

<b>Institution:</b> University of Liverpool		
<b>Unit of Assessment:</b> Six, Agriculture Food and Veterinary Science		
<b>Title of case study:</b> Sustainable Control of Digital Dermatitis in Livestock		
<b>Period when the underpinning research was undertaken</b> Jan 2008 to July 2020		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b> <b><u>Pls:</u></b>	<b>Role(s) (e.g., job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Dr NJ Evans	Senior Lecturer Infection Biology	<b>2005-Present</b>
Dr J Duncan	Senior Lecturer Livestock Health and Welfare	<b>2003-Present</b>
<b><u>Co-Is:</u></b>		
Dr D Grove- White	Senior Lecturer Livestock Health and Welfare	<b>2000-2018</b>
Prof S Carter	Professor of Veterinary Pathology	<b>1985- 2018</b>
Dr R Blundell	Senior Lecturer in Veterinary Pathology	<b>2010-Present</b>
Dr H Williams	Senior Lecturer in Livestock Health and Welfare	<b>2005 to Present</b>
<b><u>Other Researchers:</u></b>		
Dr Joseph Angell	Tenure Track Fellow	<b>2016-2017</b>
Dr H Crosby Durrani	Lecturer in Veterinary Pathology	<b>2019 -Present</b>
Miss A Gillespie	Lecturer in Farm Animal Health and Welfare	<b>2016-2018</b>
Dr Simon Clegg	Research Assistant	<b>2013-17</b>
<b>Period when the claimed impact occurred:</b> 1 <sup>st</sup> August 2013 to 31 <sup>st</sup> July 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> No		
<b>1. Summary of the impact</b> <p>Lameness is the most important animal welfare issue for farmed ruminants across the world, with digital dermatitis (DD) the most common infectious cause. DD is a bacterial infection which produces severe foot lesions in infected animals causing substantial suffering and significant economic loss. DD affects 1,200,000 dairy cattle and 1,100,000 sheep annually in the UK alone, costing an estimated GBP80,700,000 per year. Control is challenging, with no vaccines, and disease management has substantially relied on inappropriate large scale antibiotic use.</p> <p>University of Liverpool research into DD aetiology, epidemiology and control in multiple species has led to a commercial PCR diagnostic test and significant changes in national and international veterinary and livestock industry policies and practice for DD control. We have developed evidence-based treatment and prevention protocols that reduce reliance on antibiotics and encourage their responsible use. These protocols have changed the professional practice of 70% of sheep vets and 52% of sheep farmers and 45% of dairy industry professionals working across 3,800 farms and 658,320 cattle.</p>		
<b>2. Underpinning research</b> (indicative maximum 500 words) <p>Digital dermatitis (DD) is a severe, common infectious bacterial foot disease of ruminant animals affecting livestock farming industries worldwide. The disease is very painful, generating substantial welfare issues, and has significant economic consequences. Since emerging in dairy cattle in 1974, DD has spread globally, crossing multiple species barriers.</p>		

Treatment and control of DD are difficult, and many practices have been criticised for irresponsible antibiotic use.

The University of Liverpool (UoL) DD group has been the major team internationally leading research into ruminant DD (>50 papers since 2008) and the principal research group studying DD in sheep. Our group was the first to identify, routinely culture and isolate treponeme bacteria as the causal microbes of DD (3.1). This was a major step forward in DD research. Using our novel isolation methods, we have been able to identify a new pathogenic bacterial species (*Treponema pedis*), establish a polytreponemal aetiology for the disease (3.1), develop an *in vitro* antimicrobial susceptibility testing method (3.2), characterise the clinical and pathogenic features of the bacteria (3.1, 3.3) and undertake fundamental epidemiology studies (3.4). This underpinning research has enabled the group to develop evidenced-based treatment and preventative intervention studies (3.5, 3.6) which have resulted in substantial changes in industry and veterinary policy and practice in DD control.

#### **Research on Diagnosis of DD in all Species**

- We developed novel PCR diagnostics for DD treponemes (2009) which are now the basis for diagnostic testing for the disease (3.1).
- We developed the first published sheep DD lesion scoring system which are used by farmers and vets nationally and international for disease diagnosis (2015).
- These clinical and PCR diagnostics allowed us to detect and track the continued emergence of the disease (2009-2020) in new host breeds and species (beef cattle, sheep, goats and wild elk) and in new countries (Ireland, Germany, Sweden, USA) (3.3).

