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What Impact Has the COVID-19 Pandemic Had on the Fight Against Malaria?

Series | COVID-19 and other pandemics

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[This document forms part of a series of discussion notes addressing fundamental questions about global health. Its purpose is to transfer scientific knowledge into the public conversation and the decision-making process. These documents are based on the best information available and may be updated as new information comes to light.]

7 October 2022

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Malaria is the leading parasitic infection worldwide, and one of the most important global causes of disease and death. Plasmodium parasites have infected humans for millennia with devastating effects, making malaria one of the ancient scourges of humankind. Today, malaria still causes approximately 241 million clinical episodes, between two and four million cases of severe disease and an **estimated 627,000 deaths**,[1] **particularly in Africa among children under 5 years of age**. Therefore, despite different initiatives to control this disease, it still vents its rage on most vulnerable populations, contributing to perpetuating social disparities and global health inequity.

In such a long history, **the first global attempt to eradicate malaria started in the 1950s**. The international community succeeded in eliminating malaria from many countries and areas of the world, but never managed to interrupt transmission globally, and was followed by the recognition that malaria could not be eradicated with the existing tools. In fact, the deflation of global efforts, funding shortages, and the increasing resistance to drugs and insecticides used against malaria led, in the period **1970-2000,** to **a dramatic increase in cases and deaths and to devastating epidemics in countries that were approaching elimination**. The Research and development (R&D) attempts leading to new and more effective drugs and, importantly, the massive upscale of such better control strategies and prevention tools[2] led to **significant reductions in**

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[1] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[2] Resulting from the significant injection of new international available funding following the creation of the Global Fund and the US President's Malaria Initiative (PMI) in the early 2000s.

the malaria burden during the first 15 years of the new millennium.

On the other hand, the **stall in progress witnessed from 2015 onwards**[3] evidenced the many challenges faced by malaria control in many countries, making malaria eradication an unforeseeable mid or even long-term perspective.[4] Such consideration was made assuming that current available tools may not suffice, and that sustained investments would be required not only to maintain progress, but also to support research activities for a new generation of preventive, diagnostic and therapeutic tools.[5] Moreover, the coincidence with different humanitarian and health emergencies, including most notably the COVID-19 pandemic, has further jeopardized many of the gains achieved in the past two decades in the fight against malaria, and thus making urgent a renewed response to countries facing the highest malaria burden, although still supporting those that are steadily advancing towards eliminating malaria from their territories ●

Figure 1. Countries with indigenous cases in 2000 and their status by 2020.

Source: World Health Organization: World malaria report 2021. Note that in 2021 both China and El Salvador have now certified their status of "Certified malaria elimination".

[3] Alonso, Pedro and Noor, Abdisalan M. (2017), 'The global fight against malaria is at crossroads', *The Lancet*, 390 (10112), 2532-34. https://doi.org/10.1016/S0140-6736(17)33080-5

[4] Although *The Lancet Comission*, not without a huge controversy around its conclusions, stated that eradication of malaria within a generation was ambitious, achievable, and necessary. See 'Feachem RGA, et al. (2019) Malaria eradication within a generation: ambitious, achievable, and necessary'. *The Lancet*;394(10203):1056-1112. https://doi.org/10.1016/S0140-6736(19)31139-0

