Conquering Malaria: Enhancing the Impact of Effective Interventions Towards Elimination in the Diverse and Changing Epidemiology

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ABSTRACT

Malaria remains a major global disease burden causing just under a million deaths each year, mainly of children and pregnant women in sub-Saharan Africa. It consumes up to 40% of public health expenditure of these poor countries, causing in Africa US$ 12 billion in lost GDP every year. This should not be acceptable since malaria is preventable, and there is clear evidence that optimal use of current tools can reduce much of the suffering and deaths. Three major factors allowing this to happen include: (i) inadequate funding to implement a massive initial surge, to achieve universal coverage, (ii) weak country capacities for rapid scale up of such interventions and little or no use of evidence-guided methods, and (iii) insufficient coordination of efforts between national programmes, donors and technical agencies in strategic planning for sustaining gains and in building capacity. We discuss the importance of the surge and the kind of approaches that would accelerate the pace toward elimination and eventual eradication.

Key words: Effective interventions, Elimination and eventual eradication, Malaria global burden, Preventable, Regional and subregional collaboration, Universal coverage

INTRODUCTION

Malaria affects 106 countries causing estimated 225 million cases and 781,000 deaths each year.[1] Africa carries 90% of the burden bearing heavily on <5 years old children and pregnant women. It consumes up to 40% of public health expenditure in high transmission areas. Africa alone suffers US$ 12 billion in lost GDP every year. Yet it is preventable and optimal use of available effective tools can reduce suffering and deaths.[1-7] Achieving universal coverage, as emphasized in the Global Malaria Action Plan (GMAP) and which would require $4.5 billion per year, has the potential of halving the 2000 levels of malaria cases by 2015, contributing to millennium development goals (MDGs) targets 4, 5, and 6.[1] How this could be done has stirred positive discussions on priorities and effective strategies for malaria elimination.[8-14] We wish to re-emphasize the role of a rapid surge targeting high malaria burden countries accompanied by strategic capacity building and subregional collaboration in accelerating achieving elimination and finally eradication.

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The complex parasite cycle

The four *Plasmodium* species causing malaria, *P. falciparum, P. vivax, P. malarie*, and *P. ovale*, have managed to live for ages with man and mosquitoes by developing capacity to evade the host defense system.[15,16] Evasion is possible at several stages of the parasite complex life cycle in which it undergoes several morphological and genetic transformations, thus posing big challenges to the development of effective drugs and vaccines. This has necessitated the need for multiple tools and integrated approaches are needed and there can be no single "magical bullet".

Achievements and challenges

As we pass the 2010 milestone, major achievements have been registered, and the number of countries which have achieved ≥50% reduction in number of cases has risen.

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However, reaching all persons at risk for malaria with insecticide-treated nets (ITN) or indoor residual spraying (IRS) and provision of laboratory-based diagnosis for all suspected cases of malaria and effective treatment of all confirmed cases[1,17,18] is still challenging. At the end of 2010, 289 million Long-Lasting insecticide-treated nets (LLNs) had been distributed. If each of these nets lasted 3 years and protected two people, this would be sufficient to cover 76% of the 765 million at risk in Africa. However, few countries have achieved ≥50% coverage[1] of households with at least one net (average 45% in Africa). The majority of under five children and pregnant women do not sleep under a net.[1]

Indoor residual spraying (IRS) was effective in eliminating *Anopheles gambiae* in Carpe Verde 1950–1967, *Anopheles funestus* in the Kenya and Tanzania–Pare Taveta IRS Project 1955–1959 and *Anopheles funestus* in Mauritius 1949[10,19] Except in Mauritius, resurgence occurred following cessation of control efforts. In 2007–2009 countries which achieved ≥50% reduction in malaria cases by reaching >70% coverage of IRS include Botswana, Namibia, South Africa, and Swaziland.[1] Coverage of IRS has indeed increased, but there is need to assess how far it is reaching the targeted populations and where else it would have added effect. In parts of Africa where infrastructure is especially weak, universal vector control coverage may not be achieved with IRS alone, and LLNs will continue to be needed to achieve and sustain this goal.

Public sector provision of artemisinin combination therapy (ACT) covering >100% of reported cases has increased from 5 to 11 of the 43 endemic African countries by 2009 compared to 2005.[1] However, children treated at home or through the private sector are highly unlikely to receive ACTs. Available data show <20% of malaria suspected cases having parasite-based tests in 42 countries in Africa, while most of countries in other regions have reached 80% of testing.

Coverage of pregnant women attending Antenatal Clinic with two doses of IPT remains in most countries below 50% ranging from 2.4% to 62%.

