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Evaluation of the quality of current literature in the field of bovine, canine and equine reproduction and the manageability of its assessing by using a previously validated checklist

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Meinem Sohn

„Wenn du etwas machst, wie du es seit zehn Jahren gemacht hast, dann sind die Chancen recht groß, dass du es falsch machst.“

Charles F. Kettering

1. Introduction

Evidence-based medicine (EBM) equips practitioners with skills to integrate high quality information from research in clinical decision making and improves the quality of health care (Rengerink et al. 2011).

The philosophical origin of EBM extends back to mid-19th century and earlier (Sackett et al. 1996). Since 1970 the implications of EBM have been debated more intensively in the literature as e.g. Cochrane published on the importance of randomized clinical trials (Cochrane 1972). Furthermore, technology - as computers and database software which allowed compilation of large amounts of data - has played a large role in the advancement of EBM (Claridge et al. 2005). However, the term EBM had been established many years later in 1992 by a Canadian workgroup at the McMaster University in Hamilton (Group 1992; Antes et al. 2006). Then in 1996, the term was more formally defined by Sacket et al. (Claridge et al. 2005) as *'the conscientious, explicit and judicious use of current best evidence about individual patient care'* (Sackett et al. 1996).

Following the establishment of EBM in human medicine evidence-based veterinary medicine (EBVM) is the application of EBM to the veterinary field (Cockcroft et al. 2003). The concept of EBM had been transferred to veterinary medicine in the early 2000s (Vandeweerd et al. 2012a). Veterinarians are among other things responsible for the health and welfare of animals. In addition, veterinary medicine includes the care for health and life of humans regarding e.g. the compassion with owners, quality of food, zoonoses and scientific research. In conclusion, the quality of information used in veterinary decision making is of great importance.

In veterinary and human medicine, a great amount of time is spent in making diagnostic, therapeutic and preventive decisions (Vandeweerd et al. 2012d). Evidence-based veterinary medicine should rely on multiple sources of information (Kastelic 2006). In this regard veterinarians should use both individual clinical expertise and the best available external evidence, and neither alone is enough (Sackett et al. 1996). To receive external evidence one option would be to take evidence from literature and apply it in clinical practice. However, publications in veterinary journals vary widely in their quality (Kastelic 2006; Arlt et al. 2010). Studies of low quality should be used with caution. This necessitates that veterinarians reading published studies should be able to recognize and appreciate both the advantages and limitations inherent in the evidence generated by a variety of study designs (Vandeweerd et al. 2012d). Therefore, it is important to identify limitations in recent publications and to formulate recommendations for future studies. To demonstrate

possibilities and weaknesses of publications an analysis on the quality of veterinary literature has to be done in general and species specific. Achieved results have to be introduced to other researchers and practitioners.

Being aware of the limitations of publications veterinarians have to assess the quality of literature before implementing information into the clinical practice. Hence, practicing EBVM requires clinical expertise, and expertise in retrieving, critically appraising, interpreting, and applying the results of published scientific studies (Arlt et al. 2011). However, a lack of understanding of some common terms concerning EBM exists (Yousefi-Nooraie 2007). In surveys of practicing veterinarians relating to their familiarity with the concepts of EBVM many practitioners did not express confidence in their understanding of common EBVM-related terms (McKenzie 2011; Haimerl et al. in press). EBVM is rarely part of the education of German veterinarians (Arlt et al. 2012). Therefore, students may capture information without thinking about their quality. Information learned decades ago at university or in the early years at work has to be renewed over time. Because, in medicine, knowledge is rapidly changing and developing (Baum 2008). Furthermore, incorporation of EBM in practice faces several barriers to implementation e.g. lack of time (Rengerink et al. 2011). However, limited time to keep up to date with the current literature is not an adequate argument against the usefulness of EBVM (Vandeweerd et al. 2012d). Tools, like literature and databases with summarized information, to help students as well as practitioners to stay up to date for a lifetime would be beneficial. Furthermore, checklists have been developed to support the appraisal of the quality of literature. These tools could be useful to keep practitioners abreast of medical advances reported in veterinary literature. Furthermore, these checklists could help veterinarians to master terms important to EBVM. However, their usability for veterinarians has to be investigated.

Overall, the objectives of this thesis were 1) to discuss implementation of EBVM into veterinary medicine, 2) to evaluate and compare the quality of a randomly selected sample of literature on reproduction in cattle, dogs and horses and 3) to determine the inter-observer agreement utilizing a checklist for the evaluation of scientific literature in the field of animal reproduction.

2. Research Papers

Original research articles about the studies have been published in the peer reviewed Journals 'Tierärztliche Praxis Großtiere' (Impact Factor 2011: 0.283), 'Theriogenology' (5-Year Impact Factor: 2.274) and 'Journal of Veterinary Medical Education' (Impact Factor 2011: 0.573). The three papers are presented in the format outlined in the guide for authors of the respective journal. They are presented in a logical order rather than in order of their publication date.

2.1 Die evidenzbasierte Veterinärmedizin im Praxisalltag

C. Simoneit, W. Heuwieser, S. Arlt.

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Die evidenzbasierte Veterinärmedizin im Praxisalltag

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Zusammenfassung

Für den praktizierenden Tierarzt ist es von großer Bedeutung, Entscheidungen hinsichtlich Diagnostik und Therapie auf der Grundlage aktueller und solider Erkenntnisse zu treffen. Im Praxisalltag ist er insbesondere bei schwierigen Fragestellungen auf Informationen aus der Fachliteratur, Gesprächen mit Kollegen, dem Internet oder anderen Quellen angewiesen. Als große Herausforderung erweist es sich dabei, in angemessener Zeit die richtigen Informationen aus einer großen Fülle von Angeboten zu finden. Ferner stellt sich die Frage, wie hochwertig und aktuell die Angaben tatsächlich sind und ob sie sich überhaupt auf die aktuelle Fragestellung anwenden lassen. Im Idealfall sollten die Informationen eine hohe Evidenz aufweisen. Das heißt, es sollte möglichst sicher sein, dass sie tatsächlich richtig sind. Die Basis sollten gut durchgeführte, praxisrelevante und hochwertige Studien bilden. Zu beurteilen, ob dies zutrifft, stellt oftmals eine erhebliche Herausforderung dar. Zudem sind nicht immer gute Studienergebnisse verfügbar. Daher sollte von Seiten der Hochschulen, der Zeitschriftenverleger und der Berufsverbände künftig weiter daran gearbeitet werden, aktuelle Forschungsergebnisse für die Praxis so aufzubereiten, dass diese für Entscheidungsfindungen zielgerichtet eingesetzt werden können.

