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PROTOZOOLOGY - REVIEW

Malaria diagnostic methods with the elimination goal in view

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Abstract
Malaria control measures have been in use for years but have not completely curbed the spread of infection. Ultimately, global elimination is the goal. A major playmaker in the various approaches to reaching the goal is the issue of proper diagnosis. Various diagnostic techniques were adopted in different regions and geographical locations over the decades, and these have invariably produced diverse outcomes. In this review, we looked at the various approaches used in malaria diagnostics with a focus on methods favorably used during pre-elimination and elimination phases as well as in endemic regions. Microscopy, rapid diagnostic testing (RDT), loop-mediated isothermal amplification (LAMP), and polymerase chain reaction (PCR) are common methods applied depending on prevailing factors, each with its strengths and limitations. As the drive toward the elimination goal intensifies, the search for ideal, simple, fast, and reliable point-of-care diagnostic tools is needed more than ever before to be used in conjunction with a functional surveillance system supported by the ideal vaccine.

Keywords Malaria · RDT · Diagnostics · Elimination · Microscopy · Surveillance · Vaccine

Background

Malaria is still a major cause of death in human history (Gómez-Luque 2020), most especially among low-income classes which are largely located in Sub-Saharan Africa (SSA) and Asia, both of which house about 40% of malaria's burden (WHO 2018; WHO 2019). Nevertheless, malaria can also cause great health problems in urban areas where the transmission can affect both the middle- and upper-income population (De Silva and Marshall 2012). Among the diseases with great public health impact, it holds a significant place and so poses serious public health concern (Dewald et al. 2016; Gwitira et al. 2018; Arrow et al. 2004) (Table 1).

Malaria is caused by the protozoan *Plasmodium*. About five known species of this are capable of causing infection in humans. These are *Plasmodium falciparum*, *Plasmodium vivax, Plasmodium ovale, Plasmodium malariae*, and *Plasmodium knowlesi* (Talapko et al. 2019). In sub-Saharan Africa, *P. falciparum* is the dominantly observed species (de Jong et al. 2020), whereas *P. vivax* is widespread in Asia and Central and South America (Baird 2013). Of these, *P. falciparum* and *P. vivax* have been extensively studied more than other species of *Plasmodium*. Studies have shown that *P. falciparum* is more deadly than the others causing the majority of the mortality, especially in sub-Saharan Africa (Zuzarte-Luis et al. 2014), while *P. ovale* and *P. malariae* are known to cause chronic infection (Richter et al., 2016) and *P. knowlesi*, which was found in South-East Asia primarily causing infection in monkeys, has been identified to also cause infection in humans (Antinori et al. 2012).

The vector organisms for malaria transmission are the female mosquitoes. Depending on geographical location, different species of the Anopheles mosquito are responsible for human-parasite transmission. In sub-Saharan Africa, the species which are notable for malaria transmission include the *Anopheles gambiae*, *Anopheles funestus, Anopheles coluzzii,* and *Anopheles arabiensis. While the Anopheles funestus* and *Anopheles gambiae are favorable for indoor behavioral pattern, Anopheles arabiensis is known for outdoor activities* (Drake and Beier, 2014; Sinka et al. 2020).

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Table 1 The diagnostic approaches implemented by various countries in different regions

Region	Country	Diagnostic method	Reference
Sub-Saharan Africa	Nigeria	Microscopy and RDT	FMOH 2005; Abdulkadir et al. 2015
	Burkino Faso	RDT	Zongo et al. 2016
	Republic of Niger	Microscopy and RDT	PMI 2020
	Mozambique	RDT	Plucinski et al. 2019
	Tanzania	RDT	Masanja et al. 2015
	Democratic Republic of Congo	Microscopy and RDT	Hawkes et al. 2009
	South Africa	RDT	Frean et al. 2013
South-East Asia	India	Microscopy and RDT	Nema et al. 2019
	Bangladesh	RDT	Islam et al. 2013
	Sri Lanka	Microscopy and RDT	Karunasena et al. 2019
	Myanmar	Microscopy and RDT	Kang et al. 2017
	Indonesia	Microscopy and RDT	Hill et al. 2018
Western Pacific	China	RDT	Badmos et al. 2021
	Papua New Guinea	RDT	Senn et al. 2011
Eastern Mediterranean	Saudi Arabia	RDT	Coleman et al. 2014
	Iran	Microscopy and RDT	Hemami et al. 2013
Southern America	Brazil	Microscopy and RDT	Recht et al. 2017
	Colombia	Microscopy and RDT	Recht et al. 2017
	Peru	Microscopy	Recht et al. 2017
	Venezuela	Microscopy	Recht et al. 2017

The species diversity differs from what is obtained in Europe and the Mediterranean, where the dominant vectors are Anopheles atroparvus, *Anopheles labranchiae*, *Anopheles messeae*, *Anopheles sacharovi*, *Anopheles sergentii*, and *Anopheles superpictus* (Sinka et al. 2011; Hertig 2019), and in the Americas, the reported dominant vector species that were identified include *Anopheles albimanus, Anopheles albitarsis, Anopheles aquasalis, Anopheles darlingi, Anopheles marajoara, Anopheles freeborni, Anopheles marajoara, Anopheles quadrimaculatus, Anopheles pseudopunctipennis*, and *Anopheles nuneztovari* (Hay et al. 2010; Sinka et al. 2010).

In general, diagnosing malaria occupies an important aspect of malaria management; misdiagnosis has potential ripple effects on the disease treatment, prevention, and ultimately its elimination. Clinical diagnosis of malaria by medical practitioners is a common practice that is widely documented and notably inexpensive, although prone to errors, due to other febrile clinical conditions that tend to be assumed as malaria (Tangpukdee et al. 2009). Proper diagnosis is expedient for administering appropriate treatment, thereby mitigating the chances of progression to severe illness; the time to recovery becomes significantly shortened while the possibility of drug resistance is minimized. In the long run, proper diagnosis allows for effective policy-making, proper/effective planning, and budgeting (Malaria consortium 2015).

Achieving the elimination goal cannot be possible without proper diagnostic methods. From the causative organism point of view, various biological-based diagnostic methods have been developed over the years ranging from the popular Giemsa-violet microscopic method (Wongsrichanalai et al. 2007) to molecular-based diagnostics (Tangpukdee et al. 2009; CDC 2020). In this article, we review from the literature, various approaches used in malaria diagnostics with a focus on methods favorably used during the pre-elimination, elimination, and post-elimination phases of malaria.

