## Imported malaria and its implication to achievement of malaria-free Bhutan

- **Running title: Implication of imported malaria in Bhutan** Kinley Penjor<sup>a,b\*</sup>, Ugyen Zangpo<sup>a</sup>, Dorji Tshering<sup>b</sup>, Benedikt Ley<sup>c</sup>, Ric N Price<sup>c,d,e</sup>, Kinley Wangdi<sup>f</sup> <sup>a</sup>Vector-borne Disease Control Program, Department of Public Health, Ministry of Health, Bhutan <sup>b</sup>Central Regional Referral Hospital, Department of Medical Services, Ministry of Health, Gelephu Bhutan <sup>c</sup>Global and Tropical Health Division, Menzies School of Health Research and Charles Darwin University, Darwin, Northern Territory, Australia <sup>d</sup>Mahidol-Oxford Tropical Medicine Research Unit, Mahidol University, Bangkok, Thailand <sup>e</sup>Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom <sup>f</sup> Department of Global Health, National Centre for Epidemiology and Population Health, College of Health and Medicine, Australian National University, Acton, ACT 2601, Australia. \*Corresponding author kinleyp@health.gov.bt Address: Central Regional Referral Hospital, Department of Medical Services, Ministry of Health, Gelephu Bhutan Email: KP: kinleyp@health.gov.bt UZ: uzangpo@health.gov.bt DT: dorjigyarab7@gmail.com BL: Benedikt.Ley@menzies.edu.au RP: Ric.Price@menzies.edu.au KW: kinley.wangdi@anu.edu.au

## 39 Highlight

40 As Bhutan nears malaria elimination goal, imported malaria through cross-border human mobility has emerged 41 as major source of transmission. This report highlights key epidemiological characteristics of imported 42 infections and the need to strengthen pro-active and targeted surveillance and response interventions by the 43 national elimination program to achieve elimination and sustain it.

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- 45 Keywords: Bhutan, malaria, imported, surveillance, elimination, epidemiology

The WHO's *Global Technical Strategy for Malaria 2016–2030* (GTS) envisages to eliminate malaria in at least 25 countries by 2025 known as E-2025, including Bhutan.<sup>(1)</sup> While the number of recorded malaria cases has declined by over 99% between 2000 (5935 cases) and 2020 (54 cases) and local malaria transmission is successfully contained in most of the districts, imported malaria, particularly along the southern border has emerged as a major threat to elimination efforts.<sup>(2)</sup> We report some of the epidemiological characteristics of imported malaria and its potential implications for a sustainable malaria elimination program in Bhutan.

52 We collated information from malaria surveillance records collected between 2013 and 2021, maintained by the 53 national malaria program of Bhutan. All reported cases were classified as indigenous or imported according to National surveillance guidelines adapted from WHO case classification definitions.<sup>(3)</sup> Imported cases were 54 55 defined as patients with a positive malaria diagnosis by blood film microscopy or rapid diagnostic tests (RDTs) 56 and a history of travel to a malaria endemic country other than Bhutan within one month prior to the diagnosis. 57 Between 2013 and 2021 a total of 515 malaria cases were recorded and 317 were classified as imported malaria 58 (62%). Besides 2020, the proportion of annual imported cases was consistently higher than that of indigenous 59 cases, ranging from 57% to 76%. Imported malaria cases were detected in 15 of the 20 districts in Bhutan, 60 though 71% (225/317) of cases were reported from the border districts of Sarpang (26%, 83/317) and Chukha 61 (20%, 64/317) and the interior districts of Wangdi Phodrang (14%, 43/317) and Trongsa (11%, 35/317) (Figure 62 1). Almost all of imported cases originated from India (99%, 314/317), while three infections originated from African countries of Sudan (2) and Liberia (1). Seventy percent (222/317) of imported malaria cases were among 63 64 Indian nationals, and 55% (122/222) of them were recorded as daily visitors seeking medical treatment in 65 Bhutanese health centers. Among infections that were determined with source in India, 26% (81/314) originated 66 from the Indian states of Assam (54) and West Bengal (27) followed by Uttar Pradesh (7), Bihar (5), Jharkhand 67 (4) and Bihar (3) while in the remaining cases from India did not have specific Stats specified in the surveillance 68 records.

