical review of six veterinary specialities (each 25 studies) via approved checklist with an agree/disagree scale ($n = 150$): (a) number of animals adequate; (b) description of statistics is adequate and comprehensible; (c) handling of missing data is adequate and comprehensible

like epilepsy or the difficulty of having enough animals or funding for prospective studies. These circumstances are also reflected when it comes to the study type. The most interventional studies can be found in surgery, the lowest number in neurology. This seems to indicate that surgery trials may be more designed to assess new treatment protocols or procedures rather than evaluating established methods. According to our results, most studies were prospective. In the context of an appeal by Kastelic,[24] who described a shortage of prospective randomised, controlled studies in veterinary medicine in 2006, it seems that the situation has improved.

It is remarkable that for nearly 90% of the studies no details about housing and husbandry of the dogs were given. This is in accordance with earlier findings after assessing literature on canine reproduction.[17] This was especially the case for privately owned dogs. It can be hypothesised that housing and feeding was so heterogeneous that a detailed description was regarded not possible or not reasonable. However, depending on the research question it might be of interest if dogs, for example, are kept in kennels or in the household and if they were fed a conventional diet or raw meat. For experimental animals, housing and feeding were usually specified in detail. Articles on reproduction seem to stand out with nine articles mentioning the housing.

The number of enrolled dogs was given in most articles, even for retrospective studies with high numbers of animals. When it comes to the specification of inclusion criteria, most deficiencies were found in

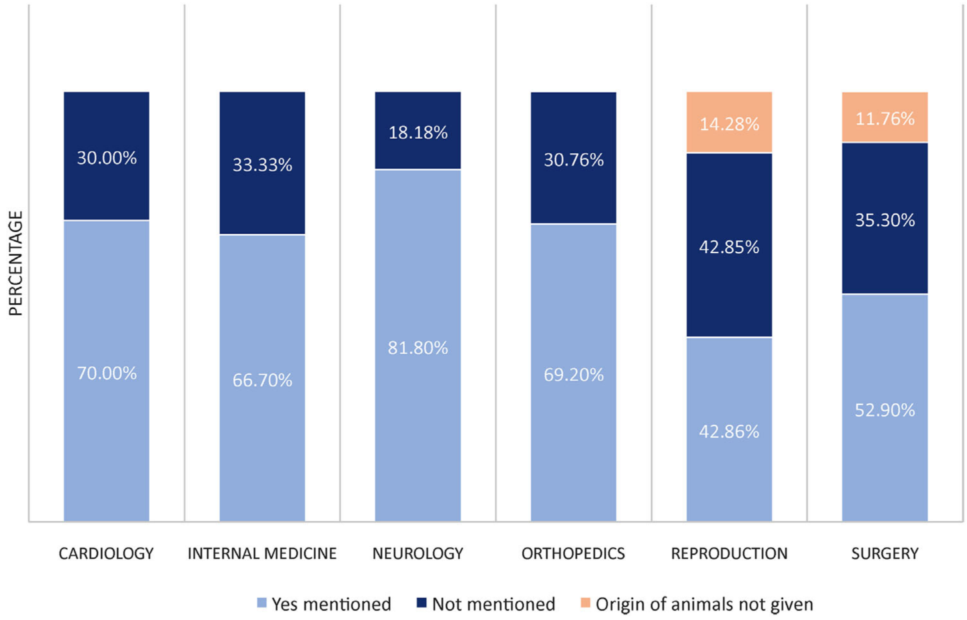

FIGURE 5 Percentage of articles with client owned dogs per speciality that mentioned the written informed consent of owners in prospective studies ($n = 80$)

cardiology and orthopaedics. Clear criteria and definitions of diseases should always be given in scientific articles. In many trials, the presence of specific diseases or conditions was used as an inclusion criterion. For readers, definitions of inclusion and exclusion criteria are essential to decide if a present case is comparable to the study population or not.

The breeds of the dogs were given in most articles, although this information was missing in a higher proportion in articles on internal medicine and orthopaedics. Since the risks of the development of many diseases such as hip dysplasia, incontinence and heart diseases are breed specific, it is important to report the breeds of the dogs used in studies. Besides, on the occurrence and severity of diseases, breeds may also have effects on parameters like treatment outcomes, side effects, survival time or recurrences.

The age and the weight of the dogs often were documented as a range, mean or median. Standard deviations or quartiles or individual data were not given in all articles, which does not allow the reader to get an impression of whether particularly old or young animals were included in the study. Especially in the context of, but not limited to, trials on age dependent diseases or studies with small sample sizes, these data should be available. It is noticeable that in our sample the individual age of the dogs was given in none of the articles on reproduction. For the studies on cardiology, the age of the dogs was given in only one publication. Also, in the majority of the articles belonging to the other specialities information about the age was missing. The age of a dog is a crucial confounder to nearly every major cause of mortality,[25] treatment success and side effects and therefore relevant for almost all diseases.

A documentation of a sample size calculation was presented in only few articles. This is in accordance with the findings of Wareham et al.,[26] where only 14.3% reported a sample size calculation and Giuffrida[16] with 22.0%. In addition, in most studies the number of animals was low. This fact was discussed by most authors as a limitation of the study. Nevertheless, an appropriate number of animals should be included in all trails since some authors even regard studies with small sample sizes as unethical because the results are highly prone to bias.[27] Our findings are in accordance with conclusions of Girolamo and Reynders[23] which compared interventional human versus veterinary RCTs and revealed that only 2% of veterinary RCTs reported a power calculation. They also reported that the median sample size for crossover trials was eight patients and stated that this might be due to additional expenses for bigger sample sizes. The low prevalence of rare diseases might also play a role. The median sample size seems to have improved as it is 31 according to this study and 30 animals within the trial of Wareham et al.[26]

A limitation of this study is that we did not recalculate the power of the studies. A recalculation, however, would not have been reasonable for most studies because main target parameters were not specified for most studies.

Documentation of handling of missing data is lacking in a high proportion of articles. Haimerl et al.[28] stated that this might be due to incomplete reporting and needs not a priori be judged as low quality. In both human and veterinary medicine research articles, key pieces of information are often lacking due to loss or withdrawal of patients or samples and might lead to biased results.[29] In order to prevent a type I (i.e. false positive) error[30] an 'intent-to-treat' (ITT) analysis should be performed with the help of the CONSORT diagram.[29] If patients had to be excluded or got lost in the follow-up the missing data should be clearly identified in the 'Results' section.[12]

The description of the statistics was adequate in most of the articles examined. In many articles more complex statistical tests were used. This is in contrast to the study of Girolamo and Reynders[23] who found that in veterinary articles mostly just statistical significances were given.

Regarding ethical approvals, it is noteworthy that around 30.5% of the reviewed published clinical trials did not contain appropriate information. About 46.0% of the surgery articles and 38.0% of the reproduction articles did not report ethical approvals. Especially for surgery studies, one should assume that an ethical approval is necessary, due to the interventional character. There might be a difference between academic versus privately assessed studies. The latter may not have to obey the same regulations. This issue was not assessed in this research project but might be interesting for follow-up studies.

When it comes to ownership and written informed consent of the owners, it is remarkable that in research on cardiology far more experimental dogs were used than in the other veterinary specialities. In the field of internal medicine and neurology, the authors, the reviewers or the editors of the journals seem to pay more attention to the documentation of written informed consent of the owners because it was reported for about 52.0% and 75.0% of the clinical trials, respectively. Nevertheless, there seems to be an improvement as Lund et al.[31] found 91.0% of their evaluated studies did not state a written informed consent.

It is important to accept that just because a study has been published it does not necessarily mean it is any good[32] and may have significant insufficiencies regarding the study design or reporting.[28] Nevertheless, veterinary practitioners should rather rely on good and actual peer-reviewed journal articles than on information of questionable quality or potential outdated sources.[33] Evidence-based medicine is nowadays a common and established method in human medicine, while high-quality evidence base is still lacking in many areas of veterinary medicine.[34] The number of RCTs increased in human medicine over the time period from 2006 to 2013 by 16.0%, while in veterinary medicine the amount of RCTs was still low and lacking adequate reporting of key methodological domains.[23] The impact of missing methodological quality has also been reported by Sargeant et al.,[20] as there is evidence that these deficiencies lead to a likelihood of positive outcomes being reported. This publication bias may lead to misinterpretation of research results, and therefore needs to be taken into account when reading papers and especially when working on reviews, systematic reviews and meta-analyses.[35]

To the authors' knowledge, this is the first project assessing the quality of articles in relation to veterinary medicine specialities. It seems that research in different specialities is influenced by different factors, which cannot be deduced by the presented evaluation results. Nevertheless, these differences provide important research approaches. After all, it needs to be stated that in all specialities methodology and reporting of research results needs to be improved. Although reporting checklists are available,[36] such as ARRIVE for animal research or STROBE for observational studies, which seem to improve the recording of RCTs,[37] there are still deficits present. It can be assumed that these checklists are not consulted to the full extent by some authors and reviewers. This is in accordance with the findings of a study by Grindlay et al.[38]

In order to improve the quality of scientific literature, it is important that authors, reviewers and journal editors pay attention to proper reporting. To support this, reporting guidelines should be implemented within education of veterinary students and researchers. In order to achieve better case management in veterinary practice, the recently published evidence-based veterinary medicine manifesto[2] should be heeded by all veterinarians and researchers.