ENHANCING IMPACT OF INTERVENTIONS: DISCUSSION

Impact of public health interventions hinges on achieving rapid high coverage and its sustenance. Key factors include the availability (production, procurement, and distribution), equity of access (reaching isolated populations, affordability), acceptance (knowledge of benefits, willingness to pay), gender and social barriers as well as robust delivery systems and mechanisms.

Concerted action and coordinated efforts have been recognized as key to success since the Eradication Campaign 1955–1969.[9,10] Taking lessons from past failures and errors, new global strategies for malaria elimination have been developed culminating in the current three part strategy.[4,9-11] Its effective application promises high impact and hope for elimination and eventual eradication. We wish to emphasize five key elements to the success of this strategy based on previous lessons: (1) A strong initial surge targeting high burdened countries, (2) coordinated regional or subregional collaboration, (3) national strategic capacity building, (4) district strategic capacity building and sustained support, (5) research that is linked to intervention and targeting critical problems toward elimination [Boxes 1-4].

Targeting high burdened countries for a strong and rapid initial surge will produce high impact. Recent evidence shows sharp decline in malaria mortality and morbidity in countries that have rapidly scaled up coverage of effective interventions.[1-6] Globally 42 countries have registered ≥50% reduction in cases (including 11 countries from Africa) and global deaths have decreased to less than a million in the last 5 years. Should larger

Box 1: National capacity strengthening needs

- Capacity to identify needs and set priorities
- Capacities to produce and manage quality data
- To seek and use evidence for policy and implementation
- To apply implementation research for shaping implementation approaches and achieve better impact.
- Forge stronger linkage between research and implementation (Collaboration between researchers and programme implementers)

Box 2: District capacity needs

- Strong disease surveillance and resistance monitoring
- Establish vector control capacities
- Capacities for malaria case management
- Engage and train the private sector
- Apply integrated treatment and vector control packages
- Establish effective workforce both public and private
- In rural and hard to reach populations establish and maintain village or community health workers

high burdened countries such as Democratic Republic of Congo (DRC) and Nigeria achieve universal coverage, the global malaria burden would shrink substantially.

Skilled manpower at all levels of the health system able to deliver interventions, adapt to local or changing conditions or develop new tools in response to emerging challenging is critical for sustained effective malaria control and achieving elimination. The resurgence of malaria in the last quarter of the 20th century was largely due to disillusionment and loss of malariologists.[10] As the vector control was withdrawn and the limited repertoire of anitmalaria drugs became less effective due to resistance, financial support also declined and management of malaria became ineffective for lack of robust response. Malaria control programs contracted or completely disappeared in several places.[1,9,10] In order to avoid marginalization of expertise in malaria control and research during the anticipated contraction of the malaria map, resource allocation for capacity building should be a priority to meet both the national and district capacity needs [Boxes 1 and 2].

Box 3: Regional and subregional collaboration and joint action

- Fosters common needs assessment, setting of common priority and policies,
- Networking among the countries with similar problems,
- Sharing experience and lessons.
- Creates peer pressure for action and implementation,
- Greater sense of ownership and maintenance of commitments.
- Allow malaria elimination agenda to gain priority in the regional or subregional financial or economical settings.
- Guards against disillusionment, loss of local and international commitments, collapse of the programme and easy withdrawal of support,
- And against external manipulation of the priorities and agenda

Motivating individual countries singly to maintain momentum is arduous and time consuming. On their own, countries still struggle to access the funds from the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM), and when the funds are accessed, delays in implementation have been common. It has taken too long to scale up ITNs/LLNs, and access to ACT for those who need them most remains low in Africa. There is need to scale up ACT use in the private sector. Left alone countries have little incentive for change. Therefore, it is necessary to create subregional coalitions to forge networking and implementing malaria interventions as united fronts. This will establish the backbone for continuous capacity generation and support for interventions at the country level reinforcing the regional strategic approach of the GMAP. Countries could move forward as block with big impact and advantages [Box 3].

Infections, especially mosquito- borne ones, can be transmitted easily across borders in Africa. This demands strong subregional approaches, greater awareness, and greater collaboration between governments of these countries. In cases like Central Africa, deliberate concerted actions and support will be necessary to make things work. Leaving behind and alone big countries with high burden may make it impossible to eliminate malaria in the adjacent countries. Major achievements in solving cross border issues and setting joint strategies have been achieved in the WHO EURO and EMRO Regions.[20,21] Establishing regional or subregional support centre may prove to be critical for long-term sustainability of capacities.

