Institution: University of Glasgow (UofG)

Unit of Assessment: UoA 6 (Agriculture, Veterinary and Food Sciences)

Title of case study: Tools that assess pain in cats and dogs have changed veterinary and pharmaceutical practice

Period when the underpinning research was undertaken: 2005–2014

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:
Prof. Andrea Nolan	Professor of Veterinary Pharmacology	1998–July 2013
Prof. Jacky Reid	Professor of Anaesthesiology	1983–2011
Prof. Marian Scott	Professor of Environmental Statistics	1983–present
Gillian Calvo	Specialist Veterinary Nurse	Dec 2006–Sept 2014

Period when the claimed impact occurred: August 2013–2020

Is this case study continued from a case study submitted in 2014? Yes

1. Summary of the impact

Animal pain and quality of life are key vital signs in veterinary practice. UofG researchers developed robust tools to measure acute and chronic pain in dogs, with adaptations to do likewise in cats. Animal healthcare companies use the tools to support regulatory approvals for new products and markets. The tools have changed veterinary practice in how pain and quality of life are assessed, and support joint decision-making by owners and veterinarians. The Glasgow Composite Measure Pain Scale (CMPS) is considered the gold standard for assessing acute pain in dogs in clinical settings as recommended in World Small Animal Veterinary Association (WSAVA) pain guidelines. A new company, Newmetrica Ltd, was formed in November 2013 to commercialise the UofG tools.

2. Underpinning research

The assessment of pain and quality of life for companion animals is highly subjective, with the need for psychometrically valid and robust statistically designed tools long recognised. From the early 2000s, Professors Andrea Nolan and Jacky Reid (School of Veterinary Medicine Pain and Welfare group) worked in an interdisciplinary research programme with Prof. Marion Scott (School of Mathematics & Statistics) to develop world-leading studies and statistically-validated tools that establish how pain can be practically assessed and managed by veterinarians. These tools are used to assess either acute pain or chronic pain (through its health-related impact) in dogs and cats; they are essential to the formulation of pain management strategies to improve animal welfare.

Acute pain tools for dogs and cats

In 2001, Nolan, Reid and Scott published the first validated acute pain scale for dogs [3.1]. Taking a psychometric approach to their tool design, the UofG researchers surveyed 69 practising veterinarians, to identify words and expressions (items) describing behaviours shown by dogs experiencing pain. This work produced 47 items, grouped into seven behaviour categories; each item was assigned a pain intensity value, with statistical testing for validity, reliability and sensitivity. The final questionnaire, the Glasgow Composite Measure Pain Score (CMPS), offered precision suitable for clinical trials. In 2007, the UofG researchers developed a short-form version (CMPS-SF) for routine clinical use where the emphasis is on speed, ease of use and guidance for analgesia provision [3.2]. The CMPS-SF refined the questionnaire to 30 items within six categories: vocalisation, attention to wound, mobility, response to touch, demeanour, and posture/activity. To generate a pain score, a user selects the item that best describes the dog's behaviour, summing the scores to produce a maximum of 24 (or 20 if mobility cannot be assessed). The CMPS-SF was the first pain scale to assign a clinically defined threshold for pain relief intervention in dogs, at scores of 6/24 and above (or 5/20). The validity and responsiveness of the tool was further demonstrated in clinical studies of dogs with acute orthopaedic or soft-tissue pain, as well as those suffering with non-surgical pain.

Dealing with feline pain has been a particular challenge, due to poor recognition of pain in cats and potential toxicity of traditional analgesics. In 2012–2013, UofG researchers Calvo & Senior Clinical Resident Dr Eleanor Holden worked with Profs Nolan, Reid and Scott to develop an acute pain tool for cats (CMPS-Feline), initially using the same approach as for the CMPS-SF

with the same six behavioural categories [3.3]. The team defined 16 behavioural expressions to describe cat pain and validity was tested in cats hospitalised for surgical, traumatic or medical conditions. As with CMPS-SF, an analgesic threshold was determined in cats undergoing postoperative care, with pain relief recommended at a score of 4/16. Calvo was awarded the 2016 British Small Animal Veterinary Association PetSaver award, which recognised the author of the best clinical research paper [3.3] published in the *Journal of Small Animal Practice*. In a parallel study, the team were the first to show that facial expression could be used as an indicator of acute pain in cats [3.4]. This work used statistical spatial, shape and landmark analysis to identify anatomical features that discriminate between pain-free and pained cats. Following rounds of discriminatory analysis and evaluation with experts in pain assessment, the team developed a feline faces categorical scale depicting increasing level of pain. The scale is presented as cartoon images highlighting the key pain related changes in ears and muzzle on a three-point scale. Used together with CMPS-Feline, the combined tool improves pain assessment, as well as training observers to recognise pain.

