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## Diagnosing malaria and other febrile illnesses during the COVID-19 pandemic



As the global malaria community observes World Malaria Day on April 25, 2020, we have plenty to celebrate. Yet this year, the coronavirus disease 2019 (COVID-19) outbreak is greatly dampening the spirits. While the Asia-Pacific region has made substantial progress against malaria, with a 42% reduction in confirmed cases between 2010 and 2018,1 the emergence of COVID-19 could undermine elimination efforts. Like malaria, one of the most common symptoms of COVID-19 is fever.2 Diagnosis of fever in the Asia-Pacific region has always been a challenge due to the large number of febrile diseases prevalent in the region, including malaria, dengue fever, scrub typhus, typhoid fever, and leptospirosis, among others, and to health systems' insufficient capacity to cope with them.3 With COVID-19 added to the mix, differentiation between these diseases becomes even more difficult. Furthermore, due to physical distancing measures and personal protective equipment (PPE) requirements, COVID-19 is limiting access to health care. To ensure that health emergencies such as COVID-19 do not impede progress towards elimination of malaria, health-care workers at the frontline must be better equipped to tackle such threats.

Initial diagnosis of febrile disease in the Asia-Pacific region is commonly done by frontline community health-care workers. In the Greater Mekong subregion,

more than 33 000 community malaria volunteers are trained and deployed with support from the Global Fund to Fight AIDS, Tuberculosis, and Malaria as part of the Regional Artemisinin-resistance Initiative (RAI2E) programme, which brings malaria services to vulnerable rural communities. However, in some places, physical distancing measures implemented to manage COVID-19 are making it difficult for volunteers to access patients with fever, potentially compromising progress towards malaria elimination. This is compounded by a lack of knowledge of infection control and prevention methods and of access to effective PPE by many community-level and primary health-care workers, making safe interactions with suspected COVID-19 cases difficult.

WHO has clearly stated that ongoing malaria interventions such as RAI2E must continue to ensure that elimination gains are not jeopardised.<sup>4</sup> Challenges to continuation must therefore be overcome to empower providers with the means to care for patients with malaria, both during the COVID-19 pandemic and in preparation for future disease outbreaks. To ensure that malaria efforts stay on track, health-care workers' toolkits could be expanded to include improved tools and training to safely identify patients with malaria. Adapted health-care packages that include pragmatic advice on PPE options, training on the use of triage

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For more on the RAI2E programme see https://raifundorg

	Short term: in times of COVID-19	Long term: planning beyond COVID-19
Community health care	Improved guidance on infection control and pragmatic PPE use and selection in facilities Additional dengue fever testing alongside malaria for further differential information Reiterated training for severity signs such as respiratory rate as per ICCM Reiterated training around temperature taking and updating equipment if needed Reiterated community behavioural change communication for personal hygiene and protective measures for broader infectious diseases Digital guidelines and contact tracing apps to support data collection Package to account for non-communicable diseases and increased risk for COVID-19 <sup>5</sup>	Digital guidelines (ICCM based) to support adherence, with a link to surveillance Tools for improved tuberculosis triage Package to account for rise in non-communicable diseases such as hypertension, diabetes, or cardiac issues Additional dengue fever testing alongside malaria for further differential information Reiterated training for severity signs such as respiratory rate as per ICCM Improved community referrals and better linkages with public health systems
Primary health care	Improved guidance on infection control and pragmatic PPE use and selection in facilities Additional dengue fever testing alongside malaria for additional differential information Reiterated training for severity signs such as respiratory rate as per IMCI Reiterated training around temperature taking and updating equipment if needed Digital guidelines and contact tracing apps to support data collection Package to account for non-communicable diseases and increased risk for COVID-19 <sup>s</sup>	Digital guidelines (IMCI based) to support adherence, with a link to surveillance testing to guide antibiotic use  Package for pathogens that respond to doxycycline (eg, leptospirosis or typhus)  Additional rapid diagnostic tests for common respiratory pathogens (eg, group A streptococcus)  Package to account for rise in non-communicable diseases such as hypertension, diabetes, or cardiac issues  Lifestyle guidance coupled with non-communicable disease and malnutrition management Training and tools for basic biochemical and haematological measurements

Table: Recommendations for health-care packages in community and primary health care to differentiate febrile diseases

tests such as respiratory rate measurements, and digital tools to support data collection and contact tracing could all support health-care workers in their task in the short term, as well as building the foundation for more integrated fever management in the future (table).

