POLICY BRIEF

GLOBAL MALARIA DIAGNOSTIC AND ARTEMISININ TREATMENT COMMODITIES DEMAND FORECAST

2016 – 2019

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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 second in a series produced by the consortium, and includes several changes from the previous report. In this report, the forecast is extended to 2019, and new data on PMI's expanded malaria budget, revised data on historical Global Fund procurement, current procurement plans for some high-volume countries, likely existing expenditures for the GF's Co-Payment Mechanism program, and more recent estimates of malaria prevalence in sub-Saharan Africa were incorporated into the forecast. In addition, this report includes a baseline forecast along with scenarios projecting the impact of potential changes in donor funding for malaria treatment and diagnostic commodities, and an analysis of the impact of a hypothetical termination of the Global Fund's Co-Payment (CPM) mechanism.

KEY MESSAGES

- In 2016, global demand for antimalarial medicines was estimated to be 1.5 billion (B) treatment courses and we forecast that demand for antimalarial medicines will grow to approximately 1.6B treatments by 2019. Demand for artemisinin-based combination therapies (ACTs) – inclusive of both quality-assured ACTs (QAACTs) and non-quality assured ACTs (non-QAACTs) – comprised approximately 33% of global antimalarial demand in 2016, and is expected to grow to 45% of global antimalarial demand by 2019. Non-QAACTs comprise about 25% to 28% of estimated global ACT demand, with most of this demand coming from the private sector.
- Global procurement of QAACTs is projected to decline from 350 million (M) treatments in 2016 to 310M treatments in 2017, due to a decrease in procurement through the private sector co-payment mechanism (CPM). QAACT procurement will rebound slightly to 332M treatments in 2018, and 329M treatments in 2019 owing to the increase in the annual budget for programs supported by the President's Malaria Initiative (PMI). 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.
- Public sector orders for quality-assured injectable artesunate (QAINJAS) will reach 30M 60mg vials in 2016 and 2017 before declining to 26M 60mg vials in 2019. The changes in QAINJAS procurement between 2016 and 2019 are driven by shifts in total malaria funding available through the Global Fund, which will have a peak funding year in 2017, followed by decreases in the subsequent years. 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 was approximately 257M tests in 2016, and will rise to 303M in 2017, before declining to 274M, and 262M in 2018 and 2019, respectively. This increased procurement is a result of a

projected increase in Global Fund grant disbursements during the end of the current funding cycle, in 2017, and an increase in the average percentage of the disbursements spent on RDTs. Conversely, the decrease in RDT procurement from 2018 to 2019 is driven by a decrease in projected funding available for malaria during the subsequent funding cycle.

- Artemisinin demand for production of active pharmaceutical ingredients (APIs) will decrease from 197 metric tons (MTs) in 2016 to 193MTs in 2017, before growing to 214MTs in 2018 and 226MTs in 2019. 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: http://unitaid.org/images/marketdynamics/publications/Global_malaria_diagnostic_and_artemisinin_treatment_commodities_demand_forecast_forecasting_methodology.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; new or expanded funding 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 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

