

Institution: Newcastle University		
Unit of Assessment: 6		
Title of case study: Improving rabbit welfare through effective pain assessment and alleviation policy and practice		
Period when the underpinning research was undertaken: 2005 - 2012		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Dr Matthew Leach	Senior Lecturer	2005 - present
Period when the claimed impact occurred: 2014 - 2020		
Is this case study continued from a case study submitted in 2014? Y		
<p>1. Summary of the impact</p> <p>Newcastle researchers have changed practice and policy relating to the assessment and alleviation of pain in rabbits, with an estimated ~4M laboratory, ~14M pet and ~180M farmed rabbits benefitting globally. Newcastle researchers developed two novel and effective pain scoring systems. These have resulted in changes to national, academic, veterinary & industry policies and individual researcher, clinician and farmer practice. These changes have produced clear benefits to the welfare of laboratory, pet and farmed rabbits. Communication and education from this research help to satisfy growing public concerns regarding animal welfare.</p>		
<p>2. Underpinning research</p> <p>Rabbits are unique in that they are a common research (~4M/yr), pet (~14M/yr) and farmed (~1B/yr) animal, and during their lifetime each individual will experience at least one painful procedure. Unalleviated pain compromises animal health and welfare, scientific outcomes in research and reduces the production/growth in farmed animals, conflicting with the drive for food sustainability and security. Consequently, effective prevention and alleviation of pain is critical and enshrined in legislation around the world (e.g., EU Directive 2010/63/EU).</p> <p>However, such legislation has had little impact on the use of analgesics in laboratory [R3, R6], pet [R4] or farmed rabbits (no data exists) as the effective alleviation of pain depends on the ability to recognise pain and assess its severity. Until the Newcastle work in 2005 [R1], there was little evidence-driven development or validation of rabbit pain assessment methods, leading to a lack of practical recommendations for the assessment and alleviation of pain. Using surveys and literature reviews, we showed the traditional indicators (clinical signs and general behaviour) were ineffective for assessing pain, and lead to delayed analgesic administration, use of arbitrary doses with no evidence of efficacy, or treatment being withheld completely [R2, R3, R6].</p> <p>In response to the need for effective pain assessment techniques for rabbits, Dr Matthew Leach and Professor Paul Flecknell at Newcastle University developed two of the only validated cage-side pain scoring methods available for rabbits, the Rabbit Pain Behaviour Scale (RPBS) and Rabbit Grimace Scale (RbtGS). They demonstrated objectively for the first time that changes in specific behaviour patterns (Rabbit Behaviour Pain Scale) and facial expressions (Rabbit Grimace Scale) provide a reliable and rapid means of assessing rabbit pain [R1, R3-5]. In 2005, they demonstrated that specific pain related behaviours increase in intensity in response to post-procedural pain and so could be used as part of a clinical assessment [R1, G1]. Subsequently, they showed that the human tendency to focus on faces when assessing rabbit pain acts as an obstacle to pain recognition when using the RPBS [R3]. In order to overcome this obstacle, they then developed a facial expression-based assessment for rabbits in 2012 [G2]. Here they showed that specific facial expressions also increase in intensity in response to post-procedural pain and so could be used as part of a clinical assessment [R5]. These scales were developed and validated with support from UKRI, industrial/government funds (e.g., Boehringer Ingelheim, Swedish Dep't of Agriculture, National Centre for the 3Rs [G3]). They are now used for clinical pain recognition and to assess effective analgesia [R5].</p>		
<p>3. References to the research</p> <p>Publications</p>		