#### **Research on Responsible Antibiotic and non-Antibiotic Therapies for DD in Sheep**

- Previous DD interventions have intensively employed antibiotics, raising concerns regarding antibiotic stewardship in DD control. Our development of a novel *in vitro* antimicrobial susceptibility testing method for DD treponemes (2009) led to the identification of the most effective antibiotics and disinfectants and enabled evidenced based treatment and prevention protocols for DD infections (3.2). Large-scale randomised controlled trials (RCT) (32 farms/9,000 sheep between 2012-2016) have demonstrated the benefit of treating sheep with targeted, non-critically important, antimicrobials which are now recommended as first line treatments for sheep (3.5). Data from our RCT studies also provided strong evidence against whole flock prophylactic antibiotic treatments, and this damaging practice has subsequently been discouraged by the sheep industry and the veterinary profession (3.6). No vaccine is currently available for DD and in one study we identified significant benefits of vaccinating sheep with a repurposed vaccine (Footvax MSD) for DD control (3.5). There has been wide uptake of our advice on the use of this vaccine for DD control in sheep, both by farmers and vets.

#### **Research on Farm Management and Biosecurity for DD Control in Sheep**

- Since its emergence in UK sheep in 1997, our epidemiology has shown the rapid spread of DD in the UK (affecting 35-50% of UK flocks in 2014) and identified farm and animal level risk factors that drive infection (2015-16) (3.4). These studies have changed national farm management disease control advice and biosecurity policies.

#### **Research on Biosecurity Practices for Cattle Farms**

- Using the culture and diagnostic methods we developed (3.1, 3.2), we demonstrated that DD treponemes could be transmitted on hoof trimming knives and gloves (2014-2017). Together with our *in vitro* disinfection efficacy assay methodology this has led to the creation of published evidenced based biosecurity and disinfection protocols to prevent disease spread between and within farms (2018-2020) (5.3, 5.10).

#### **3. References to the research** (indicative maximum of six references)

- 3.1. Evans, N.J., Brown, J.M., Demirkan, I., Singh, P., Getty, B., Timofte, D., Vink, W.D., Murray, R.D., Blowey, R.W., Birtles, R.J., Hart, C.A., Carter, S.D., 2009. The association of unique, isolated treponemes with bovine digital dermatitis lesions. *J Clin Microbiol* 47, 689-696. doi: 10.1128/jcm.01914-08 (78 citations).

- 3.2. Evans, N.J., Brown, J.M., Demirkan, I., Birtles, R., Hart, C.A., Carter, S.D., 2009. *In vitro* susceptibility of bovine digital dermatitis associated spirochaetes to antimicrobial agents. *Vet Microbiol* 136, 115-120. doi: 10.1016/j.vetmic.2008.10.015 (19 citations).
- 3.3. Clegg, S.R., Carter S.D., Birtles R.J., Brown J.M., Hart C.A., Evans N.J. Multilocus Sequence Typing of Pathogenic Treponemes Isolated from Cloven-Hoofed Animals and Comparison to Treponemes Isolated from Humans. *Appl Environ Microbiol*. 2016 Jul15;82(15):4523-4536. doi: 10.1128/aem.00025-16 (10 citations).
- 3.4. Angell JW, Grove-White DH, Duncan JS. Sheep and farm level factors associated with contagious ovine digital dermatitis: A longitudinal repeated cross-sectional study of sheep on six farms. *Prev Vet Med*. 2015 Nov 1;122(1-2):107-20. doi: 10.1136/vr.104553 (20 citations).
- 3.5. Duncan, J. S., D. Grove-White, E. Moks, D. Carroll, J. W. Oultram, C. J. Phythian, and H. W. Williams. 2012. 'Impact of footrot vaccination and antibiotic therapy on footrot and contagious ovine digital dermatitis', *Vet Rec*, 170: 462. doi: 10.1136/vr.100363 (48 citations).
- 3.6. Angell, J. W., D. H. Grove-White, H. J. Williams, and J. S. Duncan. 2016. 'Whole-flock, Metaphylactic tilmicosin failed to eliminate contagious ovine digital dermatitis and footrot in sheep: a cluster randomised trial', *Vet Rec*, 179: 308. doi: 10.1136/vr.103625 (15 citations).

#### **4. Details of the impact** (indicative maximum 750 words)

Digital dermatitis (DD) is a severe, common, infectious, bacterial foot disease of ruminant animals causing substantial animal welfare issues and economic consequences in livestock production. This disease is prolific and has emerged in countries worldwide with the UK alone having 1,200,000 dairy cattle and 1,100,000 sheep infected annually, costing an estimated GBP80,700,000 per year.

University of Liverpool research into DD aetiology, epidemiology and control, across multiple species, has resulted in a commercial diagnostic test and evidence-based treatment and prevention protocols that enable both reduced and responsible antibiotic use. Our research has resulted in significant changes in national and international veterinary and livestock industry policies and practice to control DD.

