Section A

Institution: Durham University

Unit of Assessment: UoA 5 Biological Sciences

Title of case study: Changing the way we do Global Vector Control

Period when the underpinning research was undertaken: 2002 to present

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:**
Professor S. Lindsay	Chair in Public Health Entomology	1996 – 2009 & 2012 – present
Dr Ulrike Fillinger	Post Doctoral Research Assistant	2003 – 2015
Dr Matthew Kirby	Post Doctoral Research Assistant	2001 – 2005
Dr Silas Majambere	Post Doctoral Research Assistant	2004 – 2008
Dr Anne Wilson	Post Doctoral Research Assistant	2012 – 2018

Period when the claimed impact occurred: 2013 to present

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

Section B

1. Summary of the impact

Lindsay's research team has shaped the World Health Organisation's (WHO) policy on global vector control. Their research underpins four key publications including WHO's: (1) Global Vector Control Response 2017-2030 (GVCR), the first global strategy devoted to the control of vector-borne diseases, (2) an operational manual on larval source management, (3) a toolkit for integrated vector management in sub-Saharan Africa and (4) a methodology for designing vector control trials which forms the basis of WHO's policy for evaluating new vector control tools. Durham research informs and influences international policy that reduces the global burden of vector-borne diseases.

2. Underpinning research

The research of Lindsay and his colleagues focuses on the development of new tools for the control of vector-borne diseases, principally malaria in sub-Saharan Africa, which is transmitted by *Anopheles* mosquitoes. Their research includes testing novel types of long-lasting insecticidal nets and spraying indoors, but more importantly, they explore interventions that are not in the main toolkit for vector control, including interventions outside the health sector. Here we highlight six pieces of research that have been highly influential in helping to change global health policy on the control of vector-borne diseases.

Firstly, maps of the global distribution of seven of the most important vector-borne diseases were combined to show where these diseases overlap and estimated that more than 80% of the world's population is at risk from at least one vector-borne disease and more than 50% from two or more [R1]. This was the first time anyone had looked at these diseases collectively and

provided compelling evidence on the scale of the threat and therefore, the need to control these diseases collectively (Figure).

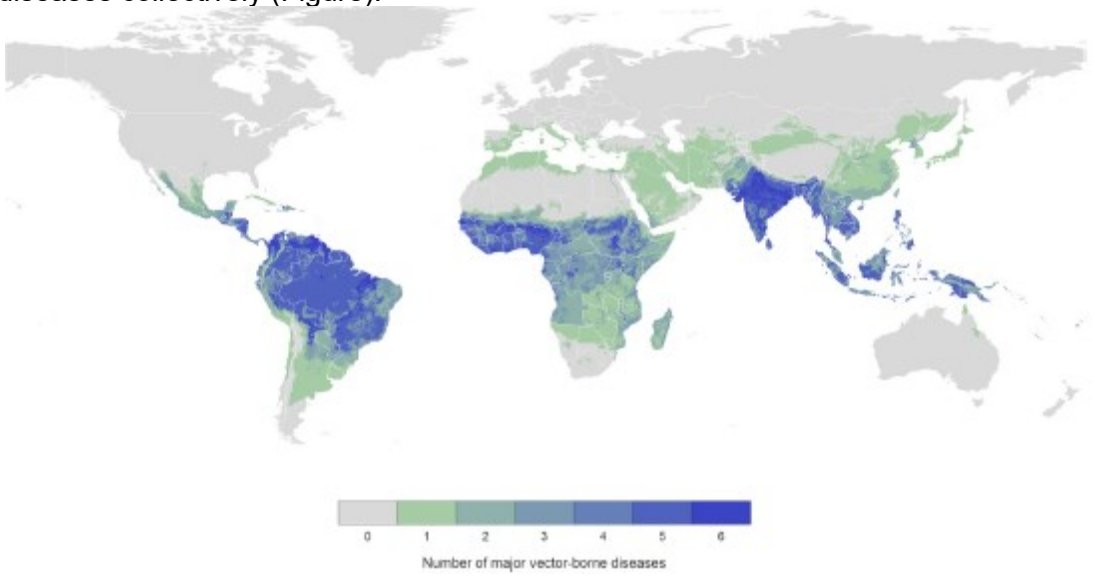

Figure. Combined distribution of the world's seven major vector-borne diseases. [R1]

Secondly and thirdly, traditional efforts to control malaria vectors in sub-Saharan Africa have focused on protecting people with insecticides in their homes. Our view was to challenge this orthodoxy and determine whether the use of microbial larvicides, which are safe to the environment, applied to the aquatic habitats of malaria mosquitoes could help reduce malaria infections in children [R2-3]. We conducted three large clinical trials, and demonstrated that in Kenya and Tanzania, in sites where the aquatic habitats of the malaria mosquito were few, fixed and findable, we could reduce malaria in children. In massive aquatic habitats bordering the River Gambia, however, application of microbial larvicides by ground teams was insufficient to reduce malaria. Thus we demonstrated that larval control was effective in specific sites.

