Unitaid

POLICY BRIEF

GLOBAL MALARIA DIAGNOSTIC AND ARTEMISININ TREATMENT COMMODITIES DEMAND FORECAST

2017 – 2020

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CLINTON HEALTH ACCESS INITIATIVE

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INTRODUCTION

This synopsis provides policymakers with a brief summary of the latest forecasts for global need, demand, and procurement of malaria diagnostics and treatments, and the implications of these projections for health and development policy. The forecasts were produced by a consortium including the Clinton Health Access Initiative, Inc. (CHAI), IMS Health (IMS), and the University of California, San Francisco (UCSF). This consortium is funded by Unitaid and operates under the guidance of a Steering Committee consisting of representatives from The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), Medicines for Malaria Venture (MMV), Unitaid, the US President's Malaria Initiative (PMI), and the World Health Organization (WHO).

The forecast includes projections for need, demand, and procurement, defined as follows:

- **Procurement** – represents the volume of commodities that will be purchased in a given year
- **Demand** – represents the volume of commodities or services that would be required to meet all consumer demand for treatment or diagnosis of presumed malaria infections.
- **Need** – represents the number of commodities that would be required to treat all febrile illnesses associated with detectable parasitemia (including cases where the malaria parasite itself is not the source of the fever).

This forecast is the third in a series produced by the consortium, and includes several changes from the previous report. This report include updates to all baseline forecast outputs that have been presented in previous reports, with key changes to the demand forecasts for injectable and rectal artesunate products, and malaria rapid diagnostic test demand and procurement. Furthermore, this report extends the forecast time period from 2016 – 2019 to 2017 – 2020.

KEY MESSAGES

- In 2017, global demand for antimalarial medicines was estimated to be over 1.5 billion (B) treatment courses and we forecast that demand for antimalarial medicines will grow to over 1.6B treatments by 2020. Demand for artemisinin-based combination therapies (ACTs) – inclusive of both quality-assured ACTs (QAACTs) and non-quality assured ACTs (non-QAACTs) – will comprise approximately 37% of global antimalarial demand in 2017, and is expected to grow to 49% of global antimalarial demand by 2020. Non-QAACTs comprise about 26% to 28% of estimated global ACT demand, with most of this demand coming from the private sector.
- Assuming no decrease in procurement through the private sector co-payment mechanism (CPM), global procurement of QAACTs is projected to rebound from 285 million (M) treatments in 2017 (its lowest projected volume since 2011) to 314M treatments in 2020, due to increased funding from donors like the President's Malaria Initiative (PMI), and increased use of QAACTs in the premium private sector. Public sector QAACT procurement will peak in 2018 with the addition of new funding from PMI, but will decline owing to a comparative decrease in total malaria funding available in 2019 and 2020 through the Global Fund, leading to projected lower spend on QAACT procurement. Procurement forecasts for QAACTs and RDTs are driven in large part by availability of financing as opposed to underlying changes in the burden of disease of patient care-seeking behavior.
- QAACT demand and procurement volumes are substantially higher than World Health Organization (WHO)-reported case estimates owing to the use of ACTs in undiagnosed febrile patients, as well as some ACT use in patients who are treated despite having received a negative diagnostic test.
- The latest national funding allocations, recently announced by the Global Fund for 2018-2020, indicate that the total amount of funding available for malaria programs is about $1billion lower (31% less) than the amount available during the prior funding window. Because countries tend to prioritize commodity purchases over other expenses, we expect that the impact of a reduction in annual Global Fund funding on ACTs and RDTs procurement

  will have a limited impact on global procurement estimates. However, this reduction in funding could

reduce National Malaria Control Program willingness to support subsidization of private-sector ACT procurement through the Global Fund's Co-Payment Mechanism, shifting ACT markets further toward public delivery channels, and potentially reducing the availability and access to WHO-quality assured ACTs in the private sector. Future forecasts will review these assumptions based on country funding requests in the new funding cycle.

- Public sector orders for quality-assured injectable artesunate (QAINJAS) will be approximately 27M 60mg vials in 2017 and 2018 before declining to 26M 60mg vials in 2019 and 25M in 2020. The changes in QAINJAS procurement between 2017 and 2020 are driven by a decrease in projected funding available through the Global Fund for malaria, with the percentage of funding earmarked for QAINJAS procurement remaining stable for each country. QAINJAS procurement through other donors is expected to remain flat over this period.
- Global procurement of malaria rapid diagnostic tests (RDTs) in the public sector will peak at 278Mtests in 2017, and begin a decline, reaching 265M in 2018, and 244M RDTs in 2019, before rebounding a bit to reach 247M RDTs in 2020. The decrease in RDT procurement after 2017 is driven by a decrease in projected funding available for malaria programs during the upcoming Global Fund funding cycle.
- Artemisinin demand for production of active pharmaceutical ingredients (APIs) will grow from 176 metric tons (MTs) in 2017 to 221MTs in 2020. This expansion, if forecast to occur, despite declining malaria prevalence, owing to increased share of ACTs among antimalarials and general use of antimalarials in the context of population growth.