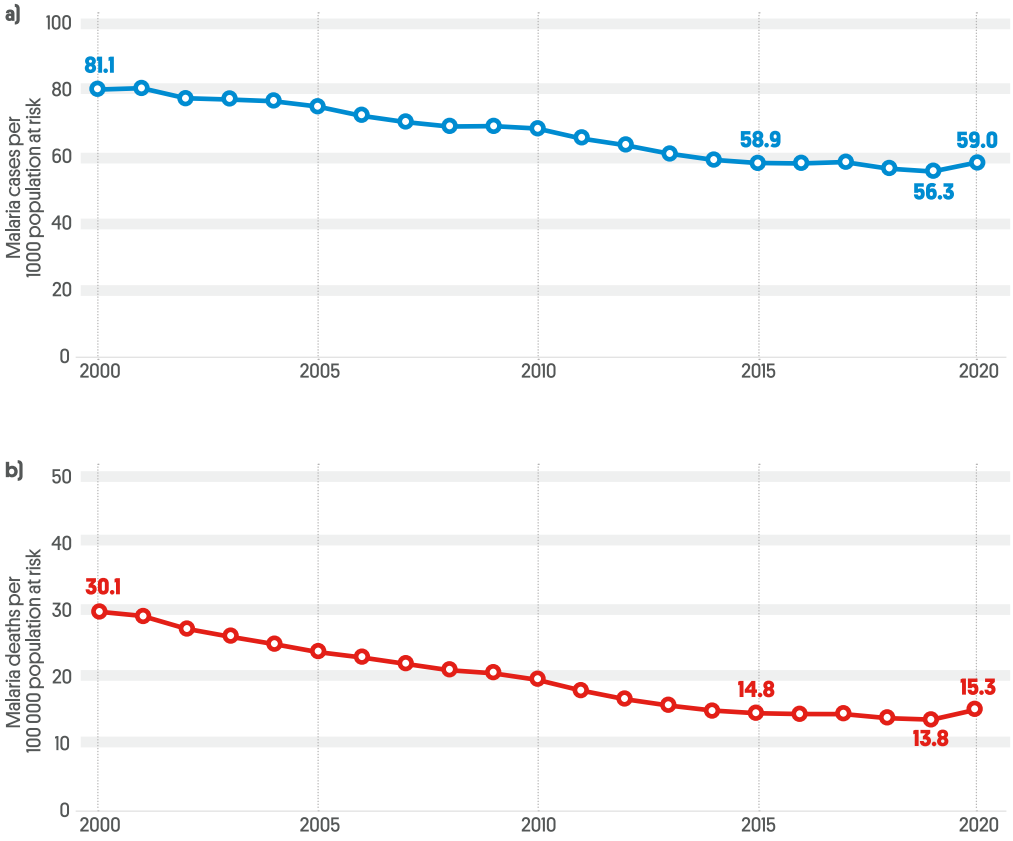
[5] malERA Consultative Group on Integration Strategies. 'A research agenda for malaria eradication: cross-cutting issues for eradication'. *PLoS Med*. 2011 Jan 25;8(1):e1000404. https://doi.org/10.1371/journal.pmed.1000404

1. Malaria Before the COVID-19 Pandemic

"In the year 2015, WHO launched its Global Technical Strategy (GTS) for Malaria 2016–2030. Two of the main objectives of such a strategy were to reduce malaria mortality rates and global incidence by at least 90% by 2030. For WHO, these very ambitious goals continue to be valid until now, but need to be reconsidered."

In the last two decades there has been an important decrease worldwide in the incidence rate of malaria with significant differences in its geographic distribution. Indeed, the first fifteen years of the millennium witnessed a 37% and 60% drop in the global malaria incidence and mortality rates, respectively, together with the interruption of transmission and eventual elimination in many countries.[6] However, and worryingly, the number of cases per 1000 population at risk had stood similar during the years before the COVID-19 pandemic. As WHO pointed out back in 2017, "**the global fight against malaria is at crossroads**", and this has caused **a rethinking on how to address the global malaria burden**, putting more emphasis on control in the countries with high burden while not putting a brake in the elimination efforts in those ready to go in that pathway. The Rethinking Malaria initiative, led by Harvard University in partnership with the WHO and other partner institutions around the world, has worked with that renewed vision.[7]

Figure 2. Global trends in malaria case incidence and mortality rate.