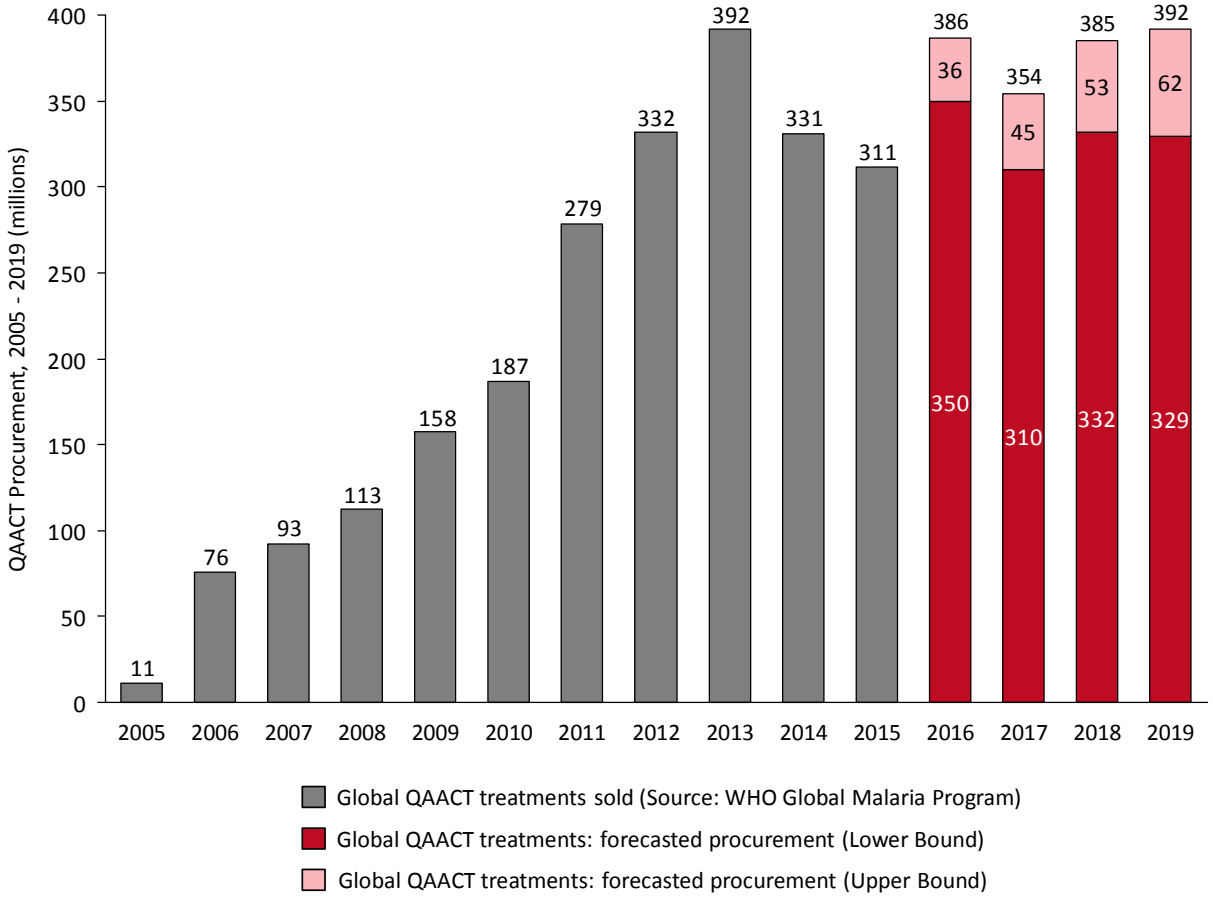
Global procurement of QAACTs is projected to decline from an estimated 350M treatments in 2016 to 310M treatments in 2017, due to a reduction in procurement under the CPM due to financial constraints within specific country grants. While the total malaria funding available in the public sector increases from 2016 to 2017 owing to an overall increase in projected Global Fund disbursements, the proportion of disbursements spent on QAACTs is projected to decrease, leading to flat public sector procurement volumes for these products (Figure 1).

Barring further reductions in ACT pricing or the introduction of additional funding for their procurement, the number of procured QAACTs will grow to 332M treatments in 2018, and 329M treatments in 2019. The increase in QAACT procurement in 2018 will be due to a small increase in public sector procurement following the additional PMI funding that will become available starting in 2018, and a projected increase in use of QAACTs in the premium private sector. While we project total malaria funding to decrease in 2018 with the start of the new Global Fund funding cycle, the projected increase in the average proportion of each grant that is spent on QAACTs will balance out the overall funding decrease. The decrease in Global Fund funding follows a year of peak malaria funding in 2017, during which time most grants from the current funding cycle are projected to end.

Global Fund-attributable public sector QAACT procurement will decline slightly in 2019, driven by a projected decrease in total malaria funding available in 2019 through the Global Fund.

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.