A chronic pain and health-related quality of life tool for dogs
Between 2001–2004, PhD student Margaret Wiseman-Orr together with Nolan, Reid and Scott, used the CMPS methodology to develop and validate the first tool to measure chronic pain in dogs, which is most commonly caused by osteoarthritis [3.5]. Chronic pain was measured on the basis of its impact on health-related quality of life (HRQL), which had not previously been defined in animals. The tool comprised a 109-item paper-based assessment (GUVQuest), which defined a core set of simple and familiar descriptors, associated with good health or chronic pain that would robustly, reliably and sensitively assess HRQL. These descriptors were placed into 13 categories, with each item associated with a seven-point numeric scale. HRQL scores could then inform decisions about euthanasia, pain treatment or cancer chemotherapy, and be used by non-clinicians. Indeed, the tool was validated with owners of either healthy dogs or those with chronic degenerative joint disease. To reduce the burden of a long assessment, in 2013 the UofG team refined GUVQuest to a 46-item web-based tool using expert judgement and factor analysis [3.6]. This tool can be completed in <5 minutes and automatically generates a score. The shortened tool has been validated to measure the change in quality of life in different medical and surgical conditions, e.g. to quantify the impact of cancer and obesity on dogs; in the latter German *et al*. (2012) quantified how quality of life is reduced in obese dogs, but improves with weight loss.

3. References to the research
3.1 Holton L, Pawson P, **Nolan A**, **Reid J**, **Scott EM** (2001) Development of a behaviour-based scale to measure acute pain in dogs. *Vet Record*. 148: 525−531 doi:10.1136/vr.148.17.525
3.2 **Reid J**, **Nolan AM**, Hughes JMP, Lascelles D, Pawson P & **Scott EM** (2007) Development of the short-form Glasgow Composite Measure Pain Scale (CMPS-SF) and derivation of an analgesic intervention score. *Anim Welf*. 16:97−104. [Note: no DOI – PDF available]
3.3 **Calvo G**, Holden E, Reid J, **Scott EM**, Firth A, Bell A, Robertson S & **Nolan AM** (2014) Development of a behaviour-based measurement tool with defined intervention level for assessing acute pain in cats. *J Small Anim Pract*. 55(12): p. 622−9. doi:10.1111/jsap.12280
3.4 Holden E, **Calvo G**, Collins M, **Bell A**, Reid J, **Scott EM** & **Nolan AM** (2014) Evaluation of facial expression in acute pain in cats. *J Small Anim Pract*. 55(12): p. 615−621. doi:10.1111/jsap.12283
3.5 Wiseman-Orr ML, **Scott EM**, **Reid J** and **Nolan AM** (2006) Validation of a structured questionnaire as an instrument to measure chronic pain in dogs on the basis of effects on health-related quality of life. *Am J Vet Res.* 67(11):1826−1836. doi:10.2460/ajvr.67.11.1826
3.6 Reid J, Wiseman-Orr ML, **Scott EM**, **Nolan AM** (2013) Development, validation and reliability of a web-based questionnaire to measure health-related quality of life in dogs. *J Small Anim Pract*. 54(5): p. 227−33. doi:10.1111/jsap.12059

4. Details of the impact
Pain is a vital sign and veterinarians widely recognise its central role in animal care and welfare. However, pain assessment in companion animals is challenging due to the inherent barriers to communication, and the species-specific response to and presentation of pain. The UK companion animal population included an estimated 10.9 million cats and 9.9 million dogs in 2019, up to 80% of which encounter pain through injury or surgery at some point in their lives.