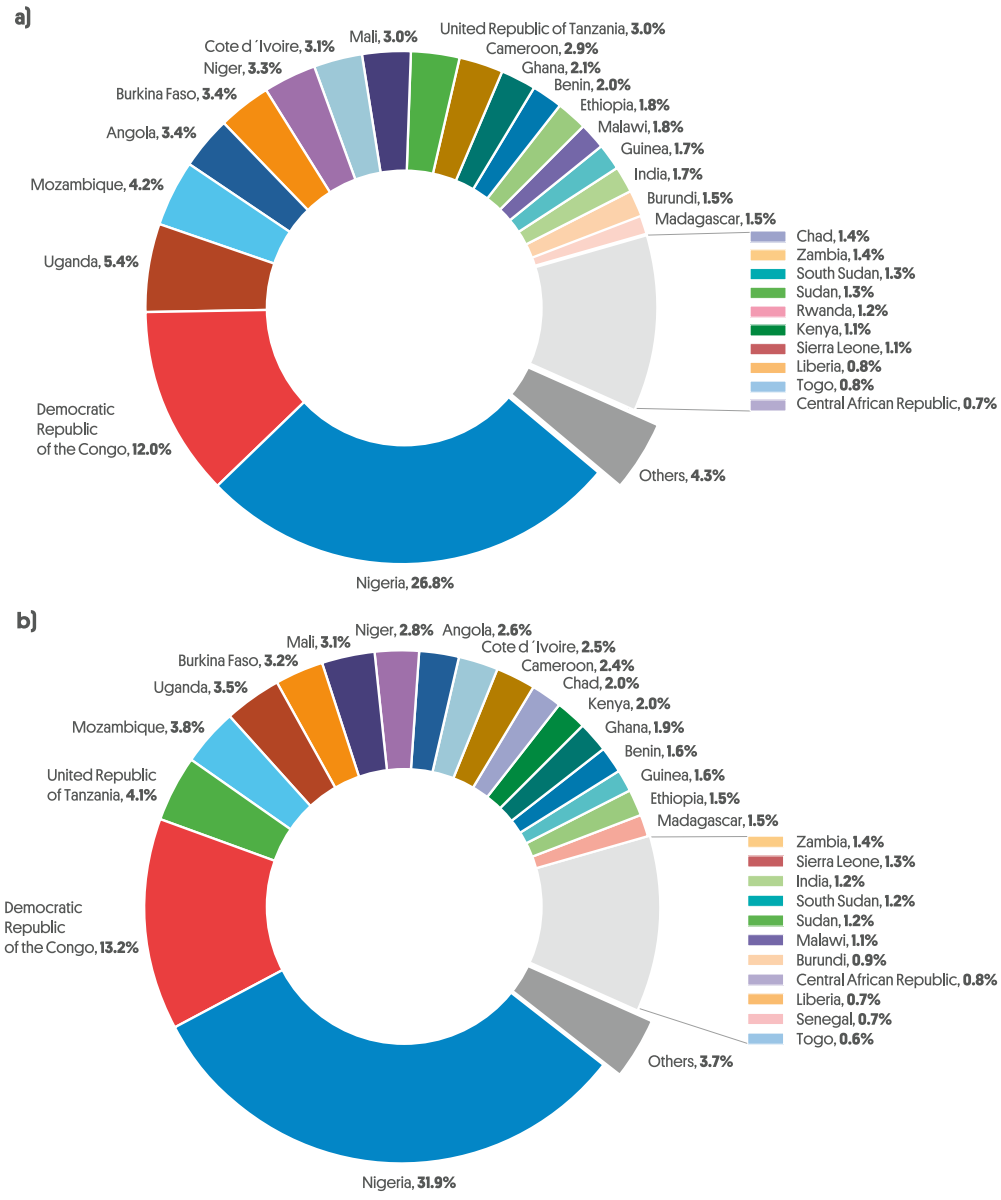
Source: World Health Organization: World malaria report 2021.

[6] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[7] https://rethinkingmalaria.org/

In any case, nearly half of the world's population continues to be at risk of malaria, which in 2020 remained endemic in eighty-five countries. The areas with ongoing malaria transmission are mainly in sub-Saharan Africa (SSA) but also in South-East Asia (SEA), Eastern Mediterranean, Western Pacific, and the Americas. However, **29 countries concentrate up to 96% of the global malaria burden, with five countries currently accounting for nearly half of all malaria cases** (Nigeria, the Democratic Republic of the Congo, Uganda, Mozambique and Angola) and deaths (Nigeria, the Democratic Republic of the Congo, the United Republic of Tanzania and Mozambique) worldwide.[8] Such **concentration of the disease burden, together with the observed stalling of the progress, led in 2018 to the design and implementation by WHO of the "High burden, High impact response"**, aiming at rapidly bringing the numbers down in those areas with major risks in order to better target resources and intensify the effect of the interventions in terms of disease reduction.[9]

Figure 3. Global trends in distribution of malaria cases and deaths by country, 2020.



Source: World Health Organization: World malaria report 2021.

[8] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[9] WHO. (2018), 'High Burden to High Impact: A Targeted Malaria Response'.

Before the start of the "High burden, High impact response", a new global strategy had been launched. Thus, in the year 2015, WHO, with the support of the main actors in the malaria stakeholders[10] map, launched its **Global Technical Strategy (GTS) for Malaria 2016–2030**.[11] Two of the main objectives of such a strategy were to reduce malaria mortality rates and global incidence by at least 90% by 2030. For WHO, **these very ambitious goals continue to be valid until now, but need to be reconsidered in the light of the changing malaria scenario and the many difficulties encountered globally and locally by countries**, including financial, implementation and biological challenges.[12] In consequence, although the goals remain the same after their update in 2021, **some of the approaches have evolved**, for example, to give more importance to country leadership in order to inform and implement policies based on their own strategic data and to strengthen their health system.[13]

Undeniably, the **difficulties faced by those initiatives have been aggravated by the global COVID-19 pandemic**, which has caused enormous harm to all national control programs. The stagnating situation in malaria control observed since 2015 has also highlighted the **need to increase the funding** for scaling up and **improve the specific design of implementation measures**, reinforcing local capacities in terms of surveillance, research, workforce capacity and decision making.[14] This has been at the basis of a major shift in the recent years in the 'mindset' of the malaria community, now highlighting the importance of increased ownership of malaria strategies by endemic countries, the need for tailoring strategies at subnational level rather than having 'one size fits all' approach, and the focus on capacity building in Africa, where most high burden countries are concentrated ●

Figure 4. Goals, milestones and targets of the Global Technical Strategy (GTS) for Malaria 2016–2030.