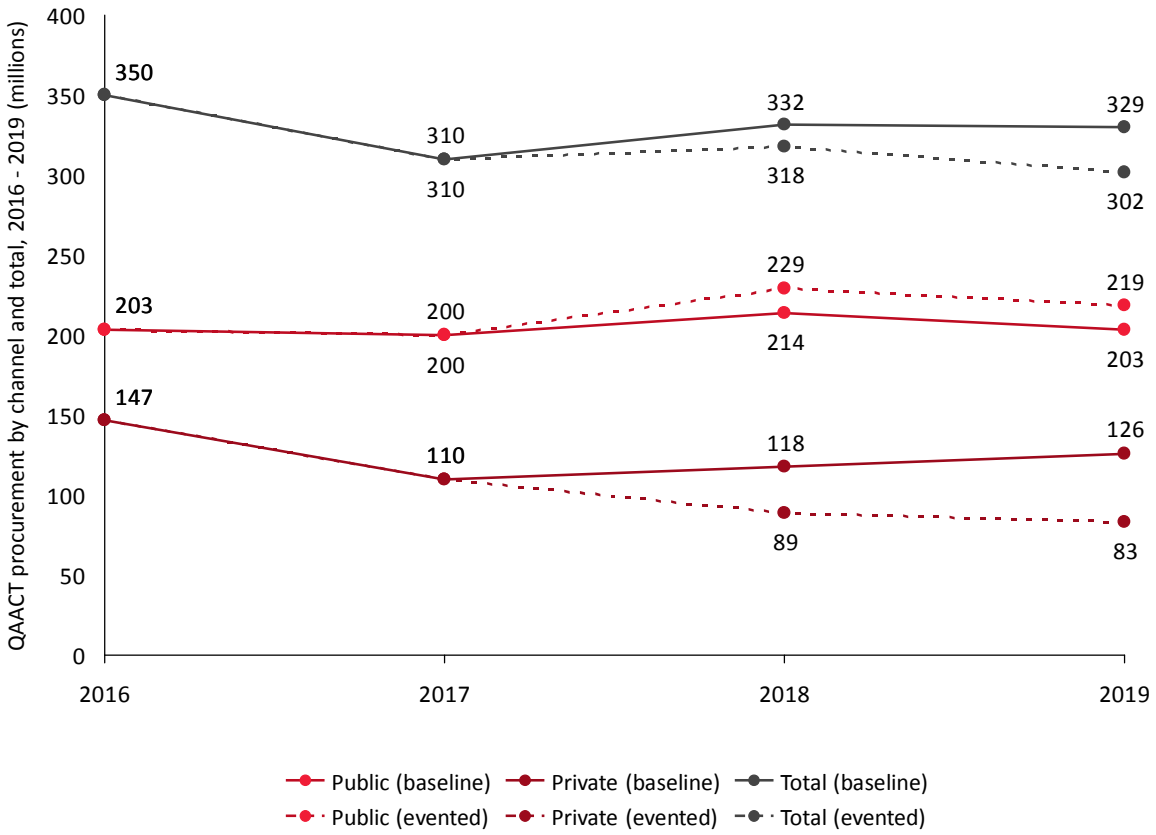
Figure 1 QAACT market: Historical and forecast growth, 2005 – 2019 (millions)



There will be a marked shift in channel mix for QAACTs in this timeframe. We project that procured QAACT volumes in the subsidized private sector will decline from approximately 107M treatments in 2016 to roughly 62M in 2017, where it will hold steady through 2019. Since estimates of public channel procurement is based on historically committed funding, unless new funding is made available, public channel procurement is expected to remain relatively flat (200M to 203M QAACTs per year) during the forecast period, with the exception of 2018, when we expect it will reach 214M QAACTs, boosted by additional PMI funds.

