Institution: University of Sussex

Unit of Assessment: UoA 5 Biological Sciences

Title of case study: Guiding treatment and leading advocacy for podoconiosis, a common but highly neglected tropical disease

1. Summary of the impact

Podoconiosis reduces the health and well-being of an estimated 4 million people globally and constrains economic development in a number of tropical countries. Our research has had significant impact on tropical societies and economies where podoconiosis is endemic. Through world-class genetic, public-health and social-science research, we have generated the evidence base for simple foot-hygiene treatment and prevention that has now reached at least 60,000 Ethiopian patients. Our team has worked with the private sector to secure the donation of several hundred thousand pairs of shoes for disease prevention, and has ensured the rapid translation of research results through assisting the development of a national podoconiosis forum in Ethiopia, and through the creation of Foot*work*, the International Podoconiosis Initiative.

2. Underpinning research

Podoconiosis is a non-infectious geochemical disease that results in swelling of the lower legs. It is caused by the long-term exposure of bare feet to red clay soil derived from volcanic rock. In southern Ethiopia, where much of our research has been conducted, and north-western Cameroon, it affects 5–8 per cent of the population and is more common than HIV, TB or malaria. Podoconiosis imposes immense economic burdens (the estimated cost to Ethiopia's economy is $208 million per year) and severe social stigma. Very little research on disease aetiology or pathogenesis has been done, yet such research is needed for the rational deployment of limited resources towards the prevention, treatment and, ultimately, eradication of the disease. To address this situation, Professor Gail Davey (2006–10 Senior Clinical Research Fellow at the Brighton & Sussex Medical School (BSMS) based in Ethiopia; 2010 onwards Reader, then Professor of Global Health Epidemiology at BSMS) established a multidisciplinary research group that covers the aetiology (genetic, mineral and biochemical), consequences (economic, ethical and social) and clinical management of podoconiosis.

The genetics arm of our group (led by Professor Melanie Newport, BSMS) has provided convincing evidence that an area of the genome commonly involved in human responses to infectious and environmental challenges plays a major role in a person's susceptibility to podoconiosis [see Section 3, R1]. Establishing the importance of genetic susceptibility has justified the use of a family-history tool in determining which children should be offered shoes for the prevention of disease when such shoes are a scarce resource. Other key research outputs include:

- an epidemiological description of podoconiosis in three endemic regions of Ethiopia [R2];
- the quantification of the severe economic impact of podoconiosis on impoverished communities [R3, R4];
- the development and testing of educational and training materials to be used in endemic communities;
- a description of the social impact on, and coping strategies adopted by, people with this debilitating and stigmatising condition [R5];
- the development and validation of clinical and quality-of-life scales;
- the novel use of a rapid ethics assessment prior to obtaining consent for genetics research in a low-income setting [R6]; and
- completion of the first genome-wide association study (GWAS) on a non-communicable disease in an African population.

Significant research grants have been awarded by the UK Medical Research Council, the Wellcome Trust, UKAid/DfID and the USA National Institutes of Health. Personal fellowships include a Wellcome Trust University Award (Gail Davey) and a Training Fellowship (Kebede Deribe). Collaborations with:

- the Addis Ababa University Schools of Public Health, Social Science and Earth Science;
- the National Human Genome Research Center, National Institutes of Health, USA;
- the Clinical Trials Facility, Kilifi, Kenya;
- the University of Buea, Cameroon; and
- the Natural History Museum, UK,

have enabled the development of research capacity through PhD and Master's training for 10 African scientists to date. Through Professor Davey's substantive appointment in 2006, BSMS has become the global hub for podoconiosis research from which international collaborations are coordinated (http://www.podo.org/research/).

3. References to the research

R1 Ayele, T.F., Adeyemo, A., Finan, C., Hailu, E., Sinnott, P., Diaz Burlington, N., Aseffa, A., Rotimi, C.N., Newport, M.J. and Davey, G. (2012) 'The HLA class II locus and susceptibility to podoconiosis', *New England Journal of Medicine*, 366(13): 1200–8.

R2 Desta, A., McBride, C., de Heer, H., Watanabe, E., Gebreyesus, T., Tadele, G., Tora, A. and Davey, G. (2012) 'The association of beliefs about heredity with preventive and interpersonal behaviors in communities affected by podoconiosis in Rural Ethiopia', *American Journal of Tropical Medicine and Hygiene,* 87(4): 623–30.