GOALS	MILESTONES		TARGETS
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least **40%**	At least **75%**	At least **90%**
2. Reduce malaria case incidence globally compared with 2015	At least **40%**	At least **75%**	At least **90%**
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least **10 países**	At least **20 countries**	At least **35 countries**
4. Prevent re-establishment of malaria in all countries that are malaria free	Re-establishment **prevented**	Re-establishment **prevented**	Re-establishment **prevented**

Source: Global Technical Strategy for Malaria 2016–2030, 2021 update.

[10] WHO regional offices; national malaria programs; global, regional and national partners; research groups and academia.

[11] WHO (2015), 'Global Technical Strategy for Malaria 2016–2030'.

[12] https://www.who.int/teams/global-malaria-programme/surveillance/malaria-threats-map

[13] Global Technical Strategy for Malaria 2016–2030, 2021 update.

[14] WHO. (2021), 'World Health Organization: World malaria report 2021'.

2. Impact of COVID-19 on the Malaria Strategy

"The worst-case scenario has been avoided, even though numbers in 2020 showed a 12% increase in malaria related mortality globally, and up to 14 million additional infections compared to 2019."

During the beginning of the COVID-19 pandemic, modelers tried to predict the consequences that the pandemic could have, directly or indirectly, on the three major diseases affecting low-income settings, namely HIV/AIDS, tuberculosis and malaria. Predictions offered many varying and glooming scenarios, including increases in mortality by 10%, 20% and 36%, respectively in the following 5 years. Regarding malaria, **major threats were predicted to come from the inability to distribute bed nets used to prevent mosquito bites that transmit the parasite**, given that this tool is considered to have played a major role in the reduction of malaria burden, and that 2020 coincided with a year of bed net replenishment for many African countries.[15] Other analyses projected a doubling of malaria deaths in the worst-case scenario of service disruptions.[16,17]

Now that all data for the year 2020 has finally become available,[10] and thanks in part to the many efforts led by National Malaria Control Programs (NMCPs) to catch up, with the support of a variety of international partners and under the guidance of WHO, it is safe to say that **the worst-case scenario has been avoided, even though numbers in 2020 showed a 12% increase in malaria related mortality globally, and up to 14 million additional infections compared to 2019**.[18]

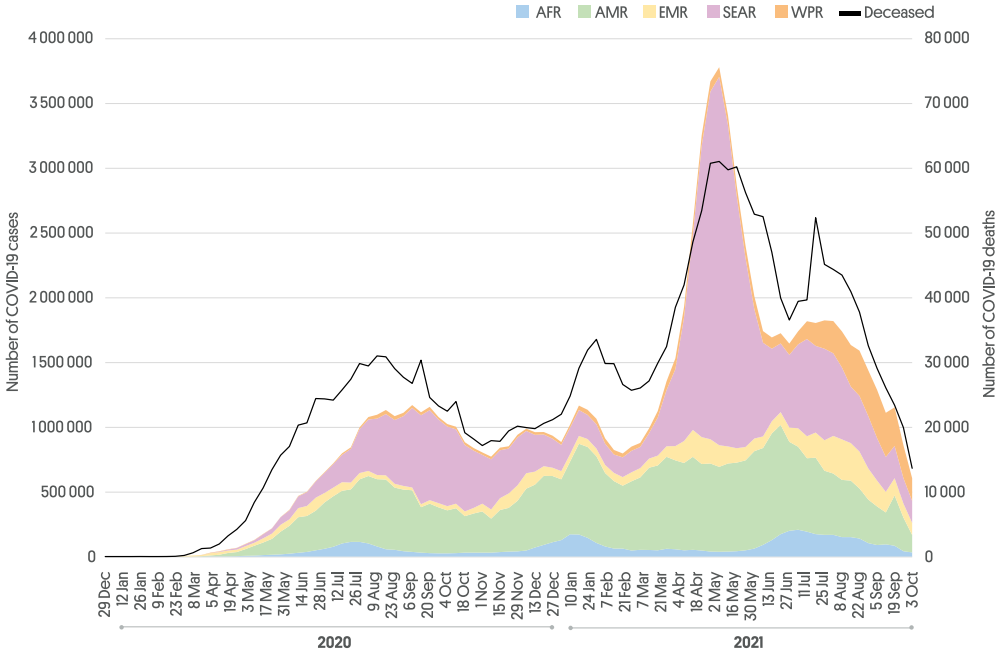
[15] Hogan, A. B., et al. (2020), 'Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modeling study', *Lancet Glob Health*, 8 (9), e1132-e41.