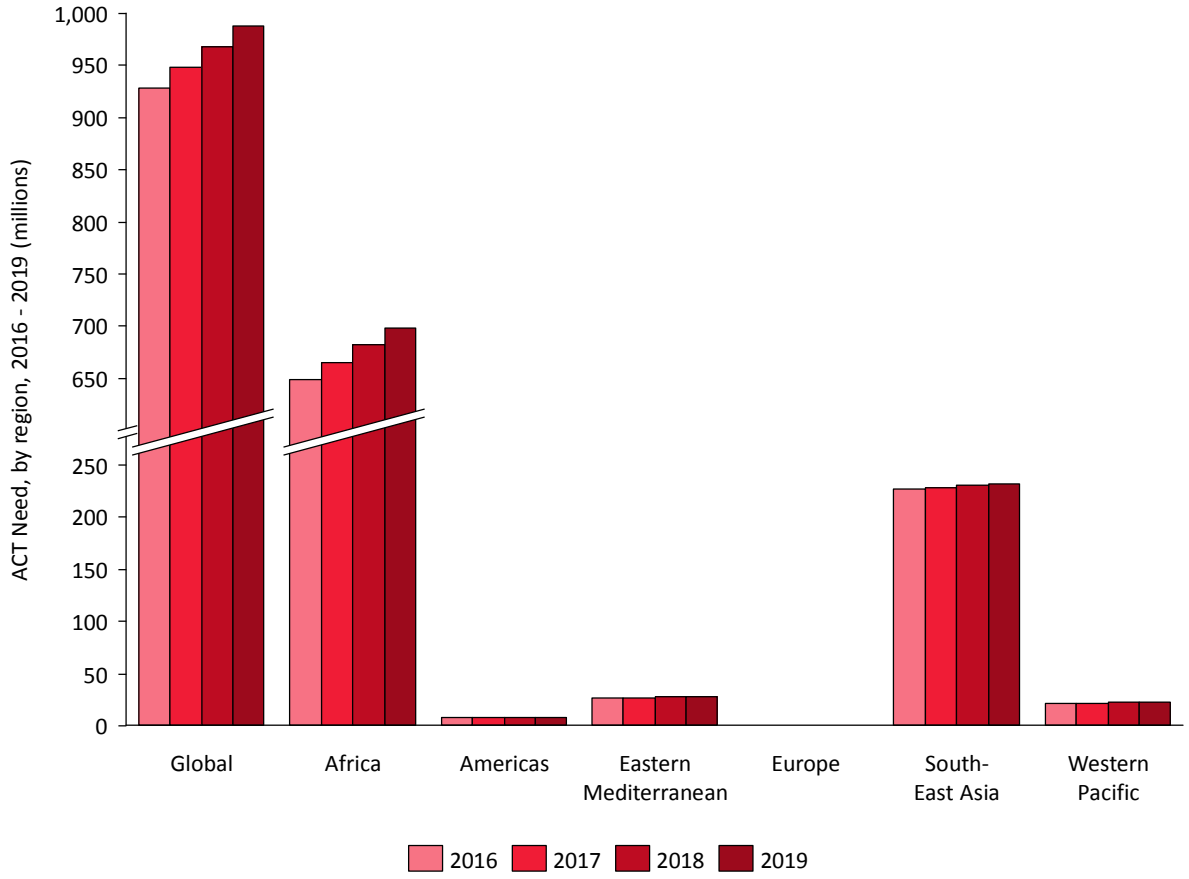
While the baseline forecast assumes that countries participating in the CPM will continue to invest in private sector treatment subsidies (even at lower funding levels), we modeled the hypothetical effect of a termination of all CPM funding beyond 2017 in five high-volume countries (Ghana, Kenya, Nigeria, Tanzania, and Uganda) by modeling a scenario where CPM funding terminates after 2017. In this hypothetical scenario, we assume countries do not replace Global Fund resources with domestic sources of funding for subsidized QAACTs. This results in a decline, when compared to the baseline forecast, in QAACT procurement in 2018 and 2019, with the QAACT market reaching a potential plateau by 2019 at levels not seen since 2012 (Figure 2). Most of the projected decline would be the result of rapid erosion of QAACT sales in the private informal sector once the QAACT's retail price advantage over non-QAACTs no longer exists to confer a market advantage for QAACTs.