- R1.** Leach, M.C., Allweiler, S., Richardson, C., Roughan, J.V., Narbe, R., Flecknell, P.A. (2009) Behavioural effects of ovariohysterectomy & oral administration of meloxicam in laboratory housed rabbits. *Res Vet Sci.* 87: 336-347 [10.1016/j.rvsc.2009.02.001](https://doi.org/10.1016/j.rvsc.2009.02.001). **121 cites**
- R2.** Allweiler, S., Leach, M.C., Flecknell, P.A. (2010) Use of propofol & sevoflurane for surgical anaesthesia in New Zealand White rabbits. *Lab Anim.* 44:113-117 [10.1258/la.2009.009036](https://doi.org/10.1258/la.2009.009036). **22 cites.**
- R3.** Coulter, C.A., Flecknell, P.A., Leach, M.C., Richardson, C.A. (2011) Reported analgesic administration to rabbits undergoing experimental surgical procedures. *BMC Vet Res* 7: 232-238 [10.1186/1746-6148-7-12](https://doi.org/10.1186/1746-6148-7-12) **43 cites**
- R4.** Leach, M.C., Coulter, C.A., Richardson, C.A., Flecknell, P.A. (2011) Are We Looking in the Wrong Place? Implications for Behavioural-Based Pain Assessment in Rabbits (*Oryctolagus cuniculi*) & Beyond? *PLoS ONE* 6 e13347 [10.1371/journal.pone.0013347](https://doi.org/10.1371/journal.pone.0013347). **66 cites, 8,773 views**
- R5.** Farnworth, M.J., Walker, J.K., Schweizer, K.A., Chuang, C.L., Guild, S.J., Barrett, C.J., Leach, M.C., Waran, N.K. (2011) Potential behavioural indicators of post-operative pain in male laboratory rabbits following abdominal surgery. *Anim. Welf.* 20: 225-237; available on request. **21 cites**
- R6.** Keating, C.J., Thomas, A.A., Flecknell, P.A., Leach, M.C. (2012) Evaluation of EMLA Cream for Preventing Pain during Tattooing of Rabbits: Changes in Physiological, Behavioural and Facial Expression Responses. *PLoS One*, 7, e44437 [10.1371/journal.pone.0044437](https://doi.org/10.1371/journal.pone.0044437) **252 cites, 32,720 views.**
- Grants:** Total value of awards related to above: >£1.3 million (2001-2020) including:
- G1:** Boehringer Ingelheim sponsorship (2007) 'Recognition & alleviation of pain in rabbits' £50K.
- G2:** NC3Rs Research Grant (2012) 'The use of facial expressions to assess pain in various laboratory animal species', £247K.
- G3:** NC3Rs Research Grant (2013) 'Quantifying the behavioural and facial correlates of subjective states in laboratory animals', £150K

Indicators of research quality

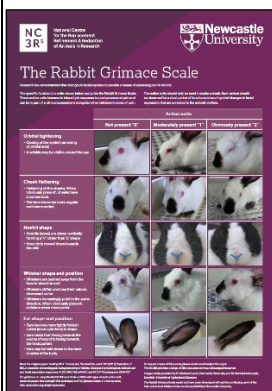
- Scales have been further used and validated by 373 peer-reviewed scientific publications
- Scales feature in 3 leading texts for laboratory animal professionals: Handbook on the Care and Management of Animals used in Research 9th Ed. 2010, Wiley & Sons (ISBN: 9781405175234); 10th Ed. 2021 Wiley & Sons (Due to be published); and Laboratory Animal Anaesthesia, 4th Ed. 2015: Elsevier (ISBN 9780128000366)
- Scales feature in 10 leading veterinary texts including: Textbook of Veterinary Nursing, 6th Ed, 2020: British Small Veterinary Association (ISBN: 978-1910443385).
- Group received Charles River Animal Welfare Award (2012) for pain assessment research.

4. Details of the impact

Ensuring the welfare of rabbits (as with all animals) is a legal and moral imperative for the public, regulators, and those who use and care for rabbits. Globally, animal-protection legislation mandates that pain is effectively controlled, which requires effective means of assessing pain. Matthew Gurney (Anderson Moores Veterinary Specialists) highlights '*there are gaps ... regarding rabbit pain management and part of this is due to our poor ability to assess pain*' [E8.C]. Consequently, the techniques developed at Newcastle provide important mechanisms for organisations and individuals to meet statutory and ethical requirements, and have benefited the welfare of rabbits globally, including those used in research and kept as pets and livestock.

Laboratory rabbits: Our techniques are recommended as an effective means of assessing pain in national, institutional and individual policy and guidance in 35 countries, annually benefitting ~4M rabbits globally [E1.A, E2.E]. Our techniques are mandated for assessing pain in rabbits used for research in Europe [E1.A-C], North [E1.D+E] and South America [E1.F], Oceania [E1.G], and Asia [E1.H]. European regulatory authorities, including those in the UK, Austria, and the Netherlands routinely use and recommend our techniques when enforcing legislation [E1.A-C]. The UK and Austrian regulatory inspectorate state that they frequently use our techniques '*...when evaluating research procedures in rabbits..., recommending research workers, veterinarians or animal care staff to refer to this work...*' and our research has '*...had a significant impact on the welfare of rabbits used in research in the UK, Europe and internationally*' [E1.A+B]. Our techniques and training materials form part of the mandated training required for scientists using animals in research in the UK, Europe and Canada,

