Modeling the Economic Impact of Substandard and Falsified Antimalarials in the Democratic Republic of the Congo

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Abstract. Substandard and falsified medicines pose significant risks to global health, including increased deaths, prolonged treatments, and growing drug resistance. Antimalarials are one of the most common medications to be of poor quality in low- and middle-income countries. We assessed the health and economic impact of substandard and falsified antimalarials for children less than 5 years of age in the Democratic Republic of the Congo, which has one of the world's highest malaria mortality rates. We developed an agent-based model to simulate patient care-seeking behavior and medicine supply chain processes to examine the impact of antimalarial quality in Kinshasa province and Katanga region. We simulated the impact of potential interventions to improve medicinal quality, reduce stockouts, or educate caregivers. We estimated that substandard and falsified antimalarials are responsible for \$20.9 million (35% of \$59.6 million; 95% CI: \$20.7–\$21.2 million) in malaria costs in Kinshasa province and \$130 million (43% of \$301 million; \$129–\$131 million) in malaria costs in the Katanga region annually. If drug resistance to artemisinin were to develop, total annual costs of malaria could increase by \$17.9 million (30%; \$17.7–\$18.0 million) and \$73 million (24%; \$72.2–\$72.8 million) in Kinshasa and Katanga, respectively. Replacing substandard and falsified antimalarials with good quality medicines had a larger impact than interventions that prevented stockouts or educated caregivers. The results highlight the importance of improving access to good quality antimalarials to reduce the burden of malaria and mitigate the development of antimalarial resistance.

INTRODUCTION

Substandard and falsified medicines are a substantial problem in low- and middle-income countries (LMICs), where a recent meta-analysis found 13.6% (95% CI: 11.0–16.3%) of essential medications including 19.1% (15.0–23.3%) of antimalarials to be of poor quality.¹ The World Health Organization (WHO) defines substandard medicines as “authorized medical products that fail to meet their quality standards, specifications, or both.”² Medical products that “deliberately and fraudulently misrepresent their identity, composition, or source” are classified as falsified.² Inadequate supply chain and storage conditions, as well as poor quality or illegal manufacturing, can result in medications that contain no active pharmaceutical ingredients, improper ingredients, or subtherapeutic concentrations of the stated ingredients.^{3–5} Poor-quality medicines introduce risks of prolonged illness, disability, and even death due to treatment failure.² Patients who would otherwise recover with proper treatment remain sick or could experience adverse effects after consuming substandard or falsified medicines. Beyond the individual patient, subtherapeutic doses of medicines increase the risk of drug resistance for entire communities.^{6–8} Falsified medicines with improper ingredients may trigger additional illnesses or create the need for more medical treatment. Over time, poor clinical outcomes associated with substandard and falsified medicines undermine trust in the healthcare system and its legitimate providers.^{6,9}

Treatments for malaria are one of the most commonly found medications to be substandard or falsified in LMICs. These poor-quality malaria medications are estimated to result in between 31,000 and 116,000 additional deaths in sub-Saharan Africa annually, with the large range due to differences in malaria case estimates by the World Malaria Report and the Clinton Health Access Initiative.² Poor-quality antimalarial medicines not only threaten the global progress made toward reducing malaria morbidity and mortality but also risk compromising the effectiveness of medications through antimicrobial resistance.¹⁰ This is particularly concerning in developing countries, where many antimalarials are available without a prescription from a variety of private vendors (e.g., formal and informal pharmacies and street vendors), or are not available in public facilities.¹¹ In addition to the health effects, substandard and falsified antimalarials impose avertable economic costs on already poor patients who face increased morbidity and mortality, and who must use up their limited resources to pay for healthcare out-of-pocket.^{6,12} No studies to date have examined the country-level impact of substandard and falsified antimalarials or simulated the effects of potential interventions to improve malaria medication quality in LMICs.