The results of this study are in accordance with earlier studies, which appraised the quality of published literature and detected deficiencies.[11,17,39] The overall quality of the studies seems to have improved slightly but there are still some attributes such as sufficient sample size, missing data handling and ethical approvals, which need further attention.

Limitations of the own study

There are some limitations of the present study. Even though there was a pretesting with three raters assessing study quality, the investigation was performed by just one person, which may have led to bias. This approach, however, has been used in several other studies before.[17,40,41] Furthermore, the person who evaluated the literature was not blinded to any manuscript details during the evaluation, which potentially may have led to biased interpretation. Lack of blinding may lead to biased assessment in terms of geographical origin or gender of the authors. It has been shown, for example, that human medicine studies from Asia are five times more likely to be rejected from publication in a journal than studies from European or American countries.[42] In addition, Wareham et al.[39] found that RCTs are more likely to be published if they had pharmaceutical industry funding or involvement. While Hopewell et al.[43] found that studies with positive outcomes are more likely to be published. Therefore, the selection of the studies used for this literature search may have been biased based on a publication bias.

Another limitation is the relatively small sample size of 25 articles per speciality. Since a number of 25 articles per speciality led to a total number of 150 articles eligible for a throughout assessment, the inclusion of more literature was not possible within this project. In that regard it may be worthwhile to re-evaluate some of the presented speciality-specific findings on a larger scale with a high number of articles and to start scoping reviews with involvement of librarians.

CONCLUSION

The findings of this study revealed deficits in methodology and reporting of studies published in peer-reviewed journals in general, with moderate variations between different veterinary medicine specialities. In order to provide veterinary practitioners and clinicians reliable, valid and concise information, authors, reviewers and journal editors should pay attention to proper design and reporting by making use of the different developed guidelines. According to our findings, authors should pay more attention to aspects such as sample size calculation, details of the animals such as breed, housing and feeding, inclusion and exclusion criteria and handling of missing data. Even if there is no data missing, this should be mentioned in the paper for clarity.

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Since no animals were used in context of this manuscript, no ethical permit was required.

AUTHOR CONTRIBUTIONS

All authors drafted and revised the manuscript.

CONFLICT OF INTERESTS

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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2.2. What kinds of dogs are used in clinical and experimental research?

Schulte, E.; Arlt, S.P. 2022:

Animals. 2022, 12, 1487, doi:10.3390/ani12121487 animals

Article

What Kinds of Dogs Are Used in Clinical and Experimental Research?

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Simple Summary: The objective of this study was to evaluate the signalment of dogs used in veterinary research in six different specialties. In total, 150 randomly chosen clinical studies (25 studies per specialty) published between 2007 and 2019 were evaluated for the breed, sex, neuter status, age, and weight information of the dogs used. Breed information was given for 5.7% of the included animals. Beagles were used 1.9% of the time, which was a less significant role in research than we expected. Information about the sex of the dogs was lacking for 16.2% of the included animals, while age and weight information were missing for 22.7 and 32.7%, respectively. The neuter status was not given in 38.7% of the clinical studies. The results show deficits in the reporting of demographic data for the dogs. The need for an improvement in the documentation and/or reporting of animal signalment is obvious and should be addressed by authors, reviewers, and journal editors in the future.

Abstract: Background: Dogs are widely used in research to answer questions about canine or human conditions. For the latter, research dogs are often used as models, since they are physiologically more similar to humans than other species used in research and they share similar environmental conditions. From a veterinary perspective, research findings are widely based on academic research, and thus are generated under experimental conditions. In that regard, the question arises: do the dogs used for research adequately represent the dog population seen in veterinary practice? It may, for example, be assumed that Beagle dogs are often used as experimental animals. The objective of this study was to evaluate the signalment of dogs used in veterinary research. Furthermore, we aimed to assess other relevant criteria regarding the validity of clinical trials in the context of six different veterinary medicine specialties: cardiology, internal medicine, neurology, orthopaedics, reproduction, and surgery. Methods: A literature search was conducted and 25 studies per specialty were randomly selected. The breed, sex, neuter status, median age, and median weight of the dogs used for clinical studies (n = 150) published between 2007 and 2019 were evaluated. Results: In total, 596,542 dogs were used in the 150 trials. Breed information was given for 33,835 of these dogs (5.7%). Of the latter, 1.9% were Beagles. Nine clinical trials exclusively used Beagles. The most frequently used breeds were German Shepherds (7.3%), Labrador Retrievers (6.7%), and Golden Retrievers (4.7%). The major reporting deficits found were missing breed specification in 25.3% of the articles; missing information about the sex of the dogs in 16.2%; missing age and weight information in 22.7 and 32.7%, respectively; and missing neuter status in 38.7% of the clinical studies. The median sample size was 56 (Q1:29; Q3:365) dogs. Conclusions: The presented project revealed that Beagle dogs represent only a small proportion of dogs in veterinary research. Based on the evaluated publications, it seems that some relevant dog attributes differ between the specialties. The results, however, show deficits in the reporting of demographic data for the dogs. The need for an improvement in the documentation and/or reporting of animal signalment is obvious and should be addressed by authors, reviewers, and journal editors in the future.

Keywords: research dogs; Beagles; breed; evidence-based medicine; literature quality; trial dogs

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1. Introduction

In medical research, dogs have been and still are widely used as testing animals [1], although worldwide, actual and precise figures are not easy to retrieve because relatively few countries collate and publish research-animal statistics [2]. It has been estimated that 79.9 million animals, out of which 207,724 were dogs, were used worldwide for experimental or scientific purposes in 2015 [3]. This was a 36.9% increase in the equivalent estimated figure of 58.3 million animals in 2005 [2,3]. The most widespread use of experimental animals occurs in China, followed by Japan and the United States [4]. Around 800,000 laboratory animals were used in 2019 in the US, of which 7% (56,000) were dogs [5]. In the EU from 2017 to 2018, the number of animals used in research decreased by five per cent to around nine million animals, of which 0.3% (27,000) were dogs and cats [6]. The purposes of research projects on dogs include gaining basic biological knowledge; answering questions regarding human health by using dogs as models for the development of drugs, diagnostic tests, vaccines, and medical devices; and answering questions directly linked to canine physiology or diseases [7]. Dogs are often preferred as models for human conditions because they are physiologically and clinically more similar than other species such as mice [8], and pet dogs also share the environmental conditions of their owners. In addition, the domestic dog, *canis familiaris*, reportedly bears over 450 diseases; approximately 360 of these are analogous to human diseases [9]. These analogous conditions include diabetes, cancer, epilepsy, eye diseases, and autoimmune diseases, not to mention the high numbers of rare monogenetic diseases [8]. It has been stated that the most suitable and frequently utilized breed in clinical trials is the Beagle. These dogs are commonly kept in kennels in homogenous groups based on age, weight, sex, and neuter status in the research facilities of universities or pharmaceutical companies [10]. Beagles are medium-sized and have a short coat and an even temperament, which makes them particularly suitable for medical research in contrast to other breeds [11]. These advantages make it easier to standardise specific and relevant conditions in research settings and help keep the costs of the experiment lower [12].

Worldwide, more than 354 dog breeds are registered at the FCI (Federation Cynologique Internationale) [13]. Searching for "Beagle dog" in the PubMed database for results between 2007 and 2019 (http://www.pubmed.gov, accessed on 21 May 2022) leads to more than 4790 results. When performing the same search with the breed "Labrador dog", which has been the most popular breed in the US since 1991 [14], the results are much less (1008 results). These figures support the assumption that Beagles may be the most utilized research dogs by far.

Both dog breeds can be found in the top ten list of the most popular dog breeds in the US [15] (Table 1). Beagles often serve as models for research focusing on human health, such as the toxicology of medications [16]. Research on Beagles has led to various relevant findings for human medicine, such as information about infections with *Helicobacter Pylori* [7], or better insights into the effects of the frequency of tooth brushing [17].

