

# Defining the Geographical Range of the *Plasmodium knowlesi* Reservoir

Catherine L. Moyes<sup>1\*</sup>, Andrew J. Henry<sup>1</sup>, Nick Golding<sup>1</sup>, Zhi Huang<sup>1</sup>, Balbir Singh<sup>2</sup>, J. Kevin Baird<sup>3,4</sup>, Paul N. Newton<sup>4,5</sup>, Michael Huffman<sup>6</sup>, Kirsten A. Duda<sup>1</sup>, Chris J. Drakeley<sup>7</sup>, Iqbal R. F. Elyazar<sup>3</sup>, Nicholas M. Anstey<sup>8</sup>, Qijun Chen<sup>9,10</sup>, Zinta Zommers<sup>11</sup>, Samir Bhatt<sup>1</sup>, Peter W. Gething<sup>1</sup>, Simon I. Hay<sup>1,12</sup>

**1** Spatial Ecology and Epidemiology Group, Department of Zoology, University of Oxford, Oxford, United Kingdom, **2** Malaria Research Centre, Universiti Malaysia Sarawak, Kuching, Sarawak, Malaysia, **3** Eijkman-Oxford Clinical Research Unit, Jakarta, Indonesia, **4** Centre for Tropical Medicine, University of Oxford, Oxford, United Kingdom, **5** Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit, Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR, **6** Primate Research Institute, Kyoto University, Inuyama, Aichi, Japan, **7** Department of Immunology and Infection, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom, **8** Global and Tropical Health Division, Menzies School of Health Research, Darwin, Northern Territory, Australia, **9** Institute of Pathogen Biology, Chinese Academy of Medical Sciences, Beijing, China, **10** Key Laboratory of Zoonosis, Jilin University, Changchun, China, **11** Division of Early Warning and Assessment, United Nations Environment Programme, Nairobi, Kenya, **12** Fogarty International Center, National Institutes of Health, Bethesda, Maryland, United States of America

## Abstract

**Background:** The simian malaria parasite, *Plasmodium knowlesi*, can cause severe and fatal disease in humans yet it is rarely included in routine public health reporting systems for malaria and its geographical range is largely unknown. Because malaria caused by *P. knowlesi* is a truly neglected tropical disease, there are substantial obstacles to defining the geographical extent and risk of this disease. Information is required on the occurrence of human cases in different locations, on which non-human primates host this parasite and on which vectors are able to transmit it to humans. We undertook a systematic review and ranked the existing evidence, at a subnational spatial scale, to investigate the potential geographical range of the parasite reservoir capable of infecting humans.

**Methodology/Principal Findings:** After reviewing the published literature we identified potential host and vector species and ranked these based on how informative they are for the presence of an infectious parasite reservoir, based on current evidence. We collated spatial data on parasite occurrence and the ranges of the identified host and vector species. The ranked spatial data allowed us to assign an evidence score to 475 subnational areas in 19 countries and we present the results on a map of the Southeast and South Asia region.

**Conclusions/Significance:** We have ranked subnational areas within the potential disease range according to evidence for presence of a disease risk to humans, providing geographical evidence to support decisions on prevention, management and prophylaxis. This work also highlights the unknown risk status of large parts of the region. Within this unknown category, our map identifies which areas have most evidence for the potential to support an infectious reservoir and are therefore a priority for further investigation. Furthermore we identify geographical areas where further investigation of putative host and vector species would be highly informative for the region-wide assessment.

**Citation:** Moyes CL, Henry AJ, Golding N, Huang Z, Singh B, et al. (2014) Defining the Geographical Range of the *Plasmodium knowlesi* Reservoir. PLoS Negl Trop Dis 8(3): e2780. doi:10.1371/journal.pntd.0002780

**Editor:** Ananias A. Escalante, Arizona State University, United States of America

**Received:** October 31, 2013; **Accepted:** February 23, 2014; **Published:** March 27, 2014

This is an open-access article, free of all copyright, and may be freely reproduced, distributed, transmitted, modified, built upon, or otherwise used by anyone for any lawful purpose. The work is made available under the Creative Commons CC0 public domain dedication.

**Funding:** CLM and AJH are supported by the Wellcome Trust [091835]. NG is funded by a Bill & Melinda Gates Foundation grant [OPP1053338]. ZH is funded by the Vector-Borne Disease Network. PNN is funded by the Wellcome Trust of Great Britain. MH is funded by the Asia Africa Science Platform Program of the Japan Society for the Promotion of Science and Grants-In-Aid for Overseas Research, Japanese Ministry of Education Science awarded to Shusuke Nakazawa. CJD is funded by a ESEI/UKRC programme grant on Plasmodium knowlesi [G1100796]. IRFE is supported by a Wellcome Trust Research Training Fellowship [B9RZGS0]. NMA is supported by a National Health and Medical Research Council Practitioner Fellowship. PWG is a Medical Research Council Career Development Fellow [K00669X] and receives support from the Bill and Melinda Gates Foundation [OPP1068048] that also supports SB. SIH is funded by a Senior Research Fellowship from the Wellcome Trust that also supports KAD [095066]. SIH also acknowledges support from the RAPIIDD program of the Science & Technology Directorate, Department of Homeland Security, and the Fogarty International Center, National Institutes of Health (<http://www.fic.nih.gov>). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

\* E-mail: catherine.moyes@zoo.ox.ac.uk

## Introduction

The *Plasmodium knowlesi* parasite, found in wild monkey populations, is a serious public health concern yet almost nothing is known about its geographical extent. It is known to cause severe and fatal disease in humans [1–4] and is the most common cause

of clinical malaria in high transmission regions of Malaysia [5,6] where it is three times more likely to cause severe malaria than *P. falciparum* [4]. However, costly *P. knowlesi*-specific molecular diagnostic techniques are only used to confirm diagnosis by microscopy in one area, Malaysian Borneo, whereas human cases have been reported from Brunei [7,8], Cambodia [9], Indonesia