Programmatic phases of malaria control

The World Health Organisation (WHO), in conjunction with various partners, has worked over the past decades to stem the tide of the malaria menace. Going by the WHO technical report, the ultimate vision of the health body and indeed the malaria community globally is to attain a malaria-free world (WHO 2015). Currently, the process of achieving this is by using the following four programmatic phases: malaria control, pre-elimination of malaria, malaria elimination, and prevention of malaria reintroduction (Shretta et al. 2017). In the malaria control phase, parameters such as incidence, prevalence, morbidity, and mortality are the main points of focus, with the goal of reducing these indices to locally acceptable levels.

According to the World Malaria Report (2009), pre-elimination (test positivity rate <5%) is described as "the period of re-orientation of malaria control programs between the sustained control and elimination stages, when coverage with good quality laboratory and clinical services, reporting and surveillance are reinforced, followed by other program adjustments to halt transmission nationwide." The elimination phase has to do with achieving a zero number of cases within a geographical area. However, in a situation where there is the occurrence of three or more indigenous cases of malaria (same species) per annum for three consecutive years in a country where it has been previously eliminated, this is referred to as re-establishment (WHO 2016, 2017).

Different factors like socio-demographic conditions, biological determinants, environmental factors, and politico-economic realities tend to affect the outcome of the elimination drive. Achieving the successful outcome of these programmatic phases requires determination and continuous efforts by the stakeholders involved in each geographical setting (Hasyim et al. 2019), keeping in view the key role of accurate diagnosis.

Malaria diagnostic methods

The diagnosis of malaria consists of the identification of malaria parasites or antigens in the host's blood (Tangpukdee et al. 2009). Different methods can be used to achieve this, including the use of microscopy, rapid diagnostic tests (RDTs), loop-mediated isothermal amplification (LAMP), and polymerase chain reaction (PCR). The choice of a diagnostic tool to be utilized can be affected by various factors, including local circumstances, the skill level of laboratory staff, patient load, and the malaria epidemiology in the specified locality (Moonasar et al. 2007).

Microscopy

This is the standard method for diagnosing malaria over the years and is still applicable as the primary method in many health settings worldwide. It prides itself in the ability to distinguish all the major *Plasmodium species* as well as the gametocytes of *P. falciparum.* However, the use of a microscope requires the availability of functioning equipment, the reagents applied, an efficient quality control system, and competency on part of the handler—being able to identify 100–200 parasites per microliter (good handlers) or 50 parasites per microliter, in the case of the expert handler (WHO 2010; Ngasala and Bushukatale 2019). According to WHO Report (2012), the sensitivity and specificity of light microscopy are dependent on the followings: the quality of the stained slide, time available to read a blood film, and the competency of the person handling the microscope.

Rapid diagnostic tests (RDT)

Rapid diagnostic tests are immune-chromatographic lateral flow devices that are extensively used for the diagnosis and prevalence estimation of malaria based on the principle of detecting malaria antigens in the blood (Jang et al. 2020). The technique involves the application of a blood specimen to the test card (or cassette, depending on the manufacturer) followed by a buffer reagent (3–5 drops). The presence of specific bands in the test card (after 15–30 min) indicates the presence of plasmodium (CDC 2020). All human malaria parasites can express the antigens Histidine-rich protein (*hrp*2) and Plasmodium lactate dehydrogenase (*pLDH*), which are commonly detected by malaria RDTs (Mouatcho and Goldring 2013; Cunningham et al. 2019). However, false negativity can occur in areas with variants of *P. falcuparum* that do not express hrp2 (Cheng et al. 2014). RDTs tend to be more preferred for diagnostic checks because of the simplicity of application, little infrastructure requirements, the capability of detecting >100 parasites/μl, and quick results with a turn-around time of less than 30 min (Mbabazi et al. 2015; Moody 2002). However, humidity and extreme temperatures tend to easily affect their performance, while antigen persistence in the blood circulation of the patient after treatment may result in false positives (Yan et al. 2013).

Molecular method

Molecular methods of malaria diagnosis include polymerase chain reaction (PCR) and loop-mediated isothermal amplification (LAMP). These methods display great potential in areas with a low density of infections which can easily be missed by RDTs. PCR method amplifies the parasite deoxyribonucleic acid (DNA), thus resulting in high sensitivity (0.004 parasites/μl) (Tambo et al. 2018). When compared with microscopy, PCR-based assays have 100-fold greater sensitivity, especially for low parasitemia infections. However, the main limitations of PCR include the complexity of its application in clinical settings, the high cost involved, and the long turn-around time; thus, limiting its wide use for malaria detection, but the method has acknowledged value in research settings (Bharti et al. 2009).

On the other hand, LAMP uses *Bacillus stearothermophilus* deoxyribonucleic acid (DNA) polymerase and four specific primers, which recognize six distinct regions of the target DNA. The amplification and detection can be completed in a single isothermal step (Sirichaisinthop et al. 2011). This technique uses simpler equipment and is cheaper when compared to PCR. The whole process is relatively simple, less time-consuming, and field adaptable (Sattabongkot et al. 2014). LAMP demonstrated sensitivity and specificity of 98.3 and 100%, respectively, compared to microscopy when using heat-treated clinical samples (Sirichaisinthop

et al. 2011). Therefore, in endemic areas where a reduction in costs is vital, LAMP overcomes the disadvantages of PCR—simpler, cheaper, and faster—while maintaining a high level of accuracy, thus making it a promising tool for malaria diagnosis (Ocker et al. 2016).

Diagnostic approach and challenges in different malaria regions

Sub-Saharan Africa region

Malaria endemicity is still persistent in many countries of SSA. Challenges to accurate diagnostics in such countries continue to retard global malaria elimination efforts. For instance, in 2019, the World Health Organisation (WHO) noted that Nigeria, the Democratic Republic of the Congo, Tanzania, Mozambique, Burkina-Faso, and the Republic of Niger reported the highest malaria mortality worldwide (World Health Organisation 2020a). Given this, the diagnostics method incorporated in the malaria control programs in these listed countries, which also fall under different regions of the continent as delineated by the United Nations, is discussed in brief (UNECA 2012).

West Africa

The gold standard for malaria diagnosis in endemic countries remains microscopy (Uzochukwu et al. 2009; Mayengue et al. 2018), but this has its limitations, which include a lack of trained personnel to operate the microscope and a shortage in the number of microscopes available (Hume et al. 2008). The national policy in Nigeria, for instance, recommends the use of microscopy or RDT for testing in all suspected cases of malaria (FMOH 2005; Abdulkadir et al. 2015).

