RSPCA ANIMALS IN SCIENCE

5th UK Focus on Severe Suffering meeting report

"Avoiding mortality"

Animals in Science Department

January 2026

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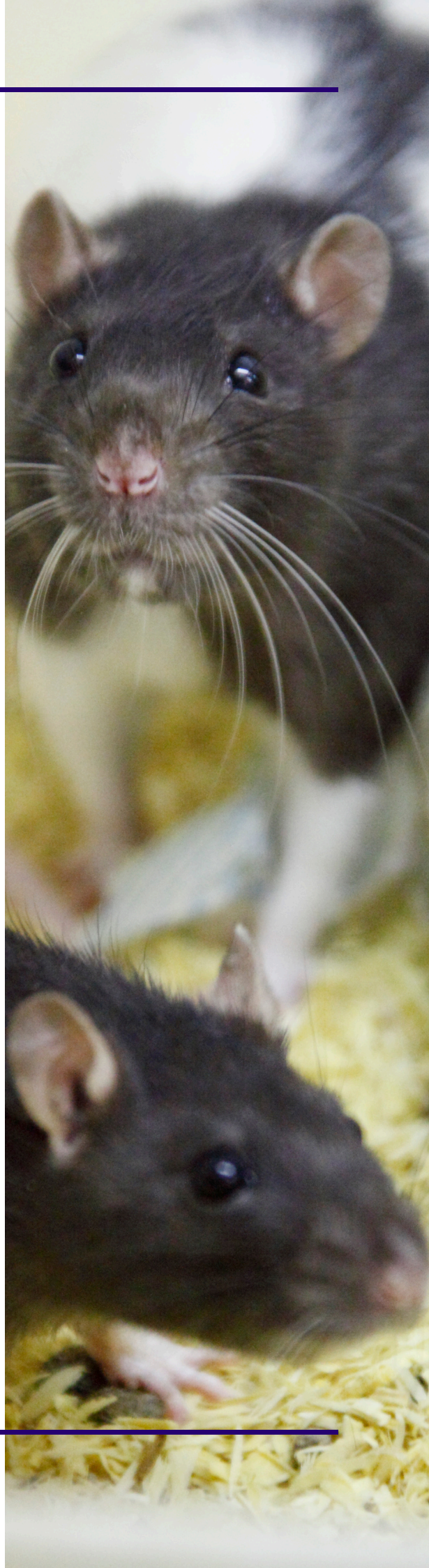

Introduction

On November 5th, 2025, participants from industry and academia joined us for our 5th UK Focus on Severe Suffering meeting, held at King's College London. The topic, 'Avoiding Mortality', was selected because mortality is a key cause of severe suffering for animals in science, and we are aware of the considerable efforts made by the scientific community to avoid this wherever possible. The meeting consisted of four sessions: 'Models of animal diseases', 'Models of human diseases', 'Use of technology to predict animal mortality', and 'Looking to the future'.

The meeting opened with an introduction to the RSPCA's 'Focus on Severe Suffering' initiative by Lorena Sordo from the RSPCA's Animals in Science Department. Her talk introduced attendees to this important initiative and key resources, and guided them through the main steps for avoiding animal mortality, as discussed in the RSPCA's 'Avoiding mortality in research and testing' report.

The next speaker was Julie Keeble, from King's College London, who presented the benefits of using study plans within animal research facilities. She highlighted the opportunity they offer to review potential experimental refinements after the project licence has been granted, as study plans are usually written once the experimental approach has been decided. Her talk included examples of situations where study plan discussions supported specific welfare refinements and helped to reduce severity and avoid mortality at King's College.