Figure 2 Cessation of the private sector Co-Payment Mechanism (CPM) after 2017. QAACT procurement by channel and total, 2016 - 2019 (millions)



NEED

Figure 3 ACT Need, by region, 2016 - 2019 (millions)



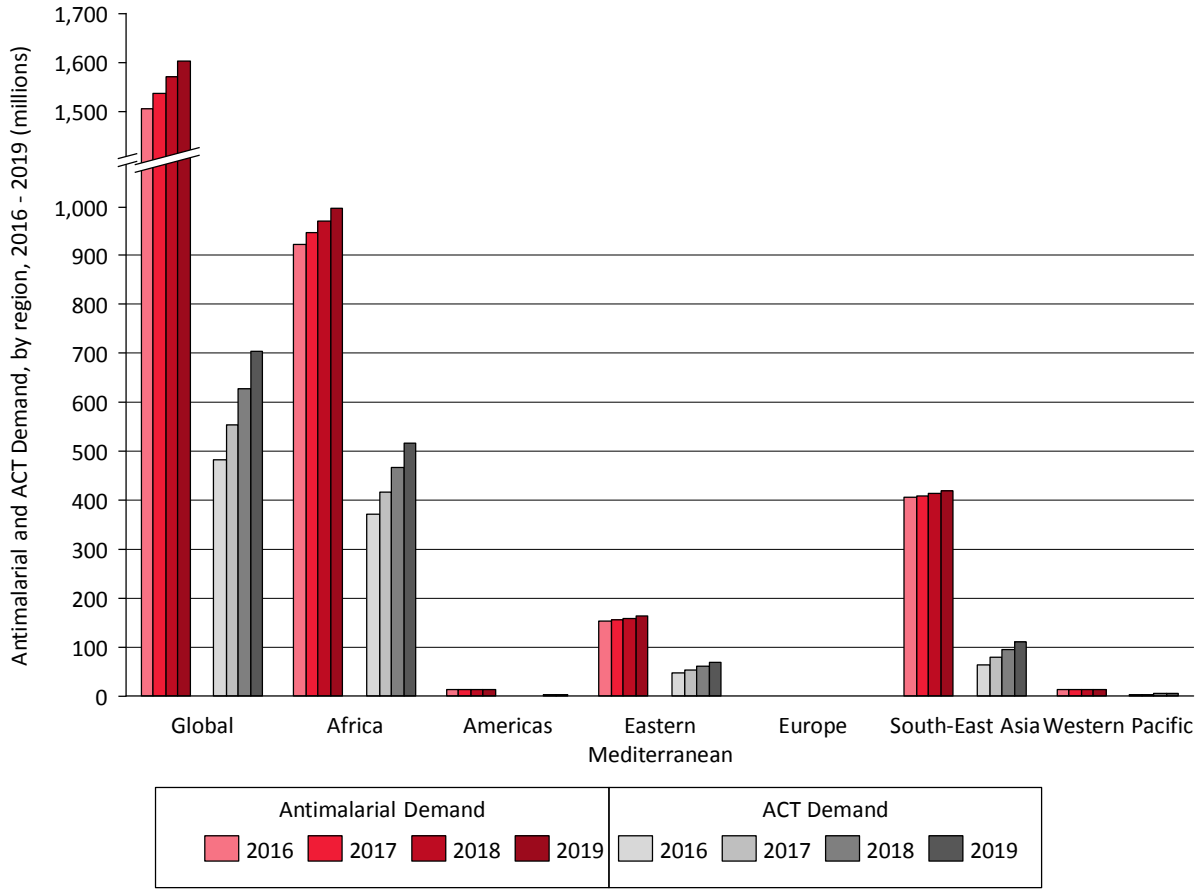
We estimate that the need for ACTs will rise between 2016 (929M) and 2019 (987M), largely in line with population growth among at-risk populations. (Figure 3) This is driven by estimates of 15B fevers in 2016 among-at-risk populations, approximately 6% of which likely were associated with detectable 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 2016, the global demand for antimalarial medicines was estimated to be 1.5B treatment courses. In the baseline forecast, we project that demand for antimalarial medicines will grow to 1.6B treatments by 2019. ACTs, both quality-assured and non-quality assured, currently make up roughly one third of the antimalarial market, with demand for ACTs in 2016 estimated at 483M 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 704M treatments in 2019 (Figure 4).

