Communication

The Value of Evidence Synthesis in Animal Sciences: A Discussion and Call to Action

Alex Whittaker * , Edoardo Aromataris Aromataris , Rachel Ankeny , Lisbeth Rem Jessen , Karolina Scahill , Marnie Brennan , Kapil Chousalkar , Zachary Munn , Timothy Barker

Posted Date: 9 February 2024

doi: 10.20944/preprints202402.0553.v1

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The Value of Evidence Synthesis in Animal Sciences: A Discussion and Call to Action

Alexandra L. Whittaker [1,*], Edoardo Aromataris [2], Rachel A. Ankeny [3], Lisbeth Rem Jessen [4], Karolina Scahill [5,6], Marnie L. Brennan [7], Kapil K. Chousalkar [1], Zachary Munn [8] and Timothy H. Barker [8]

1 School of Animal and Veterinary Sciences, Roseworthy Campus, The University of Adelaide, Roseworthy, SA 5116, Australia
2 JBI, Faculty of Health and Medical Sciences, The University of Adelaide, Adelaide, SA, Australia
3 School of Humanities, University of Adelaide, Adelaide, South Australia 5005, Australia
4 Department of Veterinary Clinical Science, University of Copenhagen, 1870 Frederiksberg C, Denmark
5 University of Edinburgh, College of Medicine and Veterinary Medicine, Edinburgh, EH16 4SB, United Kingdom
6 Evidensia Södra Djursjukhuset Kungens Kurva, Månskärarvägen 13, Kungens Kurva, 14175, Sweden
7 Centre for Evidence-based Veterinary Medicine, School of Veterinary Medicine and Science, University of Nottingham, Loughborough, Leicestershire, UK
8 Health Evidence Synthesis, Recommendations, and Impact (HESRI), School of Public Health, University of Adelaide, Adelaide, SA, Australia
* Correspondence: alexandra.whittaker@adelaide.edu.au

Abstract: Population growth, climate change, changes to land use, and the advent of emerging infectious disease agents has put our abilities to feed the growing global population at risk, which is of particular concern in low- or middle-income countries. Research to improve the profitability and sustainability of common livestock production systems is key to tackling this issue. However, despite considerable research investment to address this concern, there has been little attention paid to development of robust methodologies for the synthesis of existing research evidence and its re-use in the broader animal sciences discipline. Syntheses of evidence are critical for fostering best practices, minimising wastage of valuable research resources, and enabling informed decision and policy making. Whilst the use of evidence syntheses is well entrenched in human healthcare, with some evidence of their use in veterinary and agricultural sciences, their use within the broader animal sciences field is limited and specific methodologies for performing them are underdeveloped. In this call to action, we propose some methodological development activities that should be undertaken within this field of research to increase the potential of evidence syntheses to contribute to tackling pressing societal issues relating to livestock agriculture.

Keywords: evidence synthesis; agricultural policy; systematic reviews

Introduction

It has been suggested that the demand for food from animal agriculture will double by 2050. [a] This demand is resulting from a growing population, as well as limits placed on the availability of land, water and energy as a result of these population pressures.[1] Strategies to address these increasing demands require a strong foundation in animal, veterinary and agricultural research in

[a] There is much current work on methods to increase food availability via non-animal production using alternate protein sources. There is also controversy from some quarters around over-reliance on animal production as a food source given environment and sustainability issues. We acknowledge this but do not consider this within the current discussion.

 doi:10.20944/preprints202402.0553.v1

order to increase productivity, food safety, and animal welfare whilst decreasing costs to consumers and negative environmental implications.[1] Furthermore, these strategies require research into changing consumer preferences associated with animal products in various locales.

There are clear evidence gaps about food systems stemming from a lack of primary data and fragmentation across systems and actors.[2] These absences have led to a situation where the impact of legislation on livestock animals and the economics of farming practices can only be approximated with limited precision or accuracy due to lack of underlying data.[2] However, we argue that it is not just a lack of primary data that thwarts progress: secondary sources of data have been underdeveloped and could greatly assist in identifying evidence gaps.

