

Impact case study (REF3)

Institution: The University of Manchester		
Unit of Assessment: 5 (Biological Sciences)		
Title of case study: Improved infection awareness, prevention and treatment in hard-to-reach groups.		
Period when the underpinning research was undertaken: 2010-2020		
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:
Sheena Cruickshank	Professor Senior Lecturer Lecturer	2016 – present 2014 – 2017 2007 – 2014
Kathryn Else	Professor of Immunology	2009 – present
Joanne Pennock	Senior Lecturer Lecturer	2016 - present 2007 - 2016
Richard Grecnis	Professor	1998 – present
Andrew MacDonald	Professor of Immunology	2013 – present
Phil Withers	Regius Professor of Materials	1998 – present
Period when the claimed impact occurred: August 2013 – July 2020		
Is this case study continued from a case study submitted in 2014? N		
1. Summary of the impact		
<p>Many infectious diseases such as parasitic worm infections are preventable if there is awareness as to their transmission. A lack of awareness and misunderstanding leads to stigma and avoidance of preventative measures. University of Manchester researchers studying parasites have worked with diverse communities in the UK and Madagascar, to share research findings and develop resources and toolkits to raise awareness, understanding and dialogue about infection. This has changed behaviour and attitudes, leading to greater confidence for healthcare use and adherence to preventative measures. Furthermore, this work led to a policy-change to start deworming treatment in Marolambo in Madagascar, enhanced uptake of treatment and reduced worm infection intensity.</p>		
2. Underpinning research		
<p>Parasitic worm infections including gut helminth worms and schistosomiasis affect approximately two billion people worldwide, with the burden predominantly in countries within Africa, Asia and South America. As these infections cause morbidity and mortality, there is a need to develop better strategies to monitor, treat and prevent infection. Research from University of Manchester (UoM) immunologists focuses on understanding the relationship between pathogen and host and the control of infection by the immune system. The researchers have made several fundamental discoveries about the interaction of parasites in hosts. For example, in 2010, the mechanism of how a common parasite infection – whipworm - relies on the host microbiome to facilitate its hatching within the host was demonstrated [1]. The team subsequently showed in 2015 that altered gut microbial populations were associated with resistance and susceptibility to infection and differing dynamics of the immune response [2].</p> <p>The immunology researchers also characterised an important role for the cells that line the gut – the epithelial cells - in initiating the immune response to infection [3, 4]. They showed that epithelial cells recognise the damage caused by infection and this drives production of factors that promote immune cell recruitment to the site [4]. Additionally, akin to their</p>		

Impact case study (REF3)

observations of infection altering microbial populations [2], their research demonstrated that changes in epithelial responses are associated with resistance or susceptibility to infection [3]. In 2019, this research led them to identify receptors and pathways involved in the epithelial response to infection-mediated damage [4].

Changes in parasite-specific immune response can cause pathologic tissue changes, which in turn cause morbidity. The UoM team therefore investigated and identified the underlying mechanisms underpinning pathology and schistosome egg expulsion [5]. A vigorous immune response helps expel the parasite eggs into the environment but also causes pathology, and the team's research findings have clarified how this immune response is developed in the specific body tissues (liver and gut) [3]. Imaging tools developed by the UoM immunology team in collaboration with colleagues in the Department of Materials (UoM) have enabled visualisation of these tissue-specific pathology features in three dimensions [6]. This has provided unprecedented insight into parasite lifestyle, revealing novel therapeutic targets. This imaging research has also enabled the development of 3D printed model and videos to allow the team to share the findings with communities who have first-hand experience of worm infections, to increase their awareness [6].

3. References to the research

1. Hayes KS, Bancroft AJ, Goldrick M, Portsmouth C, Roberts IS, **Grencis RK**. (2010) Exploitation of the intestinal microflora by the parasitic nematode *Trichuris muris*. *Science*. 328: 1391-1394. DOI: [10.1126/science.1187703](https://doi.org/10.1126/science.1187703)
2. Houlden A, Hayes KS, Bancroft AJ, Worthington JJ, Wang P, **Grencis RK**, Roberts IS. (2015) Chronic *Trichuris muris* Infection in C57BL/6 Mice Causes Significant Changes in Host Microbiota and Metabolome: Effects Reversed by Pathogen Clearance. *PLoS ONE* 10(5): e0125945. DOI: [10.1371/journal.pone.0125945](https://doi.org/10.1371/journal.pone.0125945)
3. Huang SW, Walker C, **Pennock J, Else KJ**, Brough D, Muller W, Lopez-Castejon G, **Cruickshank SM**. (2017) P2X7 receptor-dependent tuning of gut epithelial responses to infection. *Immunology and Cell Biology*. 95 (2): 178-188. DOI: [10.1038/icb.2016.75](https://doi.org/10.1038/icb.2016.75)
4. Bramhall M, Rich K, Chakraborty A, Logunova L, Han N, Wilson J, McLaughlin J, Brass A, **Cruickshank SM**. (2020) Differential expression of soluble receptor for advanced glycation end-products in mice susceptible or resistant to chronic colitis. *Inflammatory Bowel Diseases* 26(3): 360-368 DOI: [10.1093/ibd/izz311](https://doi.org/10.1093/ibd/izz311)
5. Lundie RJ, Webb LM, Marley AK, Phythian-Adams AT, Cook PC, Jones LH, Brown S, Maizels RM, Boon L, O'Keefe M, **MacDonald AS**. (2016) A central role for hepatic conventional dendritic cells in supporting Th2 responses during helminth infection. *Immunology and Cell Biology* 94: 400-410. DOI: [10.1038/icb.2015.114](https://doi.org/10.1038/icb.2015.114)
6. O'Sullivan J, **Cruickshank S**, Starborg T, **Withers P, Else K**. (2020) Characterisation of cuticular inflation development and ultrastructure in *Trichuris muris* using correlative X-ray computed tomography and electron microscopy *Scientific Reports* 10: 5846. DOI: [10.1038/s41598-020-61916-0](https://doi.org/10.1038/s41598-020-61916-0)