Fourthly, there are few applications that are in use that do not rely on insecticides. We have been exploring ways in which mosquito-screened housing could help reduce malaria transmission and we carried out a clinical trial of two types of house screening in The Gambia. Both screening methods reduced the number of malaria vectors entering a house by half and reduced the likelihood of anaemia in children by half, which is a major killer of African children under two years old. Thus screening may stop children dying [R4].

Fifthly, a rigorous systematic review of 15,526 studies on housing and malaria and a meta-analysis of these studies demonstrated that improved housing reduced the likelihood of malaria infection by 47% and that of clinical malaria by 45-65% compared with traditional houses [R5].

Lastly, Lindsay and Wilson developed the first methodological framework for designing clinical trials to measure the efficacy of vector control interventions [R6]. This work was based on a critical review of thousands of scientific papers carried out during four systematic reviews by the team. This is important since the major way of controlling vector-borne diseases is by controlling the vector.

3. References to the research

Names in bold are Department of Biosciences staff at the time of doing the research.

R1. Golding, N., Moyes, C.L., **Wilson, A.L**., Cano, J., Pigott, D.M., Velayudhan, R., Brooker, S.J., Smith, D.L., Hay, S.I. & **Lindsay, S.W.** (2015). Integrating vector control across diseases. *BMC Medicine*, **13,** 249. https://doi.org/10.1186/s12916-015-0491-4. (This article has been accessed on more than 10,000 occasions and ranked 1st of the tracked articles of a similar age in *BMC Medicine*).

R2 **Fillinger, U**., Ndenga, B., Githeko, A. & **Lindsay, S.W.** (2009). Integrated malaria vector control with microbial larvicides and insecticide-treated nets in the western Kenya: a controlled trial. *Bulletin of the World Health Organization*, 87, 655-665. https://dx.doi.org/10.2471%2FBLT.08.055632 (This article was published in the World Health Organisation's own journal and has been cited in 107 articles).

R3 **Majambere, S**., Pinder, M., Fillinger, U., Ameh, D., Conway, D.J., Green, C., Jeffries, D. Jawara, M., Milligan, P.J., Hutchinson, R. & **Lindsay, S.W.** (2010). Is mosquito larval source management appropriate for reducing malaria in areas of extensive flooding in The Gambia? A cross-over intervention trial. *American Journal of Tropical Medicine and Hygiene*, **82,** 176-184. https://doi.org/10.4269/ajtmh.2010.09-0373 (This work was funded by the United States' National Institutes of Health and was presented at the Annual Meeting of the American Society of Tropical Medicine in 2010. It is published in the United States' leading journal on Tropical Medicine).

R4 **Kirby, M.J**., Ameh, D., Bottomley, C., Green, C., Jawara, M., Milligan, P.J., Snell, P.C., Conway, D.J. & **Lindsay, S.W.** (2009). Efficacy of two different house screening interventions on exposure to malaria vectors and on anaemia in children in The Gambia: a randomised controlled trial. *The Lancet*, **374,** 998-1009. http://doi.org/10.1016/s0140-6736(09)60871-0 (*The Lancet* is the 2nd highest ranked journal in medicine and is a leading journal in Global Health).

R5 Tusting, L.S., Ippolito, M.M., Willey, B.A., Kleinschmidt, I., Dorsey, G., Gosling, R., **Lindsay, S.W.** (2015). The evidence for improving housing to reduce malaria: a systematic review and meta-analysis. *Malaria Journal*, **14**, e209. https://doi.org/10.1186/s12936-015-0724-1. (This article has been accessed on 9,472 occasions and is ranked 1st of the tracked articles of a similar age in the Malaria Journal and is in the top 2% of articles of a similar age).

R6 **Wilson, A.L**., Boelaert, M., Kleinschmidt, I., Pinder, M., Scott, T.W., Tusting, L.S. & **Lindsay, S.W.** (2015). Evidence-based vector control? Improving the quality of vector control trials. *Trends in Parasitology*, **31**, 380-390. https://doi.org/10.1016/j.pt.2015.04.015. (*Trends in Parasitology* is a leading review journal).

References R1-6 have been used as exemplars in guidance documents published by the World Health Organisation (E1, 2, 4, 5, 7-10), illustrating the international importance of this research.