Depending on the research question, alternatives for the use of research dogs may be the enrolment of client-owned dogs or the retrospective evaluation of medical records. Findings from these approaches might even better represent the heterogeneity of dogs seen in daily practice and better address real clinical conditions. However, depending on the research question, a high level of heterogeneity regarding breed, age, sex, weight, neuter status, housing, feeding, and other parameters in a study population may lead to a significant influence of confounders [18,19]. If potential confounders are not taken into account during the analysis and interpretation of research results, this may lead to biased outcomes and conclusions. There is evidence that the sex, weight, age, breed, and neuter status of the dogs that take part in a clinical trial are important when it comes to different conditions and diseases, such as joint disorders [20,21], metabolic conditions [22], and periodontal diseases [23]. In addition, breed differences significantly affect the incidences of specific diseases such as pyometra [24], dilatative cardiomyopathy [25], and granulomatous colitis [26], as well as sex-steroid-influenced diseases such as diabetes [27] and hyperadrenocorticism [28].

Table 1. Top 10 dog breeds in the US in 2019 and the number of publications found in PubMed for each breed (search date: 21 May 2022).

Dog Breed	2019 Rank	Number of Publications Between 2007 and 2019 Resulting from the Breed Used as a Search Term in PubMed in May 2022
Labrador Retriever	1	824
German Shepherd	2	625
Golden Retriever	3	551
French Bulldog	4	115
Bulldog	5	488
Poodle	6	243
Beagle	7	5.199
Rottweiler	8	214
German Shorthaired Pointer	9	45
Pembroke Welsh Corgi	10	49

The objective of this study was, therefore, to evaluate what kinds of dogs were utilized in clinical trials. We aimed to assess and compare information about the dogs, including the breed, sex, age, weight, and neuter status in the context of six different veterinary medicine specialties. In addition, we aimed to evaluate the extent to which Beagles have been used in veterinary research.

2. Material and Methods

A literature search in the databases PubMed (http://www.pubmed.gov accessed on 31 October 2020) and CAB Abstracts (https://www.cabdirect.org/, accessed on 31 October 2020) was conducted on 31 October 2020. The same literature search and selection process for articles was used and described in detail in another research project [29] assessing different literature parameters. In brief, the following search keywords were used: clinical trial AND dogs AND specialty. For each search procedure, "specialty" was replaced by cardiology, internal medicine, neurology, orthopaedics, reproduction, or surgery.

Publications had to be in the English or German language and published in or between the years 2007 and 2019. Case reports or case series with a number of animals lower than $n < 10$, opinions, clinical experiences, and abstracts with less than 500 words were excluded. Studies or case reports without statistical analysis and studies on other species, such as humans or cats, were also excluded. In addition, in vitro studies were not included. From the final 150 articles, 134 articles were accessed via online databases, nine papers were retrieved in the veterinary library at the University of Berlin, and two articles were obtained via inter-lending from other libraries. As a first step, the literature was evaluated using a slightly modified version of the checklist developed in 2010 by Arlt and Heuwieser [30]. The results have been published in a previous article [29]. In addition to the validated checklist, the following items were assessed for the presented project: number of dogs, number and type of dog breeds, gender, neuter status, median weight, and median age.

Statistical Analysis

All statistical analyses were conducted in IBM SPSS for Windows (Version 24.0; SPSS Inc., Munich, Germany). Categorical data were presented descriptively as raw numbers and percentages. To identify differences between the specialties, the non-parametric Mann–

Whitney U test was used as indicated by the distribution. The statistical significance was set at $p < 0.05$.

3. Results

From the 150 examined studies, 108 (72.0%) were prospective and 42 (28.0%) were retrospective. Considering the study design, 91 publications were classified as interventional studies (60.7%) and 59 were observational studies (39.3%). In total, 596,542 dogs were used in the 150 clinical studies assessed in this project. For one study, the number of dogs was not specified; instead, the number of limb fractures over a given period of time was reported. For statistical reasons, we set the number of limb fractures equal to the number of dogs. In 100 articles (66.0%), the breeds of all enrolled dogs were specified, leading to 33,835 dogs with breed information. Out of the remaining 50 trials, breed information was not given at all for 38 studies and was incomplete for 12 studies. Most studies with no or incomplete breed information were retrospective. In several studies, the breed was not specified for all dogs included, but only for the numerical top ten breeds. Analysing breed information in the 12 studies with incomplete data led to another 7792 dogs with given breeds and 5384 with missing information. Overall, breed information was available for 41,627 dogs, which was 6.9% of the overall number of dogs. The overall median number of dogs used in each of the studies was 56 (Q1:29; Q3:365). Retrospective studies had a larger number of included animals (Median: 62; Q1:35; Q3:384) than prospective ones 24 (Q1:13; Q3:41), $p < 0.05$. Out of the dogs with known breeds, 643 dogs (1.5%) were Beagles. In nine studies, the dog population consisted of Beagles only. The median sample size of these studies was 12 dogs (Q1:12; Q3:24). These studies included five experimental studies (two related to human research) and four clinical trials (one related to human research) carried out to determine the effectiveness or administration route of drugs. All studies took place under laboratory conditions. One article was published in each of the years 2007, 2008, 2014, and 2015, two articles were published in 2017, and three were published in 2018. Furthermore, in 32 studies, Beagle dogs were used among dogs belonging to other breeds. In Section 3.4, more information about the dogs used in experimental trials is given. Out of 150 studies, 16 (10.6%) were related to human research using dogs as a model, and three of these used study populations consisting of Beagles only.

Within the individual specialties, the number of Beagles used as clinical trial dogs was heterogenous (Table 2). The greatest numbers of Beagles were used in internal medicine and surgery studies (each $n = 8$, 32.0%).

Table 2. Use of Beagles as trial dogs within six veterinary specialties in 150 clinical trials (25 per specialty).

Specialty	Number of Studies (n = 25 per Specialty)	
	Using Beagles	With Missing Breed Information
Cardiology	4 (16.0%)	7 (28.0%)
Internal medicine	8 (32.0%)	10 (40.0%)
Neurology	5 (20.0%)	5 (20.0%)
Orthopaedics	4 (16.0%)	10 (40.0%)
Reproduction	3 (12.0%)	8 (32.0%)
Surgery	8 (32.0%)	6 (24.0%)
Total	32 (21.3%)	46 (30.7%)

For dogs with a known breed, the proportion of Beagles differed between the specialties. In internal medicine, we found the highest proportion of Beagles, with 12.9%. Orthopaedics followed with 5.6% and cardiology with 4.4%. The proportion was smallest in reproduction, with 0.4% (Table 3).

Table 3. Numbers and proportions of Beagle dogs utilized in clinical trials within six veterinary specialties (*n* = 150).

Specialty	Total Number of Dogs per Specialty (25 Studies)	Total Number of Dogs with Breed Specification	Proportion of Beagles in Relation to All Dogs with Known Breed
Cardiology	3319	850	4.4%
Internal medicine	24,696	286	12.9%
Neurology	2004	639	2.0%
Orthopaedics	433,347	784	5.6%
Reproduction	102,104	744	0.4%
Surgery	31,072	30,532	1.2%
Total	596,542	33,835	1.9%

The highest amount of missing breed information was found in internal medicine (48.0%), followed by orthopaedic studies (40.0%), reproduction (36.0%), cardiology (28.0%), and neurology (20.0%). Only a portion of the dogs used in the 31 prospective studies (20.6%) and the 19 retrospective studies (12.6%) had their breeds specified. The median number of breeds was four for prospective studies (Q1:1; Q3:10), while retrospective studies had a median number of sixteen breeds (Q1:3; Q3:27). For the different specialties, the median number of breeds was one for cardiology (Q1:1; Q3:9.5), ten for internal medicine (Q1:4; Q3:15), nine for neurology (Q1:1; Q3:21), five for orthopaedics (Q1:1; Q3:16), four for reproduction (Q1:1; Q3:8.5), and nine for surgery (Q1:4; Q3:13). For 40 (26.7%) studies, there was only one breed utilized; 14 (56.0%) of these studies were cardiology trials with mostly mongrel dogs. Table 4 lists the US top ten breeds of 2019 and the number of dogs belonging to each breed that have been used in clinical veterinary research worldwide. The popularity of the dog breeds in Europe are similar [31]. These dog breeds seem to play an important role in research, since they make up around 25.2% of all study dogs with given breed information. Interestingly, despite their popularity, Bulldogs were not extensively used in the studies selected in this project.

Table 4. Numbers and proportions of dogs belonging to the US top ten breeds of 2019 used in research (*n* = 150).

Dog Breed	Number (and Percentage) of Dogs of the US Top Ten Breeds of 2019 Used in 150 Clinical Trials
Labrador Retriever	2828 (6.7%)
German Shepherd	3055 (7.3%)
Golden Retriever	1780 (4.7%)
French Bulldog	51 (0.1%)
Bulldog	46 (0.1%)
Poodle	750 (1.8%)
Beagle	640 (1.5%)
Rottweiler	1228 (2.9)
German Shorthaired Pointer	78 (0.1%)
Pembroke Welsh Corgi	1 (0.002%)

3.1. Sex of the Dog Population

In total, the sex of the dogs was specified in 83.8 % (*n* = 150) of the trials (Figure 1). Dogs of both sexes were used in 89 studies (59.3%), solely females in 25 trials (16.7%), and only male dogs in 11 studies (7.3%). Both sexes were predominantly mixed in 22 neurology studies (88.0%) and 20 internal medicine studies (80.0%). In studies relating to reproduction, dogs of only one sex were used in most trials (n = 20, 80.0%). In seventeen studies, female dogs were used (68.0%), and in five studies, both female and male dogs were used. In contrast to the other specialties, the sex of the dogs was determined for all 25 reproduction studies. In around 40% (n = 10) of the studies on cardiology, the sex of the dogs was not documented, followed by six orthopaedic studies and six surgery studies with an unknown sex for the dogs used (24.0%).