4. Details of the impact**Context:**

Lack of knowledge about infection transmission leads to stigma and avoidance of preventative measures. Sharing research on parasitic infection with diverse communities in England (including those directly affected by parasitic disease and non-native English speakers) and Madagascar has raised awareness, promoted dialogue and de-stigmatised infection. This is relevant to many common UK conditions with similar mechanisms of infection, provoking similar immune responses, such as pinworm, tapeworm and norovirus. Targeted engagement work has changed behaviours to prevent infection and informed policy change in Madagascar for targeted treatments.

Impact case study (REF3)**Raising awareness of infections and improving education around transmission****Pathway to Impact:**

Diverse methods made research accessible to the public. E.g. the team produced downloadable games and videos, with BBSRC funding, to visualise mechanisms of parasite hatching [1,2]. Immune function in disease [3,5] was demonstrated in interactive stands and exhibitions. Reach was increased via public lectures, lay articles and media commentary (e.g. The Guardian, BBC Breakfast, World Service). Activities targeted varied demographic groups, including non-native English speakers, often held in e.g. community centres.

Impact:

Between 2013 and 2018 the team engaged approximately 42,500 people in face-to-face interactions. Online resources received over 190,000 views, and articles and media appearances have reached up to an estimated 26,000,000 people [A].

Activities have raised awareness of infections and immunology, evidenced by feedback [A], e.g. *"I've learned so many new things about ... worms, how they cause infections..."* (Teen, Manchester Museum, 2015) and *"Left more knowledgeable and inspired"* (adult music festival visitor, Jodrell Bank, 2016) [Figure 1]. Work with immigrant communities destigmatised infection: *"Infections with worms were ignored, people were embarrassed as it was dirty."* (community centre, 2013) and *"People would come to our village..."* [in their previous country] *"...and offer blessings for money to treat our worm infections. Now I know this was wrong"* (community centre, 2013) [A]. Participants apply their new knowledge e.g. *"Not washing your hands and your food can give you worms!"* (child, BBSRC Great British Bioscience Festival, Tower Hamlets, London, 2016) [A]. Engagement activities highlighted the need for tools aiding parasite visualisation and understanding, stimulating research on imaging technology [6] (Figure 1 (ii)).



Figure 1. (i) Drawing showing dendritic cell recruitment to gut in infection illustrating research paper [3] done by Y3 child. (ii) Image of schistosome from EPSRC imaging project used to create videos and 3D models. Resources for parasite lifecycle education at use in (iii) UK and (iv) Madagascar.

Improved infection awareness and enhanced confidence in non-native English speakers**Pathway to Impact:**

Cruickshank's engagement work identified language difficulties as a barrier to accessing science and medical advice, prompting development of English lessons introducing the team's research [1,3,5]. The 'Infection, Inflammation and Immunology' course (developed in partnership with ESOL teachers - English for Speakers of Other Languages) explained the scientific terms and built into more nuanced discussions of the mechanistic research findings [1,3] such as how immune responses differ in resistance versus susceptibility to infection [3,4]. In 2015, teachers and researchers began delivering classes to adult ESOL learners at Bolton College, assessed as part of the students' City & Guilds exams.

Impact:

Courses have run annually to approximately 250 students since 2015, and independently of Cruickshank since 2017. In 2018, resources were adapted for free online learning, enabling wider access (5 star rating, with >200 views in week 1). Course evaluation in 2015 and 2016 (questionnaires and assessment of the students' written work) showed successful promotion of dialogue about, awareness of and enhanced confidence in discussing health and science

Impact case study (REF3)

[B]. Both the original evaluation [B] and follow-up in 2020 [C], demonstrated that the students found the ESOL course useful in their day-to-day lives, e.g. enhancing confidence in discussing infections with NHS, friends and family. This impact is enduring, e.g. *“Because it’s helping me to conversation with the people about health issues”* [C]. Students felt empowered by their new knowledge, regularly sharing course content with families and friends (UK and international) - e.g. *“I have talked with my family – how you get germs, how they transmitted to one person to another”* [C]. Another former student shared information about parasitic worms with family and friends in Somalia (a country with endemic worm infection). Tutors confirmed the students’ enhanced confidence, evidenced by sharing their experiences and performing independent research [C]. Tutors said that teens newly arrived in UK particularly benefitted, as it opened doors to possibilities for further study [C]. Tutors also felt more confident and were empowered to independently adapt the course e.g. for teens or less-advanced learners.