Schlüsselwörter

Evidenzbasierte Tiermedizin, kritische Informationsbewertung, valide Entscheidungsfindung

Summary

The veterinary practitioner should base decisions concerning diagnostic procedures and treatments in practice on recent, valid and clinically relevant information. He may rely on journal papers, colleagues, the internet or other sources. It is a great challenge to find appropriate information in a reasonable time. Furthermore, the practitioner has to judge the information regarding its actuality and validity. Ideally, such information should provide a high level of evidence. This means that this information is more likely to be “correct”. Good information can be obtained through high quality trials, such as randomized and blinded controlled clinical trials. Universities, publishers and professional organizations should promote editing of scientific information to support practitioner in decision making.

Key words

Evidence based medicine, clinical reasoning, decision making

2.2 Evidence-based medicine in bovine, equine and canine reproduction: quality of current literature

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Evidence-based medicine in bovine, equine and canine reproduction: quality of current available literature

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Abstract

The objective was to evaluate deficits and differences of published literature on reproduction in cattle, horses and dogs. A literature search was conducted in the databases Medline and Veterinary Science. Approximately five times more articles on clinical bovine reproduction (n = 25 910) were found compared to canine (n = 5 015) and equine (n = 5 090) reproduction. For the evaluation of the literature, a checklist was used. A subset of 600 articles published between 1999 and 2008 was randomly selected. After applying exclusion criteria a total of 268 trials (86 for cattle, 99 for horses and 83 for dogs) were evaluated and used for further analysis. For the field of canine and equine reproduction, there were fewer clinical trials with a control group compared to bovine reproduction (cattle 66%, horses 41% and dogs 41%). For all three species investigated, few publications were identified (4%) with the highest level of evidence, i.e. controlled, randomized and blinded trials, or meta-analyses. In cattle 33% of the publications were graded adequate to draw sound conclusions; however, only 7 and 11% were graded adequate in dogs and horses, respectively. Therefore, the veterinarian should always assess the quality of information before implementing results into practice to provide best available care for the animals. In conclusion, improvement of the quality of well-designed, conducted and reported clinical trails in animal reproduction is required.

Keywords: *Evidence-based medicine; Reproduction; Quality of literature; Cattle; Horses; Dogs*

Introduction

Veterinarians provide a wide range of services and play an important role in protecting animal welfare and maintaining animal and public health. Therefore, it is of great relevance that veterinarians use the most current diagnostic methods, preventive measures, and therapeutic interventions based on the best available evidence. Evidence is the extent of sureness that scientific findings are true [1]. This conscientious, explicit and judicious use of current best evidence in making decisions regarding the care of individual patients is called evidence-based medicine [2]. In order to stay up to date, however, the veterinarian has an enormous amount of information to process and assimilate. In a survey regarding the influence of various information sources conducted with medical staff (n = 41), reading was seen as the most influential information source on the decision-making [3]. No research is available yet for veterinary medicine, but we expect the situation to be similar. Finally, literature is an important link between research and practice [4].

The number of biomedical journals worldwide has risen from 2 300 in 1940 to 25 000 in 1995 [5]. This equals a more than 10-fold increase during a period of 50 y. In current veterinary medicine, an information explosion is observed [6]. Unfortunately, veterinary publications vary widely in their quality [7,8]. Scientists developed checklists to improve the quality of publications. These checklists report important aspects of conducting a trial. The CONSORT and the PRISMA statements aim to improve the reporting of randomized clinical trials, as well as systematic reviews and meta-analyses [9,10]. The REFLECT statement is a modification of the CONSORT statement for veterinary science as livestock and food safety [10]. These checklists may also be useful for critical appraisal of published reviews, but they are not explicitly designed as quality assessment instruments to gauge the quality of articles. It is important to identify specific deficits of publications to define their quality and to critically evaluate validity and practicability of findings. Arlt et al. [7] developed and evaluated a checklist for readers to systematically assess the quality of a veterinary publication. Furthermore, this study on the quality of literature on reproduction in dogs revealed that 67.9% of the articles published were evaluated to be not sufficient to draw valid conclusions [7].

The objective of the current study was to evaluate and compare the quality of a randomly selected sample of published literature on reproduction of cattle, horses, and dogs.

Material and methods

A literature search was conducted on 02 July 2009 utilizing the two online databases Medline (http://www.ncbi.nlm.nih.gov/pubmed/) and Veterinary Science (http://www.ovid.com). Medline was accessed using the search engine PubMed. These are the two major databases in veterinary medicine. The advantages of databases are the use of descriptors with which the search process can be specified. The descriptors are controlled vocabulary to index literature and had to be adjusted to the thesaurus of the database. In PubMed the terms “genital diseases AND female AND cattle”, “genital diseases AND male AND cattle”, “pregnancy AND cattle” or “obstetrics AND cattle” were used, respectively. In Veterinary Science, the keywords “female genital diseases AND cattle”, “male genital diseases AND cattle”, “pregnancy AND cattle” or “obstetrics AND cattle” were used to cover the same subject area. In both databases each search was repeated using the term horses or dogs instead of cattle. Terms were connected with the Boolean operator ‘AND’. The literature was managed using EndNote (Version X; Thomson Reuters EndNote, USA). All obtained articles were included into a list for each species and double entries deleted. Only articles published between January 1999 and December 2008 were included. All articles of the three lists were assigned a unique number. Two hundred articles were randomly selected per species using “Random sample of cases” by SPSS (Version 16.0; SPSS inc., Munich, Germany). Thereafter specific exclusion criteria defined before the literature search were applied to the references. Journal articles that were not published in English or German were excluded. Papers that were indexed incorrectly in the databases (e.g. articles about human, sheep or urinary diseases) and literature reviews without statistical analyses were excluded. Due to the clinical focus of our study pathological case reports, basic research (e.g. identification of proteins without a clinical context) and *in vitro* studies were also excluded. Articles that were not available via the internet or interlibrary loan were excluded, respectively.