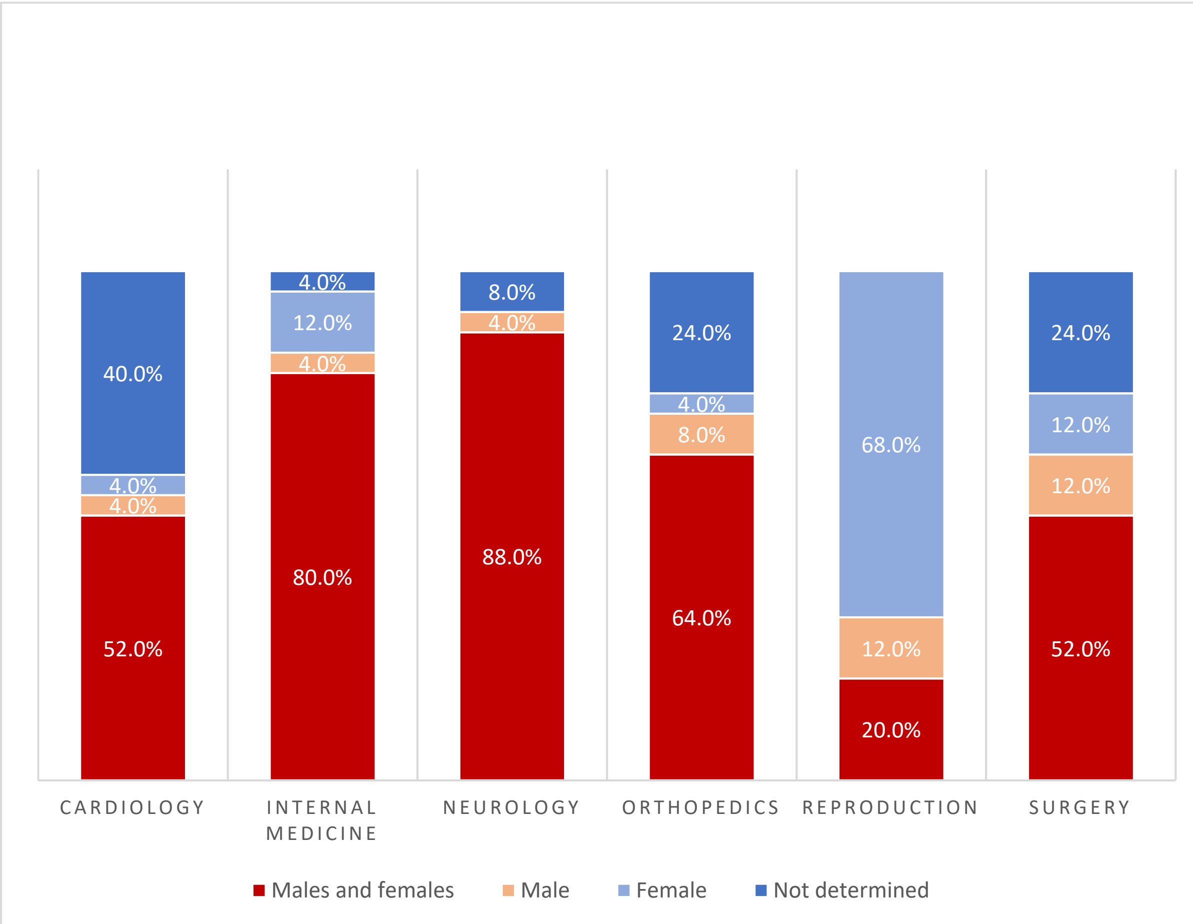

Figure 1. Sex of the dogs utilized in 150 clinical trials within six veterinary specialties (25 each).

Spay and neuter status of the study population. The spay and neuter status of most dogs used in the 150 studies was not specified in 38.7% of the studies (Figure 2). In four studies (2.7%), all dogs used in the trial were neutered. In 34.7% of the studies, both neutered and intact dogs were used, and in 24.0% of the studies, all dogs were intact. Except for studies in the field of reproduction, the neuter status was not specified as an inclusion or exclusion criterion. In 23 studies (92.0%) belonging to the reproductive field, intact dogs were enrolled ($p < 0.05$). In 18 neurology studies (72.0%) and 13 internal medicine (52.0%) studies, both neutered and non-neutered dogs were used. The spay and neuter status of the dogs used was not specified in 16 (64.0%) studies each on cardiology and orthopaedics.

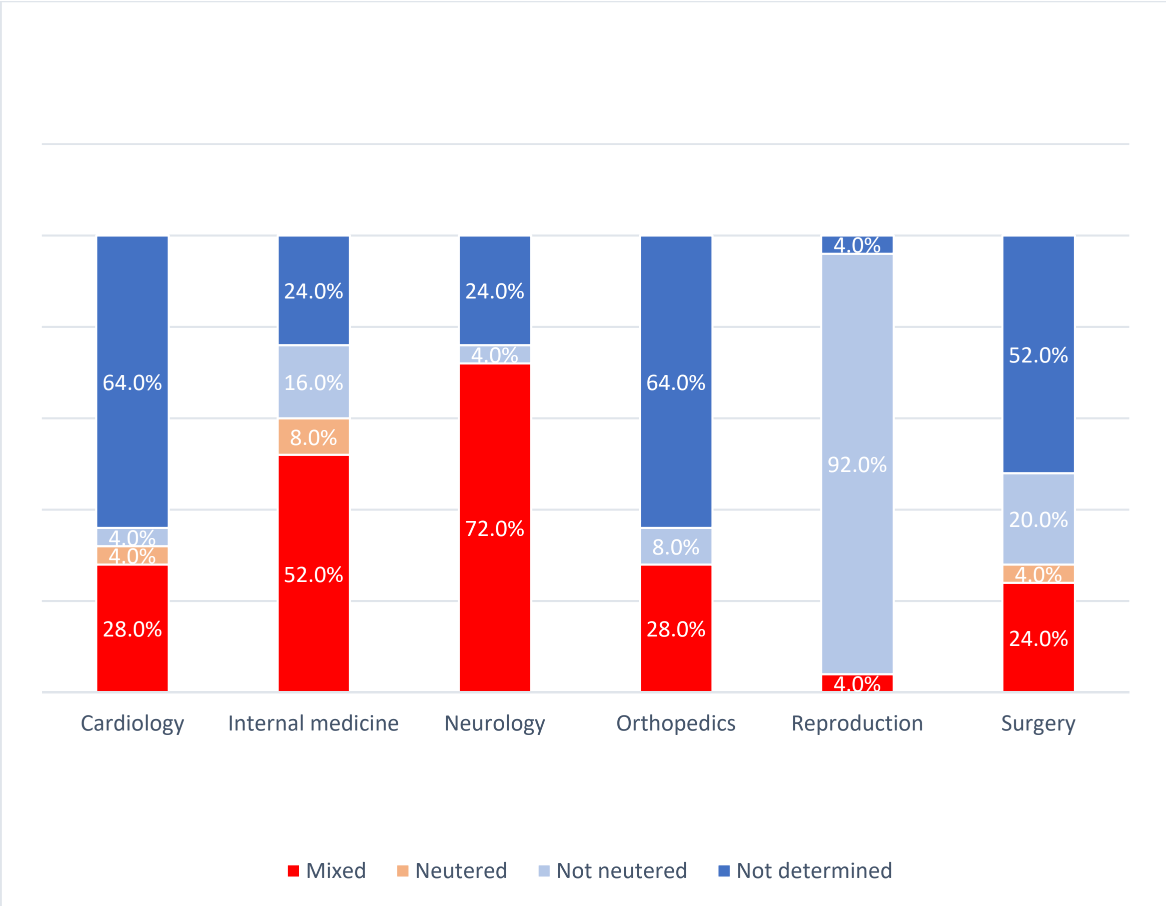

Figure 2. Spay and neuter status of the dogs utilized in 150 clinical trials within six veterinary specialties (25 each).