Syntheses of the best available evidence are critically important as enablers of translation of research into practice, whether through practical implementation or via policy reform. It is also increasingly recognised that evidence syntheses can assist in reducing wastage of declining research resources by highlighting which types of potential research are truly novel and justified based on what is already known.[3] However, many of the current synthesis tools, methods, and processes are limited and not applicable to disciplines of science involving animals where outcomes go well beyond health, and considerations about external validity and applicability are often varied and inconsistent both within the animal science discipline and in comparison to traditional fields. In this paper we present an overview on the importance of incorporating robust evidence syntheses to the animal sciences and suggest priority areas for methodological development in this field. This call to action is directed towards policy makers and those conducting evidence synthesis is this field, with the hope to stimulate international collaboration and investment in methodological development.

Why should we care?

Today's society demands safe, affordable, and high-quality animal products. Production should occur in sustainable and culturally sensitive ways with attention to increasing animal welfare and reducing adverse environmental impacts arising from animal agriculture.[4] There is growing interest in new technological advances such as improved breeding methods in relation to production goals, automation of systems, and nutritional or therapeutic interventions to maximise productivity. There is an abundance of research evidence around these topics, as well as continued funding of this type of research by governments and industry bodies to further improve productivity, revenue, welfare, and sustainability. These topics are ripe for evidence syntheses which would help to inform both whether these new technologies and approaches *should* be introduced to practice and, if so, *how* they should be.

However, it is not unusual for goals associated with animal production to conflict with each other, requiring the determination of a point of compromise or establishing trade-offs. For example, whilst antimicrobial use in animal feed creates increased productivity and farm income, it threatens both human and animal health through increasing the development of antimicrobial resistance.[5] Another common example is the well-established relationship proposed by McInerney[6] on livestock productivity and animal welfare: even though livestock productivity can be increased beyond maximal animal welfare (Figure 1, point B), social acceptability is compromised by these further productivity gains due to the negative impacts on animal welfare. These points highlight the need for evidence syntheses not to be constrained to production-based and/or animal-based impacts which may only provide part of the story, but to consider environmental, economic, and human health impacts amongst others.

As a result, it is imperative that evidence synthesis be undertaken by a cross-disciplinary team with expertise across multiple fields of inquiry. In addition to animal and veterinary scientists, these teams should include agricultural economists, social scientists, information specialists, statisticians, and public health scholars, as well as experts in evidence synthesis. Without robust evidence syntheses, millions in research funding is likely to continue to be directed into projects where the answers are already known (if only we'd looked robustly!), or where findings may not actually be as useful as assumed due to subject matter myopia or lack of awareness of previous findings. In

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addition, lack of well-grounded research may indirectly allow negative outcomes to continue to occur with serious effects for animal welfare, human health, and agricultural productivity.