Since August 2013, the UofG acute pain tool for dogs (CMPS/CMPS-SF) has continued to broaden its reach geographically as a widely used resource in veterinary practice and to support drug trials within pharmaceutical companies. Within this period this tool is now joined by new tools based on UofG research—to assess acute pain in cats and chronic pain through HRQL in dogs—which have also been further developed and promoted through a new commercial enterprise.

Commercial development of the UofG pain and quality of life assessment tools
In November 2013, Prof. Reid founded NewMetrica Ltd. (newmetrica.com) to commercialise and support wider adoption within the veterinary community of the tools developed at the UofG. NewMetrica acquired the UofG research through an EasyAccessIP knowledge transfer agreement [5.A1] and continued to build on the core UofG research, to refine the tools. In 2014, NewMetrica launched a discrete website for the 46-item GUVQuest [3.5, 3.6] and re-branded it as VetMetrica-Canine (vetmetrica.com), for use by veterinary surgeons and pet owners in the UK and Europe to assess HRQL. In 2018, NewMetrica refined VetMetrica-Canine into a shorter (22-item) tool that retains the capacity of the prototype to measure HRQL, but improves owner compliance with completing such assessments [5.B]. NewMetrica also built an alert system into the online tool, which notifies veterinary practices of changes in the health status trend of a canine patient detected through an owner's use of the tool. In 2017, NewMetrica also produced a definitive version of the CMPS-Feline (acute pain assessment tool for cats) for use in veterinary practice, by integrating the UofG feline pain assessment [3.3] and facial expression scale [3.4] into a single tool [5.B].

NewMetrica currently employs two staff members (increasing to four, as required, to support research operations), and has commercialised the tools within two key markets: 1) providing the pharmaceutical industry with valid, reliable and responsive outcome measures to support their clinical trials for post-marketing and regulatory purposes; and 2) in clinical veterinary practice, where the tools deliver benefits for vets and pet owners through improved clinical monitoring, better communication and decision-making [5.A1]. These activities have led to the following impacts:

Pharmaceutical industry: regulatory changes and medicines approval
A number of pharmaceutical companies have used the acute pain and HRQL tools in clinical trials to support regulatory approval and are included in official documentation that accompanies veterinary products:

1. Elanco Animal Health Inc (Indiana, USA) used CMPS-SF to assess efficacy in two studies for two preparations of the nonsteroidal anti-inflammatory robenacoxib for dogs (oral and injectable), demonstrating their effectiveness for postoperative pain and inflammation. **These formed part of the regulatory submission to the US Food & Drug Administration (FDA), approved in May 2016**. The same studies were also described in a post-authorisation approval (tablet and injection) from the European Medicines Agency (EMA) for a new indication of postoperative pain and inflammation in dogs (December 2019) [5.C].
2. Aratana Therapeutics (Kansas, USA) used CMPS-SF in field studies to assess product effectiveness of their novel local anaesthetic bupivacaine liposome injectable suspension (NOCITA) for cranial cruciate ligament surgery. **These formed part of the regulatory submission to the FDA, approved August 2016. Between 2016–18, Aratana earned USD10.8 million on NOCITA product sales, with year on year growth.** The slow-release formula addressed an unmet need for postoperative pain control post-surgery in the home environment. The Massachusetts Society for the Care & Protection of Animals stated, "*The introduction of NOCITA into the veterinary market has allowed us to greatly improve how we provide post-operative analgesia to our patients*" [5.D].
3. In November 2015, Royal Canin (Gard, France) launched their Weight Management Programme for vet practices across the UK. Canine obesity affects nearly 60% of dogs in the UK. Royal Canin used the UofG HRQL-canine tool to provide the first scientific evidence that weight loss improves quality of life (German *et al*., 2012), which is now one of the key scientific marketing claims for their weight loss programme [5.E].

Since its incorporation Newmetrica has worked closely with the US FDA Center for Veterinary Medicines (CVM) to ensure compliance with the US government's 21 CFR 11 standard for electronic data capture. This ensures that the data and modelling resulting from the web-based apps meets the FDA CVM's stringent quality assurance, opening the market for wider use in US clinical trials [5.F].