Models of animal diseases

The first session opened with a talk by Hugh Simmons, from the Animal and Plant Health Agency. Hugh shared how refinements, such as using clinical score sheets, blood sampling, and implementing early humane endpoints, have resulted in severity reductions, from severe to moderate, particularly for classical and African swine fever, and in bovine spongiform encephalopathy. However, these refinements cannot always be translated to other species, such as transmissible spongiform encephalopathy (TSE) in mice. In this case, the inability of animals to get up, a humane endpoint used in cattle and sheep with TSE, is more difficult to detect in mice due to rapid disease progression and their exceptionally high strength-to-weight ratio, allowing them to easily support or lift their body weight. This highlights species-specific challenges, including how animal size may influence the application of refinements and welfare outcomes.

The following speaker was Tim Connelley, from The Roslin Institute, who shared their efforts to establish a feasible artificial tick feeding system for East Coast fever, a deadly cattle disease. This alternative approach would allow the generation of cryopreserved stocks of *Theileria parva*, a tick-borne protozoan parasite, that can be used for vaccine development. Currently, generation of these stocks rely heavily on *in vivo* feeding, resulting in severe clinical symptoms and animal deaths. If successful, the artificial tick feeding system would replace *in vivo* feeding and eliminate the need for using animals to produce these stocks.

The last speaker of the session was Thomas Tzelos, from the Moredun Research Institute, who shared a refined bovine respiratory disease complex (BRDC) challenge model. Typically, BRDC studies result in a high post-challenge mortality rate. For this model, Thomas is integrating transthoracic ultrasonography into the animal inclusion and monitoring process. The integration of this quick and easy imaging technique allows for early identification of at-risk animals and minimises unnecessary suffering. Moreover, this refinement improves consistency in disease expression and has significantly reduced post-challenge mortalities.

Models of human diseases

Elaine Bignell, from The University of Exeter, opened the second session on models of human diseases. In her talk, she shared how she has avoided severe outcomes and reduced mortality in mice models of aspergilloses (fungal infections). For example, in acutely invasive fungal disease, the use of high sensitivity pathogen quantitation has proven to be a robust and reproducible pre-emptive endpoint. Furthermore, refinements in the experimental design, including intensive monitoring, using clinical scoring sheets, and implementing pre-emptive endpoints, have allowed her to identify and implement sub-acute endpoints and to achieve a 30–fold reduction in mouse usage.

The next speaker was Satomi Miwa, from Newcastle University, who presented on a common challenge and ethical dilemma in ageing research: investigators are trying to capture scientifically meaningful endpoints while ensuring that animals do not endure unnecessary suffering. She described how ageing animals typically progress toward humane endpoints or unexpected deaths, including those due to senescence. Notably, she highlighted that senescent cell accumulation and stress sensitivity to senescence may differ between sexes, underscoring the need to integrate sex-specific criteria for health and welfare assessments[1].

The last speaker of the session was Andy Trafford, from the University of Manchester, who presented the development and validation of a refined, minimally invasive ovine model of ischaemia–reperfusion–infarction. This model replicates a specific clinical scenario and electrocardiogram change, the ST-elevation myocardial infarction (MI), a serious type of heart attack, treated by percutaneous coronary intervention. Andy highlighted the importance of procedural refinements and careful protocol design to minimise animal suffering and mortality. This was demonstrated by a reduction in mortality from 43% (typically seen in large models of MI) to 6.7% in the refined model, and an overall reduction in severity, from severe to moderate.

[1] See also: Karp et al. (2025) The Sex Inclusive Research Framework to address sex bias in preclinical research proposals. Nat Commun 16, 3763. https://doi.org/10.1038/s41467-025-58560-5

Use of technology to predict animal mortality

The third session, on the use of technology to predict animal mortality, was opened by Jordi Tremoleda from Queen Mary University. He shared how home cage monitoring has advanced welfare assessments in preclinical models subjected to central nervous system injury. For instance, this technology has enabled them to identify long-term effects on activity patterns, changes in non-stimulated behaviour patterns (e.g. social interactions), and alterations in circadian behaviour responses. He highlighted the importance of establishing interdisciplinary collaboration to fully harness the potential of home cage monitoring systems, improve welfare assessments in severe models, and identify and implement early humane endpoints.