RDT usage in Nigeria among health care workers, especially in the primary health care setting, has witnessed an increased uptake since 2011, although the national malaria testing rate in the country is still low. In one of the northern states of Nigeria, the Global Fund (GF) rolled out RDTs in 2012 in 250 public health facilities and simultaneously provided malaria-specific health management information system (HMIS) training and documentation to strengthen, as well as broaden, malaria diagnostic testing in the country (Awoleye and Thron 2016). Another study conducted in the same country recommended a combination of microscopy and a highly sensitive and specific RDT kit be used as a means to diagnose malaria (Ugah et al. 2017). This double-verification would account for the shortfalls of each method. A study by Mokuolu et al. (2018) involving multiple regions of Nigeria reported that most health care workers demonstrated a positive perception of RDT as well as a good compliance rate.

Dependence on clinical diagnosis without corroborating clinical test is still widely practised but has been shown to be unreliable (sensitivity of 47.2%), with possible outcomes of misdiagnosis, treatment failure, and emergence of drug resistance (Wogu and Nduka 2018). Molecular methods for malaria diagnosis are not routinely used but are reserved for research groups for experimental purposes. This may be due to the ease of use and availability of RDTs and microscopy compared to the requirements for molecular methods.

Similar to Nigeria, Burkina Faso recommended microscopy as the primary method for malaria diagnosis. However, the country began promoting the use of RDT in 2012 as part of the national policy, following which health workers are expected to administer ACT in treating-malaria positive cases (Zongo et al. 2016). This was corroborated by Maltha et al. (2014), who noted that during passive surveillance of febrile patients in Bobo Dioulasso and Banfora (south-west of Burkina Faso), RDTs for malaria diagnosis were incorporated into the malaria control policy; hence, RDT gained popularity (Bisoffi et al. 2010).

In spite of these commendable steps by complying with WHO recommendation of testing before treatment administration (WHO 2006), it was reported that some health workers still rely on symptomatic diagnosis for treating malaria even in the presence of a negative RDT result (Bisoffi et al. 2009; Zongo et al. 2016). A study that included 15,932 children from Burkina Faso, Nigeria, and Uganda was conducted in which 97.3% were febrile, but only 82.1% were RDT positive—this would indicate that 15.2% were at risk of being treated with antimalarial when they were not necessarily infected. It was also found that 47.6% of non-febrile cases were positive by RDT (Ajayi et al. 2016)—if a healthcare worker were to base diagnosis only on some symptoms, there would have been missed infections. This leads to incorrect usage of antimalarials, which promotes drug resistance. Zaongo et al. (2020) showed that although RDT implementation significantly reduced malaria cases in Burkina Faso, the method failed in sub-microscopic detection of malaria when compared with PCR. The study also highlighted that the accuracy of PCR is required, but the ease of use of an RDT is ideal.

The annual incidence of malaria in Cape Verde, located in West Africa, is below 0.1%. However, the Island still records a few cases of indigenous infections and imported cases, mostly originating from neighboring African countries. The country aimed at eliminating malaria by 2020 but experienced an epidemic in 2017 however; its last local case was in January 2018 (DePina et al. 2020; Da Veiga Leal et al. 2021) and has currently applied for malaria elimination status (WHO 2021a, b, c). As part of its strategic plan to attain elimination, the country ensured that quality-assured

diagnoses were done in all health facilities and, as such become the main source of passives cases following, which confirmed cases are reported within 24 h and hospitalized for treatment (WHO 2021a, b, c). The availability of personnel made it easy to make a diagnosis based on RDT followed by microscopy. Health posts that are not capable of doing microscopy do have technicians who are competent in slide preparation for analysis in laboratories. In order to allow for wider coverage, the RDT used has the capacity to detect *hrp2* and *pLDH*; it also has the competence to differentiate among the four common malaria species. The major identified challenge is in the area of implementing diagnostic quality control systems as well as capacitating in molecular diagnostic techniques. Cape Verde has an existing good surveillance system that aims at monitoring and evaluating the test, treats, and track system as well as monitoring therapeutics efficacies (DePina et al. 2018a, b).

Central Africa

In terms of disease burden, malaria accounted for over 20% of all illness in the Republic of Niger, making it one of the leading causes of illnesses in the country (IHME 2020; PMI 2020). In a study by Doudou et al. (2012), it was noted that the overestimation of malaria incidence in the Republic of Niger was due to the fact that presumptive diagnosis was predominantly used. The presumptive diagnosis of malaria is a situation whereby diagnosis is based on clinical symptoms rather than a specified diagnostic tool. Although malaria is endemic throughout the country, some gains (7.9% reduction) were recorded in the number of illnesses between 2015 and 2019 (World Health Organisation 2020a). Like most endemic countries, microscopy and RDT formed the basis of malaria diagnosis in the Republic of Niger, with the national treatment guideline requiring every suspected malaria case to have either RDT or microscopy (PMI 2020). A significant uptake in the use of RDT at the health facility level was recorded in 2019 compared with preceding years among health personnel available in about 61% of the health facilities (SMO 2020).

In the Democratic Republic of Congo (DRC), which is also a malaria-endemic country (Mayengue et al. 2018; Ngatu et al. 2019), both microscopy and RDT were commonly used. Among the challenges with the use of RDT in DR Congo is the issue of cost and sustainability of the purchase and supply of the RDTs (Hawkes et al. 2009). It has been demonstrated in the DRC, which is a setting with high malaria prevalence and low economic income, that RDTs are likely to produce a cost-saving effect only in situations where malaria prevalence is <58%, but the contrary is the case where >80% prevalence is recorded (Shillcutt et al. 2008; Bath et al. 2020). On another note, instances of RDT being affected by temperature and/or environmental humidity either during transportation or storage have been reported. Overall, these tend to have an impact on the quality of the RDT in that high humidity can lead to degradation of the RDT while the high ambient temperature can affect the RDT sensitivity. In view of these, it must be ensured that rapid diagnostic kits are kept at optimal recommended conditions (WHO-WPRO 2009; WHO 2011).

Acceptability of the method of diagnosis by field health workers is another challenge that was identified in some local settings in the DRC (Hawkes et al. 2009).