For the evaluation of the literature, a checklist which had been recently developed, used and established [7] was used (Figure 1). It comprised 40 criteria in the categories materials and methodology, study design, statistics, presentation and information content, applicability and conclusions. The evaluator was able to indicate the level of agreement to each specific criterion on a likert scale [11] providing five possible statements: strongly agree, agree, neutral, disagree or strongly disagree. Statements that were not accessible had to be characterized with the answer ‘not determined’.

Figure 1: Checklist to assess the quality of publications

Material and methodology	strongly agree	agree	neutral	disagree	strongly disagree	not determined
1. The objective of the study is presented	☐	☐	☐	☐	☐	☐
2. Following information about the animals is given						
a) Number of animals	☐	☐	☐	☐	☐	☐
b) Inclusion criteria	☐	☐	☐	☐	☐	☐
c) Housing	☐	☐	☐	☐	☐	☐
d) Breed	☐	☐	☐	☐	☐	☐
e) Age	☐	☐	☐	☐	☐	☐
f) Sex	☐	☐	☐	☐	☐	☐
g) Preconditions and pretreatments	☐	☐	☐	☐	☐	☐
→ Description of material is clear and detailed	☐	☐	☐	☐	☐	☐
3. The examinations are described in detail	☐	☐	☐	☐	☐	☐
4. Treatments						
a) Information about the remedies or interventions (pharmaceutic agents, trade name, manufacturer) are given	☐	☐	☐	☐	☐	☐
b) The application of the remedy (pharmaceutical form, dose, treatment intervals) or conduction of interventions are described	☐	☐	☐	☐	☐	☐
→ Information about treatments or interventions are adequate	☐	☐	☐	☐	☐	☐
5. The monitoring is described in detail	☐	☐	☐	☐	☐	☐
6. Results are presented completely	☐	☐	☐	☐	☐	☐
7. Results are discussed critically	☐	☐	☐	☐	☐	☐

Study design	strongly agree	agree	neutral	disagree	strongly disagree	not determined
1. The study was controlled	☐				☐	☐
2. The study was randomized	☐				☐	☐
3. The study was blinded	☐				☐	☐
4. Studydesign is described in detail regarding						
a) Prospectivity/Retrospectivity	☐	☐	☐	☐	☐	☐
b) Adequate control group (No. of animals, comparability)	☐	☐	☐	☐	☐	☐
c) Type of randomisation	☐	☐	☐	☐	☐	☐
d) Type of blinding	☐	☐	☐	☐	☐	☐
→ Description of study design is clear and detailed	☐	☐	☐	☐	☐	☐

Statistics	strongly agree	agree	neutral	disagree	strongly disagree	not determined
1. Statistical tests are adequate	☐	☐	☐	☐	☐	☐
2. Sample size is adequate	☐	☐	☐	☐	☐	☐
3. Level of significance is adequate	☐	☐	☐	☐	☐	☐
4. Handling of missing data is adequate and comprehensable	☐	☐	☐	☐	☐	☐
5. Analysis of data is adequate (intention-to-treat-analysis/ per-protocol-analysis, drop-out-analysis)	☐	☐	☐	☐	☐	☐
6. Description of statistics is adequate and comprehensible	☐	☐	☐	☐	☐	☐

Presentation and information content	strongly agree	agree	neutral	disagree	strongly disagree	not determined
1. The article is written objectively	☐	☐	☐	☐	☐	☐
2. The summary represents the content sufficiently	☐	☐	☐	☐	☐	☐
3. Other studies dealing with the topic are discussed	☐	☐	☐	☐	☐	☐
4. The bibliography is adequate (comprehensive, current)	☐	☐	☐	☐	☐	☐

Practical applicability	strongly agree	agree	neutral	disagree	strongly disagree	not determined
1. Information is relevant for practice or science	☐	☐	☐	☐	☐	☐
2. Applicability is discussed (techniques, equipment and knowledge, costs)	☐	☐	☐	☐	☐	☐
3. Alternatives are discussed	☐	☐	☐	☐	☐	☐
4. Side effects, limitations and complications are discussed	☐	☐	☐	☐	☐	☐

Conclusions

1. Data is sufficient to draw valid conclusions

☐ strongly agree ☐ agree ☐ neutral ☐ disagree ☐ strongly disagree

2. Level of evidence of the article

☐ Meta-analysis ☐ Randomized controlled trial ☐ Controlled trial

☐ Not experimental descriptive trials ☐ Case report, general information, description of experience

To measure the repeatability among investigators in our study, a pre-test was performed. The evaluation of six randomly selected articles was initially performed by the three authors. A Fleiss' kappa test was used to calculate the degree of agreement in the classification of the articles by the investigators over that which would be expected by chance. It can be adapted for more than two evaluators [12]. The range of possible values is from -1 to 1 [13].

For each article, the checklist only was assessed by one evaluator and all articles were assessed by the same single evaluator. Subsequently these data were compiled. Deficits of literature on each species were defined if a criterion was evaluated as disagreeable or strongly disagreeable for approximately 50% of the publications. The statistical significance of differences of the species specific likert scale results was evaluated by Chi-square tests. Due to a low number of criteria with significant differences the centralization of the extreme position by combining 'strongly agree' and 'agree' as well as 'strongly disagree' and 'disagree' was conducted. Furthermore, clinical trials ('Randomized controlled trial', 'Controlled trial without randomization' and 'Not experimental descriptive trial') were combined with one 'Meta-analysis'. All analyses were conducted by SPSS software. The level of significance was set to $P < 0.05$.