3.2. Age of the Study Population

Overall, age information was not given in 34 (22.7%) studies (Figure 3). The median age of all dogs with given information was 5.0 years (Q1:2.4; Q3:6.9), the minimum age was 2 weeks, and the maximum age was 12.5 years. In six studies (4.0%), dogs with a median age of under one year were used. Age information was missing most often in cardiology studies (n = 11, 44.0%), followed by reproduction studies (n = 8, 32.0%). The median age for dogs enrolled into cardiology studies was 9.0 years (Q1:6.4; Q3:11.7), internal medicine was 6.0 years (Q1:4.9; Q3:7.6), neurology was 4.4 years (Q1:2.7; Q3:6.9), orthopaedics was 4.8 years (Q1:2,4; Q3:5.6) reproduction was 3.3 years (Q1:2; Q3:5.2), and surgery was 4.0 years (Q1:2.1; Q3:5.45).

3.3. Weight of the Dogs

Weight information was not given in 49 publications (32.7%) (Figure 4). The overall median weight was 20.3 kg (Q1:10.8; Q3:27.2), the lowest median weight of a study population was 3.7 kg, and the highest median weight of the dogs used within one study was 50.3 kg. Weight information was missing most often in reproduction studies (n = 17, 68.0%), followed by neurology studies (n = 12, 48.0%), cardiology and orthopaedics studies (each n = 6, 24.0%), and surgery and internal medicine (each n = 4, 16%). The median weight of the dogs used in cardiology studies was 14.5 kg (Q1:9.3; Q3:22.0), internal medicine was 20.2 kg (Q1:9.3; Q3:23.7), neurology was 19.3 kg (Q1:12.5; Q3:20.6), orthopaedics was 31.2 kg (Q1:25.6; Q3:33.8), reproduction was 17.8 kg (Q1:11.8; Q3:21.1), and surgery was 22.0 kg (Q1:10.7; Q3:25.2). One study in the field of surgery used dogs with an average weight of over 50 kg. The weight differences of dogs used in orthopaedics compared with neurology and cardiology were significant ($p < 0.05$).

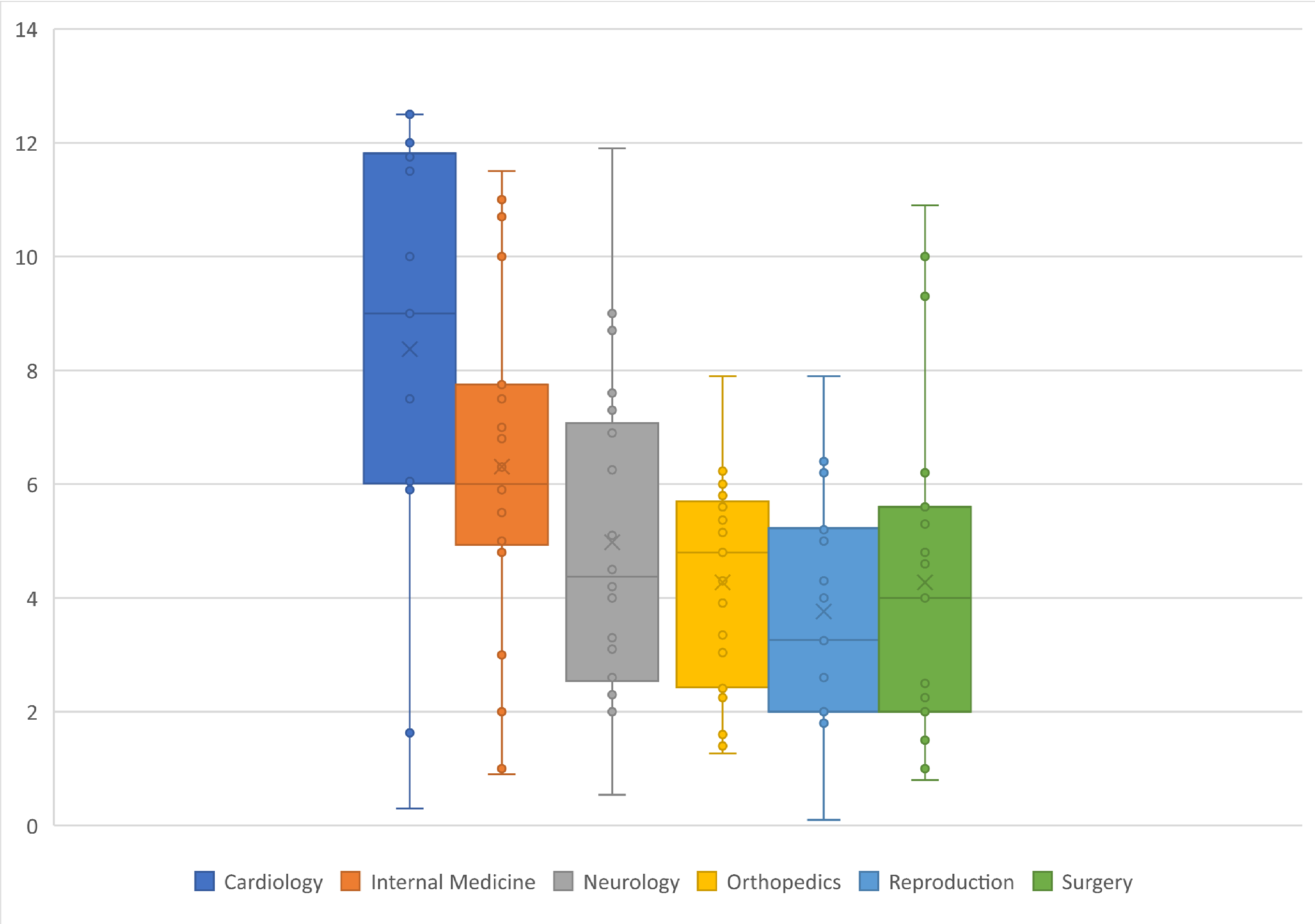

Figure 3. Age (in years) of the dogs utilized in 150 clinical trials within six veterinary specialties (25 each).

3.4. Origin of Study Population and Overall Number of Animals

Information on the ownership of the dogs and the number of dogs used for the different studies has already been presented in a previous paper [29]. The dogs were either experimental animals owned by the research institutions (18.7%), privately owned (76.0%), mixed (0.7%), or the origin of the dogs was not specified (4.7%). For research in the field of cardiology, experimental animals were used in 11 of the articles (44.0 %). The dogs used for the 28 experimental studies had a median age of 2.3 (Q1:2; Q3:4.6) years and a median weight of 15.5 kg (Q1:11.9, Q3:22.5). The neuter status of the dogs was not given in twenty articles, seven study populations were not neutered, and one had a population with a mixed neuter status. For the experimental studies, the gender of the dogs was unknown for eleven study populations, only female dogs were used in five studies, only males in seven studies, and a mixed population in five studies. The median number of dogs used for experimental studies was 21.0 (Q1:11.5, Q3:24.3) and the median number of breeds was 1.0 (Q1:1.0; Q3:1.0). In 27 out of the 28 experimental studies, the breed of the dogs was specified. The study population of nine studies consisted of cross-bred dogs and seventeen study populations were purebred dogs. Most of the experimental studies (n = 9) consisted of Beagles only, followed by three studies with a mixed study population of Beagles, Labradors, Rottweilers, and German Shepherds, and one each of Foxhounds, Sheepdogs, Pitbull Terriers, and Coonhounds.