The following speaker was Cèline Gommet, from Sanofi, who shared their work using digital ventilated cages to improve animal monitoring. As part of this work, they developed and optimised the night welfare check algorithm, which was tested in three different establishments. This new approach detects animals in distress before verifiable clinical signs appear to human observers, preventing them from reaching the severity threshold or being found dead. Notably, these algorithms are able to raise automatic alerts for cages up to six days prior to animal deaths. These new models offer a valuable tool for preventing mortality through efficient, early detection of health impairment.

The last speaker of the session was Joanna Moore from the University of Glasgow. In her talk, she highlighted how real-time monitoring can help to better understand the impact of an experiment, explaining how integrating home cage monitoring into research practice allows for timely interventions and more humane study design. For instance, alterations in activity are useful predictors and can inform interventions in several research fields such as neuropathic pain studies, cancer and atopic dermatitis models.

Looking to the future

In this session led by Penny Hawkins from the RSPCA's Animals in Science Department, participants were asked to reflect on the 'Wish list' included in the 'Avoiding mortality in research and testing' report. This wish list details key developments, identified by contributors to the report, that would further assist in avoiding mortality (Appendix A).

During this session, participants discussed which of the wish list items they believed had been achieved and which were no longer realistic (Figure 1). Notably, the discussion revealed a divergence in perspective regarding certain items. Most significantly, the item 'Regulatory bodies jointly committing to end requirements for death as an endpoint within tests that currently require this' appeared in the top three for both 'already achieved' (50%) and 'no longer realistic' (62%). It is likely that these variations stem from sector differences; some items might be achieved in one sector but remain completely unrealistic in others, leading participants to vote differently based on their specific field.