Results

Literature search in the databases Medline and Veterinary Science revealed 25,910 articles in the field of reproduction for cattle, 5,090 articles for horses, and 5,015 articles for dogs, after doublets had been excluded. According to the exclusion criteria, 360 publications (119 for cattle, 116 for horses, and 125 for dogs) had to be withdrawn from the 600 publications which had been randomly selected. To minimize selection bias, clear and reproducible criteria were defined. Hence, a total of 240 articles (81 for cattle, 84 for horses, and 75 for dogs) were eligible for further analysis. A standardized checklist was used to investigate the articles systematically. If more than one study was described in a given publication each study was evaluated as a separate entity using a separate evaluation form. Therefore, 86 evaluation forms were used for cattle, 99 for horses, and 83 for dogs (n = 268). Articles published in German were 4% for cattle, 6% for horses, and 2% for dogs. The reliability in the pre-test was Kappa = 0.55, indicating a moderate agreement [14]. Total agreement was reached regarding important review categories (100%) such as study design comprising a control group, randomization or blinding, as well as level of evidence.

Considering the study design, 238 of 268 (89%) publications were classified as clinical trials and one meta-analysis (Table 1). The meta-analysis was on equine reproduction. The remaining 30 publications (11%) contained case reports or information

Table 1

Level of evidence of 268 randomly selected publications on reproduction in cattle, horses, and dogs (numbers of articles).

Level of evidence	Cattle	Horses	Dogs	Total
Meta-analysis	0 (0.0)	1 (0.4)	0 (0.0)	1 (0.4)
Randomized controlled trial	29 (10.8)	20 (7.5)	8 (3.0)	57 (21.3)
Controlled trial without randomization	23 (8.6)	19 (7.1)	22 (8.2)	64 (23.9)
Not experimental descriptive trial	34 (12.7)	48 (17.9)	34 (12.7)	116 (43.3)
Case report, personal experience or expert opinions	0 (0.0)	11 (4.1)	19 (7.1)	30 (11.2)
Total	86 (32.1)	99 (36.9)	83 (31.0)	268

based on personal experience (i.e. report on management of dystocia without any reference of trials to verify the statement). The number of case or personal reports on reproduction of dogs was higher ($P < 0.001$) compared to the number of case or personal reports on reproduction of cattle and horses. However, for all three species, at least three-quarter were clinical trials. The predominant level of evidence corresponded to 'Not experimental descriptive trials' (i.e. clinical trails without a control group [case series] or observational studies).

The description of the animals as clear and detailed was predominantly rated with 'strongly agree' and 'agree' (cattle 57 articles = 66%; horses 50 articles = 51%; and dogs 52 articles = 63%). The reported information on housing and feeding of the animals was most detailed in literature about cattle ('strongly agree' and 'agree': cattle 40 articles = 47%; horses 17 articles = 17%; and dogs 15 articles = 18%). Conversely, age information was predominantly provided in publications on dogs ('strongly agree' and 'agree': cattle 29 articles = 34%; horses 40 articles = 40%; and dogs 52 articles = 63%). Information given regarding the examination ('strongly agree' and 'agree': cattle 35 articles = 41%; horses 53 articles = 54%; and dogs 43 articles = 52%), monitoring ('strongly agree' and 'agree': cattle 37 articles = 43%; horses 42 articles = 42%; and dogs 38 articles = 46%) and treatment or intervention ('strongly agree' and 'agree': cattle 72 articles = 84%; horses 79 articles = 80%; and dogs 67 articles = 81%) was similar between the three species. Overall, 49% of the studies had included control groups (cattle 57 articles = 66%; horses 41 articles = 41%; and dogs 34 articles = 41%). In articles on bovine reproduction the criterion control group was rated more adequate ($P < 0.01$) in respect to the number and comparability of subjects such as breed, housing, and feeding. Randomization was conducted in 34% (cattle 29 articles), 22% (horses 22 articles) and 12% (dogs10 articles), and blinding in 4% (cattle 3 articles), 6% (horses 6 articles) and 7% (dogs 6 articles) of the articles, respectively. In total, three articles of each species and overall 3% of the evaluated articles were classified as randomized, controlled and blinded clinical trials.

Statistical procedures were determined more adequate (P< 0.001) in articles related to bovine reproduction (‘strongly agree’ and ‘agree’: cattle 75 articles = 87%; horses 59 articles = 60%; and dogs 39 articles = 47%). The criterion number of animals was estimated more often as adequate in cattle (‘strongly agree’ and ‘agree’: 43 articles = 50%) compared to horses (29 articles = 29%) and dogs (13 articles = 16%). The summaries represented the content sufficiently (‘strongly agree’ and ‘agree’) in 78 articles = 91%, 74 articles = 75% and 55 articles = 66% for cattle, horses and dogs, respectively. However, in the field of canine reproduction, no summaries at all or summaries of lower quality were more frequent (P < 0.001) (‘disagreeable’ or ‘strongly disagreeable’: cattle 0 articles = 0%; horses 11 articles = 11%; and dogs 19 articles = 23%). Alternative treatments were less often (P < 0.001) discussed in articles on bovine reproduction (‘strongly agree’ and ‘agree’: cattle one articles = 1%) compared to horses (15 articles = 15%) and dogs (9 articles = 11%). The statement that data were adequate to draw sound conclusions (Table 2) was confirmed more often (P < 0.001) in cattle (‘strongly agree’: 28 articles = 33%) and less common (P < 0.001) in dogs (‘strongly disagree’: 19 articles = 23%). In horses, it was predominantly estimated with ‘neutral’ (30 articles = 30%).

Table 2

The adequacy to draw valid conclusions of publications (n = 268) on reproduction in cattle, horses, and dogs(numbers of articles).