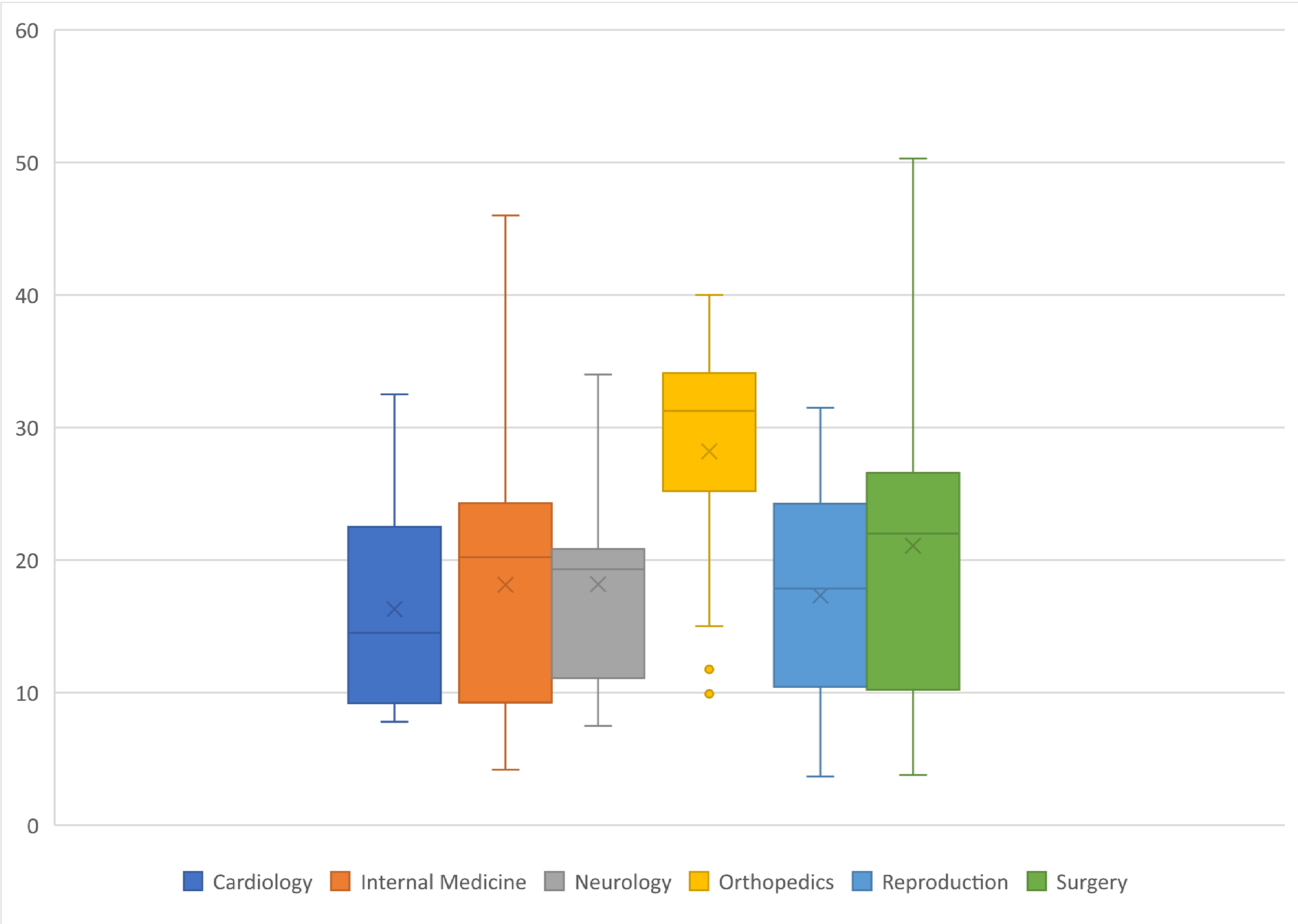

Figure 4. Weight (in kg) of the dogs utilized in 150 clinical trials within six veterinary specialties (25 each).

The number of animals was given in most of the articles in all different specialties. For two studies—one on reproduction and one on orthopaedics—the authors did not specify the number of enrolled animals. The median sample size for all the included studies was 31 dogs (Q1:16; Q3:64). For the different specialties, the median sample size was 32 for cardiology (Q1:22; Q3:207), 31 for internal medicine (Q1:14; Q3:53), 33 for neurology (Q1:15; Q3:56), 36 for orthopaedics (Q1:19; Q3:95), 35 for reproduction (Q1:18; Q3:74), and 25 for surgery (Q1:16; Q3:40).

4. Discussion

This study focused on the assessment of the signalment, such as breed, sex, neuter status, age, and weight, of dogs used in controlled clinical trials. These data were analysed with consideration of the veterinary specialty that each publication belonged to. The results of a critical appraisal of the quality of the clinical studies have been published in an earlier paper [29]. The articles were randomly selected from a list generated after a literature search in two relevant databases. There were sixteen studies using dogs that served as model for human health, but only three studies used Beagles as a study population. Interestingly, nine of these studies belonged to the specialty of cardiology.

The proportion of Beagles in our literature sample was less than we expected and less than several authors have claimed [10]. A reason could be that some studies focus on conditions that occur naturally in specific breeds, such as diseases related to brachycephaly. In 2020 in the UK, 99% of dogs used in experimental research (medical and veterinary) were Beagles [32]. In other European countries, breed information is not given in the statistics about animal testing [6]. Obviously, the Beagle has not been a predominant breed used for clinical veterinary studies in the past years. In fact, the breed of dogs used in research more or less reflects the most popular breeds, with the exception of Bulldogs. The reason for the latter remains open and should be further investigated. Nevertheless, the presented data may imply a slight increase in the use of Beagles over the last years, but the number of the assessed articles is much too small to conclude a trend. On the contrary, the number of dogs used as experimental animals seems to be declining [5], albeit a lack of comprehensive data on the worldwide use of dogs in experimental research and clinical trials. The use of Beagles and dogs in general for basic research and research related to human medicine may have become less popular in the past decades because of an increasing awareness of animal welfare [4]. Just recently, a Beagle-breeding company was inspected and found itself confronted with allegations of severe animal welfare violations, which were reported in different media [33]. Over the years, the European Union, Canada, the United States, and several other countries have introduced laws to regulate the use of laboratory animals for medical research after consulting the main stakeholders [4]. In addition, laboratory dogs are often rehomed nowadays into private households after their use in research [34,35]. However, it has been claimed that they still experience an extreme change in their life situation because they leave their familiar, limited environment in the research facility and encounter a multitude of animate and inanimate stimuli in their new home [36,37]. For 50 studies (33.3%), the amount of missing or incomplete information about the breeds used for the clinical studies is relatively high, which shows that this kind of information seems to be considered unimportant by authors, reviewers, and editors. However, since breed may be a relevant confounder, this information is essential data that needs to be given according to the STROBE statement [38]. The median number of breeds used for the clinical trials does not differ significantly between the veterinary specialties. It is noticeable that most of the cardiology studies were conducted with experimental dogs and most of the studies consisted of just one breed. The evaluation of the other parameters showed that, for most trials, both female and male dogs were used, meaning that sex was not set as an inclusion or exclusion criterion. The sex of all dogs was only given in reproduction trials, and more than 60% of these trial dogs were female. It is plausible that studies on gynaecology usually relate to conditions found in intact bitches. For the other veterinary specialties, the sex of the dogs seems to be considered unimportant, and this might indeed be the case. Similar findings have been documented regarding the neuter status. More than 90% of the dogs used for reproduction trials were intact, while in the studies belonging to the other veterinary specialties, both intact and neutered dogs were often used. It can be concluded that the neuter status seems to be considered an irrelevant factor or confounder for most research questions beyond reproduction. It is noticeable that the median age of the dogs used for cardiology was nearly double that of the ages of the dogs enrolled into studies belonging to the other veterinary specialties. This might reflect the fact that cardiac diseases tend to occur or be diagnosed in older dogs. The median age of the dogs used for the reproduction studies was the lowest. This may be related to the optimal breeding age of bitches. The median body weight of the dogs was highest in the orthopaedic studies, at around 30 kg. It is common knowledge that especially large and heavy dogs have a higher risk of suffering from joint diseases [20]. For other disorders, factors such as age and weight may also play a role concerning a studied condition. Therefore, this information should be given in scientific articles. The presented review has revealed documentation and reporting deficiencies. Based on the presented data, it is not possible to judge whether the study methodology or reporting is better or worse in specific veterinary specialties. In fact, it seems that even if some aspects are better presented in one specialty, other factors are missing more often in the same specialty. Similar shortcomings have been described by Reynolds et al. [39] and others [29,40,41]. Demographic data for dog populations used in clinical trials is very important, since it is needed to draw sound conclusions and extrapolate the findings [42]. In addition, comprehensive information about the used animals is important for readers to assess whether the given scientific information should be applied in an actual case. It has been proven that the signalment such as age, sex, and breed are highly relevant aspects for examining the prevalence of conditions and the interpretation of various study outcomes. Besides the examples mentioned earlier, age is a key factor for the outcomes of electrocardiographic exams [43], fertility [44], behaviour [45], and several canine diseases [46–48]. Belic et al. found that the sex of a dog plays an important role in biochemical markers for the bone turnover [49]. Anatomical or hormonal differences between male and female or neutered and intact dogs can also have an impact on the prevalence of diseases [50–52] or the outcome of clinical studies [53]. In addition, it has been shown that the breed has an effect on renal size [54], and genetic and phenotypic differences across dog breeds have an influence on the safety and efficacy of pharmaceutical substances and their doses [55] and the occurrence of genetic diseases [56] such as MDR1 mutations [57]. Several studies on the methodological and reporting quality of clinical trials in veterinary medicine have been published in the past years. Limitations have been criticized, such as small numbers of included animals; a lack of sufficient reporting on the specifications of animals, diagnoses, and treatments; and undocumented inclusion and exclusion criteria [29,42,58]. Our results show that relevant reporting deficiencies in clinical studies were found and essential information about the dogs used in clinical trials was missing. This may considerably limit the validity of research results. More attention should be paid to reporting guidelines, such as the STROBE statement for observational trials or the CONSORT statement for randomised studies [59], as they have been developed to improve the quality of scientific articles.

The estimated number of dogs used worldwide for medical research is still high. Attempts have been made to replace laboratory animals by in vitro and in silico methods [1,60–62]. For laboratory animals in most countries, the consideration and implementation of replacement, refinement, and reduction (3Rs) strategies, proposed by Russell and Burch in 1959, is mandatory [63]. For some purposes, animal testing has been forbidden by some authorities. For instance, the use of animals for cosmetic testing has been prohibited in Europe as of March 2013 [64].