Change in veterinary professional practice
The acute pain dog tool (CMPS-SF) has been translated into Italian, German, Spanish, Norwegian, French and Swedish, addressing the absence of validated pain assessment tools in these languages. Each translation required cross-cultural validation (e.g. Italian in 2018 [5.G]) to define behavioural expressions. The CMPS-SF tool and GUVQuest (now 'VetMetrica-Canine') are available online via NewMetrica and are also described in the WSAVA Guidelines for the Recognition, Assessment and Treatment of Pain, which was published in May 2014 and is endorsed by veterinary associations in 67 countries [5.H1]. The full text of the WSAVA pain guidelines have been accessed 38,595 times (with 13,842 PDF downloads) since publication [5.H2]. Furthermore, the British Small Animal Veterinary Association (BSAVA) re-printed the CMPS-SF in their BSAVA Pocketbook for Vets (2nd Ed., February 2019) and BSAVA Guide to Pain Management in Small Animal Practice (March 2019) with 2,497 and 6,256 copies issued, respectively, either through direct sales or provided through member benefits [5.I].

Veterinary practice and owner engagement with the pain and quality of life assessment tools
The UofG-research based acute pain tools are widely used in clinical practice. Between January 2016 and December 2020, **Newmetrica issued online licenses to 2,455 practices in 76 countries, permitting use of the CMSF-SF tool (dogs),** with the greatest volume in the UK, USA, Spain, Australia and Canada [5.A2]. Over the same period, **Newmetrica issued online licenses to 2,206 practices in 67 countries for the CMPS-Feline tool**, primarily in the USA, UK, Spain and Canada [5.A3]. These numbers reflect changing practice in veterinary clinics. The President of the European College of Veterinary Anaesthesia and Analgesia said, "*The short form of the GCMPS has allowed us to considerably raise the bar in terms of quality of analgesia in dogs. However, cats are a very different matter. Assessing pain in cats has always been difficult… the Glasgow group has given the acute pain scale for cats the robustness required for it to succeed in practice and be used after many different procedures*" [5.J].

Meanwhile, Newmetrica's online chronic pain tools platform vetmetrica.com **has raised awareness among pet owners of subtle changes in behaviours related to pain and welfare issues, thus extending the reach beyond veterinary practice**. Since launch in January 2014, vetmetrica.com has registered 169 veterinary practices and 2,179 owners (N.B. pharmaceutical companies also count as a single owner). The tool allows vets to involve owners with clinical follow-up, or to monitor an otherwise healthy pet and alert the vet to a change in health status. **To date, 12,194 owner assessments and 2,428 vet assessments have been completed** [A], showing active engagement with the tool. Referring to owner-reporting on their pets, the Director of a veterinary practice stated, "*[VetMetrica's] real time monitoring allows for early identification of problems leading to quicker intervention and the results can be used to help guide owners' decisions and monitor responses to treatment"* [5.K].

This change in collaborative vet-owner pet monitoring is recognised by the pharmaceutical industry. On their Rimadyl® (carprofen) product page, Zoetis Inc. describe the value of helping owners to work collaboratively with vets to understand, monitor and manage their dog's osteoarthritis to improve their quality of life [5.L1]. This claim cites a 2018 study, undertaken with NewMetrica, in which owners used the VetMetrica-Canine tool to monitor the improvement in chronic pain of their dogs while on long-term treatment [5.L2]. Zoetis have licensed the tool from Newmetrica (November 2013–present) and use it in their Osteoathritis Checklist—a tool designed to facilitate collaboration between vets and owners for this purpose [5.L3]. Zoetis partnered with the National Association of Veterinary Technicians of America (NAVTA) in 2018 to create a professional training course to introduce the tool [5.L4]. Zoetis have also incorporated the VetMetrica tool into their PetDialog mobile app, which is offered via veterinary practices to allow owners to assess quality of life, build a pet profile and monitor health [5.L5].