BACKGROUND

While sustained international funding for long-lasting insecticidal nets (LLIN), indoor residual insecticidal spraying (IRS) campaigns, quality-assured artemisinin-based combination therapies (QAACTs), and malaria rapid diagnostic tests (RDTs) has led to sharp declines in malaria prevalence and deaths, continuing mortality and morbidity indicate that LLIN and IRS campaigns provide incomplete transmission and infection prevention coverage, and many patients still do not receive prompt and effective treatment. RDTs have not been fully adopted in many markets, especially in the private sector, and a large number of fevers in malaria endemic regions are incorrectly presumed to be caused by malaria, resulting in extensive inappropriate use of antimalarial treatments.

Most of the global supply of artemisinin, the key raw material in production of artemisinin-based combination therapies (ACTs) (the WHO's recommended treatment for uncomplicated malaria), and injectable artesunate (the WHO's preferred treatment for severe malaria) is derived from agricultural sources. This vegetal product requires a 12 to 14-month cycle from initial planting of the crop to production and shipping of an ACT. Semi-synthetic artemisinin production has a shorter lead-time, but current total global capacity for synthesis of the semi-synthetic product is equivalent to only 25% of global artemisinin demand. Volatility in the artemisinin market has led to concerns over possible ACT supply tightening, resulting in significant risk for market participants and patients whose lives depend on ready access to these medicines.

In order to address these issues, the forecasting consortium was established to provide global malaria treatment and RDT forecasts, to identify and assess the uncertainties, and to provide better information to policy makers and market participants on potential shifts in these markets. The forecast methods have been published separately and can be found here: https://www.unitaid.eu/assets/Global_malaria_diagnostic_and_artemisinin_treatment_commodities_demand_forecast_forecasting_methodology-1.pdf. The consortium's forecasts project the impact of different trends on the market for malaria commodities at three levels, based on analysis of data from multiple sources including incidence of malaria-like fevers, surveys of treatment-seeking behavior,

market data on product imports and sales, surveys of treatment penetration in private and public channels, and country-level procurement trends.

Demand has been projected across three access channels: public sector, formal private sector, and informal private sector, where the formal private sector includes private not-for-profit and for-profit hospitals, clinics, and pharmacies, and the informal private sector includes private drug shops, vendors and general retailers that sell medicines. ACT procurement has been projected across three market categories as well: public sector, subsidized private sector market, and the non-subsidized (premium) private sector market.

Several caveats are important to keep in mind when assessing these forecasts. The antimalarial need and demand forecasts are based on extrapolation of historical household survey data on fever prevalence, malaria prevalence, treatment seeking, testing, and antimalarial treatment, collected from children under age five. New and dramatic shifts in any of these trends will take time to be reflected in the forecasts; we expect to incorporate such changes in disease and market dynamics with the addition of updated survey data, which is made available only periodically. ACT and RDT procurement forecasts are based in large part on currently committed funding and historical trends, as opposed to shifts in burden of disease or patient behaviors; changes to contributions by international donors or annual national funding allocations could change overall procurement estimates. Unforeseen events – such as the use of ACTs for Mass Drug Administration campaigns, the impact of malaria vaccine rollout on ACT demand, and others – could also alter the outlook for these products at regional and global levels, and we aim to analyze additional hypothetical scenarios in future reports.