Box 4: Research needs at the initial surge and during elimination phase

- Surge phase
- Needs assessment and priority/setting
- Operational and implementation research skills
- Scale up integrated interventions for treatment and case management - Mixture of public health skills, social science, epidemiology, vector control, economic skills
- Engaging the private sector
- Effective campaigning, advocacy and messaging
- Clinical and epidemiological skills
- Maintaining interventions
- Strengthening surveillance and prompt response actions
- Quality data collection, management and interpretation
- Diagnostics and fever case management
- Optimal combination of interventions for impact and delaying resistance
- Better drugs killing liver stages and gametocyte to prevent transmission
- Vaccine to block transmission

Research is crucial and implementation research will be critical in all the stages toward elimination and will serve as a torch to provide light to implementation.[22-24] Scaling up ACTs in the surge will be challenged by the retail cost. Establishment of the Affordable Medicines Facility for malaria (AMFm)[25] is therefore timely, and the pilot phase will provide guidance to how effective ACT scale up can be made at affordable and competing retail price to drive out monotherapies and substandard drugs. Engaging the private sector is among the well-recognized challenges.

As countries progress toward elimination, new tools will be required to complement or replace current tools. Better diagnostics to capture low parasitemia and drugs that clear early stages of gametocytes and combinations that can prevent or delay artemisinin drug resistance will be essential [Box 4].

Surveillance is another critical element.[8,26] Capacities will be required to generate quality and representative routine data, identify needs for specially targeted research such as identifying hidden transmission foci and early signs of both drug and insecticide resistance. Country capacities for rapid action and to devise appropriate mitigating measures is essential especially with current threat of artemisinin resistance.[27-29] The WHO's Global Malaria Programme (GMP) plays a critical role in strengthening both subregional and national surveillance capacities and in helping to establish mitigating measures against the threat of drug resistance. GMP is also collaborating with key partners such as the Worldwide Anti-malaria Resistance Network (WWARN)[30] in this respect.

That elimination would be more feasible in countries of the Americas and Asia than central and western Africa because of technical and operational factors[31] is predictable given poor infrastructure, access, and political instability of these latter countries. However, evidence suggests that it will become possible, if evidence is used to guide the undertaking.[4-7,23] Modeling with real field data may provide valuable guidance on critical actions and conditions to accelerate the elimination process and prevent loss of motivation.[31,32] We should be reminded that although Africa was de facto excluded from the main Global malaria eradication campaign, it was declared not feasible for eradication on the basis of a few pilot projects in savannah areas, that had failed to interrupt local transmission. Pilot projects that had succeeded in interrupting malaria transmission in some forest areas were neglected. This was followed by two decades of disillusionment and neglect of malaria specific interventions. Thus, the current call for universal coverage represents not just a rallying cry, but also a major policy change for diagnosis and vector control. From 1975 to 2005, WHO malaria vector control policies were based on the assumption that universal coverage with vector control, and universal parasitological diagnosis of malaria infection, were unfeasible. Therefore, the central policy questions were about rationing and targeting who should benefit from these limited resources. It is the technology revolution of the 1990s and 2000s, and the advent of LLNs and Rapid Diagnostic Tests (RDTS), that showed that universal coverage was feasible.

Understanding and considering ecological factors on the effectiveness of malaria interventions have been discussed elsewhere.[33] This should be given due considerations in the African context and especially when dealing with large countries like DRC and populous countries like Nigeria. The need to manage insecticide resistance and to introduce new vector control products and technologies must be given immediate and urgent priority.

CONCLUSION

A successful surge would move the whole malaria spectrum from high to low burden as is the expectation of the Global Malaria Action Plan. It could accelerate halving global deaths within the next few years or at least reach closer to meeting the 2015 target. On the contrary if the surge is not made, we risk missing this opportunity. Without it, we might still see pockets of success here and there, especially in small countries with already low transmission, but we would also see stagnation and occasional resurgence (in the forms of epidemics). This in turn could lead to donor fatigue and shift of global health priorities to other needs. The East and Southern African subregion classifies countries according to their malaria burden into (1) high burdened with limited or no evidence of decrease, (2) high burdened with good coverage and showing a clear downward trend and low burden countries moving toward elimination. This classification may help to bring countries together, to draw common strategies and priorities and conduct similar interventions.

The surge will not be possible without sufficient funding to allow universal coverage. To maximize the impact of increased funding, we suggest making it a condition upon countries to include a research component. This should be designed to strengthen the health system, and to ensure that (a) interventions are well executed and well targeted (and thus good value for money) and (b) that intervention methods can track and respond to developmental changes in the parasite, the vector, the human and their environment to remain effective in the

long term (thus sustainable). One way to proceed would be to develop support for centers of excellence for such research that are recognized as such within the countries and regions, as well as independent scientists with a proven track record of research that informs the policy and practice of malaria control programmes. Working through WHO, the special programme for research and training in tropical diseases (WHO/TDR) is in the process of developing curricula and action-oriented activities that could promote the establishment of such centers. There are signs of substantial gains, and it is for this reason that stronger evidence guided surge and research capacity strengthening is needed to accelerate the pace and prevent falling back.

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