exclusively delivered by our e-learning page (<https://researchanimaltraining.com>) [E1.I-K]. Annually, approximately 357K rabbits in Europe and Canada receive enhanced care and better quality of life from the application of our research (Data sourced from European Commission, Canadian Council for Animal Care [E2.G]). The US Dep't of Agriculture recommends the RbtGS as a 'valid and rapid means of assessing pain' in their Welfare Assessment Guidance [E1.D]. The US National Academy of Sciences Report on Recognition and Alleviation of Pain in Laboratory Animals [E1.E] recommends the RBPS, and this forms the mandatory guidance used in National Institutes of Health (NIH) policy. NIH are the largest source of funding for medical research in the world (supports 2,500 institutes), benefitting over 130K rabbits per year in the US. The president of Australian and New Zealand Laboratory Animal Association (ANZLAA) states that the '*...RbtGS has become standard in institutions working with rabbits in Australia and New Zealand...*', allowing them to meet the mandated requirements to monitor pain set out in their National body's Code of Practice for the Care and Use of Animals for Scientific Purposes [E1.G]. This benefits approximately 6K animals per year. In Brazil, the Board of the National Council of Animal Experimentation of the Science and Technology Ministry (CONCEA) state our techniques have proved '*...outstanding to support the guidelines about the care and management of laboratory animals*' [E1.F]. In Korea, the mandated national guidance includes the RbtGS and is used by institutional ethics committees and researchers to assess pain and effectively meet ethical requirements of research using animals [E1.H]. In many countries, specific guidance on how to meet the mandated requirements for pain assessment and



alleviation are provided by 3Rs (Replacement, Reduction, Refinement) organisations, who recommend our techniques. The UK National Centre for the 3Rs (most influential 3Rs organisation globally) have distributed over 7000 RbtGS posters (see opposite) in 3 languages to over 1,080 research facilities, veterinary practices, and animal shelters in 68 countries and recommend our techniques [E2.A]. These materials have been viewed '*...over 15,500 times by over 10,800 individuals globally, demonstrating the wide reach and educational impact of this research*' according to the Director of Policy and Outreach [E2.B]. These resources are recommended for usage to monitor rabbit pain by other national 3Rs organisations, including the Danish 3Rs Centre [E2.C], and the National Consensus Platform for the advancement of the 3Rs in Norway

(norecopa) [E2.D]. The Secretary of norecopa states that our work has had '*...significant impact on the assessment and alleviation of pain in rabbits worldwide*' [E2.E].

Our techniques are widely utilised and highly valued by membership organisations that represent laboratory animal professionals and provide guidance, training and information. The Institute of Animal Technology (UK) CEO states that our work '*...has directly led to improvements in the recognition and management of pain*' in UK research organisations and that these techniques are routinely referred to by Animal Welfare Groups '*with some 160 members*' who are responsible for institutional compliance and standards [E1.I]. The UK Laboratory Animal Veterinary Association (LAVA) president states '*...impact of this work is clearly illustrated by the use made of the rabbit... scales by LAVA members in their roles as Named Veterinary Surgeons*' [E1.A]. The Australian and New Zealand Laboratory Animal Association president states '*the RbtGS is widely incorporated and documented in the post procedural monitoring regimes that are required when caring for animals.*', and that their members report that it has introduced '*...more empathy for the animals... and ...objectivity into their evaluations*' [E1.G]. The European College of Laboratory Animal Medicine (ECLAM) president states our research has '*had a significant impact on the welfare of rabbits used in research worldwide and have changed working practices of professionals in this field*' [E3.A], a sentiment echoed by the President of the European Society of Laboratory Animal Veterinarians (ESLAV) [E2.F].

Our research has changed attitudes and practice of individual researchers and care staff. Prior to our research, we would routinely hear statements such as '*...rabbits do not show overt signs of pain making effective assessment impossible*', and '*analgesic efficacy is difficult to assess as we do not have validated means of assessing pain*' (Presidents of ECLAM [E3.A], LAVA [E1.A] and ESLAV [E2.F], and national inspectors in UK & Austria [E1.A-B]). The introduction of our materials led to '*...a significant impact on the welfare of rabbits used in research in the UK*' and made it '*more likely that pain will be effectively detected and alleviated*' according to the Head of

the RSPCA Animals in Science Dep't [E3.B]. This is supported by a short survey of laboratory animal professionals [E3.C] showing that ~60% (n=130) regularly used our techniques and found them valuable. The Chief Executive Officer and Scientific Director of the Universities Federation of Animal Welfare (UFAW) states we have '*made a significant contribution to the reduction of animal suffering...*' and our efforts have led to '*...increased awareness amongst researchers and animal caretakers of the signs [of] pain in rabbits used for research purposes... undoubtedly leading to better diagnosis, treatment and prevention of pain and suffering*' [E4.A]. Recommendations in three leading laboratory practice texts [E4.A-C] mean our techniques are part of institutional standard procedures and individual practice at universities in the US [E5A-D], Europe [E1.A, E1.J], Australia [E5.E], Canada [E5.F], Brazil [E1.F] and Sri Lanka [E5.G].