Species	Answer					Total
	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	
Cattle	28 (10.5)	29 (10.8)	19 (7.1)	10 (3.7)	0 (0.0)	86 (32.1)
Horses	11 (4.1)	23 (8.6)	30 (11.2)	24 (9.0)	11 (4.1)	99 (36.9)
Dogs	6 (2.2)	13 (4.9)	23 (8.6)	22 (8.2)	19 (7.1)	83 (31.0)
Total	45 (16.8)	65 (24.3)	72 (26.9)	56 (20.9)	30 (11.2)	268

Discussion

Based on the results of the sample evaluated in this study, approximately five times more articles regarding clinical bovine reproduction have been published compared to canine and equine reproduction. We did not validate the correct species indexing conducted by the databases throughout all articles. Nevertheless, it can be assumed that indexing errors occurred independent of specific species. Thus a bias was unlikely to be present. The

hypothesis that there are significantly fewer publications in the area of reproduction of horses and dogs compared to that of cattle was confirmed.

Regarding the considerable difference in studies published in the area of bovine reproduction compared to canine and equine reproduction, it needs to be considered that there is a high economic value [15,16] and public health interest in trials related to bovine reproduction. Products from cattle such as milk, meet and leather are fundamental to society. The importance of reproduction is also substantiated by the number of offspring born in the three species. In Germany, there were 2,694,519 calves [17], 46,661 foals [18] and 87,821 puppies [19] reported to be born in 2009. However, not all offspring born had to be registered, and animal import and export were conducted. Nevertheless, achieving effective clinical research was encumbered by the smaller canine and equine population.

In this study, we used Medline and Veterinary Science as databases and did not additionally search by hand. Each database has its strengths and weaknesses and no database provides adequate indexing to all relevant veterinary literature [20]. Therefore, it is highly unlikely that the literature search included all studies conducted in the area of reproduction in cattle, horses, and dogs. We decided to use these two databases since Medline is one of the most powerful databases for journals of human and veterinary medicine [21], with 37,665 available journals. Veterinary Science is specific to veterinary medicine and encompasses 2,413 journals. Furthermore, we wanted to obtain a transparent, repeatable, and non-biased data set.

Some limitations regarding material and methods of this study have to be discussed. An increase of the sample size of assessed articles may have improved the validity of the study results. However, our approach of using a subsample of 600 randomly selected articles resulting in 268 evaluated trials was a compromise based on feasibility and scientific validity. It is routine for peer reviewed journals to utilize two to three reviewers to minimize person-based bias. In a pre-test, the reliability of agreement among three evaluators was assessed using the Fleiss' kappa test. As repeatability of classification conducted by independent investigators was moderate and repeatability of important review categories was high, only one investigator continued with the assessment of all 268 trials. However, if difficulties in the assessment were encountered, the criteria were discussed by all three authors. The information of the Fleiss' kappa test only values the agreement among investigators. It does not provide evidence if the investigators assessed the quality of the articles correctly compared to a gold standard (which is not available in these types of studies). Therefore, in further trials, an accurate definition of a good standard of quality for each criterion or a higher number of investigators would be instrumental to increase interobserver agreement. Nevertheless, the checklist has been demonstrated to be a useful and reliable tool ($\kappa = 0.56$) for systematically assessing the quality of a publication by one investigator [7].

Controlled, randomized, and blinded studies are essential to minimize bias and to obtain scientifically valid outcomes [22]. Therefore, these criteria are essential to achieve the highest level of evidence. Other evidence levels do not inevitably imply that results or conclusions are wrong. The reader and user of information, however, has to consider that the certainty with which the results represent the truth is weaker. Additionally, lower evidence levels, e.g., case reports, are important, as they enable rapid publication of new and rare information and stimulate ideas for future studies. The finding of a previous observation without a systematic evaluation of studies that blinded, placebo-controlled, randomized trials are scarce in equine medicine was supported in the present study [23]. Clinical trials were identified in 77% of canine publications. In contrast, Arlt et al. [7] evaluated literature published between 1996 and 2006 on canine reproduction (n = 287) and identified 31.4% as clinical trials. Therefore, progress has been made regarding the percentage of clinical trials. Although we randomly selected 200 publications out of the body of literature, it cannot be excluded that the number of clinical trials was overestimated. Also, the two approaches (comparison of bovine, equine, and canine versus general canine reproduction) might have influenced the percentage of clinical trials. It became obvious, however, that in equine and canine reproductive medicine, considerable fewer trials existed with an adequate control groups compared to bovine reproduction.

The hypothesis that there are important deficits in the description of the animals, study design, statistics, and validity of conclusions in bovine, equine, and canine reproduction was confirmed in the present study (Table 3). Substantive deficits exist in the reporting of methodological quality criteria and in the completeness of reporting in bovine and canine publications [24,25], as well as bovine and porcine conference proceedings [26].

Table 3

Deficits ('disagree' and 'strongly disagree' in %) in articles (n = 268) on bovine, equine and canine reproduction

Criterion	Species		
	Cattle (n = 86)	Horses (n = 99)	Dogs (n = 83)
Housing	32.6	67.7	62.7
Age	51.2	27.3	18.1
Preconditions and pretreatments	53.5	66.7	65.1
The study was controlled	33.7	57.6	56.6
Randomisation is conducted	65.1	76.8	85.5
The study is conducted in a blinded manner	96.5	92.2	90.4
Number of animals is adequate	32.6	53.5	66.3
Alternatives are discussed	36.0	36.4	48.2
Data is sufficient to draw valid conclusions	11.6	35.4	49.4

These deficits hamper critical evaluation by readers. Also, deficits of publications are species specific ($P < 0.001$ to $P < 0.01$). Based on our data, we can not offer a science-based explanation for these differences. One major reason for the scarcity of adequate clinical trials may be the high costs involved in performing them. The veterinary pharmaceutical market represents only a tiny fraction of the entire pharmaceutical industry, and the industry is therefore unlikely to conduct studies whose costs could exceed potential returns and may imply even nonpharmacological modalities [23]. Furthermore, species-specific animal husbandry system might also have a role. Although dairy and beef cattle are kept in herds of constantly increasing sizes [27,28], horses and dogs are considered companion animals and housed either on smaller farms or individually with a family. These animal husbandry practices lead to a high individual variance of information about the animals given and potentially lower compliance of companion animal owners. In bovine research, animals fitting certain inclusion criteria are more easily available and adequate control groups are easier to implement.