[16] Sherrard-Smith, E., et al. (2020), 'The potential public health consequences of COVID-19 on malaria in Africa', *Nat Med*, 26 (9), 1411-16. https://doi.org/10.1038/s41591-020-1025-y

[17] WHO. (2020), 'World Malaria Report 2020: 20 Years of Global Progress and Challenges'.

[18] Ibid,.

Figure 5. Trends in COVID-19 cases and deaths in malaria endemic countries.



AFR: WHO African Region; **AMR:** WHO Region of the Americas; **EMR:** WHO Eastern Mediterranean Region; **SEAR:** WHO South-East Asia Region; WHO: World Health Organization; **WPR:** WHO Western Pacific Region.

Source: World Health Organization: World malaria report 2021.

A considerable proportion of that increase **(two-thirds of the new deaths) may be attributable to disruptions in the provision of prevention, diagnosis and treatment services for the disease during the COVID-19 pandemic,**[19] and has been observed predominantly in Africa, where more than 95% of patients and global deaths from malaria are concentrated. The COVID-19 pandemic has taken us back to mortality figures similar to those of a decade ago.[20] Nonetheless, WHO states that "with support from global, regional and national partners, countries have mounted an impressive response to adapt and implement WHO guidance to maintain essential malaria services during the pandemic".[21] Having this in mind, the impact of the pandemic needs to be evaluated specifically in the following areas:

a) Access to health care services, clinical disease pathogenesis and management

At the beginning of the pandemic, many countries (including most malaria-endemic ones) imposed severe restrictions to citizen's movements, as a first response to control the expansion of COVID-19. These included, among others, and with varying severity, **travel restrictions, lockdowns or curfews**. Such restrictions impacted the accessibility of sick patients to health care, which was further limited by **fear of getting infected** or COVID-19 **quarantines**; closure of health facilities and reduced health care workforce capacity.[22,23] The generalized difficulties in accessing the health system (together with shortages in global supplies, described below), may explain the increase in malaria mortality during the coronavirus pandemic, similarly

[19] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[20] Heuschen, A. K., et al. (2021), 'Public health-relevant consequences of the COVID-19 pandemic on malaria in sub-Saharan Africa: a scoping review', *Malar J,* 20 (1), 339. https://doi.org/10.1186/s12936-021-03872-2

[21] Ibid,.

[22] Babalola, O. J., et al. (2022), 'The influence of first wave of COVID-19 outbreak on routine healthcare services, Liberia, August 2020: a mixed study approach', *BMC Health Serv Res*, 22 (1), 684. https://doi.org/10.1186/s12913-022-08074-3

[23] Hakizimana, D., et al. (2022), 'The impact of Covid-19 on malaria services in three high endemic districts in Rwanda: a mixed-method study', *Malar J*, 21 (1), 48. https://doi.org/10.1186/s12936-022-04071-3

to what was observed during the Ebola epidemic in 2014 in West Africa.[24] However, given the short nature of those restrictions, and the subsequent catch-up efforts made by NMCPs, the overall impact of such restrictions has finally been transitory and smaller than predicted.[25,26]

Otherwise and considering clinical aspects of both diseases, malaria and COVID-19 infections have **overlapping symptomatology** and one initial concern, particularly during the first waves of the pandemic -when no rapid diagnostic tools for COVID-19 were available- was that the two diseases could easily be misdiagnosed, resulting in an overall increase in morbidity and mortality secondary to any of them. However, and despite the challenges mentioned, COVID morbidity and mortality in endemic areas, such as those of SSA countries, have been not only proportionally lower than anticipated, but also lower than what has been documented in high-income countries (HIC). This may have resulted from differing population pyramids (with a higher proportion of young population, less prone to severe COVID disease), climatic differences, genetic factors, preexisting immunity, or a lower burden of chronic comorbidities (diabetes, hypertension, obesity etc.) predisposing to severity.[27]

b) Malaria infection control and prevention

Major disruptions in the distribution and supply of malaria diagnostic tools and antimalarial drugs were expected, particularly as a result of the aforementioned generalized restrictions imposed by many governments. Therefore, the **reduced delivery of global supplies** despite strenuous efforts of countries and institutions may also explain the impact on disease control, justified by the limited availability of curative and preventive malaria commodities. For instance, **problems in the distribution of the antimalarial drugs** used for seasonal malaria chemoprevention or insecticide-treated bed nets, have been associated with the significant increases in the malaria burden.[28] In addition, **redirection of investments and human resources** from malaria programs to emergency relief for the COVID-19 pandemic may have had an important effect in malaria control programs.[29] Other increased costs for countries may have resulted from the prevention measures adopted against COVID-19, and in particular as a result of **disturbances of global transport** [30]

[24] Walker PG, et al. (2015), 'Malaria morbidity and mortality in Ebola-affected countries caused by decreased health-care capacity, and the potential effect of mitigation strategies: a modelling analysis', *Lancet Infect Dis*, 15(7):825-32. https://doi.org/10.1016/S1473-3099(15)70124-6

[25] The Global Fund. (2020), 'Mitigating the Impact of COVID-19 on Countries Affected by Hiv, Tuberculosis and Malaria'.