69 Our analysis revealed increasing trend in imported malaria which will continue to pose a significant challenge 70 to Bhutan's malaria elimination program. Throughout the entire surveillance period between 2013 and 2021 71 annual number of imported cases exceeded local cases with the exception of 2020, when the COVID-19 72 pandemic imposed lockdowns not only halted cross border population movement but also disrupted the national 73 malaria control program resulting in local malaria outbreak in Sarpang district.<sup>(4)</sup> Bhutan shares a border with 74 the Indian states of Assam and West Bengal that report some of the highest case numbers in India.<sup>(5)</sup> An 75 estimated 1000 daily migrants cross the border from India into Bhutan and this group of visitors is currently not 76 screened for any *Plasmodium* infection, though a recent study reported 0.42% (2/739) of immigrants to be positive for a *Plasmodium* infection by polymerase chain reaction.<sup>(6)</sup> These group of daily migrants enter and 77 78 exit border on the same day for various purposes including for seeking healthcare in Bhutanese health facilities 79 who accounted for 39% of imported cases in this study. These category of migrants pose a significant infectious 80 risk to the local population in the absence of routine screening for the malaria parasite. Hence appropriate 81 surveillance needs to be designed that target this high risk group. The priority should be accorded these group 82 of cross border migrants who live across the international border and come to Bhutan for empolyment, particularly considering the difference in disease transmission level and malaria control measures on the two 83 side of the borders.<sup>(7)</sup> 84

85 Although importation risk are mainly in bordering areas, the interior districts of Wangdi Phodrang and Trongsa 86 accounted for a quarter of imported cases, possibly due to the large number of Indian migrant workers employed 87 at two mega hydropower projects (Figure 1). The detection of sporadic imported cases from other malaria free 88 or low risk districts pose a risk of re-introduction and re-establishment of malaria in the country. While short 89 term daily migrants are unlikely to move beyond the border districts, long term migrants will proceed to interior 90 districts and could potentially trigger local outbreaks in districts where the conditions are favourable. However 91 imported cases were reported at low frequencies from almost all districts of the country. Considering the 92 continuous threat of introduction and re-establishment of malaria transmission despite sound control measures 93 within the country, comprehensive screening including the daily migrants originating from adjacent border areas 94 for *Plasmodium spp*. at border crossings and airports and a strengthening of the current 1-3-7 response system<sup>(3)</sup> 95 within the country are needed. An integrated malaria screening posts for mobile populations at strategic 96 locations including border crossings and migration port could be established to tackle the risk of imported malaria.<sup>(8)</sup> These measures must be complimented by continuous training of health workers to diagnose malaria 97 98 and maintain a high level of vigilance for any case of malaria, irrespective of origin.<sup>(9)</sup>

99	Since the majority of imported cases were from India, comprehensive cross-border collaborations around
100	Plasmodium surveillance and control strategies must be strengthened between Bhutanese and Indian authorities.
101	In addition, strategies for mandatory testing of daily workers from India and Bhutanese citizens returning from
102	malaria endemic areas must be developed and implemented as priority intervention until regional malaria
103	elimination is achieved as is implemented in Sri Lanka. <sup>(10)</sup> Ideally these measures should include sensitive
104	diagnostics for the detection of sub-clinical parasitaemia especially among long term migrants and high
105	throughput screening methods at border crossings and airports for all migrants irrespective of nationality.
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107	Declarations
108	Authors have nothing to declare.
109	Data availability
110	The datasets underlying the results of this study are available from the corresponding authors upon reasonable
111	request.
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115	Contributions
116	KP and KW conceived, accessed, cleaned, analysed and drafted the original manuscript. All other authors
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- 149 countries. Malaria journal. 2019;18(1):210.

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## 152 **Tables and Figues**

- 153 Figure 1: Distribution of imported malaria in Bhutan 2013-2021. Purple circles and green circles are the
- 154 locations of two hydro projects in Bhutan. Note: Locations of 22 long term migrants were missing.

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