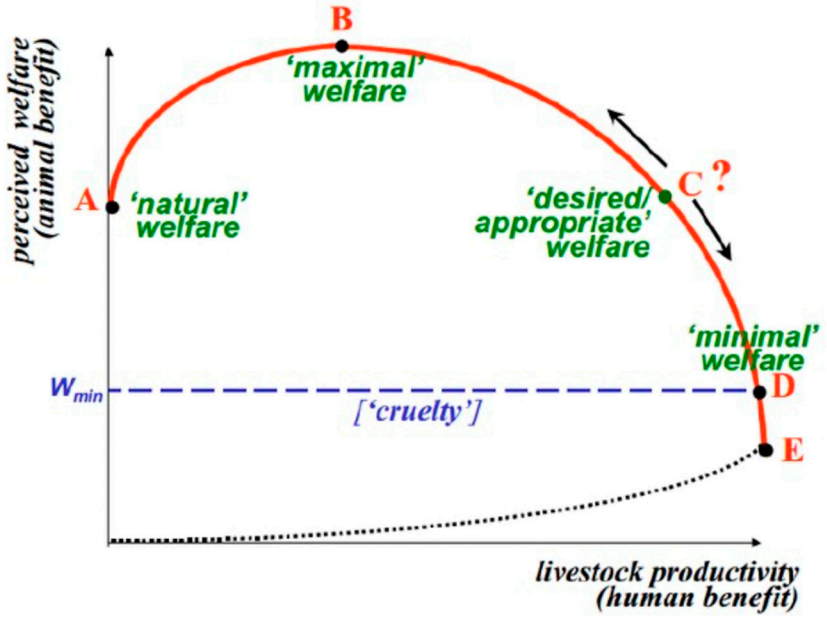

Figure 1. The relationship between livestock productivity and animal welfare as proposed by McInerney 2004.[6]

A further challenge for animal scientists is that livestock farming is heavily influenced by external factors such as weather, geography, type of production system, and labour training and availability. As an example, an intervention that improves productivity in an intensive system may not work as well or be unfeasible in an extensive system. Similarly, given different geography and climatic conditions as well as distinct breed preferences, evidence from studies conducted in Europe may be poorly translatable to farming enterprises in the tropics.

Farming is subject to significant regulatory oversight including in terms of animal welfare, veterinary practice, environmental management, biosecurity, and food safety.[7] Laws are typically (but should always be) drafted against the backdrop of the best available scientific evidence,[8] also taking into consideration prevailing societal and economic viewpoints. However, challenges for regulators include how to source and assimilate this scientific evidence in a non-biased fashion; how to assess relevancy and certainty in the evidence; and how to evaluate the quality and rigor of the research. It has also been acknowledged that methods in other disciplines are not likely to be directly applicable.[9] A final consideration is that of transparency about the science that informs law reform agendas, which feeds into trust. If the data and methods upon which decisions are made is publicly available, others can assess the validity of the research and how that research supports the decision-making process.[10]

We argue that robust methods for evidence syntheses are necessary to address these issues. However, there currently is both lack of awareness and lack of knowledge within the agricultural and animal sciences about best practices for robust evidence assimilation techniques. While there has been some development into tools specific to clinical veterinary medicine, these too are limited in terms of offerings. There has been limited attention paid to methodological development around evidence syntheses, likely due to erroneous assumptions that clinical veterinary or human medicine-related tools can be applied. Below we briefly present some priorities for methodological development in this area and call for greater attention to research into these methods as well as to the fostering of cross-disciplinary networks and outlining of key considerations necessary to develop a new and robust evidence ecosystem for the animal sciences (Figure 2).

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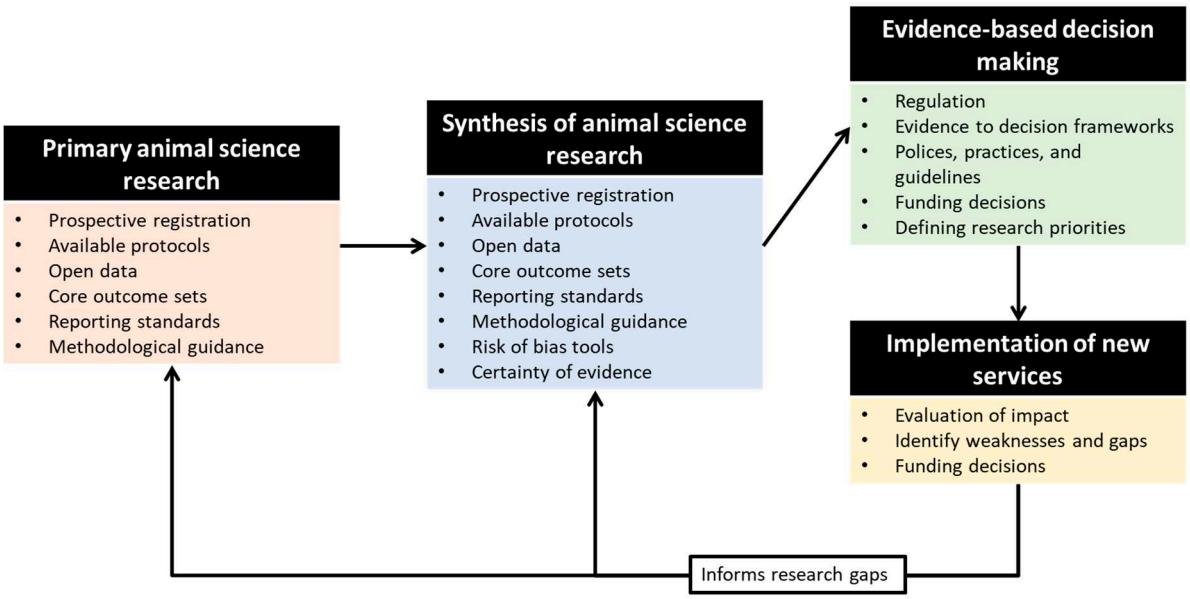