[26] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[27] Maeda JM, Nkengasong JN. (2021), 'The puzzle of the COVID-19 pandemic in Africa'. *Science*. 1;371(6524):27-28.

[28] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[29] Hussein, M. I. H., et al. (2020), 'Malaria and COVID-19: unmasking their ties', *Malar J*, 19 (1), 457. https://doi.org/10.1186/s12936-020-03541-w

[30] WHO. (2021), 'World Health Organization: World malaria report 2021'.

3. Post-Pandemic Challenges

"Financial streams for malaria control remain insufficient, and biological challenges such as insecticide or drug resistance, genetic parasite variants eluding rapid diagnostic tests (RDTs), or climate change can still overthrow many of the successes achieved in recent years."

The global fight against malaria continues to be threatened by the **same problems** that were already well-established before SARS-CoV-2 appeared, although **some of those have clearly worsened** as a result of COVID-19. Financial streams for malaria control remain insufficient, and biological challenges such as insecticide or drug resistance, genetic parasite variants eluding rapid diagnostic tests (RDTs), or climate change can still overthrow many of the successes achieved in recent years.

Vector control: Scale-up home-centered interventions such as long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS) have been important contributors to the significant decline in the malaria burden witnessed globally.[31] However, such success is threatened by the emergence of mosquitoes resistant to pyrethroids and to other insecticides used as part of other vector control strategies. Additionally, mosquito behavioral changes to elude these preventive measures (such as biting outdoors to avoid the effect of bed nets) are important biological challenges to consider in the fight against malaria. Innovative approaches are needed to control the so-called 'residual transmission', such as the use of drugs (for example ivermectin) that kill mosquitoes feeding upon treated people or animals, attractive targeted sugar baits and spatial repellents.

Diagnosis: RDTs are now the most widely available option and often the first-line investigation method in the presence of malaria suspicion, as they provide rapid, simple and near-patient, sensitive and specific diagnosis. HRP2-based diagnostic tests, which are those most widely available, may produce negative results in infections caused by *P. falciparum* parasites that do not express the PfHRP-2/3 proteins, rendering these RDTs useless, and those infections "invisible". As the deletion mutants increase in prevalence, the need for better data and the potential for transitioning to non-HRP2-based RDTs may be required.

Treatment: Emergence of antimalarial drug resistance threatens effective antimalarial drug treatment, prevention, and elimination. Resistance has been observed for most antimalarials including artemisinins. Artemisinin resistance appears to be "partial", characterized by a slower parasite clearance, and has emerged (like all other resistances documented for antimalarial drugs) in the Greater Mekong Subregion,[32] although major containment efforts in the region have decreased its importance as a global threat. However, artemisinin-resistance has recently been also described as emerging de *novo* and independently in at least two African countries, namely Uganda[33] and Rwanda.[34,35] While we wait for the next generation of antimalarial drugs with different mechanisms of action to those already in use, it appears critically important to establish surveillance systems to closely monitor the emergence and spread of parasite resistance to currently available drugs, and to develop alternative strategies to protect currently used antimalarial drugs (such as triple artemisinin-based combination therapy).

[31] Bhatt, S., et al. (2015), 'The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015', Nature, 526 (7572), 207-11. https://doi.org/10.1038/nature15535

[32] Menard, D. and Dondorp, A. (2017), 'Antimalarial Drug Resistance: A Threat to Malaria Elimination', *Cold Spring Harb Perspect Med*, 7 (7).