Improving infection education, access and uptake of treatment for Schistosomiasis in Madagascar**Pathway to Impact:**

Targeted engagement work sought to change infection awareness and prevalence in rural Madagascar via ‘MADEX’ (Madagascar Medical Expeditions) programme (collaboration with Madagascar Ministry of Public Health (MoH) and Antananarivo University). Cruickshank, MacDonald and Else used their research [1, 5] to train UoM medical students in parasite identification. Cruickshank provided education resources (developed for ESOL classes above) and training in engagement approaches. In 2017, co-designed participatory workshops with Madagascan communities and researchers led to a tailored education program for 5-14 year olds that was subsequently delivered to approximately 400 children in 6 schools (2017-18). Findings were shared with MoH to inform and change policy about targeted Mass Drug Administration (MDA) for Schistosomiasis.

Impact:

In 2015, MADEX researchers found schistosomiasis in virtually all children (~90%) at two schools in Marolambo, associated with significant morbidity and potentially mortality [D]. *“MoH ... are shocked by the very high rates and will start arranging for MDA to treat the town of Marolambo...”* (MADEX researcher) [E]. Since 2015, MoH have provided MDA annually to treat schistosomiasis [F]. Infection awareness is paramount for MDA compliance, as evidenced in 2016 when, in one village, only 20% of children took MDA. *“...families...were either unaware of the risk of Schistosomiasis or suspicious of the treatment”* [E]. The MDA, where taken, impacted positively, with heavy infections that cause the worst morbidity declining from 24% to 10% after four rounds of annual MDA (2015-2019) [G]. The education program resulted in substantive improvements in knowledge and significantly improved MDA uptake, from 64% in 2016 to 91% in 2017, compared to a decline in uptake where there was no education programme, from 74% in 2016 to 42% in 2017 [H]. Children reported altered behaviour around defecation (an infection source), also reducing their risk of infection.

5. Sources to corroborate the impact

- A. Summary of infection education and engagement activities (2013-2018), including testimonial and survey responses from participants at events, evidencing reach and raised awareness of infection and immunology.
- B. Peer reviewed paper reporting the benefits of the ESOL health education course: Mclean, I., Rushton, M., Griffiths, R., Lizio, M.G., Dawson, E. and Cruickshank, S. (2018) ‘A community-based public engagement with health experiment: Using English for speakers of other languages (ESOL) classes to empower immigrant communities with science’. *Research for All*, 2 (1): 131–142. [DOI 10.18546/RFA.02.1.12](https://doi.org/10.18546/RFA.02.1.12). – co-authored with teachers from Bolton College.
- C. Report of long-term impact of ESOL classes collated by independent assessor, including testimonial statements from learners and Bolton College teachers.

Impact case study (REF3)

- D. Paper first describing the high burden of Schistosomiasis in Marolambo that led the Madagascar MoH to change MDA targeting (co-authored by the Madagascar MoH): Spencer et al. High burden of *Schistosoma mansoni* infection in school-aged children in Marolambo District, Madagascar. Parasite Vectors. 2017;10(1):307. [DOI 10.1186/s13071-017-2249-7](https://doi.org/10.1186/s13071-017-2249-7).
- E. Summary report of MADEX activity and outcomes, 2015-2019, including testimonials from MADEX researchers describing steps leading to changes in targeted MDA and the outcomes of this in Madagascar.
- F. Letter from the former head of department for the Fight Against NTDs (Neglected Tropical Diseases) at the Madagascar Ministry of Public Health (received 11 January 2021) (in post in 2015 when the MDA began), confirming how the MADEX work led to annual MDA to treat school-aged children in the remote Marolambo district.
- G. Data from follow-up of schistosomiasis burden in Marolambo showing reduced intensity of infection in children following education and MDA (co-authored by the Madagascar MoH): Spencer et al. Five year follow-up on the prevalence and intensity of infections of *Schistosoma mansoni* in a hard-to-reach district of Madagascar. The American Journal of Tropical medicine and Hygiene (*in press*).
- H. Paper evidencing benefits of education work about Schistosomiasis from 2-year study with children (increased knowledge, improved MDS uptake and behaviour change) (co-authored by the Madagascar MoH): Spencer et al. Impact of a novel, low-cost and sustainable health education programme on the knowledge, attitudes and practices related to intestinal schistosomiasis in children in a hard-to-reach district of Madagascar. PLOS NTDs 2020 (*under revision*).