R3 Taye, B., Alemayehu, B., Birhanu, A., Desta, K., Tsegaye, A., Addisu, S., Petros, B. and Davey, G. (2012) 'Podoconiosis and soil-transmitted helminths (STHs): double burden of neglected tropical diseases in Wolaita zone, rural southern Ethiopia', *PLoS Neglected Tropical Disease*, 7(3): e2128.

R4 Davey, G. (2010) 'Podoconiosis', in Warrell, D.A., Cox, T.. and Firth, J.. (eds) *The Oxford Textbook of Medicine*, 5th ed.

R5 Sikorski, C., Ashine, M., Zeleke, Z. and Davey, G. (2010) 'Effectiveness of a simple lymphoedema treatment regimen in podoconiosis management in southern Ethiopia: one year follow-up', *PLoS Neglected Tropical Disease*, 4(11): e902.

R6 Tekola, F., Bull, S.J., Farsides, B., Newport, M., Adeyemo, A., Rotimi, C.N. and Davey, G. (2009) 'Tailoring consent to context: designing an appropriate consent process for a biomedical study in a low income setting', *PLoS Neglected Tropical Disease*, 3(7): e482–7.

Outputs can be supplied by the University on request.

Grants in the last five years

2013–18 Wellcome Trust Strategic Award for the WT-Brighton and Sussex Centre for Global Health Research: £251,000.

2013–16 University of Sussex Chancellor's International Research Scholarship for Henok Negussie. 'Defining and managing acute adenolymphangitis in podoconiosis lymphoedema in Northern Ethiopia': £48,600.

2013–16 Wellcome Trust PHATIC Training Fellowship for Kebede Deribe. 'Nationwide mapping of podoconiosis in Ethiopia': £299,000.

2013–15 Wellcome Trust Enhancement Award. Validating a combined geo-epidemiological approach to sampling for a geo-chemical disease: £161,412.

2013–16 MRC/DfID/Wellcome Trust. RCT of podoconiosis treatment in Northern Ethiopia: £791,000.

2013–15	NIH Social and Behavioral Research Branch. Using Behavioural Research to Optimize Shoe Use and Enhance Prevention of Podoconiosis – Community Intervention Trial: $193,148.
2012–15	MRC IIB Research Grant. Discovering podoconiosis susceptibility genes: from molecules to disease control for a 'neglected' NTD: £504,188.
2012–13	Association of Physicians of Great Britain and Northern Ireland. Identification of reasons for loss to follow up of patients with podoconiosis: £9,980.
2012–13	Higher Education Innovation Fund, University of Sussex. 'Shoes are the New Bednets': Engagement with US and UK Shoe Companies to Prevent Neglected Tropical Diseases: £4,200.
2011–13	NIH Social and Behavioral Research Branch. Using Behavioural Research to Optimize Shoe Use and Enhance Prevention of Podoconiosis – Phase 2: $29,025.
2011–12	TOMS Shoes. Advance support for Ethiopian Nationwide Podoconiosis Mapping: $26,800.
2010–15	Wellcome Trust University Award. PI. Gene-environment interactions in podoconiosis: £550,000.
2009–11	NIH Social and Behavioral Research Branch. PI. Using Behavioural Research to Optimize Shoe Use and Enhance Prevention of Podoconiosis – Phase 1: $45,625.
2008–10	Association of Physicians of Great Britain and Ireland. Building links in Histopathology and Geology between Ethiopia and the UK through elucidation of the role of ultrafine particles in the pathogenesis of podoconiosis: £9823.
2007–10	Wellcome Trust. The genetic basis of podoconiosis – a model for gene-environment interaction?: £280,187.

4. Details of the impact

Our research has had a direct impact on patient care, community-wide disease prevention, the training of health professionals in disease management, the raising of awareness of podoconiosis in scientific and policy fora, and the mobilising of the private sector to engage in disease prevention.