Professional education and supporting prescribing
A key impact pathway for the tool uptake into clinical practice has been through continuing professional development (CPD) delivered to drug companies and their partner veterinary practices. Five veterinary pharmaceutical companies have licenced the CMPS or HRQL tools for marketing and educational purposes since November 2013 (Boehringer Ingleheim, Germany; Zoetis Inc., USA; Animalcare Ltd., UK; Ceva Animal Health, UK; and Dechra Pharmaceuticals, UK) [5.A4]. Between January–December 2016, Boehringer Ingelheim partnered with NewMetrica to deliver CPD on CMPS-Feline in 630 veterinary practices and to 3,779 professionals (vets and vet nurses); the tool was well-received, with the majority of attendees adopting it for use in their practices. Boehringer also offer an online white-label version of the tool to support prescribing of their Metacam® (meloxicam) drug in cats (www.metacam-painscale.co.uk), which has been loaded 5,171 times since launch in March, 2020—even though Covid-19 has interfered with marketing of the app. Accompanying this were five education webinars on using the CMPS-Feline tool, viewed collectively 2,800 times as part of the Boehringer Academy [5.M1]. Similarly, AnimalCare Ltd. offer their own branded versions of the Glasgow CMPS tools for [cats](#) and [dogs](#) within 'The PAC'—their 'Practice Assistance Centre'. The PAC is available to their network of veterinary practices, and has registered 540 users since launch in April 2020 [5.M2].

5. Sources to corroborate the impact [PDFs have been uploaded for all evidence items]
A. Testimony & data from NewMetrica: (1) Testimony from the CEO; (2) Online licences for acute pain tools, for use in veterinary practice or research; (3) Spreadsheet of commercial licenses; (4) Vetmetrica.com usage statistics 2014–2020.
B. Product developments based on UofG research: (1) Davies *et al*. (2019) Optimising outputs from a validated online instrument to measure health-related quality of life (HRQL) in dogs. *PLoS ONE*, 14: e0221869 doi:[10.1371/journal.pone.0221869](#) (Vetmetrica); and (2) Reid J *et al*. (2017) [Definitive Glasgow acute pain scale for cats: validation and intervention level](#). *Vet Rec*. 108(19): 449. doi:[10.1136/vr.104208](#) (CMPS-feline).
C. Elanco evidence dossier: (1) tablet-form robenacoxib (Elanco study doi:[10.1186/s12917-017-1100-x](#); FDA approval summary ([NADA141-463](#)), May 2016, see Section B – Substantial evidence, p.6); (2) injectable robenacoxib (Elanco study doi:[10.1111/jvim.14698](#); FDA approval summary ([NADA 141-443](#)), November 2016, see Section B – Substantial evidence, p.7); (3) [EMA assessment report](#).
D. Aratana evidence dossier: (1) Aratana study doi:[10.1186/s12917-016-0798-1](#); published, Aug 2016—a subsequent unpublished pivotal trial, also using CMSP-SF, is described in the FDA approval; (2) FDA approval summary ([NADA141-461](#)), Aug 2016, see Section A, p.4 and Section B, p. 6; (3) Today's Veterinary Practice article; (4) MSPCA comment on Aratana's NOCITA; (5) Financial results 2016–18.
E. Royal Canin evidence dossier: (1) [German *et al*. (2012)](#); (2) [Weight Management Programme brochure](#) (p.11, ref.6) & [Weight Management Clinic brochure](#) (see p.8 of PDF); (3) Testimony from Research & Development Manager, Royal Canin.
F. Letter from FDA Center for Veterinary Medicines stating regulatory data compliance
G. Della Rocca G, *et al*. (2018) Creation and validation of the Italian version of the Glasgow composite measure pain scale-short form (ICMPS-SF). *Vet Ital*. 54:251−260. doi:[10.12834/VetIt.699.3421.3](#)
H. WSAVA: (1) [2014 Guidelines for Recognition, Assessment and Treatment of Pain](#) (*J Small Anim Pract*. 55: E10–68. doi:[10.1111/jsap.12200](#)). (2) [List of endorsing countries](#); (3) Download metrics of guideline
I. Information from Head of Publishing at BSAVA.
J. Vet. Record Editorial by President of the European College of Veterinary Anaesthesia and Analgesia doi:[10.1136/vr.j2065](#)
K. Testimony from [Greenside Veterinary Practice](#)
L. Zoetis evidence dossier: (1) [Rimadyl product page](#); (2) [NewMetrica-Zoetis study](#) (2018); (3) [Zoetis osteoarthritis checklist](#); (4) [NAVTA-Zoetis course](#) (5) Zoetis PetDialog App
M. Pharmaceutical education and marketing dossier: (1) Boehringer Ingelheim information (Metacam-support app; access numbers; webinar support for CMPS-Feline use); (2) Animalcare branded pain assessment for cats and dogs, and access numbers.