The Democratic Republic of the Congo (DRC) has one of the world's largest malaria burden with approximately 25 million cases and 46,000 deaths in 2017.¹³ This accounts for an estimated 12% of the malaria cases in sub-Saharan Africa.¹³ Most of these deaths are among children less than 5 years of age.¹⁵ *Plasmodium falciparum* is responsible for nearly 95% of malaria infections in the DRC.¹⁴ Although national guidelines endorsed by the Ministry of Public Health (MOPH) and the National Malaria Control Program recommend artemisinin-based combination therapies (ACTs) for first-line treatment of malaria, alternative treatments are

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TABLE 1
Key model inputs, sources, and assumptions

	Model inputs	Kinshasa province	Katanga region	Source
Demographic and epidemiological data	< 5 population at risk	1,014,632	1,624,934	DHS 2014 ²²
	Malaria incidence (6–59 months old)	0.406	0.923	MAP ²⁵
	Case fatality rate (overall)	0.0152	0.0152	WHO 2016 ²⁴
	With medications	0.0038	0.0038	Estimated
	No medications	0.0304	0.0304	Estimated
	Probability of hospitalization			
	Quality-assured ACTs	0.050	0.050	Estimated
	Non-quality-assured ACTs/other treatments*	0.099	0.099	WHO 2015 ²³
	No treatment	0.199	0.199	Estimated
	Probability of testing	0.391	0.162	DHS 2014 ²²
Healthcare-seeking behavior	Care-seeking behavior (%)			
	Public facilities	5.28	13.09	ACTwatch 2015, ²⁶
	Private practices	6.07	19.76	DHS 2014 ²²
	Pharmacies/drug stores	74.68	49.89	
	Street vendors/hawkers	0.00	0.49	
	Self/neighbors†	6.86	4.94	
	No treatment	7.11	11.82	
Medication stock by facility	Public facilities			ACTwatch 2017 ¹⁶
	% Stock quality-assured ACTs	33.62	57.36	
	% Stock non-quality-assured ACTs	17.24	3.02	
	% Stock other treatments	50.00	39.62	
	Private practices			
	% Stock quality-assured ACTs	15.69	28.83	
	% Stock non-quality-assured ACTs	31.37	17.12	
	% Stock other treatments	54.90	54.05	
	Pharmacies/drug stores			
	% Stock quality-assured ACTs	1.36	20.48	
	% Stock non-quality-assured ACTs	42.65	28.32	
	% Stock other treatments	56.00	51.20	
	Street vendors/hawkers			
	% Stock quality-assured ACTs	0.00	0.00	
	% Stock non-quality-assured ACTs	0.00	0.00	
	% Stock other treatments	100.00	100.00	
	Self/neighbors			
	% Stock quality-assured ACTs	4.00	4.00	Assumption
	% Stock non-quality-assured ACTs	8.00	8.00	Assumption
	% Stock other treatments	88.00	88.00	Assumption
Medication in-stock probabilities	Antimalarial in-stock probabilities (%)			
	Public facilities	0.985	0.980	ACTwatch 2015 ²⁶
	Private practices	0.634	0.721	
	Pharmacies/drug stores	0	0	
	Street vendors/hawkers	0	0	
	Self/neighbor	0	0	
Medication effectiveness	Probability of cure			
	Quality-assured ACTs	0.950	0.950	WHO 2015 ²³
	Non-quality-assured ACTs	0.766	0.700	Estimated
	Other treatments	0.688	0.627	Estimated
	Other treatments (no SF scenario)	0.854	0.851	Estimated
	Other treatments (AMR scenario)	0.561	0.580	Estimated
	No treatment	0.000	0.000	Assumption

(continued)