Figure 4 Antimalarial and ACT Demand, by region, 2016 - 2019 (millions)



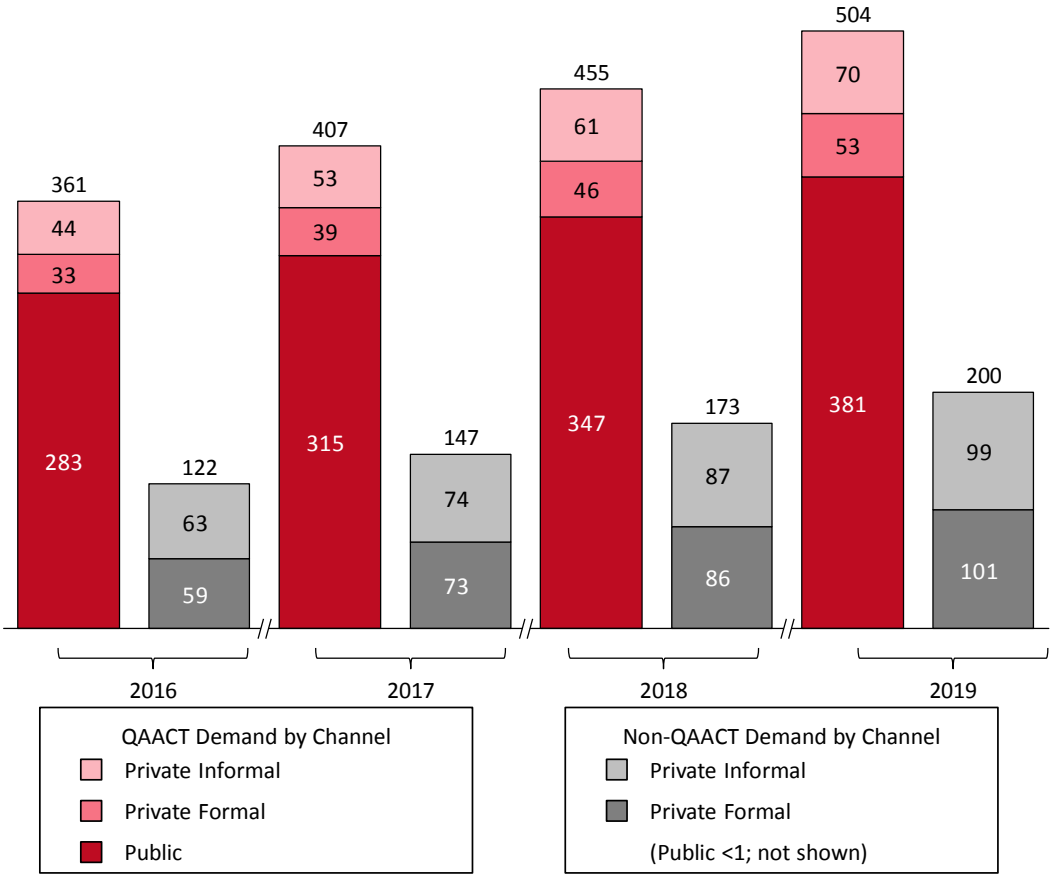
Demand for QAACTs is estimated at 361M treatments in 2016, rising to 504M treatments in 2019 while demand for non-quality-assured ACTs (Non-QAACTs) is estimated to grow from 122M treatments in 2016 to 200M treatments in 2019, with non-QAACTs comprising about 25% of estimated ACT demand (Figure 5). Although 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 259M treatments in 2016 to 362M treatments in 2019.

Artesunate-amodiaquine is projected to remain the second most commonly used ACT, with demand growing from 80M treatments in 2016 to 111M in 2019. The non-subsidized private sector (premium private sector) market for QAACTs is projected to increase over the next few years from 39M treatments in 2016 to 64M treatments in 2019. This increase in the use of QAACTs in the premium private sector would only reduce the magnitude of the QAACT decline in the CPM-termination scenario, described above.

Demand for oral artemisinin monotherapies will continue to decline, from 0.7M in 2016 to 0.3M in 2019.