East Africa

In 2010, the ministry of health and social welfare in Tanzania, through the National Malaria Control Programme, adopted a massive deployment of RDTs for *Plasmodium* diagnosis throughout the country (Masanja et al. 2015), and this was also corroborated in another study reported by Stuck et al. (2020). Within Tanzania, a study was conducted involving 168 patients at facilities with diagnostic capabilities. Of these patients, 63% were tested for malaria, and 30% were positive. However, antimalarials were still prescribed to patients with negative results, as well as some patients who were not tested for malaria (Mubi et al. 2013). An updated report in 2016 by the ACT-watch Group included a survey on malaria diagnostics in Tanzania which showed 91.8% availability of malaria diagnostics in public health facilities (18.9% microscopy and 89.3% RDTs) and 97.1% in private health facilities (68.9% microscopy and 89.3% RDTs) (Hanson and Goodman 2017).

Southern Africa

In Mozambique, the National Malaria Control Program instituted the policy of testing all malaria suspected cases with either microscopy or RDT in 2008 (Sequeira 2015). However, the outcome of a 2015 study revealed a poor attitude of healthcare workers to this government policy. Despite this, reports as of 2019 showed that RDTs were the primary diagnostic method; as opposed to microscopy in other geographic regions and that the RDT was still suitable for use in the population (Plucinski et al. 2019). Presumptive diagnosis and treatment of malaria were also common, as previously noted in the preceding SSA countries above. Furthermore, the findings noted the common prescription of antimalarials to patients who tested negative for malaria (Salomão et al. 2015).

By way of complying with WHO guidelines on malaria tests and treatment, it was in 2017 that the Mozambique national health system mandated RDTs as part of the diagnostic method in malaria case management and surveillance (Candrinho et al. 2019; Galatas et al. 2020). In a bid to improve diagnosis, a field study compared ultra-sensitive

RDT and conventional RDT (using PCR as a reference method), it was noted that there was no substantial difference in terms of diagnostic output between the two RDTs in terms of sensitivity and detection of false positives (Galatas et al. 2020). The issue of RDT stock-out arising from supply chain bottlenecks and inadequacies is a major challenge identified as a hindrance to the successful implementation of test and treat based on the use of RDT (Hasselback et al. 2014).

Some countries in the southern Africa region, such as Botswana, Swatini, South Africa, Namibia, and Zambia, have reported areas with a very low level of transmission, and thereby positioning them in the pre-elimination phase. The common practice in these areas revealed vector control and use of antimalarial as key factors, with RDT and microscopy for diagnosis forming the mainstay of diagnosis while molecular detection method is reserved for research purposes. The efficient surveillance system has been reported too, giving credence to the successes achieved so far in some of these countries (Gueye et al. 2014; Nghipumbwa et al. 2018; Moakofhi et al. 2018; Motlaleng et al. 2018; Stresman et al. 2019; Kobayashi et al. 2019; Maharaj et al. 2013a, b; Moonasar et al. 2021).

The South-East Asia region

Many countries in the WHO South-East Asia region have recorded a progressive decline in the incidence of malaria. Although countries like India, Myanmar, and Bangladesh are still malaria-endemic, Bhutan and Timor-Leste are in the pre-elimination phase, while Sri Lanka and the Maldives have achieved malaria elimination status (WHO 2019a, b; WHO 2021a, b, c). More than 85% of the malaria cases in South-East Asia are located in India, which is home to 2% of the world's malaria cases as well as 2% of malaria deaths globally (hence the main country discussed in this section). In spite of these, there was a significant decline in the number of malaria cases among the population at risk-reducing from 10 to 4 per 1000 between 2016 and 2019 (SMO 2022; World Health Organisation 2020a). India's malaria control and elimination program are divided into four segments as it is deemed applicable in the districts, using annual parasite incidence as criteria. These segments are prevention of re-establishment, elimination phase, pre-elimination phase, and intensified control phase (MoHFWGI 2016; SMO 2022). With many parts of the country being low resource settings, RDT and microscopy are the main diagnostic methods; however major shortfalls from these are challenges resulting from mixed infection and low-density cases (Nema et al. 2019). A study by Haanshuus et al. (2016) noted that with use of RDT, malaria is under-diagnosed in rural parts of India. When compared with PCR, the study showed a decrease in the sensitivity of RDT and microscopy. A major contributor to this is the presence of a high number of sub-microscopic or asymptomatic malaria cases, which can lead to under-estimation of malaria prevalence and thus have an impact on surveillance if dependent solely on the use of RDT and microscopy (Kumari et al. 2020). Some of the various challenges being faced by surveillance in India include poor coordination in the reporting, and capturing of surveillance data across the regions, delay in data reporting, and multiplicity of data resources leading to limitations in data reliability (Rahi et al. 2021). As a key factor in malaria elimination, it is important to train surveillance staff and make them operate at levels that befit international standards with regular monitoring of their output by independent external agencies (Lal et al. 2019). Digitalization of the malaria management system, most especially the surveillance, will enhance a great leap in the drive toward elimination (Nema et al. 2021).

Bangladesh has achieved a reduction in malaria burden with malaria cases confined to 13 out of its 64 districts thus making it be classified as having a "very low transmission" level. The malaria elimination drive in the country is a product of combined efforts of the national government and non-governmental organizations working in the rural interiors where malaria transmission is persistent (Noé et al. 2018). The use of commercial RDT is widely practiced and has shown to be highly sensitive (94.6%) and specific (88.5%) for *P. falciparum.* Slide microscopy is mainly available to support early diagnosis and treatment (Islam et al. 2013). With the introduction of telephone as part of early malaria diagnosis and treatment in 2010 there were observable levels of improvements in terms of the case diagnosis time (Prue et al. 2013). The Bangladesh Institute of Epidemiology, Disease Control and Research have in place an effective surveillance system for communicable, and non-communicable diseases, among which is malaria. The institute makes use of web-based integrated disease surveillance with data being collated weekly from the sub-districts (Husain et al. 2019). Since 2000, RDTs have been implemented in areas of Myanmar where there is no reliable microscopic malaria diagnosis facility (Nyunt et al. 2016). The use and feasibility of RDTs were assessed in Myanmar. A few studies noted challenges that included inadequate instructions to differentiate mixed *P. falciparum/vivax* infections from *P. falciparum* infections Sudhinaraset et al. 2015).

Since 2000, RDTs have been implemented in areas of Myanmar where there is no reliable microscopic malaria diagnosis facility (Nyunt et al. 2016). The use and feasibility of RDTs were assessed in Myanmar. A few studies noted challenges that included inadequate instructions to differentiate mixed *P. falciparum/vivax* infections from *P. falciparum* infections Sudhinaraset et al. 2015). Microscopy remains the gold standard for malaria diagnosis; however, in eastern Indonesia and other malaria-endemic regions, microscopy has challenges that start within the healthcare

system as well as the limited access to such microscopy services for the majority of symptomatic and exposed populations. Thus, in eastern Indonesia, RDTs should be able to detect both *P. falciparum* and *P. vivax* (Tjitra et al. 1999). In Sri Lanka, elimination status was achieved in 2012, and WHO certification was given in 2016. Some of the strategies applied in order to achieve the elimination goal include entomological survey, health awareness and community programs by dedicated groups, selective vector control, and parasitological surveillance with aim of early diagnosis and treatment (Premaratne et al. 2019).