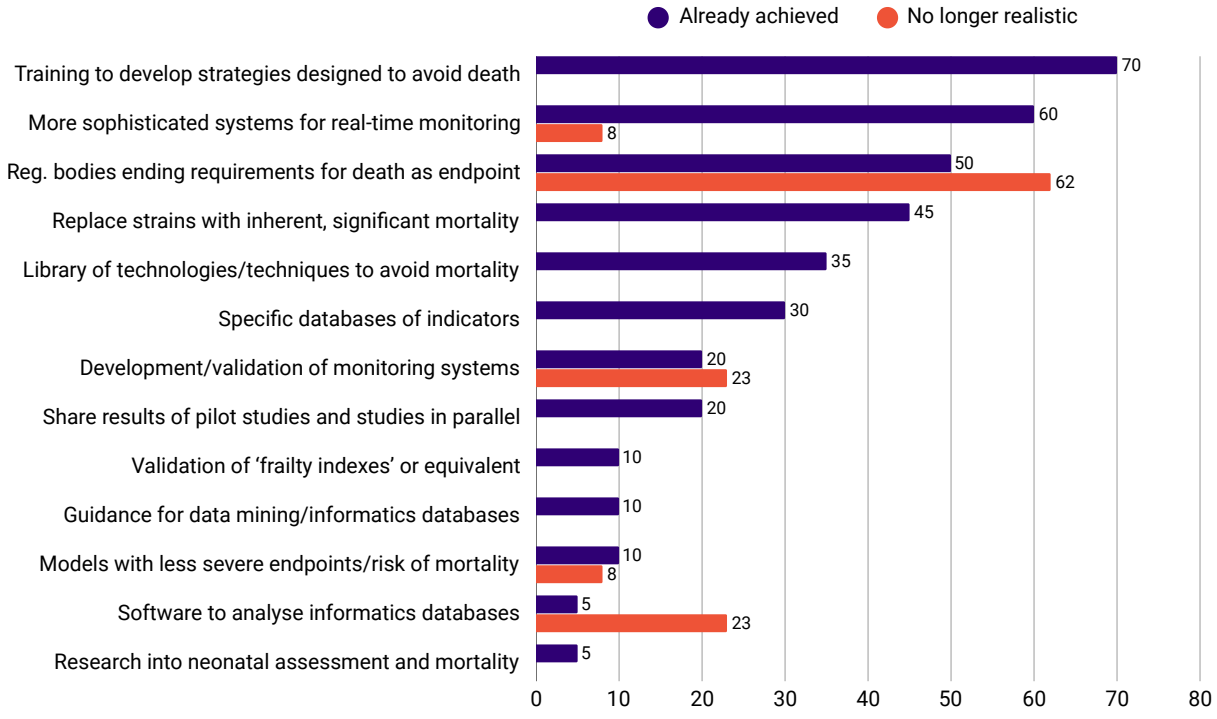

Figure 1. Wish list items from the 'Avoiding mortality in research and testing' report that had been achieved (blue) or are no longer realistic (orange) according to participants

Participants were then asked which of the wish list items should be prioritised (Figure 2). The scores presented in this report were obtained from a Slido ranking poll where points were assigned to each item based on the rank given (e.g. first choice gets the most points and the last gets the fewest). These points were aggregated to calculate a weighted average score, representing a final ranked order. The top five priorities were as follows:

1. Cheap, user-friendly software to set up and analyse informatics databases.
2. Species-specific and disease-model specific databases of indicators to help predict deaths; ideally driven by controlled lexicons, such as Mouse Welfare Terms, Fish Welfare Terms or OBO MPath.
3. Further research and development into more sophisticated, cheaper, automated systems for continuous, real-time animal monitoring (e.g. nc3rs.org.uk/rodent-big-brother).
4. A library of technologies, techniques and approaches to avoiding mortality.
5. Development and validation of multi-factorial, species- and model-specific assessment and monitoring systems to help predict impending mortality in high-risk models and situations.