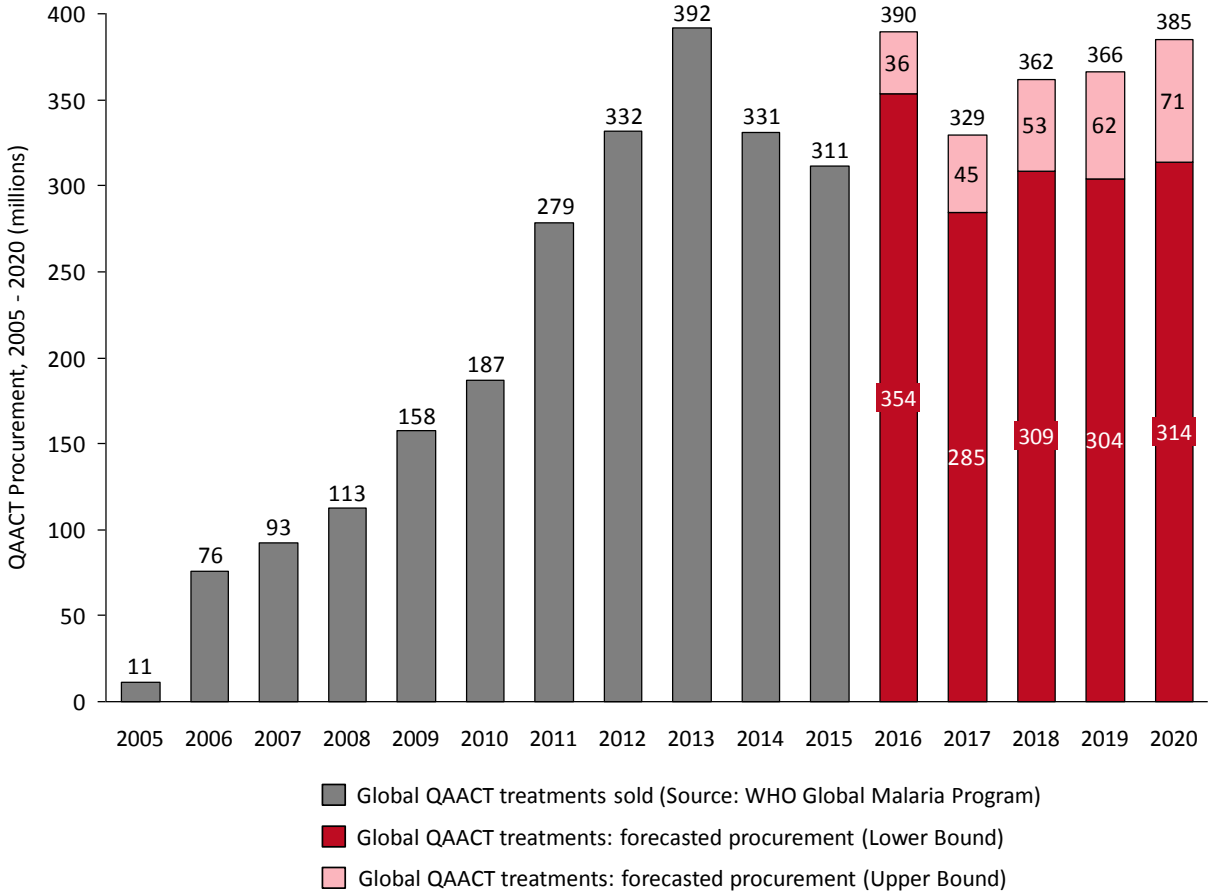
KEY FINDINGS

ACTS AND ANTIMALARIAL MEDICINES

PROCUREMENT

Barring further reductions in ACT pricing or the introduction of additional funding for their procurement, global procurement of QAACTs is projected to grow from an estimated 285M treatments in 2017 to 309M treatments in 2018, due to the introduction of additional funding for malaria programs and interventions from PMI (Figure 1). Our model assumes that procurement through the private sector co-payment mechanism will continue throughout the forecast period at volumes comparable to those in 2017 (please see our prior forecast report for analysis around this assumption). Owing to the combined effect of growth in QAACT use in the premium private sector and a projected decrease in total malaria funding available in 2019 and 2020 through the Global Fund, QAACT procurement volume will dip to 304M treatments in 2019 and bounce back to 314M treatments in 2020. QAACT demand and procurement volumes are generally higher than WHO-reported case estimates owing to the use of ACTs in undiagnosed febrile patients, as well as some ACT use in patients who are treated despite having received a negative diagnostic test.

Figure 1 QAACT market: Historical and forecast growth, 2005 – 2020 (millions)