The daily decision making of veterinarian should be based on the best available evidence. Comparing our data with the data of Arlt et al. [7], we found an improvement in the evidence of the quality of literature on canine reproduction. Therefore, the deficits are not insurmountable obstacles. To improve the quality of studies in the field of animal reproduction, the deficits (e.g., control groups, randomization, blinding, sufficient sample size) identified in this study should be considered to improve the study design. The scarcity of controlled studies seriously limits the applicability of an evidence-based approach in veterinary medicine [23]. This lack of a substantial base of primary research data makes it difficult to perform systematic reviews and meta-analyses, which represent the strongest form of evidence in making clinical decisions [22]. A high evidence level is provided only by scientifically valid data. Therefore, a poor study design or reporting does not provide necessary information for readers to interpret and apply study results [29].

Conclusion

Overall, 17% of the studies were graded strongly adequate to draw sound conclusions (‘strongly agree’: cattle 33%, horses 11% and dogs 7%). Therefore, the veterinarian should always try to assess the quality of information before implementing results into practice. To evaluate the quality of a publication, the veterinarian has to evaluate not just a single criterion as the level of evidence, a large number of animals, or the critical discussion of the data. Only the combination of all aspects assures a high quality of a

publication. For the field of canine and equine reproduction, there are not enough clinical trials with a control group. For all three species, there were only 4% controlled, randomized and blinded trails or meta-analyses. This lack of high quality trials hampers the implementation of meta-analyses. This is relevant for the practitioner, since availability of more meta-analyses would reduce the negative effects of the information explosion and would help them to remain current and to make decisions with the actual best evidence in daily practice. Hence, improvement of the quality of well-designed, conducted, and reported clinical trails is required.

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2.3 Inter-observer agreement of a checklist to evaluate scientific publications in the field of animal reproduction

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Inter-observer agreement of a checklist to evaluate scientific publications in the field of animal reproduction

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Abstract

This study's objective was to determine respondents' inter-observer agreement on a detailed checklist to evaluate three exemplars (one case report, one randomized controlled study without blinding, and one blinded, randomized controlled study) of the scientific literature in the field of bovine reproduction. Fourteen international scientists in the field of animal reproduction were provided with the three articles, three copies of the checklist, and a supplementary explanation. Overall, 13 responded to more than 90% of the items. Overall repeatability between respondents using Fleiss's κ was 0.35 (fair agreement). Combining the "strongly agree" and "agree" responses and the "strongly disagree" and "disagree" responses increased κ to 0.49 (moderate agreement). Evaluation of information given in the three articles on housing of the animals (35% identical answers) and preconditions or pretreatments (42%) varied widely. Even though the overall repeatability was fair, repeatability concerning the important categories was high (e.g., the level of agreement = 98%). Our data show that the checklist is a reasonable and practical supporting tool to assess the quality of publications. Therefore, it may be used in teaching and practicing evidence-based veterinary medicine. It can support training of systematic and critical appraisal of information and in clinical decision making.

Keywords: evidence-based veterinary medicine; literature quality; evaluation form

3. Discussion

The first article (Simoneit et al. 2012b) demonstrates the importance of evidence-based veterinary medicine. It describes the different steps of performing EBVM, e.g. an effective information search, assessing the quality of this information and deciding whether it can be applied to the case or not. This overview discusses also the advantages and obstacles of EBVM for practitioners. Further steps to establish EBVM, e.g. developing a curriculum to teach students the significance and acquaintance of performing EBVM, are recommended. Courses to deal with English publications would be beneficial. Furthermore, high quality research as systematic reviews and meta-analyses should be easier to receive for practitioners.

The results of the assessment of the literature in the second article (Simoneit et al. 2011) indicate that adequate clinical trials are rare in the field of animal reproduction. Special limitations in the literature on animal reproduction were identified. Similar studies conclude that in veterinary medicine few publications of high level evidence exist and substantial deficits in quality often occur (Arlt et al. 2010; Brace et al. 2010; O'Connor et al. 2010; Sargeant et al. 2010; Simoneit et al. 2012a).

These deficits have to be identified by readers and taken into account when deciding to incorporate information into practice or not. The recommendations which were formulated should be considered to improve future study design. It remains open if these deficits also exist in literature of other disciplines like internal medicine and surgery.

The quality of information has to be improved regarding e.g. study design and animal number. Especially in trials conducted in the field of companion animals it is often difficult to receive a significant number of animals. This might be due to the small number of animals per owner. Validity of information could possibly be enhanced by including data from practice into research. In this case animal number could easily be increased. This way e.g. one case study would not be the only source of information and by including several cases the evidence could be increased. This would necessitate implementing of and experimenting with data-collecting systems (Vandeweerd et al. 2012c). In the field of animal production databases are developed for certain specific topics e.g. antibiotics monitoring (http://www.q-s.de). However, to design these data-collection systems there may be limitations e.g. to receive sufficient and clear information from the practitioners. Further difficulties may be to harmonize different operation methods of practitioners and animal conditions as housing and feeding. Additionally, data retrieval from practice may be difficult due to the absence of sufficient funds to allow this type of data management (Vandeweerd et al. 2012a). The

willingness of owners and vets to participate could be a further problem. However, practitioners who help conduct a study may be highly interested in receiving accurate results concerning the question. Therefore, it could be an impulsion for practitioners to provide data if the database would show results as well. Although, this data management from the practice is not a replacement for conducting controlled and randomized trials. Still, this way the collaboration of research and practice could be promoted.