Western Pacific region

According to a World Health Organization press release in 2016, the Western Pacific region had achieved targets for malaria reduction as per the Millennium Development Goals in 9 out of 10 malaria-affected countries, also reporting significant reductions in fatalities and prevalence in 8 out of the 10 countries (World Health Organization 2016). On one end, Papua New Guinea makes up as much as 80% of malaria cases reported in the Western Pacific region in 2021 (World Health Organization 2021c), an increase from 71% of cases in the previous years. The use of RDT for malaria detection prior to treatment administration in Papua New Guinea is well recognized, and it has been demonstrated that treatment for malaria based on RDT is safe and feasible (Senn et al. 2011). The recent resurgence in cases of malaria witnessed in Papua New Guinea has been attributed to challenges with funding resulting in limited access to diagnostic tests and treatment, among others (Das 2021).

Conversely, the Greater Mekong sub-region has shown great strides toward achieving malaria elimination by 2030 (World Health Organization 2021c). Thus, different regions of the Western Pacific are at different points in their elimination journeys. As of the 2016–2020 regional framework for malaria control and elimination in the Western Pacific (World Health Organization Regional Office for the Western Pacific 2017), malaria case surveillance incorporated with necessary re-stratification based on malaria disease burden and entomological surveillance will be required to achieve optimal malaria interventions. For over a decade, event-based surveillance has been conducted in this region to detect any public health threats or events (Lowbridge et al. 2020). With regards to malaria specifically, surveillance is aimed to be a core intervention by the year 2030 (World Health Organization 2016) as the region aims to approach elimination.

Remarkably, China had been declared malaria-free as of June 2021, which involves increased surveillance of high-risk regions to maintain this status (World Health Organization 2021a). It is believed that this feat was at least partially due to innovative approaches to treatment and surveillance—China has sought to apply genetic epidemiological methods to promote surveillance efforts. China invested well in necessary technologies, including the implementation of rapid diagnostics for case detection (Badmos et al. 2021). The surveillance includes not only case detection, but stable systems in place for reporting and laboratory testing, identification of malaria vector resistance and *Plasmodium* species resistance (Chen et al. 2021). This was all supported by major financial contributions toward these efforts (Badmos et al. 2021). Other interesting efforts included the establishment of a network of national reference labs to ensure capacity for malaria diagnosis and the hosting of microscopy competitions by the Chinese Ministry of Health to strengthen and maintain skills (Cao et al. 2021).

Collaborative efforts with China to establish their protocols in malaria regions may assist the Western Pacific greatly in their approach toward elimination. The establishment of these malaria-reporting networks, laboratory infrastructure, and trained personnel is a long-term investment that several regions of the Western Pacific may not have funds to allocate toward, particularly during the current pandemic. Thus, collaborative approaches are needed.

Eastern Mediterranean region

In the Eastern Mediterranean region, nine countries are approved as being malaria-free by WHO, however no further additions have been made to the list since 2012 (World Health Organization 2021b). Between the years 2000 and 2015, malaria incidence in the Eastern Mediterranean region reduced by 38% (World Health Organization 2021d). Unfortunately, this was followed by a 33% increase in the number of cases between 2016 and 2020 (World Health Organization 2021d).

Similarly, the number of malaria-related deaths decreased from 2000 to 2015 but increased as of 2020 (World Health Organization 2021d). Difficulties in reducing the malaria burden in the region require financial investment to move toward their elimination goals (World Health Organization 2019). Saudi Arabia was at the verge of malaria elimination although had an outbreak in 1998, which was curtailed by effective surveillance that employed rapid case detection (RCD) using RDT. Vector control, adoption of artesunate plus sulfadoxine-pyrimethamine as first-line treatment (Coleman et al. 2014), coupled with a regional partnership with neighboring countries (Snow et al. 2013) helped the country achieve 0.1 malaria cases in 1000 population in Arabian Peninsula (Coleman et al. 2014). Conversely, in Al Hudaydah, Yemen, long-lasting insecticide mosquitoes nets (LLIN) were difficult to access among local communities, thus serving as a major factor in the continual transmission of malaria in the area (Al-Eryani et al. 2017).

Unlike Saudi Arabia, Yemen only focused on vector control measures and not on clinical and epidemiological methods hence promoting constant endemicity in the country. In addition, factors such as cultural beliefs, financial constraints, and inadequate knowledge of the disease do further encourage a high level of malaria transmission among the Yemen population (Al-Taiar et al. 2009; Bamaga et al. 2014).

The malaria elimination goal program in Iran began in 2009 with aim of achieving elimination by the year 2025. There was a great decline in Iran between 2002 and 2017 (Soofi et al. 2019; Vatandoost et al. 2019a, b). The country has successfully reduced its local cases of malaria over a period of 16 years, from an incidence of 0.24/1000 cases in 2002 to 0.01/1000 in 2017 with most cases limited to the South and Southeast of Iran (Nejati et al. 2018; Vatandoost et al. 2019a, b), while the East Azerbaijan Province of Iran has attained a zero-malaria level since 2018, which qualifies it to be classed in elimination phase (Azizi et al. 2020).

According to Soofi et al. (2019), some identified challenges responsible for delay in achieving the desired control level in the southern part of the country include delay in diagnosis and treatment due to superstitious beliefs, misdiagnosis, delay in accessing health facilities and activities of unqualified health personnel. It is noteworthy that in areas of the country that are already focusing on attaining elimination, part of the most important strategies used were early diagnosis and treatment of identified cases. Passive and active case detection by trained health workers is currently one of the surveillance strategies being employed (Vatandoost et al. 2019a, b).

The surveillance reporting system of identified cases works from the periphery to a central network using the telephone as means of communication (Rahmani et al. 2020). Hassanpour et al. (2017) noted that as the number of asymptomatic cases and submicroscopic cases arises, it is important to consider diagnosis using molecular methods. Strictly enforced policies need to be rolled out as a way of combating malaria reintroduction to areas where zero cases have been achieved. Qatar is one of such countries which had introduced a malaria surveillance system to detect local transmission as well as imported cases (Chehab et al. 2018). However, much of the success may be due to Qatar having eliminated local transmission in 1970, but the region was still subject to numerous imported cases due to migrants entering the country from malaria-endemic countries (Atta et al. 2016). Similarly, Tunisia has eliminated malaria since 1979 but still experiences some imported cases annually (Aoun et al. 2010).