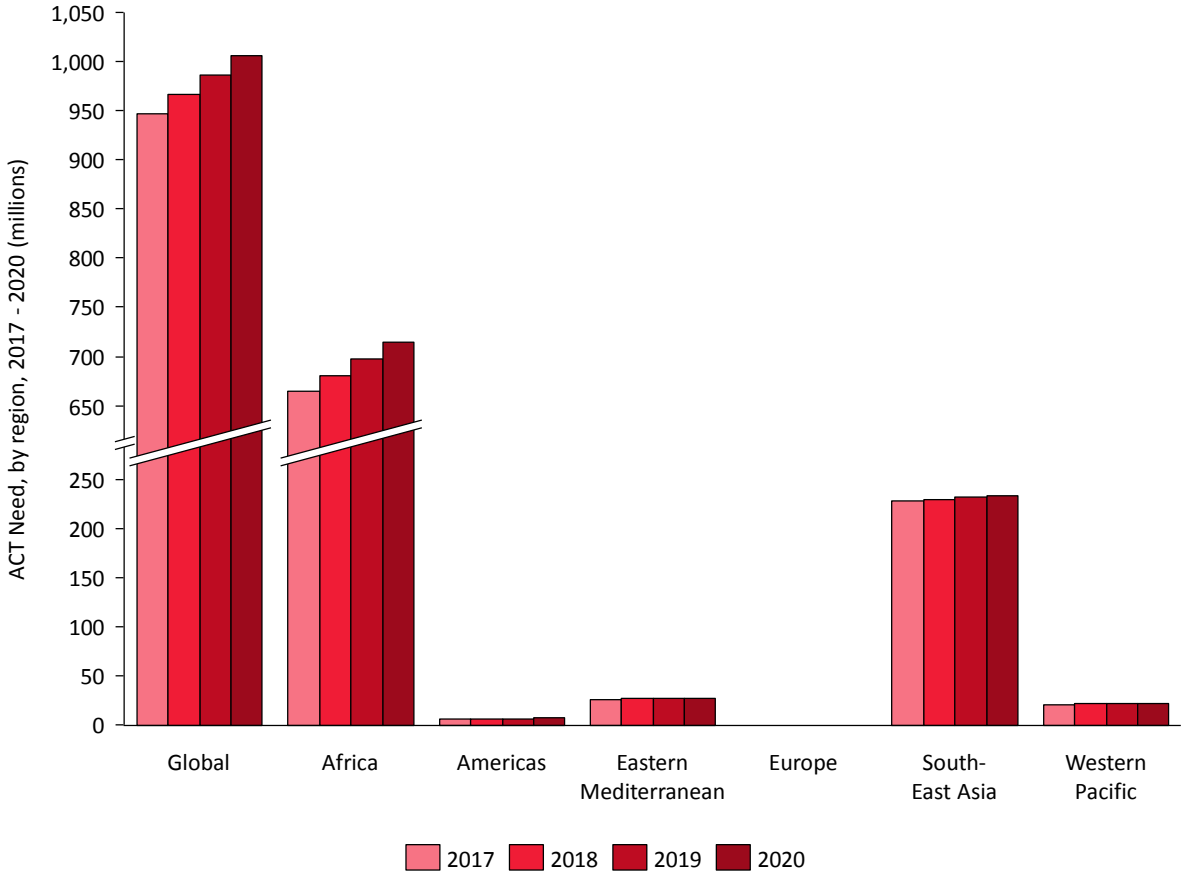
The new Global Fund funding allocations for countries applying for funding during the 2018-2020 period is approximately $3.2 billion, a figure that is about $1 billion (31%) lower than the funding allocated for spending on malaria programs in the prior Global Fund funding round (2014-2017). Many high burden malaria-endemic countries have new funding envelopes that are 25% or more below the funding allocations they had during the previous funding round. Since some countries were able to extend that prior envelope over a four-year period, the annual reduction in funding available for procurement of commodities from the Global Fund may not reflect as sharp a decline as the headline number suggests. However, many countries may feel that their funding, over a three-year period, has been reduced, and will have to manage their program needs accordingly. The deadlines for submission of Global Fund funding requests stretch across the 2017 calendar year, and while we assume that countries will prioritize QAACT, RDT, and QAINJAS commodity purchases over other programmatic expenses, there is a possibility that some countries may reduce commodity purchasing in order to assure that all programs

receive, at least, minimally adequate funding. This also means that some countries that have previously participated in the Affordable Medicines Facility malaria (AMFm) and Private Sector Co-Payment Mechanism (CPM) may reconsider their commitment to that program, and we may see some countries reduce their funding allocations for the CPM, or apply for such funding as an "above allocation" request.

The forecast period will see steady growth in QAACT volumes in the premium private sector, (from 47M treatments in 2017 to 72M in 2020), stable volumes in the subsidized private sector (62M; assuming steady state investment in the CPM), and, outside of a spike to 191M treatments in 2018 owing to the influx of additional PMI funding, steady volumes in the public sector (175M to 179M treatments).

As stated previously, the baseline forecast, presented in this report, assumes that countries participating in the CPM will continue to invest in private sector treatment subsidies (even at lower funding levels). In our prior forecast report, we modeled the hypothetical effect of a termination of all CPM funding beyond 2017 in five high-volume countries (Ghana, Kenya, Nigeria, Tanzania, and Uganda) and assumed countries would not replace Global Fund resources with domestic sources of funding for subsidized QAACTs. This scenario is not reproduced in the current report; please refer to the previous report for a review of that analysis.

Figure 2 ACT Need, by region, 2017 - 2020 (millions)