Limitations

There are some limitations to the present study, such as the relatively small sample size of 25 articles per specialty. Since this number per specialty led to a total number of 150 articles, which was eligible for a throughout assessment, the inclusion of more literature was not possible within this project. In that regard, it may be worthwhile to re-evaluate some of the presented specialty-specific findings on a larger scale with a greater number of articles.

Furthermore, the investigation and evaluation of the studies was done by just one non-blinded researcher, which may have led to a biased interpretation. This approach, however, has been used in several other studies before [29,30,41,65].

5. Conclusions

The results of our literature review concerning the kinds of dogs that are used in veterinary research indicate that we are widely not able to give a sufficient answer. The presented project revealed that Beagle dogs represent only a small proportion of dogs in clinical veterinary research. It seems that Beagles are used much more in experimental research, but this should be investigated in future analyses including more experimental research reports. The results of this study are furthermore in accordance with previous findings, and reflect once more that essential information about the dogs used in clinical trials is missing. Some parameters, such as body weight and neuter status, vary significantly between specialty-specific studies. Authors, reviewers, and journal editors should pay more attention to the reporting of basic information about the animals enrolled in veterinary research and should follow the guidelines for the specific study type.

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3. Discussion

The purpose of this study was to evaluate as a first step the study design quality of research on dogs in peer-reviewed journals. Furthermore, an aim was to compare the results within six different veterinary specialities: cardiology, orthopaedics, neurology, internal medicine, reproduction, and surgery. As a second step, the dog study population was evaluated with regard of their signalment and number. These results were again compared between the six different veterinary specialties.
As already mentioned in the introduction there are different study designs with differing importance within the Evidence-based Veterinary Medicine. Clinical appraisal is an important process through which one can identify the strength and weaknesses of a research study (Young and Solomon 2009).

Reporting guidelines

In order to improve the quality of the different clinical studies, specific guidelines providing a comprehensive framework for documenting study methodology and results and assessment of the quality of reporting have been published. In meta-analysis and systematic reviews these are called PRISMA, QUORUM (Quality of Reporting of Meta-Analyses) or AMSTAR, CASP respectively (Young and Solomon 2009). When it comes to randomised controlled trials the CONSORT (Consolidated Standards of Reporting Trials) statement should be used. The REFLECT statement is also available, which is an extension to the CONSORT reporting guideline specifically developed for RCT's with a population of livestock (Wareham et al. 2017).
For the observational studies researchers can make use of the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement in order to improve their study.

Sadly, even if these guidelines have been published and amended over the past almost 15 years, they are hardly known and used. A study published in 2014 revealed, that the majority (68.2 %) of veterinary journal editors believed that reporting guidelines should be adopted by all refereed veterinary journals (Grindlay et al. 2014). However, the authors could also show that perceived barriers to a more intensive use of these guidelines were a lack of knowledge, fear, resistance to change, and difficulty in implementation. It remains open if the situation has improved during the past 8 years. The presented studies show that certain deficiencies still are present.

Evidence syntheses for practitioners

With the aim of helping practitioners to find and apply evidence in clinical practice the critically appraised topics (CATs) can be applied. They are evidence syntheses that provide veterinary professionals with information to rapidly address clinical questions and support the practice of Evidence-based Veterinary Medicine (EBVM) (Brennan et al. 2020). A CAT is a document of usually one to three pages that includes a specific clinical question and a clinical conclusion that reflects a synthesis of one or more research articles (Arlt et al. 2012). Hence, these documents are different to scientific reviews since they focus on answering a single and simple question, only. The format of rapid reviews is typically shorter, and the statistical methods used less complex than those of a systematic review, enabling greater accessibility and enhanced readability (White et al. 2017). Here within lies the main limitation of a CAT, due to its quick research, one can miss relevant evidence sources (Brennan et al. 2020). Therefore, it is important to do a comprehensive literature search, based on a well formulated questions, ideally by using the PICO approach. A well-formatted clinical question contains four elements: (1) the patient or problem, (2) the intervention being considered, (3) a comparison intervention (when relevant), and (4) the clinical outcomes of interest (Hardin and Robertson 2006).

The development of a critically appraised topic has been included already in some veterinarian curricula with great success (Hardin and Robertson 2006;Arlt et al. 2012). It has been suggested to implement this teaching method more intensively to better train the principles of EBVM.

There were no CATs in the assessed 150 articles used for this study. The overall number of published CATS is still low in veterinary medicine compared to human medicine. But some journals such as Veterinary Evidence (https://veterinaryevidence.org) and the Veterinary Record allow submissions and publish CATs. In addition, some databases have been developed to collect and present CATs (https://bestbetsforvets.org/) and systematic reviews (https://vetsrev.nottigham.ac.uk).

Results of the research papers

The findings of the first study revealed deficits in methodology and reporting of studies published in peer-reviewed journals in general, with moderate variations between different veterinary medicine specialities. In order to provide veterinary practitioners and clinicians reliable, valid, and concise information, authors, reviewers and journal editors should pay attention to proper design and reporting by making use of the different developed guidelines mentioned above. According to our findings, authors should give more care to aspects such as sample size calculation, details of the animals such as breed, housing and feeding, inclusion and exclusion criteria and handling of missing data. Even if there is no data

missing, this should be mentioned in the paper for clarity.
The informed consent is given by the animal’s owner in veterinary medicine. It is a core ethical principle in order to inform the owner about the study's requirements, risks, and potential benefits (Sobolewski et al. 2019) and should be a crucial part for every clinical study which contains private owned animals. It is surprising that our research revealed at least 26 clinical studies where the written informed consent was not mentioned. We recommend strongly to describe this in the research paper and to pay attention to the readability of the forms as a recent study revealed, that the forms used for 53 veterinarian studies where not easily readable (Sobolewski et al. 2019). Maybe a template with a good readability should be worked out by veterinarian professionals and be available for all clinical authors.

The results of the second study concerning question ´what kinds of dogs are used in veterinary research´ is that we are widely not able to give a sufficient answer. The presented project revealed that Beagle dogs represent only a small proportion of dogs in clinical veterinary research. It seems that Beagles are used much more in experimental research, but this should be investigated in future analyses including more experimental research reports.
For transparency reasons it seems to be advisable that data about dogs and their species used in research should be available for the public. A question that remains open is to what extent research on Beagles should be used in order to study human diseases or diseases related to specific dog breeds. As mentioned in the published papers, there is a difference concerning diseases and breed, age, gender and castration status which can not be extrapolated to other study populations. This needs to be investigated and clarified in further studies.

Limitations

There are some limitations, such as the relatively small sample size of 25 articles per specialty. Since this number per specialty led to a total number of 150 articles, which was eligible for a throughout assessment, the inclusion of more literature was not possible within this project. In that regard, it may be worthwhile to re-evaluate some of the presented specialty-specific findings on a larger scale with a greater number of articles.
Furthermore, the investigation and evaluation of the studies was done by just one non-blinded researcher, which may have led to a biased interpretation. This approach, however, has been used in several other studies before**.**

Conclusion:

The results of this study are furthermore in accordance with previous findings and reflect once more that essential information about the dogs used in clinical trials are missing. Some parameters like body weight and neuter status vary significantly between speciality specific studies. Authors, reviewers, and journal-editors should pay more attention to the reporting of basic information about the animals enrolled in veterinary research and should follow the reporting guidelines for the specific study type. Further communication and education about reporting guidelines in the veterinary scientific communities and also among practitioners has the potential to increase their adoption by veterinary journals in the future (Grindlay et al. 2014). In order to improve the study and reporting quality in peer-reviewed journals it should be mandatory to present specific information in scientific papers and authors and reviewers should work with checklists, to ensure that essential data is presented.

The practitioner furthermore should evaluate and appraise the quality of every study critically by using the Evidence-based Veterinary Medicine principles because only a publication of a study in a scientific journal does not mean it is any good (Dean 2013).

Further research with a larger scale of clinical studies could be done on the comparison of the signalment of dogs used for human or veterinary studies concentrating either on interventional or observational studies.

Beyond the six different small animal specialties included in the presented studies, it would be interesting to evaluate and compare other specialties such as ophthalmology or dermatology or assess the quality of clinical studies for other species such as livestock animals and other.

4. Summary

Evelyn Schulte: Study design quality and signalment of dogs used for research published in peer-reviewed journals

In the past it has been criticised that only a low proportion of well-designed and well-reported studies in some medical specialities is available.

Dogs are furthermore widely used in research to answer questions about canine or human conditions. For the latter, research dogs often are used as models since they are physiologically more similar to humans than other species used in research and share similar environmental conditions. From the veterinary perspective, research findings are widely based on academic research, and thus are generated under experimental conditions. In that regard the question arises if the dogs used for research adequately represent the dog population seen in veterinary practice. It may, for example, be assumed that often Beagle dogs are used as experimental animals.