Although it is essential to ensure that frontline workers continue to have access to malaria rapid diagnostic tests and are trained in their correct use, negative results must be interpreted carefully. Currently, with the pandemic in the forefront of our minds, there might be a tendency to suspect malaria-negative febrile patients as having COVID-19, but other febrile diseases such as dengue fever cannot be ruled out. Dengue fever rapid diagnostic tests6 could be an easy add-on to current packages now, and to future integrated management bundles, when supported by adequate and rapidly shared training programmes to ensure correct use. This approach to tackle additional febrile illnesses and strengthen community referrals would be beneficial to support patient management as well as contributing to tracking and testing for emerging communicable diseases such as COVID-19. In the future, diagnostic assays for other febrile or respiratory diseases could be included to allow detection of other causes of fever, such as rapid tests that detect C-reactive protein, a marker of bacterial infection, or rapid diagnostic tests for prominent doxycycline-responding pathogens or group A streptococcus.7

It is unclear how long the COVID-19 pandemic will last, but there are already lessons to be learned to strengthen health systems for the future, from improved diagnosis of febrile disease to better collection of surveillance data to inform communicable disease management in general. Existing clinical decision algorithms such as the Integrated Management of Childhood Illness or Integrated Community Case Management could be adapted to consider local epidemiology, seasonal prevalence and severity of various febrile diseases, and relative accuracy of the available diagnostic tools.<sup>6</sup> Digital versions of these algorithms can support adherence and can be linked to surveillance systems.<sup>8</sup>

In summary, to ensure continued access to diagnosis and care for patients with malaria during a pandemic, frontline workers need the appropriate training, equipment, and health-care packages to distinguish between different febrile diseases. Strengthening febrile disease diagnosis and management long term will support malaria elimination efforts<sup>9</sup> and improve preparedness for future outbreaks.

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- WHO. World malaria report 2019. Geneva: World Health Organization, 2019.
- Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020; published online Feb 28. DOI:10.1056/ NEJMoa2002032.
- 3 Shrestha P, Roberts T, Homsana A, et al. Febrile illness in Asia: gaps in epidemiology, diagnosis and management for informing health policy. Clin Microbiol Infect 2018; 24: 815–26.
- 4 WHO. Tailoring malaria interventions in the COVID-19 response. Updated April 3, 2020. Geneva: World Health Organization, 2020.
- 5 WHO. COVID-19 and NCDs. March 23, 2020. https://www.who.int/who-documents-detail/covid-19-and-ncds (accessed April 15, 2020).
- 6 Pokharel S, White LJ, Aguas R, Celhay O, Pellé KG, Dittrich S. Algorithm in the diagnosis of febrile illness using pathogen-specific rapid diagnostic tests. Clin Infect Dis 2019; published online July 17. DOI:10.1093/cid/ciz665.
- 7 Althaus T, Greer RC, Swe MMM, et al. Effect of point-of-care C-reactive protein testing on antibiotic prescription in febrile patients attending primary care in Thailand and Myanmar: an open-label, randomised, controlled trial. Lancet Glob Health 2019; 7: e119–31.
- 8 Keitel K, D'Acremont V. Electronic clinical decision algorithms for the integrated primary care management of febrile children in low-resource settings: review of existing tools. Clin Microbiol Infect 2018; 24: 845–55.
- 9 McLean ARD, Wai HP, Thu AM, et al. Malaria elimination in remote communities requires integration of malaria control activities into general health care: an observational study and interrupted time series analysis in Myanmar. BMC Med 2018; 16: 183.