Figure 2. Key components and their interactions proposed to ground a robust evidence ecosystem for animal sciences.

Core Outcome Sets (COS)

Core outcome sets (COS) permit comparative effectiveness research where the benefits and harms of interventions for clinical conditions are being evaluated.[11] In medicine and veterinary medicine,[11,12,13,14] COS outline an agreed set of research outcomes that should be measured and reported in studies investigating a particular health condition.[15] Their use allows robust evidence syntheses to be conducted, minimising wastage of research resources and supporting rapid translation of evidence to practice.[16] COS are available online in a publicly available repository in order to promote their widespread development and use[11].

The selection of appropriate outcomes for research study design is fundamental as any detected differences between intervention groups are considered to arise because of the intervention.[17] Outcomes operate at different levels of specificity and across domains: for example, research in production animals may consider outcomes ranging from health, production, and welfare.[18] Conceptual outcomes focus on one aspect of the domain such as meat-related parameters in relation to production. Outcomes also may be described with varying levels of granularity. For example, an operational outcome of pain may be assessed by a variety of specific outcome measures, such as cortisol levels at a fixed timepoint. In order for COS to work effectively, each component of an outcome needs to be specified precisely to enable it to be used by others (as outlined in Figure 3).

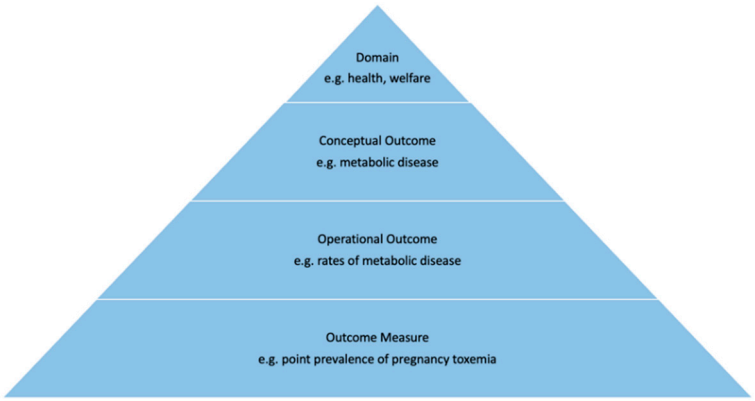

Figure 3. Hierarchy of outcomes requiring definition when establishing Core Outcome Sets (COS).

 doi:10.20944/preprints202402.0553.v1

Defining COS across a range of research areas within animal sciences will assist in building a strong body of evidence, for example about animal welfare, interventions for enhancing reproductive success or meat quantity and/or quality, or effective disease treatments. Thus, COS will ultimately lead to better translation of research to practice, less wastage of research funding through duplications and inefficiencies, and enhanced clinical decision making which will benefit animals through improved health and welfare and improved practices and profits for producers.