4. Details of the impact

In 2017, the World Health Organisation's (WHO) first comprehensive global strategy on the control of vector-borne diseases, the *Global Vector Control Response 2017-30* [E1], was approved by member states at the United Nation's World Health Assembly and aims to reduce mortality due to vector-borne diseases globally by at least 30% by 2020 and case incidence by at least 25%. Lindsay was one of the two lead authors of this strategy and the document includes a key figure showing the overlapping global distribution of seven major vector-borne diseases and provides global estimates of the global population at risk from these diseases, based on a Lindsay publication [R1, Figure above]. Reference is also made in this strategy to the WHO toolkit for integrated vector management for sub-Saharan Africa [E2], which Lindsay co-wrote and which includes references to 10 of his research papers [including R2, R3, R4]. WHO's vector control strategy is now being rolled out around the world [E3].

Global vector control practitioners have lacked rigorous evidence for many of the available tools that could be used for the control of vector-borne diseases, including the use of larvicides to control malaria in sub-Saharan Africa. Prof Lindsay and colleagues carried out three major clinical trials of microbial larvicides in Africa [R2,3], which demonstrated that larvicides could reduce malaria infection in areas where aquatic habitats of malaria vectors were few, fixed and findable. Lindsay was the chair of the Larval Source Management workstream of the Roll Back Malaria partnership, a global framework for coordinated action against malaria that informs international policy. This workstream provides technical support to WHO and national malaria

control managers around the world by providing the evidence required for decision making. Lindsay and his Durham team contributed to WHO recommending larval source management as a supplementary measure for malaria control in sub-Saharan Africa [E4]. In this publication 14 separate studies carried out by Lindsay's team were referenced to support the case for using larval source management to control malaria [E4]. In 2020, almost 60 countries carry out larval control, and 24 of 46 member states do so [E5].

One key aspect of integrated vector management (IVM) is using interventions within and outside the health sector. Again, Lindsay has been a pioneer in developing the theory behind IVM and providing case examples for policy development. He was lead writer in WHO's *A toolkit for integrated vector management in sub-Saharan Africa* [E2] which includes 10 references to his work [including R4]. Dr Al-Eryani, who is a technical officer for WHO, wrote in her testimonial 'we are adapting this tool kit for use in the East Mediterranean Region.' [E6]. 'Our tool kit is important to help member states improve their vector control strategy and save lives and reduce the burden of vector-borne diseases in the region'. Lindsay and his team have been pioneers, particularly in developing interventions for screening houses to reduce malaria, [R4] and his systematic review and meta-analysis of trials of housing [R5] have been used to justify recommendations made by Roll Back Malaria, United Nations Development Programme and UN-Habitat (Housing and Malaria Consensus Statement, November 2015) to support improved housing as an intervention against malaria [E7].

Investigators developing new vector control tools need to demonstrate evidence of efficacy against clinical infection or disease before they can get a recommendation from WHO, for wide scale deployment of the intervention in a country. The Vector Control Advisory Committee (VCAG) of the WHO has the task of reviewing all potential vector control tools. Lindsay and Wilson were both lead authors on a methodological paper describing how clinical trials for vector control interventions should be conducted [R6]. The research paper [R6] was expanded and used to write the WHO guidance on the structure and performance of vector control trials (*WHO 2017 How to design vector control efficacy trials. Guidance on phase III vector control field design provided by the Vector Control Advisory Group*) [E8]. This publication references 12 research papers carried out by Lindsay and his colleagues [including R2, R3, R4, R6]. The WHO guidance on the design and conduct of vector control trials [E8], published in 2017, must be adhered to by anyone wishing to demonstrate efficacy of a novel vector control tool, and is being used to develop a wide range of novel interventions from genetically modified mosquitoes, to spatial repellents, to novel combinations of insecticides on bednets.

The research of Lindsay and colleagues has influenced WHO global policy on the control of vector-borne diseases and has led to the development of improved methods for measuring the efficacy of vector control tools in clinical trials. Importantly, WHO's GVCR strategy for global vector control is being rolled out across the globe [E3, E6]. In February 2020 the WHO reported that their regions for Africa, the Americas, Eastern Mediterranean, Europe, South-East Asia and Western Pacific have all developed regional plans of action on vector control aligned with the GVCR road map and will be rolled out to member states [E3]. Thus this activity has the potential to reduce the threat of vector-borne diseases for every citizen on the planet. As the first steps, training courses on this strategy for control programme managers have been conducted in Cape Verde, Honduras, Maldives, Nepal, Senegal, Singapore, and 12 countries in the Eastern Mediterranean [E3]. Normative guidance providing guidelines for policy and programme implementation have been developed to facilitate the delivery of the GVCR [E3]. This resulted in a document entitled '*Framework for a National Vector Control Needs Assessment*' (VCNA), the initial draft and earlier revised versions were prepared by Dr Anne Wilson of Durham University, [E9] from Lindsay's team. The VCNA work will commence in the American Region in 2020, and has been conducted in Iran, Iraq, Morocco, Sudan and Yemen. A detailed reporting system for all Member States to analyse progress and deficiencies will be undertaken in 2020. The current implementation of the GVCR is reducing the threat of vector borne diseases around the world and will reduce the 405,000 deaths from malaria [E10] and the 390 million dengue infections each year.