[33] Balikagala, B., et al. (2021), 'Evidence of Artemisinin-Resistant Malaria in Africa', *N Engl J Med*, 385 (13), 1163-71. DOI: 10.1056/NEJMoa2101746

[34] Uwimana, A., et al. (2020), 'Emergence and clonal expansion of in vitro artemisinin-resistant *Plasmodium falciparum kelch13* R561H mutant parasites in Rwanda', *Nat Med*, 26 (10), 1602-08. https://doi.org/10.1038/s41591-020-1005-2

[35] Uwimana, A., et al. (2021), 'Association of *Plasmodium falciparum kelch13* R561H genotypes with delayed parasite clearance in Rwanda: an open-label, single-arm, multicentre, therapeutic efficacy study', *Lancet Infect Dis*, 21 (8), 1120-28. https://doi.org/10.1016/S1473-3099(21)00142-0

Concerning severe malaria, changes in malaria transmission have also led to changes in the clinical presentation. In areas where malaria was highly endemic and now transmission has decreased, children now present with severity at an older age than a decade ago[36] or have other complications, like acute kidney injury, previously more frequent in adults.[37] Promising strategies to decrease malaria-associated mortality in children, such as the use of pre-referral rectal artesunate for children with severe malaria have also shown frustratingly differing results when implemented in 'programmatic mode' to those seen in clinical trials, evidencing the importance of implementation science to better tailor and understand the efficacy of tools when scaled up in real-life health systems.[38]

In addition, there are no currently available adjunctive therapies to improve the clinical and long-term outcomes of severe malaria which, despite prompt and effective treatment with antimalarials, still carries an unacceptably high associated mortality.[39] Several adjunctive therapies have been evaluated without proving any success, and this is a field which urgently needs to be further developed.[40]

Vaccines: The great antigenic variability shown by the malaria parasite throughout its life cycle has made the design of effective vaccines a titanic task. The RTS,S/AS01 malaria vaccine, recently recommended by WHO (October 2021) for its implementation in malaria-endemic areas of SSA for the protection of young infants, is currently the only effective compound, and has shown consistently significant (albeit partial) levels of protection, both against clinical malaria and severe malarial disease.[41,42] The evaluation of the results of the pilot implementation project conducted in Ghana, Kenya and Malawi confirmed its protective effectiveness, the feasibility of administering 4 doses, the impact on overall infant mortality and the safety of its routine use in endemic countries, and importantly that such an intervention had significant public health impact and was highly equitable, paving the way to the current WHO recommendation.[43] This first-generation malaria vaccine, which should be added to existing preventive and control measures, has the potential to save tens of thousands of lives a year, and consequently, GAVI, the Global Alliance for Vaccination and Immunization, announced its immediate support – with an initial investment of 1380 million euro for the period 2022-2025- for purchase and distribution. Current shortage in supply appears as an important bottleneck for a wide scale implementation, but efforts have been made to develop a prioritization framework to guide where should scarce vaccines be first implemented.[44]

RTS,S has however opened a path for new products to be developed, with higher efficacy and safety profiles, and currently exciting candidates are well advanced in their clinical development.[45] The gigantic leap forward brought by mRNA vaccines developed against COVID should also benefit efforts in the fight against malaria.

[36] Guinovart, C., et al. (2022), 'The epidemiology of severe malaria at Manhiça District Hospital, Mozambique: a retrospective analysis of 20 years of malaria admissions surveillance data', *Lancet Glob Health*, 10 (6), e873-e81. https://doi.org/10.1016/S2214-109X(22)00125-5

[37] Conroy, A. L., et al. (2016), 'Acute Kidney Injury Is Common in Pediatric Severe Malaria and Is Associated With Increased Mortality', *Open Forum Infect Dis*, 3 (2), ofw046. https://doi.org/10.1093/ofid/ofw046

[38] Brunner NC, et al . 'Prereferral rectal artesunate and referral completion among children with suspected severe malaria in the Democratic Republic of the Congo, Nigeria and Uganda'. *BMJ Glob Health*. 2022 May;7(5):e008346. doi: 10.1136/bmjgh-2021-008346. PMID: 35580913; PMCID: PMC9114942. http://dx.doi.org/10.1136/bmjgh-2021-008346

[39] Dondorp, A., et al. (2005), 'Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial', *Lancet*, 366 (9487), 717-25. https://doi.org/10.1016/S0140-6736(05)67176-0
Dondorp, A. M., et al. (2010), 'Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial', *Lancet*, 376 (9753), 1647-57. https://doi.org/10.1016/S0140-6736(10)61924-1

[40] Varo, R., et al. (2018), 'Adjunctive therapy for severe malaria: a review and critical appraisal', *Malar J*, 17 (1), 47. https://doi.org/10.1186/s12936-018-2195-7

[41] RTS,S Clinical Trials Partnership. (2021), 'A phase 3 trial of RTS,S/AS01 malaria vaccine in African infants'. *N Engl J Med*. 2012 Dec 13;367(24):2284-95. DOI: 10.1056/NEJMoa1208394

[42] RTS,S Clinical Trials Partnership. (2014), 'Efficacy and safety of the RTS,S/AS01 malaria vaccine during 18 months after vaccination: a phase 3 randomized, controlled trial in children and young infants at 11 African sites', *PLoS Med*, 11(7):e1001685. https://doi.org/10.1371/journal.pmed.1001685

[43] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[44] Strategic advisory group of experts (SAGE) on immunization and the Malaria Policy Advisory Committee (MPAC), (2019), "Proposed framework for policy decision on RTS,S/AS01 Malaria vaccine".