South America region

There has been meaningful progress in the fight against malaria in the Americas. However, in southern America, especially the Amazon regions, not much has been achieved in reaching the zero-infection rate of malaria infection. In 2015, Brazil, Venezuela, Peru, and Colombia recorded varying degrees of the prevalence of malaria infection (WHO 2016). Over the first decade of this century, most nations in the Americas saw a significant decrease in malaria incidence (Carter et al. 2015), with the exception of Venezuela. However, from South America's four neighboring nations (Brazil, Colombia, Peru, and Venezuela), Colombia and Brazil have seen a progressive drop in the number of confirmed malaria cases per 1000 population, whereas Peru and Venezuela have seen rises. Argentina and Paraguay are in the elimination phase, with the World Health Organization (WHO) certifying malaria eradication after three years of no indigenous cases (2013–2015).

Malaria has quadrupled in the Loreto area of Peru's Amazon between 2011 and 2014, with 60,566 documented cases in 2014. Furthermore, based on data from non-WHO sources for 2016, PAHO issued a notice in February 2017 indicating a recent spike in malaria incidence in numerous countries in the Americas, including Colombia and Venezuela: In Colombia, 83.356 malaria cases were recorded, with *P. falciparum* accounting for 57% (47,497) of the cases, 39.7% (33,055) were *Plasmodium vivax* infections, whereas 3.3% (2804) were mixed infections, In 2016, 240,613 cases were reported in Venezuela, representing a 75% rise over 2015.

Venezuela, a country of interest in Southern America, has had a steady increase in malaria infection in recent times. However, national and regional initiatives focusing on the diagnosis, vector control, and stocking of adequate antimalarial treatment medications are required to restrict malaria spread, particularly in mining regions (Recht et al. 2017) thus, such initiatives are important in curbing up the rapid increase in the spread of Malaria in Venezuela.

Diagnostic in the elimination settings

No doubt, accurate malaria diagnostics are imperative for disease elimination; to achieve this, there must be active, condensed efforts to identify and act against infections (Moonen et al. 2010). In particular, the challenge is that of asymptomatic carriers that constantly contribute to the low-grade transmission of malaria (Wickremasinghe et al. 2014) and can be missed using the common diagnostics tools. Asymptomatic persons do contribute to the transmission of the parasite but are not detected by the health systems, thereby going unaccounted for since the malaria diagnostic methods used are not sensitive enough to identify these

patients. Studies have shown that the low performance of malaria microscope operators can particularly hinder species identification (Thet Wai et al. 2020), as such, newer methods are required. One of the major programs employed is the mass-screen-and-treat strategy. Unfortunately, a shortfall associated with this is that it has been shown to have low detection limits, detecting only 55% of infectious persons (Slater et al. 2015). This is much lower than a detection limit of 2 parasites per microliter which should detect 95% of the infectious reservoir (Hemingway et al. 2016; Graves et al. 2015). To reduce the number of infected people, it is imperative that tests can detect low-level blood-stage infection of *Plasmodium* species or the dormant liver stages of *P. vivax* and *P. ovale* (Slater et al. 2015). In recent years, researchers have worked on developing tests for this purpose. This resulted in the use of CRISPR-based (clusters of regularly interspaced short palindromic repeats) diagnostic methods to detect *Plasmodium* species even in asymptomatic carriers (Lee et al. 2020). Non-endemic areas provide a suitable setting to test such diagnostic methods meant for low parasite numbers. In such an environment, the illumigene LAMP assay has also been proven to be suitable. The test was designed to be able to reach a limit detection of about 0.5 parasites per microliter of *P. falciparum* and *P. vivax* (De Koninck et al. 2017). Unfortunately, the assay needed to be tested on larger populations for the results to be considered definitive. However, researchers using an ultrasensitive LAMP method had success in malaria-endemic regions having a detection limit of 0.025 parasites per microliter from whole blood and 0.050 parasites per microliter from dried blood spots (Mohon et al. 2019).

Evidently, great strides have been made in diagnostic assays to allow approaching malaria elimination. These sensitive tests are required to detect asymptomatic infection with low parasite numbers to ensure all cases of malaria are captured with very minimal or no chance of parasite transmission. Unfortunately, the worrisome aspect of it is that there is still a long way to go. In view of this, researchers must be careful and thorough before declaring malaria elimination. It becomes important for every country that is at the elimination stage to consider or enact a policy of test and treat at every border post made mandatory for every traveler by making use of a more efficient point-of-care (POC) diagnostic method. Any identified method that meets up with the required POC specification needs to be given adequate support in terms of funding and regular availability of both the diagnostic tool and operational manpower. A strict surveillance system must equally be enforced by way of complementing the aforementioned.

Roles of diagnostic test, surveillance, and vaccines in the national and regional malaria elimination programs

To achieve overall malaria elimination, regional changes must be affected to result in national impacts (Table 2). By impacting necessary changes at the national level as well as addressing compliance regionally, great strides can be made toward elimination. Precise malaria diagnosis is important for individual case management as well as disease surveillance nationally (McMorrow et al. 2011). Without proper diagnostics, surveillance, and treatment efforts are not possible. In particular, inaccurate diagnosis leads to inappropriate use of antimalarials which promotes drug resistance. Aside from correct diagnosis, it is ideal to pick up infections during early onset. Early detection of infection reduces the time between symptoms and prescription of appropriate treatment, thereby reducing the chance of transmission (Landier et al. 2016). Although RDTs have been particularly useful in

Table 2 Summarized role of diagnostic tests, surveillance, and vaccines in the national and regional malaria elimination programs

Parameter	Description	Reference
Guidelines	• For training on the use of variously approved diagnostic methods such as microscopy and RDT. • Treatment guidelines for health professionals and health care workers. • Guideline for community private drug peddlers and retailers.	Tetteh et al. 2021 Ansah et al. 2015 Bruxvoort et al. 2013
Surveillance system	• An adequate supply of technologically relevant surveillance tools in malaria-affected regions. • Implementation of the surveillance system for monitoring infections and progress toward elimination. • Regular training and retraining on surveillance for monitoring and evaluation officers. • Strengthening surveillance systems to involve private health sectors. • Integration of upcoming technology into a currently existing system for enhancing surveillance efficiency, especially in post elimination regions.	Barclay et al. 2012 Bridges et al. 2012 Lourenço et al. 2019 WHO 2018 Yukich et al. 2014
Vaccine	• Financial investments in promoting malaria vaccine research and production. • Development of vaccines with high efficacy, minimal side effect, and wide acceptability. • Promoting vaccine literacy among less-educated communities to enhance vaccine acceptability.	Targett and Greenwood 2008 Healer et al. 2017 Dimala et al. 2018

this regard, as they are simple and easy to use (Mbanefo and Kumar 2020). However, as countries approach elimination, limits of detection for microscopy and RDTs are reached while the parasite is still circulating in the population (Zimmerman and Howes 2015). Through a reduction in malaria transmission, infected persons will show low-density infections that may not be detected by RDTs (McMorrow et al. 2011) reiterating the fact that more sensitive tests are needed to reach a true elimination status.