Standardised Reporting Guidelines

Standardised reporting guidelines ensure that published research is transparent and contains all the essential information related to the design, conduct, results, and interpretation of the study. Within veterinary medicine, there are a range of reporting guidelines available which have often been adapted from counterparts developed for evidence-based medicine. Examples include the REFLECT statement based on the CONSORT statement for RCTs,[19] and STROBE-vet for observational study designs.[20] The RCVS Evidence Based Veterinary Medicine (EBVM) toolkit also contains several reporting guidelines for the most common study designs.[21] Inclusion of items in reporting guidelines is based on empirical evidence indicating the lack of report regarding a key design feature could either lead to biased effect estimates or would prevent evaluation of the reliability of the findings.[19] Adherence to reporting guidelines ensures that key information is included, enhances reproducibility, facilitates the transferability of findings, and allows systematic reviews to perform a risk of bias assessment.

There are no reporting guidelines that are specific to systematic reviews for animal or veterinary science research. While the PRISMA 2020 statement[22] can be utilised in systematic reviews in the animal sciences, these reporting guidelines have been developed for use in systematic reviews of health interventions. It has been acknowledged that the PRISMA statement is not a 'one size fits all' set of guidelines, with extensions being approved for systematic reviews of diagnostic test accuracy studies[23] and scoping reviews[24] among others. There may be scope for the development of a PRISMA extension that focuses on the unique nuances encountered in systematic reviews of animal science research.

Critical Appraisal Tools

A key component of evidence syntheses which contributes to their rigour and the ability to draw conclusions about the strength of the body of evidence is the use of methods to assess internal validity. Internal validity is defined as the degree to which a study supports a cause-and-effect relationship between the treatment (or exposure) and the observed outcome, that is the degree to which the findings represent a valid finding in the population being studied as opposed to the results being incidental or influenced by methodological factors.[25] The assessment of a study's internal validity is achieved through a risk of bias assessment.

Systematic reviewers often make a distinction between quality assessment (also referred to as a 'critical appraisal' or 'assessment of methodological quality') and risk of bias assessment. Whilst the former often vary in substance, they generally require an evaluation of design features which may in some circumstances result in assessment that goes beyond internal validity. For example, it is not unusual for appraisal criteria to include aspects of study reporting or whether the study received ethical approval. On the other hand, risk of bias tools evaluate whether study design or performance elements may have led to a biased conclusion.[26] As an example, these could cover aspects such as the completeness of the randomisation procedure or the appropriate blinding of investigators. In comparison to quality assessment, a risk of bias assessment requires a more nuanced understanding of certain design features, and the impact that these features (or lack thereof) may have on internal validity. For example, although blinding of outcome assessors is typically associated with reduction in the risk of bias, it may not be important if the outcome being measured is objective (e.g., mortality).[26]

In contrast to the reporting guidelines discussed above, there has been less focus on development of risk of bias tools within EBVM and animal science research more generally. Perhaps

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the most notable set of guidelines for veterinary clinical studies are the appraisal tools for various study designs created by the Centre for Evidence-Based Veterinary Medicine (CEVM).[27] However, these tools are not limited to examination of internal validity, and there is a need for the development of risk of bias tools for use in more comprehensive evidence synthesis approaches that align with recent advancements in the field in other disciplines. with inclusion of some items that may be more suitable in a reporting guideline as they are related to external validity or generalisability to practice. There is potential to develop a new tool in this space, that has been built from the outset to align with recent advancements within the field of risk of bias assessment. A tool such as this would be extremely valuable as it could be applied universally across study designs.[28]