5. Sources to corroborate the impact

E1 WHO (2017) Global Vector Control Response 2017-30, WHO, Geneva, includes a: (a) key illustration (Figure 2) showing the overlapping distribution of nine major vector-borne diseases, (b) reference to 80% of the world's population being at risk from one or more vector borne diseases, a statistic that appears on the main summary page of the strategy (page vii). Both the figure and the statistic were from a published paper which included Durham researchers (Golding, N., Moyes, C.L., **Wilson, A.L**., Cano, J., Pigott, D.M., Velayudhan, R., Brooker, S.J., Smith, D.L., Hay, S.I. & **Lindsay, S.W.** (2015). Integrating vector control across diseases. *BMC Medicine*, **13,** 249). This strategy also references E2.
https://www.who.int/vector-control/publications/global-control-response/en/

E2 WHO's 'A toolkit for integrated vector management in sub-Saharan Africa. Geneva: World Health Organization; 2016 which was written by Lindsay and Wilson includes ten research papers published by Lindsay's team.
https://www.who.int/neglected_diseases/resources/9789241549653/en/

E3 WHO (2020) Update on Global Vector Control Response. A presentation delivered by Dr Rajpal Yadav (WHO/Neglected Tropical Diseases) at the Vector Control Working Group meeting of Roll Back Malaria on 5th February, 2020 in Geneva, Switzerland.

E4 WHO (2013) Larval source management: a supplementary measure for malaria vector control. An operational manual, WHO, Geneva. This document refers to the clinical trials that evaluated the efficacy of microbial larvicides in Kenya (ref 21 and in The Gambia, ref 81; R2 & R3).
https://www.who.int/malaria/publications/atoz/9789241505604/en/

E5 IVCC (2017) Larviciding for malaria control in Africa. A gap analysis and change management proposal. Innovative Vector Control Consortium, UK.

E6 Testimonial letter from Dr. Samira Al-Eryani, Technical Officer (Entomologist), Malaria and Vector Control Unit, Dept of Communicable Diseases Prevention and Control, World Health Organization, Regional Office for the Eastern Mediterranean (2020).

E7 Dossier of evidence about housing and malaria. Roll Back Malaria partnership/United Nation's Development Program/UNHabitat (2015) Housing and malaria consensus statement, November 2015, Geneva, references the meta-analysis quantifying the efficacy of good housing on malaria (ref 8; R4).
https://malariaworld.org/sites/default/files/RBM%20VCWG%20Housing%20and%20Malaria%20Consensus%20Statement_final.pdf

WHO (2017) Keeping the vector out. Housing improvements for vector control and sustainable development, WHO, Geneva, references the statistic that 80% of the world's population is at threat from at least one vector-borne disease (key messages, page 5), the meta-analysis quantifying the efficacy of good housing on malaria (Tusting et al. 2015, page 14 and is listed as a key systematic review page 18).
https://www.who.int/social_determinants/publications/keeping-the-vector-out/en/

E8 WHO (2017) How to design vector control efficacy trials. Guidance on phase II vector control field trial design provided by the Vector Control Advisory Group, WHO, Geneva, states in the acknowledgements that 'this document is based on a peer-reviewed manuscript (14)' which is Wilson AL, Boelaert M, Kleinschmidt I, Pinder M, Scott TW, Tusting L & Lindsay SW. Evidence-based vector control? Improving the quality of vector control trials. Trends Parasitol. 2015;31:380–90. doi:10.1016/j.pt.2015.04.015
https://apps.who.int/iris/bitstream/handle/10665/259688/WHO-HTM-NTD-VEM-2017.03-eng.pdf

E9 WHO (2017) Framework for a National Vector Control Needs Assessment. WHO, Geneva.
https://apps.who.int/iris/handle/10665/259405

E10 WHO (2019) World Malaria Report 2019, WHO, Geneva.
https://www.who.int/publications/i/item/world-malaria-report-2019