[45] HDatoo MS, et al. (2021), 'Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial', *The Lancet*, 15;397(10287):1809-1818. https://doi.org/10.1016/S0140-6736(21)00943-0

Climate change, natural disasters and conflicts: Although important efforts have been made to try to understand and predict the potential impact that climate change[46] and other major factors (such as, for example, urbanization)[47] may have on malaria trends in the future, there are still major uncertainties that hinder our current understanding. However, there is good evidence to suggest that vector-borne diseases in general will increase.[48] Importantly, the number of people living in malaria transmission areas will significantly increase in the next few years. In addition, we have to consider that other infectious disease outbreaks (like Ebola or other viral haemorrhagic diseases), economic crisis, political instability and armed conflicts, natural disasters (hurricanes, droughts, flooding….) and populations displacements (inside and between countries) may further increase malaria transmission and thus, health risks for those people living in malaria-endemic countries ●

[46] World Health Organization. (2018), Climate Change and health.

[47] Tatem AJ, et al. (2013), 'Urbanization and the global malaria recession'. *Malar J.* 17;12:133. https://doi.org/10.1186/1475-2875-12-133

[48] Parham, P. E., et al. (2015), 'Climate, environmental and socio-economic change: weighing up the balance in vector-borne disease transmission', *Philos Trans R Soc Lond B Biol Sci*, 370 (1665). https://doi.org/10.1098/rstb.2013.0551

4. Conclusions and Future Perspectives

"We need to foster creativity at the service of malaria control, although this needs to be done in parallel to the strengthening of the health systems, and the promotion of universal health coverage, precisely because health systems are weakest in those places where malaria remains highly endemic."

In the third decade of the 21st century, malaria remains a significant global health challenge, and the situation is not likely to improve in the short term. In the pre-pandemic years, the world's malaria situation was already at a crossroads. Although less than expected, the time of COVID-19 pandemic has meant a significant regression in the number of global malaria cases and deaths, going back to 2010-2011 numbers,[49] from which it will take years to fully recover. It is now however clear that with current tools, we will not achieve the ambitious 2030 malaria control and elimination targets.[50] Thus, **it is now time for rolling back again our sleeves**, and pushing the accelerator to enhance malaria control strategies, in parallel to heightened efforts to continue **improving our understanding of the biology of malaria, but also to the cultural, social and political factors that may affect its transmission** as a mechanism to better design the new generation of tools and strategies to combat this disease, in addition to the **necessary funding schemes and systems in place to generate data and inform policies**. We need to foster creativity at the service of malaria control, although this needs to be done in parallel to the strengthening of the health systems, and the promotion of universal health coverage, precisely because health systems are weakest in those places where malaria remains highly endemic.

We encourage working for a new push in malaria innovation and research focusing on new therapeutics, diagnostics, insecticides and preventive measures. Our recommendation is that **global efforts should be focused on uncovering the biological, economic and political challenges affecting the currently existing tools, and research in all those areas may play an essential role**. In addition, further work is needed to improve capacity building; to establish a better governance of the global malaria scene to increase endemic countries' ownership; or to develop a new culture of decision making based on data with subnational granularity. **In general, it is essential to increase financial support**, to strengthen malaria programmes and global leadership, and to advance faster in research and development. In that sense, the unprecedented achievements in the containment of the coronavirus pandemic may be an example to follow, given the extraordinary speed in the development of preventive and therapeutic innovations, together with the unprecedented collaborative approaches that have occurred at a global level.

The reaction to COVID-19 pandemic has proved that the success in the fight against a particular disease is a matter of willingness. Unhappily, and despite specific initiatives that have been discussed here, malaria has still not been accounted as a main concern for the global society. The fact that this is a disease affecting the most vulnerable populations in the most vulnerable countries, as the African children, may justify this indifference. Therefore, to revert this situation, the response against coronavirus must be not only a possible model, but surely an incentive to bring malaria to the frontline of our health priorities ●

[49] WHO. (2021), 'World Health Organization: World malaria report 2021'.

[50] WHO. (2021), 'World Health Organization: World malaria report 2021'.

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How to cite this document:

Varo, Rosauro and Bassat, Quique. **What Impact Has the COVID-19 Pandemic Had on the Fight Against Malaria?** Barcelona Institute for Global Health (ISGlobal). No. 47. September 2022.

https://www.isglobal.org/

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