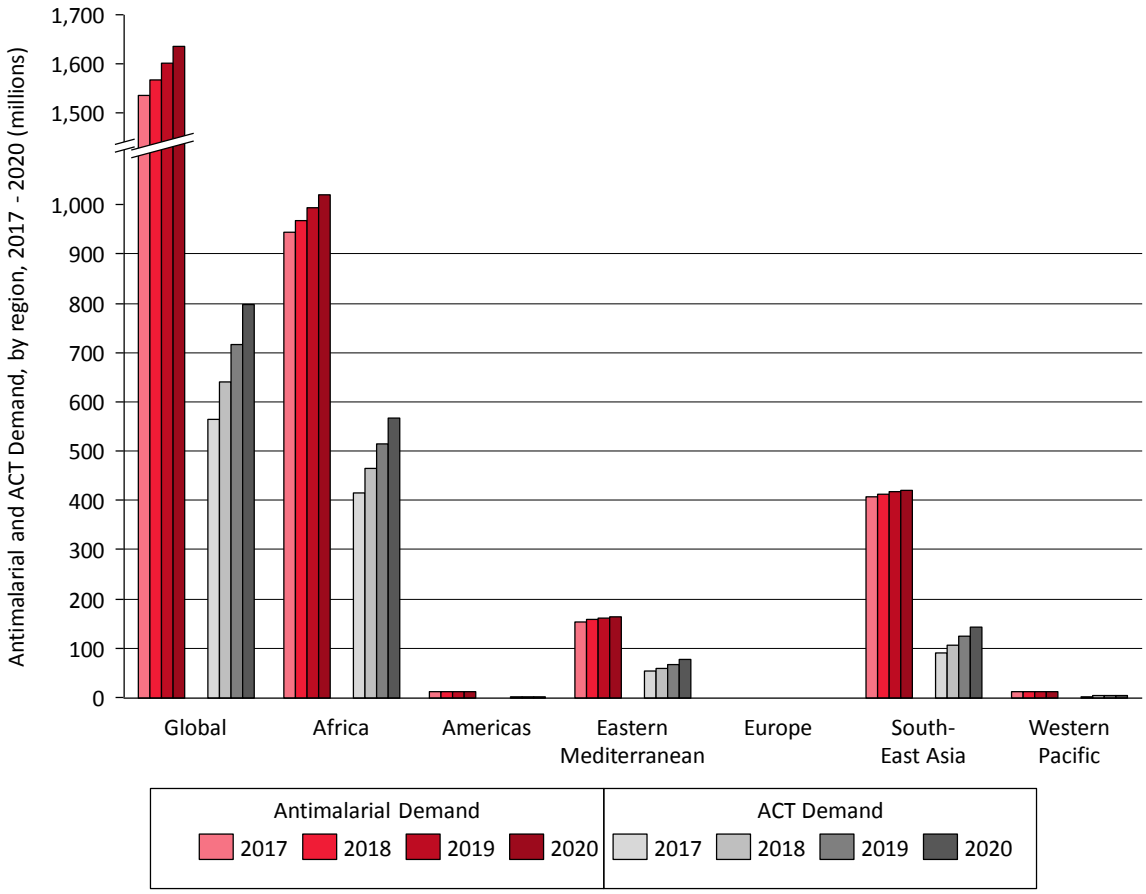
We estimate that the need for ACTs will rise between 2017 (948M) and 2020 (1B), largely in line with population growth among at-risk populations (Figure 2). This is driven by estimates of over 15B fevers in 2017 among-at-risk populations, approximately 6% of which likely were associated with detectable parasitemia. While associated with *P.falciparum* malaria infection, not all of these fevers were necessarily caused by *P.falciparum* malaria, and thus, we expect estimations of antimalarial need (based on *P.falciparum* malaria prevalence applied to febrile incidence) to be greater than reported malaria case estimates; these estimates should be interpreted as a high ceiling to the overall need for antimalarial medicines, rather than as a guide to a necessary volume of ACTs that must be produced by manufacturers and whose procurement must be funded by governments and donor agencies.

Substantial reductions in this measure of antimalarial need will require additional large and sustained reductions in *P.falciparum* malaria prevalence in areas of risk and/or elimination of malaria from large areas (i.e., shrinking the malaria map) – both of which are longer-term objectives.

DEMAND

In 2017, the global demand for antimalarial medicines was estimated to be 1.54B treatment courses. We project that demand for antimalarial medicines will grow to 1.64B treatments by 2020. ACTs, both quality-assured and non-quality assured, currently make up 37% of the antimalarial market, with demand for ACTs in 2017 estimated at 566M treatments, and (assuming continued trends in product availability and usage, and owing to population growth in endemic areas and a shift away from use of other antimalarials), will rise to 799M treatments in 2020, comprising 49% of the antimalarial market (Figure 3).

Figure 3 Antimalarial and ACT Demand, by region, 2017 - 2020 (millions)