TABLE 1
Continued

	Model inputs	Kinshasa province	Katanga region	Source
Medication costs by facility†	Public facilities			ACTwatch 2015 ²⁶
	Cost of quality-assured ACTs	\$0.56 (\$0.00–\$1.40)	\$0.56 (\$0.00–\$1.40)	
	Cost of non-quality-assured ACTs	\$0.56 (\$0.00–\$1.40)	\$0.56 (\$0.00–\$1.40)	
	Cost of other treatments	\$0.44 (\$0.33–\$0.55)	\$0.44 (\$0.33–\$0.55)	
	Private facilities			
	Cost of quality-assured ACTs	\$0.00 (\$0.00–\$0.00)	\$0.00 (\$0.00–\$1.10)	
	Cost of non-quality-assured ACTs	\$3.07 (\$1.64–\$4.17)	\$2.19 (\$1.23–\$4.38)	
	Cost of other treatments	\$0.33 (\$0.33–\$0.55)	\$0.33 (\$0.33–\$0.55)	
	Pharmacies/drug stores			
	Cost of quality-assured ACTs	\$6.47 (\$4.93–\$8.77)	\$1.64 (\$1.10–\$2.19)	
	Cost of non-quality-assured ACTs	\$3.84 (\$3.07–\$4.93)	\$4.38 (\$2.19–\$4.93)	
	Cost of other treatments	\$0.44 (\$0.33–\$0.55)	\$0.33 (\$0.33–\$0.55)	
	Street vendors/hawkers			
	Cost of other treatments	\$0.44 (\$0.33–\$0.55)	\$0.33 (\$0.33–\$0.55)	
Non-medication costs	Self/neighbors			Assumption Ilunga-Ilunga 2014 ³⁴ ACTwatch 2015 ²⁶ Kim 2010 ³⁵ World Bank 2015 ³⁶ UN Data 2014 ³⁷
	Cost of all treatments	0	0	
	Cost per hospitalization§	\$150.53 (\$10.83–\$204.68)	\$150.53 (\$10.83–\$204.68)	
	Testing costs	\$1.10 (\$0.55–\$1.10)	\$1.10 (\$0.55–\$1.10)	
	Average transportation costs	\$2.58	\$2.58	
	Productivity loss per sick day	\$1.25	\$1.25	
	Productivity loss per death	\$11,518.47	\$11,518.47	

ACTs = artemisinin-based combination therapies; AMR = antimicrobial resistance; DHS = Demographic and Health Survey; MAP = Malaria Atlas Project; SF = substandard or falsified; UN = United Nations; WHO = World Health Organization.

* Other treatments include artemisinin-containing monotherapies, sulfadoxine-pyrimethamine, and oral quinine.

† The self/neighbor category included medications obtained from friends, personal stores, or reported use of traditional medicines.

‡ All costs with ranges are median costs with the interquartile range. All other costs are means or values calculated from means. All costs are presented in 2017 US dollars.

§ Direct state hospital costs were utilized.

known to comprise more than 50% of the market share in parts of the DRC.^{16,17} In addition, non-quality-assured ACTs and substandard and counterfeit artemisinin derivatives have been found in high prevalence in the DRC, particularly in the private marketplace.^{16,18–20} Our study estimates the health and economic impact that substandard and falsified antimalarials have on children with malaria in the DRC, and examines the effects of potential interventions to inform policy.

MATERIALS AND METHODS

Development of an agent-based model (ABM). We developed an ABM using the NetLogo simulation software (Wilensky, U. Evanston IL, version 6.0) to evaluate the impact of interventions to improve medicinal quality by reducing substandard and falsified medicines in the DRC. Agent-based models can model complex adaptive systems, such as patient care-seeking behavior and medicine supply chain processes that evolve over time.²¹ We simulated the use of antimalarials in two regions in the DRC, Kinshasa province and the region formerly encompassing Katanga province, where antimalarial market data were available from ACTwatch.¹⁶ At the time of our model development, data inputs were obtained from sources citing information from Katanga province, which in 2015 was reorganized into four separate provinces (Tanganyika, Haut-Lomami, Lualaba, and Haut-Katanga). We used epidemiological, demographic, and healthcare-seeking behavior data from the Malaria Atlas Project, the Demographic and Health Survey (DHS), the WHO World Malaria Report, ACTwatch, and other sources to inform key model inputs (Table 1).^{22–25} ACTwatch provided data on antimalarial availability and costs.^{16,26}