The research group has ensured their outputs on diagnosis and management of DD have reached all levels of livestock industries by working with industry organizations and veterinary professional bodies to deliver a substantial knowledge exchange programme. This included 45 farmer and veterinarian meetings, 4 webinars, 23 national and international conference presentations, annual programmes of undergraduate and postgraduate veterinary education lectures, 12 publications in farming and veterinary press, 51 peer reviewed publications and 2 public websites aimed at directly communicating research results to the veterinary profession and farming industry (5.1).

The impact of the work on DD is broad, in terms of reach and significance. The direct beneficiaries are farmers, veterinary practitioners, industry policy makers, foot trimmers and diagnostic laboratories. The impacts are change in knowledge, understanding, policy and practice on the diagnosis and management of DD and have shifted the industries towards more responsible use of antibiotics in food producing animals, a wider societal benefit. In our recent surveys, 52% of sheep farmers and 70% of vets and 45% of dairy industry professionals have indicated they have changed their professional practices directly as a result of the UoL research (5.2, 5.3).

#### **Improvement in Veterinary and Farming Industry Practice: Diagnosis of DD.**

- Based on the pathogens we identified as causal of DD, and the PCR tests we developed, diagnostic tests for DD are now included in diagnostic lab portfolios around the world, including the UK (Axiom) and New Zealand (Gribbles Veterinary) with 444 tests per year completed in the UK alone enabling appropriate treatment and control (5.4).
- Our lesion scoring system, which details diagnostic criteria for DD in sheep, has been incorporated into the Sheep Veterinary Society Good Practice Guidelines for Lameness in sheep (5.5) and national UK sheep industry guidance on diagnosis (AHDB Manual on Lameness in Sheep) (5.6). In our impact survey, 73% of veterinarians considered their knowledge and ability to diagnose DD had improved as

a result of UoL research work, and 97% of UK sheep farmers were now aware of the disease (5.2).

- Internationally, our clinical and laboratory diagnostics work has informed the first diagnosis of DD in sheep in Ireland, Sweden and Germany (5.7).
- Our group was first to identify the ability of DD pathogens to cross host species including diagnosing DD in UK goats and wild elk in the USA (5.7). The identification of a wildlife reservoir for DD has serious implications for control and informed US government control strategies. A government website available to the public describes UoL work identifying the disease cause and provides advice for disease control and public health implications with 56,566 views since 2014. The Washington Department of Fish and Wildlife (WDFW) reports: “UoL research implicating treponemes as causal agents for elk hoof disease increased our fundamental understanding of the disease, and directly informed WDFW management policies and outreach...[This] has allowed us to enact regulations to minimize disease spread...[and] allay concerns for human health from contacting diseased material/consuming meat...[and] communicate the causes and management challenges to elected officials, other US state wildlife management personnel, the veterinary community, hunters, wildlife advocates, and public” (5.7).

#### **Veterinary and Farming Industry Policy and Practice: Improved Management of DD**

- **Responsible Antibiotic and non-Antibiotic Therapies for DD in Sheep.** The severity of DD infections previously led vets to treat whole sheep flocks with prophylactic, highest priority, critically important antibiotics for human health. This practice is contrary to WHO and UK Government positions on antibiotic use in farming. Our research demonstrated the efficacy of a lower priority antibiotic (3.2, 3.5), and the efficacy of a repurposed commercially available vaccine (Footvax, MSD) (3.5); reciprocally we provided strong field evidence against the use of prophylactic antibiotics for control of DD in sheep (3.6). These research findings led to new guidelines on treatment and prevention of DD in sheep which were quickly incorporated into Sheep Veterinary Society (SVS) Policy on Responsible Antibiotic Use (5.4), National Guidance on Responsible Antibiotic use by the Farming Industry (Sheep Health and Welfare Group) (5.8) in 2016. Since then, the veterinary profession and farming industry have rapidly and substantially changed practice with respect to antibiotic use in treatment of DD in sheep. Our 2020 Impact Survey (5.2) found that as a direct result of UoL research, 73% of vets and 51% of farmers have now changed their antibiotic selection, 45% have changed practice on whole flock antibiotic treatments, whilst 58% of vets and 34% of farmers have increased their use of the re-purposed vaccine (Footvax MSD) (5.2). Furthermore, sales of the repurposed vaccine Footvax (MSD) during this period have also increased by 16% (5.9).

Testimony from the National Sheep Association (5.6) state that our research has “significantly increased the fundamental knowledge of CODD in terms of its causes, diagnosis and treatment, whilst promoting further good practice with regards to responsible antibiotic use in our sector”; the SVS (5.5) state that we have “improved practices within the veterinary profession, concerning DD, by increasing awareness of the disease amongst vets and farmers, improving diagnosis and providing evidenced based treatment and control strategies for the profession to utilise”.