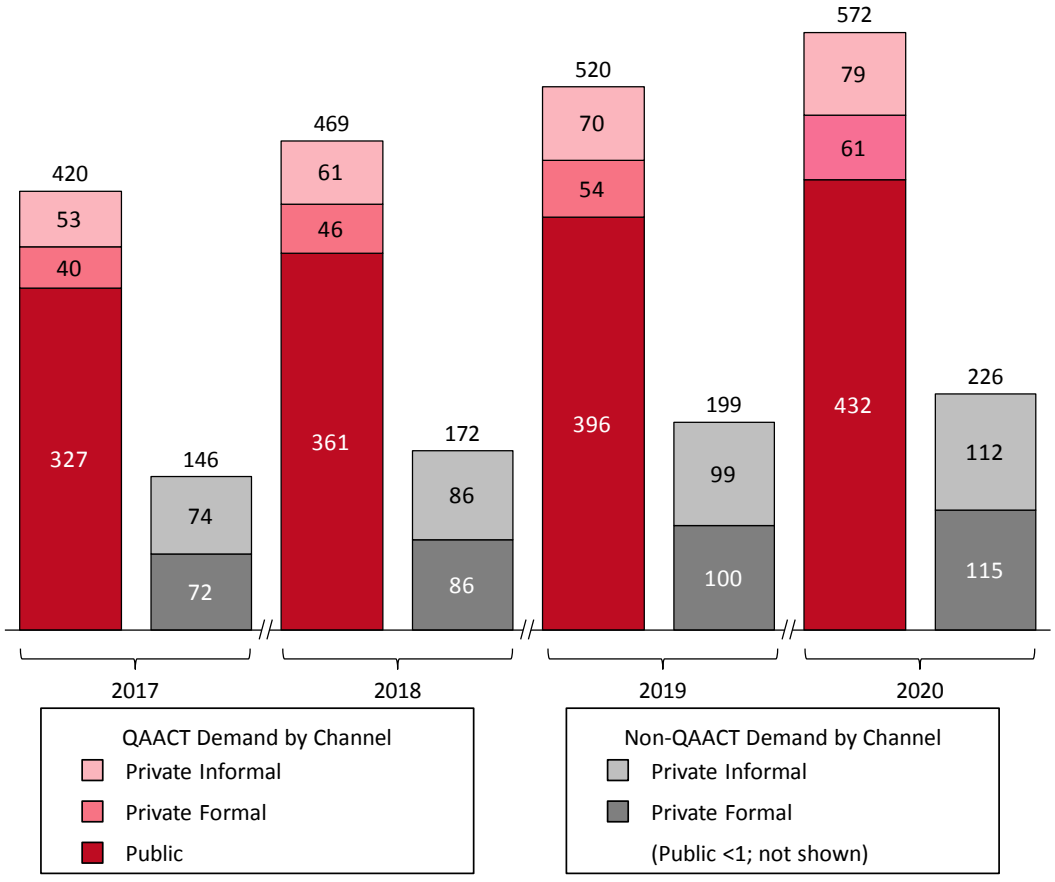


Demand for QAACTs is estimated at 420M treatments in 2017, rising to 572M treatments in 2020 while demand for non-quality-assured ACTs (Non-QAACTs) is estimated to grow from 146M treatments in 2017 to 226M treatments in 2020, with non-QAACTs comprising about 26% to 28% of estimated ACT demand (Figure 4). Although there is some use of non-QAACTs in the public sector (for example, in Viet Nam), most demand for non-QAACTs is in the private sector, split almost equally between informal and formal sources.

Among QAACT product combinations, artemether-lumefantrine will remain the leader, with consumer demand rising from 219M treatments in 2017 to 241M treatments in 2020. Artesunate-amodiaquine is projected to remain the second most commonly used ACT, with demand growing from 63M treatments in 2017 to 70M in 2020. The non-subsidized private sector (premium private sector) market for QAACTs is projected to increase over the next few years from 47M treatments in 2017 to 72M treatments in 2020.

Demand for oral artemisinin monotherapies will continue to decline, from 0.52M in 2017 to 0.24M in 2020.

Figure 4 ACT global demand, by Quality-Assured drug classification and distribution channel, 2017 - 2020 (millions)

