rates. Quantitative PCR assays showed a single copy of plasmepsin II in all edited parasites (data not shown), indicating that amplification of this initial resistance marker[4,5] was not required for piperaquine resistance.

Whole-genome sequence data of 84 Cambodian isolates support the expansion of Thr93Ser and Ile218Phe between 2013 and 2016, overtaking the prevalence of Phe145Ile (appendix p 4). Recent years showed a reduced percentage of parasites harbouring four or more copies of plasmepsins II and III, although parasites with two to three copies remained the majority (appendix p 4). *pfmdr1* amplification, a marker of reduced susceptibility to lumefantrine and mefloquine, became less common over time (appendix p 4). Survival rates of piperaquine-treated cultured parasites increased over the years (appendix p 4), mirroring increasing dihydroartemisinin–piperaquine clinical failure rates. Emerging PfCRT mutations also increased *P falciparum* susceptibility to chloroquine, amodiaquine, quinine, pyronaridine, and ferroquine, with the Phe145Ile mutation causing the greatest sensitisation (appendix pp 6, 7). Dihydroartemisinin, lumefantrine, and mefloquine were unchanged. These data highlight the broad effect of PfCRT mutations on multiple antimalarials.

To test for differences in parasite fitness between mutants, we used a competitive growth rate assay in which each parasite line was individually cocultured with an isogenic green fluorescent protein (GFP)-positive Dd2 line. Parasites expressing the Thr93Ser allele showed a negligible fitness cost compared with control Dd2 *pfcrt*-edited parasites, with both lines out-proliferating GFP-positive Dd2 parasites (figure). The Ile218Phe mutation showed a mild growth attenuation. Phe145Ile parasites showed a substantial fitness cost, potentially explaining why this allele is ceding ground to the less resistant but fitter Thr93Ser and Ile218Phe mutations.

The data support a key role for PfCRT mutations in driving the recent expansion of highly piperaquine-resistant parasites in southeast Asia and highlight the need for vigilance in screening for novel PfCRT mutations in other malaria-endemic regions, notably in Africa or South America where piperaquine use has been increasing.

We declare no competing interests.

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No measles cases during the 2019 Hajj

The 2019 Hajj took place amid a global surge in measles cases, including travel-associated infections.[1] Eduard Massad and colleagues[2] estimated that at least 110 measles importations would occur during the 2019 Hajj, mainly from six countries (Yemen, India, Nigeria, Indonesia, Pakistan, and Sudan). They warned that these imported cases could trigger a significant outbreak towards the end of the Hajj, leading to rapid international dissemination when pilgrims return to their home countries. Others voiced similar concerns regarding the importation and the potential globalisation post-Hajj of measles via returning pilgrims.[3]

Saudi Arabia implements numerous measures to prevent communicable diseases during the Hajj, including vaccination requirements, health awareness campaigns before and during the event, and public health interventions at points of entry. Additionally, during the Hajj, Saudi health authorities activate an enhanced indicator-based notifiable diseases surveillance system to ensure timely detection and prompt response to infectious disease events.[4] The 2019 Hajj also saw the first application of the Hajj early warning system (HEWS), a syndromic and event-based surveillance system that complements the existing surveillance tools at the pilgrimage.[4]

The 2019 Hajj was attended by 2 489 406 pilgrims, 74·5% of whom were international. Almost 746 000 people originated from the six counties identified as posing the greatest risk for measles importation.[2,3] Measles was identified as a high-risk event in the 2019 Hajj strategic health risk assessment conducted by the Saudi health authorities, and was an essential syndrome of the HEWS. No cases of measles or outbreaks of infectious diseases were reported during the 2019 Hajj, from early July when pilgrims started arriving in the country until the pilgrimage officially ended in mid-August.

Although this is reassuring, given the incubation period of measles, as pilgrims return to their home countries the possibility of post-Hajj spread remains. We echo others in calling for public health measures to

be implemented to reduce the risk and minimise the consequences of such spread.[2,3] These include increased surveillance among countries receiving pilgrims after the Hajj. Unfortunately, such post-Hajj surveillance is not implemented in many countries, especially in those with scarce resources, which represent the largest proportion of Hajj pilgrims. The establishment of a harmonised Hajj health information system proposed previously[5] would, among other things, allow systematic follow-up of health events among pilgrims after the Hajj, hence enabling rapid detection and management of communicable diseases potentially introduced via pilgrims and strengthening global health security.

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The long shadow post-tuberculosis

The meta-analysis investigating the excess mortality after tuberculosis published by Kamila Romanowski and colleagues[1] is an important piece of work confirming a long-held belief by health workers in the field; however, death frequently comes only at the end of prolonged periods of suffering and morbidity. We would like to highlight the hidden epidemic of chronic disease, impairment, and social costs after microbiological cure of tuberculosis, as discussed by Sumona Datta and Carlton Evans in the Comment[2] accompanying the Article.[1]

WHO estimates that 54 million people have survived tuberculosis since the year 2000,[3] with estimates of residual lung damage ranging from 18% to greater than 80%.[4] Post-tuberculosis damage straddles the intersection of communicable and non-communicable diseases, and is likely to be one of the most important causes of chronic lung disease globally, yet it has received little attention as a non-infectious complication of tuberculosis primarily affecting the world's poor.

The First International Post-Tuberculosis Symposium was held in Stellenbosch, South Africa, on July 22–23, 2019, to discuss priorities and gaps that need to be addressed in order to provide guidance in this neglected area. The symposium involved 68 delegates across 12 disciplines from five continents, representing more than 27 institutions. Historically, inconsistency and lack of consensus in nomenclature and terminology have hampered work in this field. Using the Delphi process, the Symposium voted to embrace the non-discipline-specific adjective "post-tuberculosis" for future work in this area, with a majority vote of 84% after three rounds.

During this meeting the need for a comprehensive post-tuberculosis research agenda was emphasised and various important aspects were highlighted. First, heterogeneity between patients, in terms of severity and phenotypic outcomes,[4] remains largely unexplained and contributes to difficulties in accurate estimation of disease burden. Second, to develop prevention strategies, the mechanisms of damage during tuberculosis require further elucidation. Furthermore, former patients with tuberculosis—which include large numbers of children—are known to have a heightened risk of recurrent tuberculosis,[5] highlighting the need for integrated care strategies to prevent and manage both recurrent disease and post-tuberculosis lung damage.

Seen through the eyes of several patient representatives, there is a need to advocate for health and wellbeing after completion of tuberculosis treatment, and to address socioeconomic consequences, including post-tuberculosis stigma and disabilities. The shadow of tuberculosis is long for many former patients, and in the words of one: "When we started tuberculosis treatment, no-one told us that it would never leave us".

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For more on the **First International Post-Tuberculosis Symposium** see http://www.post-tuberculosis.com