Figure 5 ACT global demand, by Quality-Assured drug classification and distribution channel, 2016 - 2019 (millions)

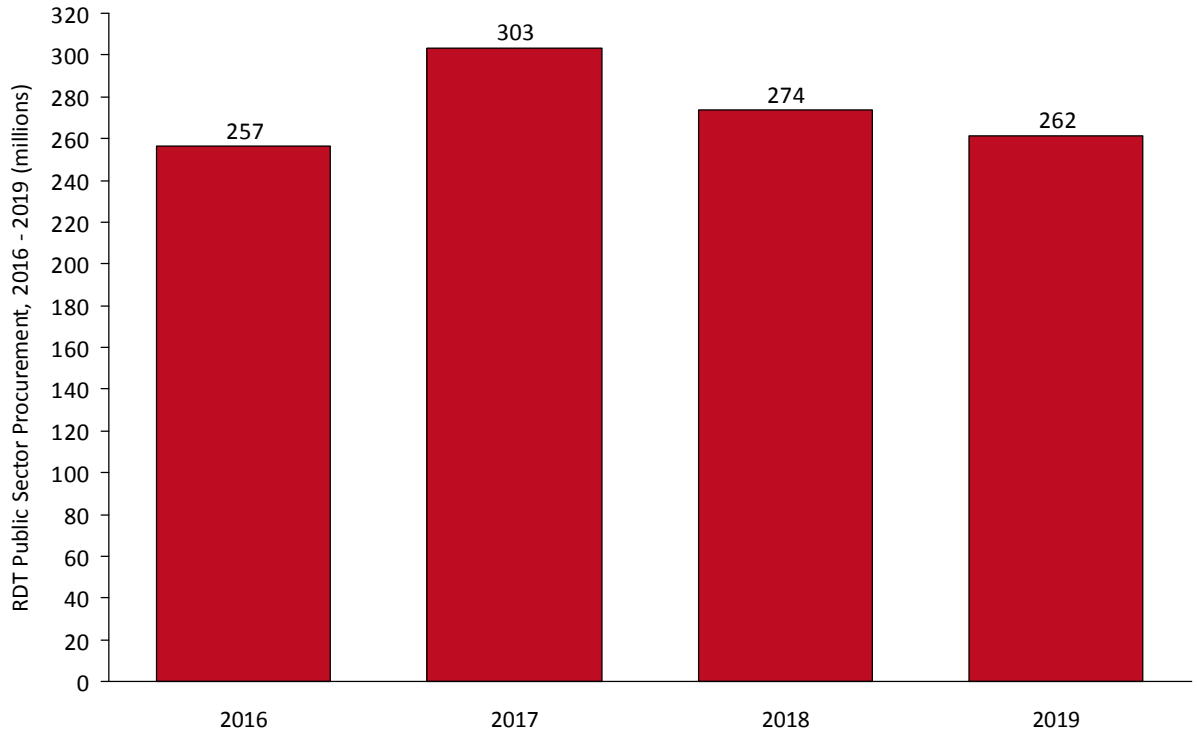


With multiple donor agencies conducting a concerted funding effort to shift severe malaria treatment away from the use of quinine and on to injectable artesunate, public sector orders for quality-assured injectable artesunate will reach 30M 60mg vials in 2016 and 2017, before declining slightly to 28M and 26M 60mg vials in 2018 and 2019, 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 257M tests in 2016, rising to 303M in 2017, before declining to 274M in 2018 and 262M in 2019 (Figure 6). This increased procurement is a result of a projected increase in Global Fund grant disbursements during the end of the current funding cycle, in 2017, and an increase on the average proportion of the disbursements spent on RDTs. Conversely, the decrease in RDT procurement from 2018 to 2019 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. Global demand for RDTs is expected to grow over this timeframe as well, from 578M tests in 2016 to 623M in 2019. 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 6 RDT public sector procurement, 2016 - 2019 (millions)