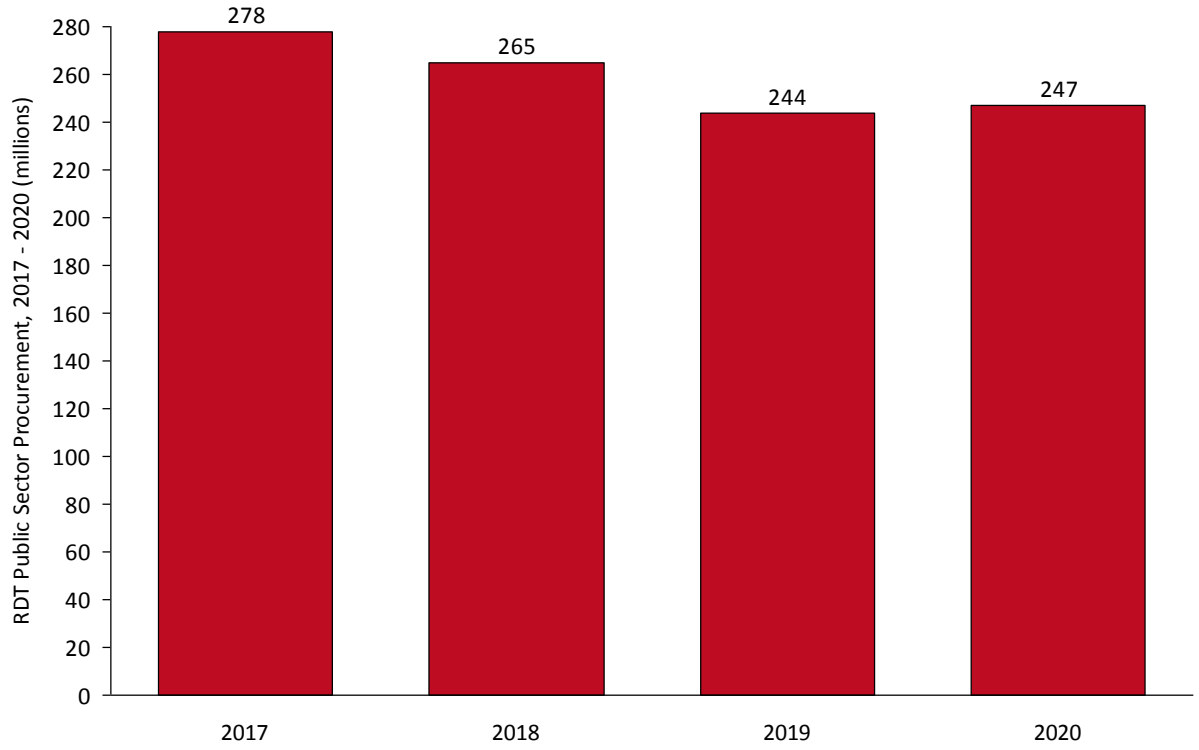


Public sector orders for quality-assured injectable artesunate will be flat in 2017 and 2018, with 27M and 28M 60mg vials procured in these years, respectively, before declining slightly to 26M and 25M 60mg vials in 2019 and 2020, respectively. The decrease in projected quality-assured injectable artesunate procurement between 2018 and 2019 is driven by a slight decrease in projected funding of QAINJAS as severe malaria burden decreases.

RDTs

Our model for RDT procurement, which is based on announced and committed funding for public sector procurement, forecasts global public sector procurement of RDTs at 278M tests in 2076, declining to 265M in 2018, and 244M in 2019 before a slight increase to 247M in 2020 (Figure 5). This decrease in public sector RDT procurement is driven by a decrease in projected funding available for malaria, with the percentage of funding earmarked for RDT procurement remaining stable, during the coming funding cycle. Conversely, global demand for RDTs is expected to grow over this timeframe, from 568M tests in 2017 to 694M in 2020. The forecast demand is significantly higher than our procurement forecast as the demand estimates rely on test data from household surveys, and extend data on the portion of diagnostic tests conducted using an RDT across all sectors, while the procurement estimates focus on historical orders and procurement plans for the public sector, and do not include estimates of private sector RDT use.

Figure 5 RDT public sector procurement, 2017 - 2020 (millions)



ARTEMISININ DEMAND

The market for artemisinin for production of derivative active pharmaceutical ingredients (API) will remain robust over the 2017-2020 forecast period, given the expansion of general antimalarial use with population growth, and shifts in ACT use as a share of antimalarial treatments (37% in 2017 increasing to 49% in 2020). Artemisinin demand will increase from 176 metric tons (MTs) in 2017 to 196MTs in 2018, coinciding with the growth in procurement for QAACTs in 2018, and will continue to grow in 2019 (205MTs) and 2020 (221MTs) with the influx of PMI's additional funding for malaria programs, and sustained growth in demand for QAACTs and non-QAACTs in the premium private sector. ACTs (both QAACTs and non-QAACTs) comprise the majority of global artemisinin demand (97%), with QAACTs accounting for a large share (53 to 61%) of artemisinin demand.

METHODS AND DATA UPDATES SINCE THE PREVIOUS REPORT

Since the publication of the previous report, a number of significant updates have been made to the source data and the forecasting methods. Chief among the data and methodological updates have been:

- RDT Demand: RDT shares were calculated at the country level, based on market specific data from the latest World Malaria Report. The recent WMR showed that the trend in suspected malaria cases receiving a diagnostic test (in Africa) has grown significantly since 2011, with a ~17% annual increase. We assume that the testing growth is predominantly driven by RDTs, and have therefore applied this growth rate to the RDT share in all countries in the African region (with a cap at 100%). We applied the regional uptake curves to all other countries; based on historical growth, these trends were assumed to be flat.
- ACT / QA usage: We have adjusted assumptions around QAACT treatment demand by ACT type in the Indian public sector, with the uptake of AL (replacing AS+SP) in that market.
- Injectable/Rectal artemisinin monotherapies: We adjusted assumptions around national trends in the private sector demand for these products. Growth of the private sector injectable/rectal artemisinin monotherapies was decoupled from the oral artemisinin market growth, and based on historical trends in the IMS data. We applied regional historical trends to all countries in a particular region.
- We updated source data to incorporate PMI's 2016 procurement data into our analysis and application of historical procurement trends, and updated Global Fund grant disbursement data to ensure that our projections of available funding for commodity procurement through the end of the current funding cycle were accurate. New Global Fund funding envelopes have not yet been incorporated into the models as (1) we expect that national programs will prioritize procurement of life-saving commodities, leading to potentially minor changes in procurement volumes, and (2) we will update these data in future iterations of this report as funding requests are submitted and reviewed.

This change in the methodology, and the review and subsequent update of data sources, has resulted in significant changes in the private sector demand outputs for injectable artemisinin monotherapies and rectal artesunate in the current forecast, as well as RDT demand and procurement forecasts, when compared to those published in the prior report.

POLICY IMPLICATIONS

Sustained and predictable donor funding for QAACTs, injectable artesunate, and RDTs is essential for continued progress toward reducing malaria mortality and morbidity, and maintaining stable and healthy markets for suppliers of malaria treatment and diagnostic commodities.