A further obstacle to the implementation of EBVM is that tools which can be applied in the daily practice of veterinarians are rarely available (Vandeweerd et al. 2012d). Therefore, a checklist was developed (Dicty 2008; Simoneit et al. 2011). This checklist was sent to scientists in the field of animal reproduction affiliated to a university to assess the inter-observer agreement (Simoneit et al. 2012c). However, its usability for practitioners as well as students has to be assessed in further trials. Additional tools that help to deal with the information explosion and variety in quality could be critically appraised topics (CAT) (Arlt et al. 2012), systematic reviews and meta-analyses (Lean et al. 2009). A systematic review should identify all relevant primary research, make a standardized appraisal of quality, and systematically synthesize the results of studies of acceptable quality (Vandeweerd et al. 2012b). CATs have been developed to have a more direct relevance to clinicians (Foster et al. 2001). The importance of presenting evidence in the form of summarized information and that this is made available for practitioners has been pointed out (Buczinski et al. 2012). However, barriers are the scarcity of primary research and the unknown extent to which systematic reviews require updating. In human medicine, a study showed that signals for updating occurred frequently and within a relatively short time (Shojania et al. 2007). These accurate, informative, and clear summarized information of high-level research studies should be obtainable quickly from free-access databases available via the internet (Vandeweerd et al. 2012c).

In conclusion, information of high evidence is provided only by scientifically valid trials. A poor study design or reporting does not provide sufficient information for readers to interpret and apply study results (Lund et al. 1998). Therefore, the veterinarian must always assess the quality of information before implementing results into practice. Further projects should focus on sensitizing veterinarians to the problem of possible low quality of published information. And it is important to conduct further studies about how to strengthen the link between high evidence publications and clinical veterinary practice.

4. Summary

Céline Simoneit: Evaluation of the quality of current literature in the field of bovine, canine and equine reproduction and the manageability of its assessing by using a checklist

Veterinarians provide a wide range of services and play an important role in protecting animal welfare and maintaining animal and public health. Publications are important to implement knowledge into the practice despite the difficulties of a continuous increase of literature and variations in quality. Thus, the systematic evaluation of the quality of veterinary literature may help to imply best available care for patients of the highest available evidence.

The overall objective of this study was to evaluate the quality of actual veterinary literature and the manageability of its assessing. First an overview of evidence-based veterinary medicine, its strengths and weaknesses regarding the establishment in a workaday life was shown.

In the first study the quality of a randomly selected sample of published literature on reproduction of cattle, horses and dogs was evaluated and compared.

A literature search was conducted in the databases Medline and Veterinary Science. Approximately five times more articles on clinical bovine reproduction (n = 25 910) were found compared to canine (n = 5 015) and equine (n = 5 090) reproduction. For the evaluation of the literature a checklist was used. A subset of 600 articles published between 1999 and 2008 was randomly selected. After applying exclusion criteria a total of 268 trials (86 for cattle, 99 for horses and 83 for dogs) was evaluated and used for further analysis.

Data of this study demonstrated for the field of canine and equine reproduction fewer clinical trials with a control group compared to bovine reproduction (cattle 66%, horses 41% and dogs 41%). For all three species investigated, few publications were identified (4%) with the highest level of evidence, i.e. controlled, randomized and blinded trials or meta-analyses. In cattle 33% of the publications were graded adequately to draw sound conclusions. Only 7% and 11% were graded adequately in dogs and horses, respectively.

Altogether, the results of this study demonstrate deficits and differences of published literature on reproduction in cattle, dogs and horses. Hence, improvement of the quality of well-designed, conducted and reported clinical trails is required.

The objective of the second study was to determine the inter-observer agreement utilizing an existing checklist for the evaluation of scientific literature in the field of animal reproduction.

Three publications on bovine reproduction (one case report, one randomized controlled study without blinding and a blinded, randomized controlled study) were selected. Fourteen international recognized scientists in the field of animal reproduction were utilized. Each reviewer was provided with the three articles, three checklists, and supplementary explanations.

Altogether, 13 of the respondents filled out over 90% of the answers of the three evaluation forms. The repeatability for the respondents using a Fleiss' kappa was 0.35. By combining 'strongly agree' and 'agree' as well as 'strongly disagree' and 'disagree' the kappa value increased to 0.49. There was a very strong agreement among the respondents concerning the classification of the level of evidence (98% of all evaluation forms). Only in one case a randomized, controlled trial was considered as a controlled trial. Evaluation of information provided regarding housing (35% identically answers) and preconditions or pretreatments (42%) of the animals varied widely in all publications.

These data illustrate that by combination of the extreme positions the kappa value raised from a fair to a moderate agreement. Even if the repeatability of classification was moderate, repeatability of important review categories was high. Our data provide evidence that such a checklist does provide a reasonable and practical tool to assess the quality of publications.

Overall, the two studies demonstrated the manageability of using a checklist to assess the quality of publications. Additionally, publications in the field of animal reproduction vary widely in their quality and the deficits are species specific. The lack of high quality trials hampers the implementation of high evidence knowledge. Therefore, the veterinarian should always try to assess the quality of information before implementing results into practice.

5. Zusammenfassung

Céline Simoneit: Beurteilung der Qualität von Publikationen im Bereich der Reproduktionsmedizin von Rindern, Hunden und Pferden und ihrer Durchführung anhand eines Fragebogens.

Veterinärmediziner haben ein weit reichendes Aufgabengebiet und spielen eine wichtige Rolle im Tierschutz und der Aufrechterhaltung der Gesundheit von Tier und Mensch. Wissenschaftliche Veröffentlichungen sind von großer Bedeutung, um Erkenntnisse in die Praxis einzuführen. Allerdings besteht die Schwierigkeit eines ständigen Anstiegs der Publikationsmenge und deren Qualitätsunterschieden. Aus diesem Grund würde eine systematische Beurteilung der Qualität von veterinärmedizinischer Literatur dem Tierarzt helfen, eine optimale Betreuung der Patienten anhand von Erkenntnissen mit der höchsten Evidenz zu gewährleisten.

Ziel dieser Arbeit war die Beurteilung der Qualität von aktueller veterinärmedizinischer Literatur und die Durchführbarkeit dieser Beurteilung. Zuerst wird ein Überblick der evidenzbasierten Veterinärmedizin und ihre Vor- und Nachteile bei der Etablierung im Praxisalltag dargestellt.

In der ersten Studie wurde die Qualität einer randomisierten Stichprobe von Publikationen über die Reproduktionsmedizin von Rindern, Pferden und Hunden bewertet und verglichen.