Farmed rabbits: Our techniques have changed national policy and guidance across Europe, and in Canada. In Sweden, our research demonstrated ear tattooing (required for identification) was painful and this pain could be effectively treated with local anaesthesia [R6]. This directly led to Jordbruksverket (Dep't of Animal Welfare & Health) [E6.A] mandating local anaesthesia



application for this procedure, and changing laws to permit all 120 producers of rabbits to administer this treatment without a veterinary surgeon present for the first time. Lotta Nordensten at Jordbruksverket stated this has improved '*...both animal welfare and farmer livelihood*' and that our techniques have had '*significant impact on the recognition and management of pain in farmed rabbits in Sweden, Europe and Internationally*'. The RbtGS is included in guidance from the National Farm Animal Care Council of Canada [E6.B]. According to their general manager, these codes and the 2000 RbtGS posters (see opposite) distributed to Canadian rabbit producers have benefited '*approximately 170,000 rabbits*' each year [E6.C], and are '*impacting directly on the welfare of these animals, and on working practices of professionals in this*

field' [E6.C].

In 2020 our scales were recommended for assessing pain in three scientific opinion documents commissioned by the European Food Standards Agency (EFSA) [E6.D-F] that form the basis of European Union (EU) and the World Organisation for Animal Health (OIE) regulations of farming practice of ~180M rabbits across Europe (Data sourced from EC Health and Food Safety Directorate [E2.H]).

Companion (pet) rabbits: Our techniques have changed institutional policy and guidance, and individual veterinary practice across the world. The 2018 Scottish Government Guidance of Rabbit Welfare [E7.A], recommended our techniques for assessing pain, enabling owners and veterinary professionals to meet their mandated requirements under the Animal Health and Welfare (Scotland) Act 2006. From 2018, this guidance has benefitted over 109,000 rabbits in



Scotland. Our techniques were incorporated into similar guidance from the local government of Hayward California (US) [E7.B]. Our techniques are used to train veterinary professionals globally. In 2018, we developed pain assessment training resources (e.g. webinars, manuals, posters (see opposite), and scorebooks) for AnimalCare Ltd's 'pain assessment toolkit' which was distributed to veterinary clients in seven European countries [E8.A]. According to the Senior veterinary manager our techniques have '*directly led to improvements in the recognition and management of pain in rabbits, impacting directly on the welfare of these animals, and on working practices of professionals in veterinary care*' [E8.A]. We have run over 60 workshops training veterinary professionals (reaching >1000 people) to use our techniques worldwide and reached more users by 'training the trainer'.

Rafael Frias, vet at the Karolinska Institut [E1.J] who was trained to deliver our package, states our techniques are '*widely considered best practice within the field*'. Aneesa Malik, a practicing veterinary nurse, also confirms this [E8.B]. Matt Gurney (Anderson Moores Veterinary Specialists - UK) has trained ~250 practitioners to use the RbtGS. Matt states the RbtGS is '*invaluable in teaching veterinary practitioners the subject of pain management in rabbits*' [E8.C]. Feedback Matt has received includes '*it allows them to tailor pain management to the individual rabbit*' and '*Practices that were previously unsure of the degree of pain that rabbits were experiencing are now more confident in their assessments*' [E8.C]. Gerry Skinner (The Rabbit Drs - Australia) has

trained ~200 practitioners to use our techniques over 7 years [E8.D]. Gerry states that our techniques *'have directly led to improvements in my clinic to the recognition and management of pain in rabbits, impacting directly on the welfare of these animals, and on working practices of professionals in veterinary care'* [E8.D]. Feedback includes *'it is reassuring to have such scales available ...to tailor pain management to the individual rabbit'*. Gerry estimates this has benefited approximately 600 rabbits a year in his practices. A survey of veterinary professionals (n=37) showed that over 60% regularly used our techniques and found them valuable for assessing pain in rabbits [E8.E]. Our techniques are recommended in ten leading veterinary texts that guide practice, as illustrated by the editor of the 'Textbook of Veterinary Nursing', who states *'...their inclusion was essential to ensure veterinary nurses had the skills to assess pain and provide adequate analgesia in these small pets'* [E8.F].