POLICY IMPLICATIONS FOR ACTS AND ANTIMALARIAL MEDICINES

- The WHO's 2016 World Malaria Report showed that the median proportion of children under five with recent or current *P. falciparum* malaria who received an ACT was 14% (Figure 4.5, 2016 World Malaria Report). While it is unclear why the remaining 86% of recent or current cases did/do not receive an ACT, our estimates of between 948M and 1B parasitemic fevers per year indicate that the currently available supply of QAACTs is insufficient to meet overall need; even if all fevers were tested and only confirmed parasitemic fevers were treated with a QAACT, the current procurement of such drugs would cover only one third of all detectable infections. This indicates that as more patients have better access to proper disease diagnosis, the supply of QAACT must grow to meet the need for appropriate treatment of all confirmed infections.

- ACTs currently comprise approximately 37% of the global antimalarial demand. We forecast that this share will grow to 49% by 2020. However, much of this growth will be from the use of non-QAACTs in the private sector, as the QAACT share of ACT demand will decrease from 74% to 72% over this period. The use of non-QAACTs is concerning owing to the potentially higher risk for mortality and/or induction of artemisinin-resistant malaria with the use of these potentially sub-standard ACTs. With growth in ACT usage, and the expected increased use of non-QAACTs, the

global malaria community should consider ways to either phase out the use of non-QAACT medicines, or provide a pathway for these products to become quality-assured, at the national, regional, or global level.

- Sustained support for procurement of malaria commodities is heavily dependent on international funding sources. The 31% decline in Global Fund funding envelopes in the current funding cycle will force countries to make difficult decisions around their health spending priorities. Given the need to sustain robust malaria case management programs, procurement of quality assured malaria commodities, at least in the public sector delivery channel will likely be prioritized over other investments. In addition, given the recent shifts in political priorities in major donor nations, the malaria community will need to monitor the funding situation and advocate for continued substantial investments to combat this disease.

- Malaria case management will continue to be provided through health systems that include both public and private providers. Policymakers can improve malaria outcomes by focusing on effective stewardship of mixed health systems and by addressing issues specific to each sector. The Global Fund's private sector co-payment mechanism is responsible for a significant fraction of the QAACT market, and any changes or reductions in this program will likely affect the market for QAACTs, and sustained access to quality-assured antimalarial medicines for many people living in high-risk regions.

- Sustained communication of WHO-recommendations for the cessation of oral artemisinin-based monotherapies is warranted to continue to drive down their use. Further pressure needs to be sustained on national regulatory authorities and on suppliers to discourage production and licensing of oral artemisinin-based monotherapies for potential use as stand-alone therapies.

POLICY IMPLICATIONS FOR RDTS

- The WHO-led focus on expansion of RDT use will help identify malaria infections across diverse settings where febrile patients seek treatment. Although we expect public sector RDT procurement to decrease by nearly 12% from 2017 to 2019 (Figure 5), increased uptake of RDTs in and of itself will not lead to a reduction in antimalarial or ACT use. Sustained donor support for RDT use must continue to be coupled with appropriate treatment follow-up: increasing the percentage of malaria-positive patients that receive appropriate treatment while decreasing the percentage of malaria-negative patients that receive an antimalarial. Such coupled interventions could improve targeting so that all confirmed cases are treated, and valuable QAACTs are not wasted by misuse in patients who do not have malaria.

- The progress that has been made in expansion of diagnostics in recent years has been remarkable. The WHO reports that there are now fewer ACTs distributed in the public sector in sub-Saharan Africa than diagnostic tests conducted in this region (Figure 2.10, 2016 World Malaria Report). We forecast 278M RDTs will be procured in for the public sector 2017, 92% of them in Africa. This RDT deployment estimate and our estimate that Africa accounts for approximately 26% of annual global fevers in malaria-endemic areas, indicate that countries outside of Africa should potentially increase their focus on expanding access to RDTs. The ratio between procured public sector RDTs and QAACTs will approach 1:1 in 2017. Although we acknowledge that malaria testing extends beyond the use of RDTs, a 1:1 test-to-treatment ratio is not sufficient given annual estimates of ~4B fevers in this region; the ratio of diagnostic tests to ACTs will have to increase significantly to achieve ubiquitous case management targets. These data reinforce the need for the expansion in the use of diagnostics, coupled with deployment of prompt and appropriately targeted follow-up treatments.

POLICY IMPLICATIONS FOR ARTEMISININ SUPPLY

- We project that despite declining malaria prevalence and increase use of malaria diagnostic tools preceding treatment, artemisinin demand for API will increase throughout the forecast period, owing to the steady increase in ACT share as a portion of antimalarial use. Semi-synthetic artemisinin (SSA), which reduces the start-to-finish production cycle to six or fewer months, has a current maximum total production capacity that is equivalent in size to approximately 25% of the global demand for artemisinin. Therefore, agriculturally-derived artemisinin will continue to play a critical role in supplying artemisinin to meet global demand for artemisinin-based medicines for at least the next three years.

- Despite sustained and stable demand that should help stabilize supply there are potential for external shocks that can impact supply such as weather (droughts or floods), and changes in the prices of competing cash crops. Thus supply should continue to be monitored to make sure global demand can be met, and policymakers should explore whether specific institutions or consortia are best placed to fulfill this monitoring function.

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