Eine Literatursuche wurde anhand der Datenbanken Medline und Veterinary Science durchgeführt. Ungefähr das Fünffache an Artikeln wurde zur Reproduktionsmedizin von Rindern (n = 25 910) im Vergleich zu Hunden (n = 5 015) und Pferden (n = 5 090) gefunden. Für die Beurteilung der Literatur wurde ein Fragebogen genutzt. Eine Stichprobe von 600 Artikeln, die zwischen 1999 und 2008 publiziert wurden, wurde randomisiert ausgewählt. Nach der Anwendung von Ausschlusskriterien wurden 268 Studien (86 für Rinder, 99 für Pferde und 83 für Hunde) bewertet und weitere Analysen durchgeführt.

Die Daten dieser Studie bestätigten für den Bereich der Reproduktionsmedizin von Hunden und Pferden weniger klinische Studien mit einer Kontrollgruppe im Vergleich zur Reproduktionsmedizin von Rindern (Rinder 66%, Pferde 41% und Hunde 41%). Für alle drei untersuchten Tierarten wurden nur wenige Publikationen (4%) mit dem höchsten Evidenzlevel (kontrollierte, randomisierte und verblindete Studien oder Metaanalysen) identifiziert. Als adäquate, um wissenschaftlich gesicherte Schlussfolgerungen ziehen zu können, wurden 33% der Publikationen aus dem Themenbereich Rind eingestuft. Nur 7% und 11% waren bei Hunden und Pferden als adäquate beurteilt worden.

Insgesamt weisen die Ergebnisse dieser Studie Defizite und Unterschiede in Publikationen der Reproduktionsmedizin von Rindern, Pferden und Hunden auf. Dementsprechend ist eine Verbesserung der Qualität der Planung, Durchführung und Beschreibung klinischer Studien erforderlich.

Ziel der zweiten Studie war die Untersuchung des inter-observer Agreements bei der Nutzung eines existierenden Fragebogens für die Bewertung von wissenschaftlicher Literatur in dem Bereich der Veterinär-Reproduktionsmedizin.

Drei Artikel zu dem Thema der Reproduktionsmedizin von Rindern (ein Fallbericht, eine randomisierte, kontrollierte Studie ohne Verblindung und eine verblindete, randomisierte und kontrollierte Studie) wurden ausgewählt. Vierzehn internationale Tierärzte mit Spezialisierung auf dem Gebiet der Veterinär-Reproduktionsmedizin haben an dieser Studie teilgenommen. Jeder Teilnehmer erhielt die drei Artikel, drei Fragebögen und eine Liste mit Erläuterungen.

Insgesamt haben dreizehn Teilnehmer über 90% der drei Fragebögen ausgefüllt. Die Übereinstimmungen der Antworten ergaben einen Fleiss' Kappa von 0.35. Die Zusammenführung von ‚trifft voll und ganz zu' und ‚trifft zu' sowie ‚trifft ganz und gar nicht zu' und ‚trifft nicht zu' führten zu einem Anstieg des Kappas auf 0.49. Es bestand eine große Übereinstimmung zwischen den Teilnehmern in Bezug auf die Einteilung der Artikel in Evidenzstufen (98% der Artikel). Nur in einem Fall wurde eine randomisierte, kontrollierte Studie als eine kontrollierte Studie eingestuft. Beurteilungen zu Informationen zur Haltung (35% identische Antworten) sowie Vorerkrankungen und Vorbehandlungen (42%) der Tiere waren zu allen Artikeln sehr unterschiedlich.

Diese Daten verdeutlichen, dass sich beim Zusammenführen der extremen Positionen der Antworten der Kappa-Wert von einer ausreichenden auf eine mittelmäßige Übereinstimmung erhöht. Trotz einer mittelmäßigen Übereinstimmung war die Übereinstimmung von wichtigen Bewertungskategorien hoch. Unsere Daten bieten Anhaltspunkte, dass die Nutzung eines Fragebogens ein angemessenes und praktisches Instrument ist, um die Qualität von Publikationen zu beurteilen.

Insgesamt verdeutlichen die beiden Studien die Durchführbarkeit der Qualitätsbeurteilung von Literatur anhand eines Fragebogens. Zusätzlich weisen Publikationen im Bereich der Veterinär-Reproduktionsmedizin Unterschiede in ihrer Qualität auf. Diese sind tierartspezifisch. Die Ermangelung von qualitativ hochwertigen Studien verhindert die Einführung von Erkenntnissen hoher Evidenz. Diese sind allerdings notwendig, um fundierte Schlussfolgerungen für veterinärmedizinische Fragestellungen zu ziehen. Aus diesem Grund sollten Tierärzte möglichst die Qualität von Informationen vor ihrer Umsetzung in die Praxis beurteilen.

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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 analyses	+++	+++
Manuscript writing	+++	+++
Manuscript editing	++	++

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

Anteil Eigener Anteil an den Studien

Beitrag	Studie 1	Studie 2
Studienplanung	+++	+
Datenerhebung	+++	++
Datenanalyse	+++	+++
Verfassen des Manuskriptes	+++	+++
Editieren des Manuskript	++	++

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

8. Publications

Research articles

Simoneit C, Gartrell B D. 2008. Treatment of Lead Toxicosis in a North Island Kaka. Kokako 15 (2): 35-41

Simoneit C, Heuwieser W, Arlt S. 2011. Evidence-based medicine in bovine, equine and canine reproduction: quality of current literature. Theriogenology 76 (6): 1042-1050

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Poster

Arlt S, Simoneit C, Heuwieser W. 2011. Quality of literature on bovine, equine and canine reproduction. The 15th annual conference of the ESDAR, Antalya/ Türkei, 15.-17.09.2011. Reprod Dom Anim. 46 (Suppl. 3): 86

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10. Declaration of Independence

Hiermit erkläre ich, dass ich alle Studien selbstständig durchgeführt und die vorliegende Arbeit selbstständig angefertigt habe. Ich versichere, dass ich ausschließlich die angegebenen Quellen und Hilfen in Anspruch genommen habe.

This is to declare that I conducted all of 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.

Berlin, den 24.09.2013

Céline Simoneit