ARTEMISININ DEMAND

The market for artemisinin for production of derivative active pharmaceutical ingredients (API) will remain robust over the 2016-2019 forecast period, given the expansion of general antimalarial use with population growth, and shifts in ACT use as a share of antimalarial treatments (33% in 2016 increasing to 45% in 2019). Artemisinin demand will dip slightly from 197 metric tons (MTs) in 2016 to 193MTs in 2017, coinciding with the decline in procurement for QAACTs in 2017, but will rebound in 2018 (214MTs) and 2019 (226MTs) with the influx of PMI's additional funding for malaria programs, and sustained growth in demand for all other artemisinin containing medicines, including non-QAACTs. ACTs (both QAACTs and non-QAACTs) comprise the majority of global artemisinin demand (97%), with QAACTs accounting for a large share (57-70%) 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 updates have been:

- Revisions to data on Global Fund historical procurement volumes and planned procurement in 2016 and beyond. Previous data had indicated the potential for higher procurement volumes in 2016 and 2017 (for some key countries e.g., Democratic Republic of the Congo), but the latest data does not support this potential.

- Revised assumptions for PMI funding, following U.S. President Obama's statements during the January, 2016 State of the Union speech, and subsequent request for increased funding for PMI programs.

    - Assumed an annual budget increase of at least $71M per year, starting in the 4th quarter of 2017.

- Incorporation of more recent estimates of malaria prevalence in sub-Saharan Africa based on data from the Malaria Atlas Project (MAP) leading to a decline in weighted average prevalence from 30% to 17% in the Africa region.

- Revised data inputs for the private sector co-payment mechanism

    - Funding continues to tighten for this program, with 2017 funding likely to be significantly less than funding in 2016. We assume the 2017 funding floor will continue through 2018 and 2019.

Chief among the updates to the methodology have been:

- Revisions to the procurement forecast methods for Global Fund funded commodities to more accurately project annual procurement of ACTs, InjAS, and RDTs. Whereas previous methods relied primarily on country-level procurement plan data, with the grant-recipient's historical spending rate for ACTs as a secondary approach, the revised method estimates future procurement primarily based on historical procurement (i.e. order data) trends, with country-level procurement plan data used only for select high volume countries. The country-level planned procurement information is gathered from a combination of sources – national malaria programs, Global Fund principal recipients, Global Fund health product managers to account for country specific nuances that shape procurement plans. This combination of historical trends and country procurement plan information was used for our 2016-17 forecasts. For 2018-19 we relied primarily on the extension of historical trends.

This change in the methodology, and the review and subsequent update of data sources, has resulted in significant changes in the procurement and need outputs of the current forecast, when compared to those published in the prior report.

1. Forecasted procurement of QAACTs has decreased significantly in the current forecast, as compared to the prior one from 457M, 431M, and 390M in the previous forecast to 350M, 310M and 332M in the current forecast in 2016, 2017 and 2018 respectively.

2. These methodological and data sourcing changes had a different effect on the RDT procurement forecast; revised projections point to a rise in RDT procurement in 2017 and 2018, based on trends in increasing use and access to these products. In 2016, the RDT procurement decreases in the current forecast to 257M compared to 278M in the previous forecast. However, there is an increase of 13% and 27% over the previous forecast in 2017 and 2018 respectively (from 267M, 216M in the previous forecast to 303M and 274M in the current forecast in 2017 and 2018 respectively).

3. Forecasted need of ACTs has significantly decreased with the incorporation of more recent estimates of malaria prevalence in sub-Saharan Africa, which show a weighted average prevalence decrease from 30% in the previous forecast to 17% in the current

forecast for the Africa region. The ACT need for 2016 has decreased from 1399M in the previous forecast to 929M in the current forecast.

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 2015 World Malaria Report showed that the portion of children under five with confirmed *P. falciparum* malaria who received an ACT was less than 22% (Figure 3.13, 2015 World Malaria Report). While it is unclear why the remaining 78% of confirmed cases do not receive an ACT, our estimates of approximately 930M 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 32% of the global antimalarial demand. We forecast that this share will grow to 44% by 2019. 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 75% 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.

- 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 as seen in this forecast, any changes or reductions in this program will likely affect the market for QAACTs.

- 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 increase by nearly 18% from 2016 to 2017 (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. We forecast 303M RDTs will be procured in for the public sector 2017, 93% 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. However, a 1:1 test-to-treatment ratio is not sufficient given annual estimates of ~3.9B 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 remain stable 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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