Clear guidelines essential

Many African countries have implemented guidelines for testing and diagnostics, but they are not always followed in local settings. This may, in part, be due to a lack of training for health care workers and medical laboratory professionals. In Ghana, it has been shown that providing microscopy training improved the ability of medical laboratory professionals to correctly identify malaria parasites from 64 to 87% (Tetteh et al. 2021) - this is indicative of a great improvement in diagnostics as the result of a relatively short training program. There is also evidence from another study in Ghana that the integration of RDTs at the informal private drug retailers will result in a reduction in the prescription of antimalarials for malaria-negative individuals. This is important to consider as many febrile individuals would approach a private drug trailer as opposed to hospitals or clinics. With the availability of RDTs in malaria-endemic regions, antimalarials are less likely to be prescribed in a fever-presenting patient who is not infected with malaria (Ansah et al. 2015). It has also been shown in Tanzania that the rollout of RDTs drastically improved diagnostic tests and reduced the incorrect usage of ACT (Bruxvoort et al. 2013). These regional training program and implementation of more RDT sites would therefore be greatly beneficial to both patients and the efforts toward malaria elimination.

Strong surveillance system

In addition to these, effective surveillance is essential in curbing the spread of malaria. Without the ability to detect and respond to outbreaks timeously, malaria elimination efforts will go in vain (Barclay et al. 2012). In the absence of surveillance, countries will not be able to monitor infections and progress toward elimination, hence at-risk regions may be overlooked (Lourenço et al. 2019). As regions approach elimination, universal coverage programs transition to localized detection and containment of individual malaria cases—this level of scrutiny requires successful surveillance (Bridges et al. 2012). An ideal surveillance system would envelope quick, accurate case reporting, incorporation of relevant data, central storage, and the ability to be analyzed well to assist with policymaking and malaria-control efforts (Ohrt et al. 2015). A study of 16 countries found that there were common issues at the national level (Lourenço et al. 2019). These included low surveillance coverage in remote communities or in the private sector, a lack of infrastructure to allow high-quality case-based data to be captured, data was not being integrated from multiple sources, and, importantly, the data was not available to guide policy-making and program decisions. While a short message service (SMS) system has been proposed to populate a central database of cases (Yukich et al. 2014), this has not been properly implemented since in some regions it is yet to be implemented and would once again require strict compliance at the regional level. Evaluations that trialed an SMS surveillance system was promising but hindered by internet coverage, data transmission, and e-literacy within regions (Win Han et al. 2021). Other studies have also pointed out a loss of accuracy of reported data through this system (Githinji et al. 2014). The World Health Organization has also recognized that the private sector is not as tightly regulated as the public sector, which results in inconsistent reporting from the private sector (WHO 2018). This is a major hindrance to surveillance and forming national policies requires coordination and collaboration from all sectors. As with testing, surveillance requires solidarity between the national policies and implementation regionally. Tracking surveillance has proven difficult regionally; particularly considering health care facilities may already be strained. Above regional challenges, the national level requires the relevant database infrastructure to be in place, as well as a means to gather information rapidly. Parts of Africa do not have reliable access to telephones, internet, or well-maintained tarred roadways to ensure that disease information is rapidly conveyed to the necessary authorities (Chaminuka et al. 2008; Barclay et al. 2012). However, with incomplete surveillance, the national bodies struggle to make policies that are relevant to the current malaria infection status.

Need for effective vaccine

A vaccine that induces complete sterilizing immunity or blocks transmission would be ideal in the race to malaria elimination (Targett and Greenwood 2008). While a transmission-blocking vaccine will not directly prevent infection, herd immunity can be reached by reducing the number of infected mosquitoes in the community (Duffy 2021). It has been postulated that in a seasonal setting, a vaccine should lower the basic malaria reproductive rate in the population. This in conjunction with other control measures may disrupt transmission (Cotter et al. 2013). Vaccines also hold a vital role in malaria post-elimination. These will play the role of preventing the re-establishment of transmission in settings where elimination has been achieved, and should there be an incidence of malaria resurgence the vaccine can

prevent disease and death (Healer et al. 2017). While malaria vaccination is an ongoing research problem, RTS,S/AS01 has been recommended by WHO for use in children in sub-Saharan Africa and regions with moderate to high *P. falciparum* transmission (WHO 2021a, b, c). This is a major breakthrough as we approach malaria elimination but does not come without its challenges. The vaccine requires 4 doses for children—the first three are monthly (Laurens 2020). It is probable that children may miss follow-up doses or not have them administered within the correct time frame. This is particularly an issue in areas where individuals have to travel through harsh environmental conditions to reach a health-care facility. A systematic review by Dimala et al. (2018) identified the major challenges, which were community hesitancy to take the vaccine due to a lack of information, concerns regarding the side effects, inefficient administration of the vaccine, and poor health services. Particularly when it comes to community engagement and awareness, there is a responsibility at the national level to organize appropriate programs and ensure correct and accurate information is available to the public. Above this, sourcing and ensuring the quality of vaccines is a responsibility to be undertaken. However, health care workers at the regional level need to be informed and able to assist patients with any questions that they may have. These individuals are also required to ensure proper storage and administration of the vaccine.