The objective of this study was to firstly systematically evaluate the quality of literature about canine medicine published in peer-reviewed journals in relation to six specific veterinary medicine specialities and furthermore to evaluate the signalment of dogs used in veterinary research.

A literature search was conducted and 25 studies per speciality were selected. The quality of the articles (*n* = 150) published between 2007 and 2019 was evaluated with a validated checklist for the first study. The breed, sex, neuter status, median age, and median weight of the dogs used for clinical studies were additionally evaluated within a second study.

The first study revealed deficits in articles related to all specialities, such as not adequate number of animals in 60.0% of the studies. In 88.0%, information about housing and feeding of the dogs were not specified. In 69.4% of the prospective clinical studies, an ethical approval was reported, and written informed consent of the owners was obtained in 46.2%. The findings revealed extensive deficits in the design and reporting of studies in canine medicine. The demand for improvement is obvious and should be addressed by authors, reviewers, and journal editors in the future. The specific guidelines for the different studies should be used. Our results underline that practitioners should critically appraise the quality of literature before implementing information into practice.

The second study revealed a total of 596.542 dogs, that were used in the 150 trials. For 33.835 dogs out of these (5.7%), breed information was given. From the latter, 1.9% were Beagles. Nine clinical trials enrolled no other breeds than Beagles. Most frequently used breeds were German Shepherds (7.3%), Labrador Retrievers (6.7%) and Golden Retrievers (4.7%). Major reporting deficits found were missing breed specification in 25.3 % of the articles. Information about the sex of the dogs was lacking in 16.2 %, age and weight

information missing in 22.7 and 32.7%, respectively. The neuter status was not given in 38.7% of the clinical studies. The median sample size was 56 (Q1:29; Q3:365) dogs.
The presented project revealed that Beagle dogs represent only a small proportion of dogs in veterinary research. Based on the evaluated publications it seems that some relevant attributes of the dogs differ between the specialties.
The results, however, show deficits in the reporting of demographic data of the dogs. The demand for improvement of documentation and/or reporting of animal signalment is obvious and should be addressed by authors, reviewers, and journal-editors in the future.

5. Zusammenfassung

Evelyn Schulte: Qualität von in Peer-Review-Zeitschriften veröffentlichten Studien und Merkmale von Hunden, die in der Forschung verwendet werden

In der Vergangenheit wurde kritisiert, dass in einigen medizinischen Fachgebieten nur ein geringer Anteil gut konzipierter und gut dokumentierter Studien vorliegt.
Darüber hinaus werden Hunde häufig in der Forschung eingesetzt, um Fragen zu veterinärmedizinischen oder menschlichen Erkrankungen zu beantworten. Für letztere werden Forschungshunde häufig als Modelle verwendet, da sie dem Menschen physiologisch ähnlicher sind als andere in der Forschung verwendete Tierarten und ähnliche Umweltbedingungen aufweisen. Aus veterinärmedizinischer Sicht beruhen die Forschungsergebnisse weitgehend auf akademischer Forschung und werden daher unter experimentellen Bedingungen gewonnen. In diesem Zusammenhang stellt sich die Frage, ob die für die Forschung verwendeten Hunde die Hundepopulation in der tierärztlichen Praxis angemessen repräsentieren. Es ist davon auszugehen, dass zum Beispiel häufig Beagle-Hunde als Versuchstiere verwendet werden.

Ziel dieser Studie war es, zum einen die Qualität der in Fachzeitschriften mit Peer-Review veröffentlichten Literatur zu wissenschaftlichen Studien mit Hunden in Bezug auf sechs spezifische veterinärmedizinische Fachgebiete systematisch zu bewerten und zum anderen das Signalement der in der veterinärmedizinischen Forschung verwendeten Hunde zu beurteilen.

Es wurde eine Literaturrecherche durchgeführt und 25 Studien pro Fachgebiet wurden ausgewählt. Die Qualität der Artikel (n = 150), die zwischen 2007 und 2019 veröffentlicht wurden, wurde anhand einer validierten Checkliste für die erste Studie bewertet. In einer zweiten Studie wurden zusätzlich die Rasse, das Geschlecht, der Kastrationsstatus, das Durchschnittsalter und das Durchschnittsgewicht der für klinische Studien verwendeten Hunde bewertet.

Die erste Studie ergab Defizite in den Artikeln zu allen Fachgebieten, wie z. B. eine unzureichende Anzahl von Tieren in 60,0 % der Studien. In 88,0 % wurden keine Angaben zur Unterbringung und Fütterung der Hunde gemacht. In 69,4 % der prospektiven klinischen Studien wurde eine ethische Erlaubnis angegeben und in 46,2 % wurde die schriftliche Einwilligung der Besitzer eingeholt.

Die Ergebnisse zeigen erhebliche Defizite bei der Gestaltung und Berichterstattung von Studien in der Veterinärmedizin. Der Verbesserungsbedarf ist offensichtlich und sollte von Autoren, Gutachtern und Herausgebern von Zeitschriften in Zukunft angegangen werden.

Dabei sollten die spezifischen Leitlinien für die verschiedenen Studien verwendet werden. Unsere Ergebnisse unterstreichen, dass klinisch tätige Tierärzte/Tierärztinnen die Qualität der Literatur kritisch bewerten sollten, bevor sie die Informationen in die Praxis umsetzen.

Die zweite Studie ergab eine Gesamtzahl von 596.542 Hunden, die in den 150 Studien eingesetzt wurden. Bei 33.835 Hunden (5,7 %) davon wurden Angaben zur Rasse gemacht. Von den letzteren waren 1,9 % Beagle. An neun klinischen Studien nahmen keine anderen Rassen als Beagle teil. Die am häufigsten verwendeten Rassen waren Deutsche Schäferhunde (7,3%), Labrador Retriever (6,7%) und Golden Retriever (4,7%). Die größten Mängel in der Berichterstattung waren fehlende Angaben zur Rasse in 25,3 % der Artikel, fehlende Informationen zum Geschlecht der Hunde bei 16,2 % der Studien, Alters- und Gewichtsangaben fehlten in 22,7 bzw. 32,7 %. Der Kastrationsstatus wurde in 38,7 % der klinischen Studien nicht angegeben. Der Median der Stichprobengröße betrug 56 (Q1:29; Q3:365) Hunde.

Das vorgestellte Projekt ergab, dass Beagle-Hunde nur einen kleinen Teil der Hunde in der tiermedizinischen Forschung ausmachen. Anhand der ausgewerteten Publikationen scheint es, dass sich einige relevante Eigenschaften der Hunde zwischen den Fachgebieten unterscheiden.

Die Ergebnisse zeigen jedoch Defizite in der Berichterstattung über die demographischen Daten der Hunde. Der Bedarf an einer Verbesserung der Dokumentation bzw. Berichterstattung über Tiermerkmale ist offensichtlich und sollte von Autoren, Gutachtern und Zeitschriftenherausgebern in Zukunft berücksichtigt werden.

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7. Contribution of doctorate student

My personal contributions to the research projects presented under this cumulative doctoral thesis are summarized in the following table.

Contribution of Doctorate Student

Contribution	Research project 1	Research project 2
Study Design	++	++
Data collection	+++	+++
Data analysis	+++	+++
Manuscript writing	+++	+++
Manuscript editing	++	++

Score: + < 50 %; ++ 50 to 70 %; +++ > 70 %

Eigener Anteil an den Studien

Beitrag	Studie 1	Studie 2
Studienplanung	++	++
Datenerhebung	+++	+++
Datenanalyse	+++	+++
Verfassen des Manuskripts	+++	+++
Editieren des Manuskripts	++	++

Legende: + < 50 %; ++ 50 bis 70 %; +++ > 70 %

8. Publication directory

Schulte, E.; Arlt, S.P. 2022:
Study design quality of research on dogs published in peer-reviewed journals.
Vet Rec. 2022;*190*:e1382. doi:10.1002/vetr.1382.

Schulte, E.; Arlt, S.P. 2022:
What kinds of dogs are used in clinical and experimental research?
Animals. 2022, 12, 1487, doi:10.3390/ani12121487

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11. Conflict of Interest

Im Rahmen dieser Arbeit bestehen keine Interessenskonflikte durch Zuwendungen Dritter.

In the context of this work, there are no conflicts of interest due to contributions from third parties.

12. Declaration of Independence

Hiermit bestätige ich, dass ich die vorliegende Arbeit selbständig angefertigt habe. Ich versichere, dass ich ausschließlich die angegebenen Quellen und Hilfen in Anspruch genommen habe.

This is to declare that I conducted all the studies described herein myself and the manuscripts were produced independently. I confirm that I have used only the specified resources and tools to complete this thesis.

Lübeck, den 09.02.2023

Evelyn Schulte