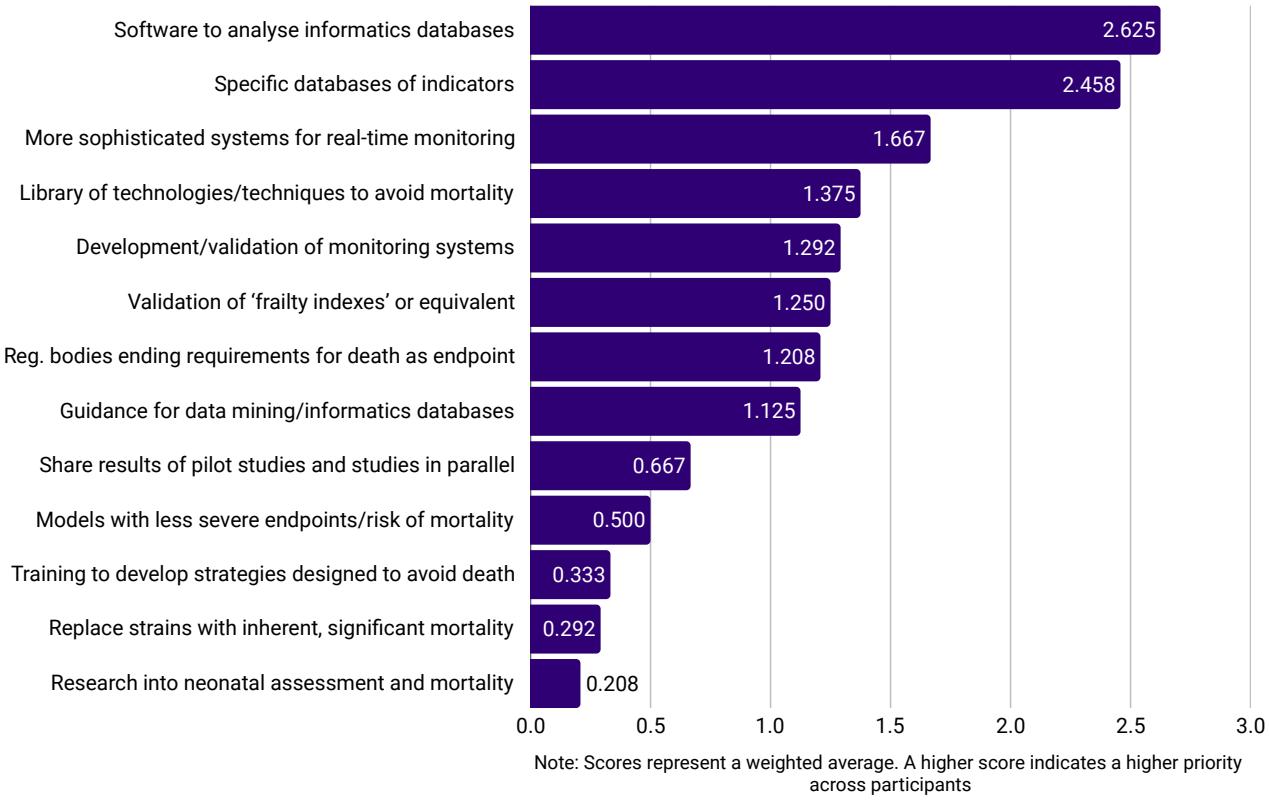

Figure 2. Wish list items from the 'Avoiding mortality in research and testing' report that should be prioritised according to participants. Scores represent a weighted average. A higher score indicates a higher priority across participants

Finally, participants were asked if a new wish list was needed. Some attendees agreed that a new wish list is needed and suggested recommendations to include in it. These recommendations focused on funding, regulatory change, refinement of procedures, and technology integration, all aimed at the ultimate goal of avoiding animal mortality.

Attendees suggested the creation of a dedicated financial budget to support the implementation of humane methods, as well as funding for refinement studies and for the validation of these refined procedures. This validation is seen as the necessary evidence to convince more scientists to move away from the *status quo*. This is linked to regulatory change, where attendees suggested revisions to requirements for severe procedures and a clear expectation from funding bodies that new monitoring technologies and reducing severity be integrated into applications.

Participants also recommended methodological refinements, particularly in how suffering is assessed. This includes shifting from simply recognising clinical signs of pain/suffering to detecting the *absence* of 'normal' behaviours associated with good health and welfare, an approach seen as enabling the detection of earlier, more sensitive indicators of distress. Furthermore, attendees highlighted the need to replace existing severe behavioural tests with refined methods and to better evaluate the cumulative effects of severity in complex models.

Finally, recommendations included improving communication and training. Attendees wanted more opportunities to discuss and share findings to facilitate rapid implementation of refinements, alongside easy access to impartial advice on techniques and methodologies, and targeted training to overcome user reluctance toward new databases and automated monitoring systems. Moreover, participants reported it would be useful to determine the most effective way to combine human expertise with AI tools to generate predictive data and prevent mortality.

The discussion, and survey results, have been captured in the action points listed below, which include measures that can be taken to reduce mortality both within individual projects and by contributing to wider policies and processes.

Action points

Tailor welfare assessment and humane endpoints

- Review the literature to identify potential model-, species-, sex-, or age-specific vulnerabilities.
- Develop tailored welfare assessments and adjust humane endpoints and monitoring frequency based on specific animal characteristics (i.e. species, strain, sex, age).
- Collect structured welfare and endpoint data to feed into species- and model-specific databases.
- Document and share specific indicators, refinements, and recommendations to allow others to adopt these into their own studies.

Minimise animal suffering

- Replace severe or invasive techniques with validated, lower-severity alternatives wherever possible.
- Assess cumulative severity over the animal's entire lifetime instead of focusing only on single, acute events.
- Monitor the absence of 'normal' behaviours (e.g. grooming, exploration, social interactions) as early signs of decline.
- Use subtle behavioural changes as triggers for prompt intervention and prevent mortality.