Maintaining elimination

The ultimate goal of the world health body is to eradicate malaria, just as was the case with some other disease condition; and until this is achieved, malaria elimination remains the aspiration and target for every affected nation. No doubt many countries (mostly outside sub-Sahara Africa) have been able to achieve malaria elimination for which malaria elimination status is issued to countries by the World Health Organization following three consecutive years of zero local malaria-free states (WHO 2019a, b). Following the award of malaria elimination status in identified settings/countries, the importance of maintaining such status cannot be overemphasized, not necessarily because of the certification but the various negative impacts arising from the reintroduction of malaria in such settings. It is important therefore that the maintenance of a malaria-free status is ensured through unwavering surveillance. Such surveillance is not time-bound but rather must be made an exercise that is continuous and gradually integrated into the mainstream health services until eradication is attained (WHO 2015). In the same vein, it is very vital to ensure that all measures leading to achieving elimination be maintained by the presence of competent leadership and constant political will. No doubt availability of an effective malaria vaccine post-elimination will augment all the structures mentioned above, hence reducing the chances of having malaria outbreaks or reintroduction.

Challenges posed by COVID-19 to malaria elimination efforts

The advent of coronavirus disease (COVID-19) caused by SARS-CoV-2 took the world by surprise with the disease becoming a pandemic in 2020 (Gorbalenya et al. 2020; World Health Organisation 2020a). It is obvious that the pandemic had its impacts on various sectors of health with malaria elimination drives not spared (Gorbalenya et al. 2020). The virus shared similar symptoms with malaria, such as fever, headache, body pain, and fatigue, thus making it difficult to clinically distinguish between the two infections (Rothan and Byrareddy 2020). The presence of COVID-19 has greatly agitated the health care system in many countries leading to a transient halt in focus on some infectious diseases (like HIV/AIDS, tuberculosis, and malaria), which are known for high morbidity and mortality rates. Over the years, the recommended interventional measures that have been applied in controlling malaria have proven to be quite effective with success reports from different malaria regions; however, the COVID-19 pandemic stands to erode these gains. It has been documented that undetected cases of the two infections have potential multiplier effects, which can be disastrous, especially in low- and middle-income communities (Zawawi et al. 2020).

The issue of misdiagnosing malaria as COVID-19 was noted in South Africa due to the fact that both disease entities present with similar symptoms (Chanda-Kapata et al. 2020; NICD SA 2022). South Africa is in the malaria pre-elimination stage; the possibility of missing out on malaria cases in the guise of COVID-19 has a propensity to cause some setbacks to the malaria elimination achievements attained. To stem the possibility of missing out on malaria cases, health workers are to ensure that every individual living in malaria-endemic areas of the country who present with fever or flu-like symptoms is tested for malaria, with all malaria positive cases commenced on medications immediately (NICD SA 2022). On another note, the trial of various medications to combat the new virus witnessed the trial of artemisia and chloroquine in some countries. Artesunate based medications are currently the mainstay of malaria treatment. With the injudicious use of COVID-19, there is the possibility of widespread resistance, which is already noted in some parts of South Asia (Kyaw et al. 2013; Aborode et al. 2020). Chloroquine is not a standard recommended treatment for COVID-19, rather its use in such instances could mitigate the effort of attaining chloroquine reintroduction as gradually being tried in a place like Malawi (Ho et al. 2021; Roux et al. 2021).

According to Diptyanusa and Zablon (2020), funds and personnel allocated for malaria control programs were diverted to combating COVID-19 and its attendant challenges, most especially in Africa and Southeast Asia countries. This ultimately had its consequences on the malaria control and elimination program in some of these countries. It is until recently that reprioritization of malaria programs began to ensue. Other major areas that were affected during the COVID-19 pandemic include challenges with executing population-wide malaria interventional programs in form of distribution of insecticide-treated nets, indoor residual spray, and seasonal malaria chemoprevention especially in affected countries (Rogerson et al. 2020a, b). These control/elimination activities were impaired due to travel restrictions resulting from COVID-19 regulations, which took the form of lockdowns, curfews, and enforcement of travel certificates depending on the prevailing situation from one locality to another (Hussein et al. 2020). The movement restriction affected supply and, consequently the availability of materials such as chemicals, diagnostic tools, and medication needed for combating malaria (Aborode et al. 2020). For instance, a high record number of deaths due to malaria outbreaks during the pandemic were reported in Cameroun and Zimbabwe as a result of inaccessibility to health care (Kindzeka 2020).

In the light of the various impacts of COVID-19, it is important for the malaria-affected regions to align the malaria elimination along the rules and regulations guiding the new COVID-19 disease as it evolves through various endemic phases that still lie ahead while staying focused on the elimination goal irrespective of the numbers spontaneous outbreaks that may ensue.

Concluding remarks

The fact that malaria affects a significant number of the world population, especially among the underprivileged and poor in society, makes it a disease that must be given utmost priority. No doubt, conquering the malaria menace and malady has been a daunting task whose panacea is multipronged, of which accurate diagnosis is inevitably non-negotiable. The age-long microscopy method remains the reference standard for diagnosis in the majority of endemic regions, but over time RDT has successfully gained wider spread in terms of usage due to its easy and rapid mode of application. Regions in the elimination phase are mainly faced with the challenges of malaria importation and recognizing asymptomatic sub-microscopic carriers, which serve as a potential source of transmission. Speeding up and lending financial support to ongoing research aimed at coming up with easy-to-use, point diagnostic care diagnostics in the elimination settings should be given a high priority on all fronts. It is not enough to have surveillance policies in countries battling malaria, there must be joint efforts to ensure effective implementation with measurable outcomes using up-to-date technologies. Taking a cue from the international support received in the development of COVID-19 vaccines, it will be worthwhile that such a level of commitment to be made to the ongoing research and development of the malaria vaccine, which has the potential and far-reaching effects in terms of reducing the malaria mortality and losses resulting from morbidity.

Abbreviations ACD: Active case detection; ACT: Artemisinin-based combination therapies; CRISPR: Clusters of regularly interspaced short palindromic repeats; DNA: Deoxyribonucleic acid; DDT: Dichlorodiphenyl-trichloroethane; DRC: Democratic republic of Congo; GF: Global funding; HMIS: Heath management information system; Hrp2: Histidine rich protein-2; IRS: Indoor residual spraying; LAMP: Loop-mediated isothermal amplification; LLINs: Long lasting insecticidal nets; LSM: Larva source management; pLDH: Plasmodium lactate dehydrogenase; NMCP: National malaria control program; *P. falciparum*: *Plasmodium falciparum*; *P. knowelsi*: *Plasmodium knowlesi*; *P. malariae*: *Plasmodium malariae*; *P. ovale*: *Plasmodium ovale*; *P. vivax*: *Plasmodium vivax*; RDT: Rapid diagnostic testing; RNA: Ribonucleic acid; SVIRE: Integrated surveillance and response to epidemics; WHO: World Health Organisation

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