Assessment of the Certainty of the Evidence: Moving from Evidence to Decision

The assessment of the certainty of the evidence is now considered a fundamental component of the evidence synthesis process. Determining the 'certainty' of the evidence involves a judgement about how certain we are that the results of research are correct to inform a decision. Established by the GRADE (Grading of Recommendations Assessment, Development and Evaluation) Working Group, the GRADE approach assigns four levels of 'certainty' to a body of evidence. Levels of 'certainty' are specific to an outcome produced as part of a research synthesis, and in descending order, these certainty levels range from high, moderate, low, or very low. The GRADE methods have been adapted for a range of review types within healthcare. The GRADE approach provides specific criteria used to lower the certainty of the evidence (risk of bias, imprecision, inconsistency, indirectness, and publication bias)[29,30] as well as criteria to increase the certainty of the evidence (magnitude of effect, dose-response gradient, and plausible residual confounding).[29,31]A secondary (but no less important) component of the GRADE approach addresses the complexities and challenges of moving from a synthesised piece of evidence to a formal decision. The GRADE Evidence to Decision Framework (EtDF) assists decision-makers in balancing the benefits and harms of a particular intervention or strategy against other considerations that are important to the decision-making process, but which are overlooked in primary and secondary research mediums. These considerations include contextual factors such as feasibility, equity, acceptability, and costs and resource implications. [32]

GRADE methodology has also been applied outside of health care disciplines, for example in environmental health,[33] public health, [34] and even preclinical animal studies.[35] However, the GRADE approach is constantly evolving, reflective of the ever-changing nature of research synthesis as a discipline. GRADE methods for 'traditional' evidence (i.e., intervention-based research) receive regular updates and attention in the form of new guidance. Although there is some active development of GRADE for use in diverse synthesis types, these efforts are not as prominent when compared to development of the framework for more 'traditional' evidence sources. However, the GRADE working group recently established the GRADE for Veterinary Medicine project group, where some of these issues can begin to be addressed.

There is also scope for greater development of GRADE methods for use in diverse forms of EtDFs. Animal and agricultural sciences, and the decision-making in these fields, are far removed from decision-making processes within healthcare, and additional considerations are likely required, including societal and economic issues that may not be considered in or captured by existing GRADE EtDF methodology. Stakeholder participation is an integral part of the guideline development process to ensure that synthesized evidence is contextualized, and recommendations are of relevance to end-users. Guidance for stakeholder engagement should be adapted to an animal health setting and should include a range of stakeholders, [36] including those whose role it is to safeguard animal welfare.

Take Home Messages and Call to Action

1. **Robust evidence syntheses in animal sciences are critical to inform future research, prevent wastage of research funds, aid adoption of research in practice, and guide policy reform.**
2. **The systematic and reproducible nature of evidence syntheses benefits law reform agendas since it provides transparency around the scientific evidence-base for a decision and assures stakeholders of this evidence base.**
3. **Methods and tools used in evidence-based medicine could be used to guide tool development within the animal sciences, but consideration is needed about discipline-specific factors such as a reliance on observational study designs, aspects of external validity such as geographic and climatic factors, and impacts that may extend beyond the animal (e.g., to humans and the environment).**
4. **In developing and strengthening techniques for evidence synthesis within the animal sciences, a multidisciplinary approach is preferable given that animal benefits may be accompanied by consequences for humans based on a one-health approach, and may be economically or societally unpalatable.**
5. **Identified deficits in the evidence-synthesis toolbox in this discipline include the lack of core outcome sets (COS), true risk of bias tools across a range of study designs, and frameworks for assessing certainty in the evidence synthesised to guide the formulation of robust recommendations.**
6. **There is a need for greater research to develop these evidence synthesis tools by academia, industry, and government. For academics, there is a need for international and multi-disciplinary cooperation to generate these tools and foster industry buy-in.**
7. **Clear strategies for dissemination and education in the use of developed tools is needed to maximise their application and realise the benefits of robust evidence syntheses for research and practice.**
8. **We propose development of a global consortium to create, host, and maintain a database on activities relevant to evidence syntheses in animal sciences, which also could drive methodological development and education efforts.**

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