- **Patients, their families and communities**

  Untreated, podoconiosis causes disability and disfigurement. Patients suffer pain and immobility, are highly stigmatised and are excluded from social and religious gatherings and marriage. Our research provides evidence that enables communities to initiate simple treatment programmes that improve physical and psychological health. These programmes now reach an estimated 60,000 patients in three regions of Ethiopia [see Section 5, C1]. Our research into genetic susceptibility has provided a robust scientific rationale to targeting shoes to children with a family history of disease [C2]. Our behavioural research in collaboration with the Social and Behavioral Research Branch at the National Institutes of Health, USA, is testing community interventions (campaign materials and household-level training sessions) to improve the use of shoes distributed to prevent disease [C3].

- **Health workers**

  At a workshop in June 2013, the Ministry of Health in Ethiopia agreed to deliver training for the trainers of community health workers based on our research outputs. This will cover 10 disease-endemic locations in Ethiopia and Cameroon and will reach approximately 300 trainers altogether [C1]. Twelve Regional Heads of Special Needs Education were trained at a workshop in Addis Ababa in June 2011. The Ethiopian Federal Ministry of Health has also approved an in-service training module on podoconiosis which will be used for the refresher training of 30,000 Health Extension Workers [C1, C4]. This module was developed by Professor Davey on the basis of research results and previous training.

- **Private sector:**

Contact with TOMS (a US-registered shoe company whose aim is to give a pair of shoes to a child in need for every pair sold, www.toms.com) developed at a time when they were looking to increase the impact of shoes being distributed in low-resource settings. TOMS founder, Blake Mycoskie, and his team visited podoconiosis-endemic sites and consulted with members of the research team to optimise the design of shoes distributed to prevent disease [C5]. As a consequence, we have also drawn in significant research and advocacy support from TOMS. TOMS have funded the preparations for a nationwide mapping of podoconiosis and recently appointed an epidemiologist (Dr Shira Shafir) to be their Director of Impact Assessment and ensure the shoes being distributed are having the impact intended. TOMS is also contributing $500,000 to the support new Foot*work* posts, including an Executive Director (www.podo.org).

- **Policy-makers, national and international agencies**

  Professor Gail Davey was a member of the Guideline Development Committee that used research generated by this group to write the Ethiopian National Guideline on Morbidity Management of Lymphatic Filariasis and Podoconiosis, which is ongoing. Our research findings have underpinned successful advocacy to include podoconiosis among eight priority Neglected Tropical Diseases in the Ethiopian National Plan for Integrated Control of Neglected Tropical Diseases which was launched in June 2013 [C6]. Professor Davey is a founding member of and now advisor to the Ethiopian National Podoconiosis Action Network (NaPAN) [C1].

  In October 2010, Professor Davey presented evidence to the Department for Control of Neglected Tropical Diseases at the World Health Organisation which led to podoconiosis being recognised for the first time as a Neglected Tropical Disease [C7]. Professor Davey serves as Director of Foot*work*, the International Podoconiosis Initiative [C8]. In November 2012, Foot*work* initiated talks between key stakeholders in lymphatic filariasis and podoconiosis in Atlanta, GA, USA, paving the way for a joint mapping of both diseases in Ethiopia and a subgroup working on improved diagnostics to enable differentiation of these diseases in tropical settings. This work is underway [C9].

5. Sources to corroborate the impact

C1 Data and corroboration available from Biruk Kebede, Director of National Podoconiosis Action Network (NaPAN), www.podo.org/ethiopia/napan/.

C2 *Ethiopian Herald* (Sunday Edition) 68(174): 1 April 2012. 'Researchers identify genetic basis of tropical foot and leg lymphoedema'.

C3 http://clinicaltrials.gov/show/NCT01160523

C4 Open University HEAT website: http://labspace.open.ac.uk/mod/oucontent/view.php?id=452781&direct=1

C5 CBS documentary on TOMS visit to podoconiosis sites: http://www.cbsnews.com/8301-18563_162-5439649.html (including patient testimony at 01:45).

C6 Copy available at: http://www.ntdenvision.org/sites/default/files/docs/national_ntd_master_plan_ethiopia_2013-2015_1.pdf

C7 WHO NTD website: http://www.who.int/neglected_diseases/diseases/en/

C8 *Lancet* profile: http://download.thelancet.com/pdfs/journals/lancet/PIIS0140673612604188.pdf

C9 http://www.ehnri.gov.et/news-and-information/144-national-lymphatic-filariasis-and-podoconiosis-mapping-launched.