Invest in monitoring technologies

- Incorporate systems, such as home-cage monitoring, digital ventilated cages, and real-time behavioural tracking where financially and logistically possible.
- Combine automated alerts with input from an interdisciplinary team (animal technologists, data scientists, veterinarians, researchers) to guide timely interventions.
- Engage with emerging AI-supported monitoring or data-analysis tools, using these insights to support (not replace) professional judgement.
- Document and disseminate case studies and examples on how these tools reduce severity, avoid mortality, and improve data quality.

Advocate for systemic change

- Challenge scientific and regulatory requirements where death as an endpoint is unnecessary or outdated.
- Contribute to the evidence base by including detailed information and data on refined procedures, endpoints, mortality, and monitoring outcomes in grant applications and publications.
- Regularly share successes and challenges at lab meetings, AWERB sessions, internal seminars, and with colleagues.
- Engage with your AWERB, or institutional ethics committee, and provide them with evidence on refinements and non-animal alternatives to help them make informed decisions.

Note

The RSPCA is opposed to experiments that cause pain, suffering, distress and lasting harm to animals, and the Society's principal goal is replacement with non-animal methods. While animal use continues, we strive to help ensure the fullest possible implementation of the 3Rs, and robust ethical review that effectively challenges whether, and how, animals are used. The Focus on Severe Suffering initiative should be regarded in this context, and the RSPCA would like to acknowledge the strong support of the scientific community for the project. This has enabled a 68% reduction in experimental procedures causing severe suffering in the UK since 2014.

Visit the RSPCA 'Focus on Severe Suffering' website for the latest information and resources on this topic, including the Roadmap and the summary and action points from previous meetings.

The RSPCA would like to thank King's College London for providing the venue for this meeting, and all the speakers and attendees for their valuable contributions. The insights gathered from the poll results and discussions will be integrated into our work on reducing severe suffering and avoiding animal mortality. This summary report has been produced by the RSPCA Animals in Science Department.

RSPCA Animals in Science website

Animals in Science on LinkedIn

Focus on Severe Suffering website

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Appendix A: Wish list to avoiding mortality

From 'Avoiding mortality in research and testing' report

- Species-specific and disease-model specific databases of indicators to help predict deaths; ideally, these would be driven by controlled lexicons, such as Mouse Welfare Terms, Fish Welfare Terms or OBO MPath (obofoundry.org/ontology/mpath.html).
- Objective validation of species-specific 'frailty indexes', or equivalent, for predicting impending mortality.
- Guidance to help facilities to implement data mining and set up informatics databases.
- Cheap, user-friendly software to set up and analyse informatics databases.
- Increased use (e.g. within drug discovery) of mechanism-based model approaches with less severe endpoints and less risk of mortality, moving away from animal 'models' of human disease that recapitulate disease symptoms.
- Active, strategic efforts to replace strains (conventional and GA) with inherent, significant mortality.
- Development and validation of multi-factorial, species- and model-specific assessment and monitoring systems to help predict impending mortality in high-risk models and situations.
- Research to empirically evaluate whether assessing neonatal rodents leads to mortality, and if so, which factors contribute to this and how to address any problems and make decisions regarding monitoring protocols.
- Further research and development into more sophisticated, cheaper, automated systems for continuous, real-time animal monitoring (e.g. nc3rs.org.uk/rodent-big-brother).
- Mechanisms to share results of the kinds of pilot studies, and studies in parallel, described in this report.
- A library of technologies, techniques and approaches to avoiding mortality.
- Regulatory bodies jointly committing to end requirements for death as an endpoint within tests that currently require this, e.g. in some toxicity testing and in vaccine potency tests.
- Training resources specifically tailored to help researchers and animal care staff develop strategies designed to avoid death, e.g. relating to welfare assessment, monitoring and humane endpoints.