5. Sources to corroborate the impact

E1: Impact on international laboratory policy: **A:** Letter: Dr. N. Dennison, President of the Laboratory Animal Veterinary Association; **B:** Letter: Dr. Akos Szakmary, Austrian Office of the Advisory Committee for Animal Experiments; **C:** Guidance of Netherlands National Committee for protection of animals used for research; **D:** U.S. Dept of Agriculture guidance on Animal Welfare Assessment; **E:** National Academy of Sciences Report: Recognition and Alleviation of Pain in Laboratory Animals; **F:** Letter: Prof Stelio P.L. Luna, Univ. of São Paulo State, Brazil; **G:** Letter: Kiri Collins, President of Australian and New Zealand Laboratory Animal Association; **H:** Korean Institutional Animal Care and Use Committee guidance on "Care and Management of Rabbits"; **I:** Letter: Linda Horan, CEO and Chair of Council, Institute of Animal Technology; **J:** Letter: Dr Rafael Frias, President-elect of the European Society of Laboratory Animal Veterinarians (ESLAV); **K:** Canadian Council on Animal Care e-Learning resource on "Assessment of Laboratory Animal Welfare".

E2: Impact on national membership organisations' policies: **A:** The National Centre for the Replacement Refinement & Reduction of Animals in Research (NC3Rs) website showcasing Newcastle techniques; **B:** Letter: Dr Mark Prescott, Director of Policy and Outreach, NC3Rs; **C:** Danish 3R Center Guidance, inc. grimace scale; **D:** Norway's 3R centre and National Consensus Platform for the 3Rs of animal experiments (norecopa) website, inc. Newcastle papers/guidance; **E:** Letter: Prof Adrian Smith, norecopa secretary; **F:** Letter: Peter Glerup, President of ESLAV. **G:** European Commission & CCAC reports; **H:** EC Health & Food Safety Directorate Report.

E3: Impact on individuals' research working practice: **A:** Letter: Patricia Hedenqvist, President of the European College of Laboratory Animal Medicine; **B:** Letter: Dr Penny Hawkins, Head, Animals in Science Dep't, Royal Society for the Prevention of Cruelty to Animals; **C:** Survey results, Lab Animal practitioners.

E4: Impact on laboratory handbooks: **A:** Letter: Dr. Huw Golledge, CEO and Scientific Director, UFAW – Science in the Service of Animal Welfare; **B:** Excerpt, UFAW handbook 2010; **C:** Details of "Laboratory Animal Anaesthesia" 4th Edition.

E5: Impact on university and industrial practice: Resources using Newcastle research by: **A** Univ. of Michigan; **B** Yale Univ.; **C** Univ. of Iowa; **D** Baylor College of Medicine (all U.S); **E** Univ. of New South Wales, Australia; **F** McGill Univ., Canada; and **G** Univ. of Colombo, Sri Lanka.

E6: Impact on international policy on farming rabbits: **A:** Letter: Lotta Nordensten, civil servant, Dept. of Animal Welfare and Health, Sweden; **B:** National Farm Animal Care Council (NFACC), Canada's "Code of Practice for the Care of Farmed Rabbits"; **C:** Letter: Jackie Wepruk, NFACC General Manager; **D:** European Food Safety Authority (EFSA) Panel on Animal Health and Welfare (AHAW), Scientific opinion concerning the killing of rabbits for purposes other than slaughter, 2019; **E:** EFSA AHAW Scientific opinion on Health and welfare of rabbits farmed in different production systems, 2019; **F:** EFSA AHAW Scientific opinion on Stunning methods and slaughter of rabbits for human consumption, 2019.

E7: Impact on international veterinary policy: **A:** Scottish Government Pet Rabbit Welfare Guidance 2018; **B:** Hayward Local Government guidance on rabbit pain.

E8: Impact on veterinary practice: Letters: **A:** Felicity Caddick, Senior Veterinary Manager, Animalcare Ltd UK; **B:** Aneesa Malik, Registered vet nurse; **C:** Matthew Gurney, Anderson Moores Veterinary Specialists; **D:** Dr Gerry Skinner, The Rabbit Drs, Aus; **E:** Results of Newcastle survey of vets; **F:** Letter: Dr Elizabeth Mullineaux, Capital Veterinary Services Ltd.