- **Biosecurity practices on sheep farms** designed to prevent DD disease transmission between and within sheep flocks have also been enhanced because of our research. In 2015, our epidemiological research identified key farm management and biosecurity practices as important risk factors for DD in sheep flocks. These findings were incorporated into the SVS Good Practice Guidelines on Lameness in Sheep (5.5) and the Sheep Industry Manual on Lameness in sheep (5.6). Following these changes, and considerable additional knowledge exchange activity, we conducted an impact survey of farmers and veterinarians. Seventy percent of vets considered that this revised guidance improved farm management advice to reduce DD transmission; 63% of vets changed biosecurity advice to farmers as a direct consequence of UoL research; 46% of farmers have up taken this biosecurity advice (5.2).



- **Biosecurity practices on cattle farms.** The research group developed evidence-based disinfection protocols for DD in cattle in 2019 which have now been adopted as policy by the national UK dairy industry (5.10). The protocols were based on our identification of foot trimming equipment and user gloves as infection reservoirs for the DD pathogens, and *in vitro* and field-based studies on disinfectant efficacy (2014-2019; detailed within 5.3).

An international dairy industry survey in 2020 demonstrated the impact of UoL research on awareness and hygiene practices (5.3). Respondents were based in the UK (56%), Europe (25%), USA and Canada (18%). 44% of dairy professionals on 3,800 farms (managing 658,320 cows a year) considered they were now more aware of the risk of spreading DD during foot trimming and 45% of respondents had enhanced their hygiene practices in line with UoL disinfection protocols in the last year with 5.6% already considering they are already observing less DD in their cattle as a result (5.3).

In summary, the research at the University of Liverpool on DD in livestock has led to improved diagnostic tools; provided an evidence base for treatment, with a focus on reduced and responsible antibiotic use; and the creation of farm biosecurity and hygiene practices to prevent disease transmission. These practices have been quickly and widely taken up by the farming and veterinary industries for animal welfare, antibiotic stewardship, and economic benefits.

#### **5. Sources to corroborate the impact** (indicative maximum of 10 references)

- 5.1 University of Liverpool CODD and BDD websites (<https://www.liverpool.ac.uk/infection-and-global-health/research/codd/> and <https://www.liverpool.ac.uk/infection-and-global-health/research/bovine-digital-dermatitis/>).
- 5.2 Duncan, JS, Angell, J.W, Grove-White D, Walsh T, Carter SD, Evans NJ (2021) Impact of Research on the Knowledge and Practices Associated with Contagious Ovine Digital Dermatitis of Farmers and Veterinarians in the UK: Veterinary Record: Accepted 6th Jan 2021. Evidence <https://www.liverpool.ac.uk/infection-and-global-health/research/codd/impactofresearch/>
- 5.3 Gillespie AV, Carter SD, Blowey RW, Staton GJ, Walsh TR, Evans NJ (2021) Measuring the impact of bovine digital dermatitis research on knowledge and practice of biosecurity during cattle foot-trimming. Journal of Dairy Research. First view, pp. 1 - 4. DOI: <https://doi.org/10.1017/S0022029921000170>
- 5.4 Axiom email corroborating PCR assay diagnostic numbers for DD pathogens.
- 5.5 Sheep Veterinary Society Policy on Responsible Antibiotic Use in Sheep 2016 & Sheep Veterinary Society Good Practice Guidelines on Control of Lameness in Sheep 2016 and Support Letter from SVS. Evidence <https://www.sheepvetsoc.org.uk/> (Individual contact1)
- 5.6 Sheep Industry National Guidelines on Control of Lameness in Sheep (AHDB Better Returns Manual Lameness in Sheep (co-authors) 2016) Evidence <https://ahdb.org.uk/knowledge-library/reducing-lameness-for-better-returns> (Individual contact 2.)
- 5.7 Testimonials from animal welfare/health organisations confirming international knowledge exchange resulted in changes to policy and practice as a result of identification of DD outbreaks: from Sweden (sheep), Germany (sheep), Ireland (sheep), USA (wild elk), UK (National Sheep Association and Goat Veterinary Society). (Individual contacts 3 and 5.)
- 5.8 Sheep Industry Guidelines on Antibiotic Use in Sheep: Evidence <http://beefandlamb.ahdb.org.uk/wp-content/uploads/2019/07/Responsible-AMU-guidance-for-sheep-Version-1.0-June-2019.pdf> (Individual contact 2)
- 5.9 Use of Vaccines in Cattle and Sheep Production: Evidence <https://ahdb.org.uk/knowledge-library/use-of-vaccines-in-cattle-and-sheep-production>
- 5.10 Disinfection guidelines included on the dairy levy board website: Evidence <https://ahdb.org.uk/knowledge-library/reducing-the-spread-of-digital-dermatitis> (Individual contact 4.)