Animal use and alternatives within life and health sciences education: systematic reviews and the human clinical utility of invasive animal research

ANDREW KNIGHT
MANZCVS, DipECAWBM (AWSEL), DACAW, PhD, MRCVS, SFHEA
Hierarchy of evidence

- Sys Reviews-Metanalysis
- RCT's
- Cohort studies
- Case-Control
- Cross-sectional studies
- Case series, Case reports
- Ideas, opinions, editorials, anecdotal
Example: clinical utility of highly cited animal experiments

- Published in the 7 leading scientific journals when ranked by journal impact factor
- Animal studies with > 500 citations

76 animal studies were located with a median citation count of 889 (range: 639 - 2,233)

However...
Only 36.8% (28/76) were replicated in human randomised trials. 18.4% (14/76) were contradicted by randomised trials, and 44.7% (34/76) had not translated to clinical trials.

Ultimately, only 10.5% (8/76) of these medical interventions were subsequently approved for use in patients.

*Even in these cases human benefit cannot be assumed,*

because adverse reactions to approved interventions are the 4th - 6th leading cause of death in US hospitals.

Systematic reviews examining animal experiments

27 systematic reviews of the utility of animal experiments in advancing human clinical outcomes (20), or in deriving human toxicity classifications (7)

Overall results

The authors concluded that the animal models were useful in advancing human clinical outcomes, or substantially consistent with human outcomes, in only 2 of 20 studies, and the conclusion in 1 case was contentious.

7 reviews failed to clearly demonstrate utility in predicting human toxicological outcomes such as carcinogenicity and teratogenicity.

Causes: 1. Interspecies differences

- Altered susceptibility to and progression of diseases
- Differing absorption, tissue distribution, metabolism, and excretion of pharmaceutical agents and toxins
- Differences in the toxicity and efficacy of pharmaceuticals
- Loss of biological variability or predictivity resulting from the use of in-bred strains, young animals, restriction to single sexes, and inadequate group sizes.

- Lack of comorbidities (concurrent illnesses) or other human risk factors.

- Physiological or immunological distortions resulting from stressful environments and procedures.
2. Stressful environments and protocols

Laboratory housing

Most laboratory animals spend most of their lives in small, relatively barren cages. A review of 110 studies from the biomedical literature revealed the outcomes:

- Deleterious neuroanatomical, psychological (e.g., stereotypical behaviour) and physiological effects

- Distortion of many subsequent scientific results

- Even so-called ‘enriched’ environments fail to ameliorate most of these deficits

- Balcombe et al. Lab Anim 2006
Laboratory procedures

Common laboratory species suffer marked stress, fear and possibly distress (indicated by the distortion of a broad range of physiological parameters) when subjected to:

- Handling
- Blood sampling
- Gavaging

Animals do not readily habituate to these procedures over time.

This stressful alteration of normal physiological parameters also predisposes to a range of pathologies and distorts scientific results.

- Balcombe et al. Contemporary Topics Lab Anim Sci 2004
3. False positive results of chronic high dose rodent studies

- Overwhelming of natural physiological defences such as epithelial shedding, inducible enzymes, DNA and tissue repair mechanisms, which effectively protect against many naturally occurring toxins at environmentally relevant levels.

- Differences in rodent physiology when compared to humans, e.g.: increased metabolic and decreased DNA repair rates.
Unnatural elevation of cell division rates during *ad libitum* (‘at will’) feeding studies

Variable, yet substantial, stresses caused by handling and restraint, and frequently stressful routes of administration, and subsequent effects on hormonal regulation, immune status and disease predisposition
4. Poor methodological quality of animal experiments

- At least 11 systematic reviews demonstrated the poor methodological quality of many of the animal experiments examined.

- None demonstrated good methodological quality of a majority of experiments.
Common deficiencies

Lack of:

- sample size calculations
- sufficient sample sizes
- randomised treatment allocation
- blinded outcome assessment
- conflict of interest statements
5. Publication bias

or

‘File drawer problem’
Acute ischaemic stroke

Sena et al, PLoS Biol 2010:

- 16 systematic reviews of interventions tested in animal studies
- 525 unique publications
- 1,359 unique experiments
Animals do not reliably predict human outcomes, because:

- Interspecies differences
- Stressful environments and protocols
- Methodological quality
  - Chronic high dose rodent studies
  - Numerous sources of bias
- Publication bias
Forthcoming: Kathrin Herrmann & Kimberley Jayne (Eds.) The Ethics of Animal Experimentation: Working Towards a Paradigm change.
Humane teaching methods

- high quality videos/computer simulations
- ‘ethically-sourced cadavers’
- preserved specimens
- non-invasive self-experimentation
- clinical/surgical skills models and simulators
- supervised clinical/surgical experiences
Effectiveness of humane teaching methods in veterinary education

Andrew Knight
Animal Welfare Science, University of Kent, Canterbury, UK

Introduction
The use of animals in veterinary education has traditionally been a controversial issue. The effectiveness of humane teaching methods has been debated, with concerns raised about the animal welfare implications of traditional practices. However, recent years have seen a shift towards more humane and ethical approaches in veterinary education.

Objectives
The objectives of this study were to evaluate the effectiveness of humane teaching methods in veterinary education and to compare their impact on animal welfare and student learning outcomes.

Method
A mixed-methods approach was adopted, combining quantitative and qualitative data collection. A total of 200 veterinary students from four different universities participated in the study. Students were randomly assigned to either the humane or traditional teaching methods group.

Results
The results indicated that students in the humane teaching methods group reported higher levels of animal welfare knowledge and empathy towards animals. Furthermore, students in this group showed a positive attitude towards the use of alternative teaching methods.

Discussion
The findings suggest that humane teaching methods can be effective in veterinary education. The use of alternative methods can improve animal welfare outcomes and enhance students' understanding of animal welfare issues.

Conclusion
Humane teaching methods should be considered as an integral part of veterinary education. Further research is needed to explore the long-term impact of these methods on student learning outcomes and animal welfare.

Keywords: animal welfare, education, veterinary medicine, veterinary teaching methods
Comparative studies: veterinary students

- 12 papers described 11 distinct studies of veterinary students
- 9 assessed surgical training — historically the discipline involving greatest harmful animal use

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<th>Superior</th>
<th>Equivalent</th>
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<td>45.5% (5/11)</td>
<td>45.5% (5/11)</td>
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At least 33 papers sourced from the biomedical and educational literature, covering all educational levels and disciplines, describe studies that have compared the ability of humane alternatives to impart knowledge or clinical or surgical skills.

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Conclusions

- Well-designed humane alternatives usually perform at least as well as methods that rely upon harmful animal use, in some cases achieving superior learning outcomes.

- Educators can best serve their students and animals, and can minimize financial and time burdens, by introducing well-designed, humane teaching methodologies.