Figure 1 presents the structure of our ABM. A one-year time horizon was used for the analysis, divided into 52 one-week

intervals. Each week, children could become ill with malaria based on the regional incidence for children less than 5 years of age.²² Those who fell ill or remained ill from previous weeks underwent simulated care-seeking for malaria treatment. Patients in the model either sought care at one of five types of locations (public facility, private practice, pharmacy/drug store, street vendor/hawker, or neighbor/home/family), or chose not to seek care, based on published data on care-seeking behavior specific to malaria in the DRC.^{22,26} Location of care-seeking is an important driver in the model, as pharmacies and informal drug stores (separate in our model from private sector health practices) play a large role in the distribution of substandard and falsified medicines in the DRC. The model was run for 1,000 modeled children less than 5 years of age in each region. Results are presented for all children less than 5 years of age in Kinshasa province and Katanga region.

Malaria treatment. We simulated each location where children could obtain malaria treatment with stock of medications, including quality-assured ACTs, non-quality-assured ACTs, and other treatments. Other treatments included artemisinin-containing monotherapies, sulfadoxine-pyrimethamine (SP), and oral quinine. Based on the WHO recommendation that quality-assured ACTs should be the first-line treatment in all uncomplicated cases of malaria, we considered quality-assured ACTs as the gold standard.²⁷ When children who sought care visited facilities, they received one of these medications or faced a stockout based on the probability of antimalarial availability at each location. The average probabilities of facilities facing stockouts in our model were based on data collected by the Global Fund to Fight AIDS, Tuberculosis and Malaria on the average number of stockout days for ACTs over a 15-month period across health centers and general reference hospitals in the DRC.²⁸ For

FIGURE 1. The model structure depicting a week in a 52-week care-seeking cycle. This figure appears in color at www.ajtmh.org.

non-quality-assured ACTs and other treatments, the published effectiveness of each medication^{23,29–31} was reduced by the prevalence of substandard and falsified medication from the literature, under the assumption that substandard and falsified medicines were ineffective. For other treatments, we estimated a combined effectiveness of artemisinin-containing monotherapies, SP, and oral quinine adjusted by market share and estimated to be substandard or falsified.²⁶ The prevalence of substandard and falsified medicines was estimated at 19.1% based on a meta-analysis of antimalarial quality.^{18,32} Without medication, it was assumed that there is no parasite clearance and no spontaneous recovery.³³

In our simulation, each modeled child faced a corresponding probability of recovering, remaining ill, or dying based on the type of medication they received.²⁴ Reported overall probability of hospitalization was adjusted for each treatment. The probability of hospitalization with only quality-assured ACTs was assumed to be half the overall rate of hospitalization and the probability of hospitalization with no medication was set at twice the overall rate. The overall reported case fatality rate (CFR) was also adjusted by treatment, where we assumed the CFR without medication was double the average CFR, and with treatment was a quarter of the average CFR.

Economic impact. Throughout each of these steps, the cost of medication and expected transportation costs, testing costs, and hospitalization costs were estimated using a cost-of-illness approach.^{26,34,35} We estimated productivity losses including short-term losses due to caretakers' lost work time as well as long-term productivity losses due to child death from malaria, using the DRC's gross domestic product (GDP) per capita from the World Bank.³⁶ Short-term productivity losses estimated the loss of daily per capita GDP of caretakers, whereas long-term productivity losses projected economic productivity loss of deceased children from age 15 years until life expectancy, discounted to the present value at 3%.^{36,37} We took a patient perspective using data on out-of-pocket costs.^{16,34,35} Transportation costs were converted from 2005 international dollars using purchasing power

parity conversions.³⁸ All costs are presented in 2017 US\$ and rounded to the nearest three digits.

Scenario analyses. We examined two extreme scenarios to help describe the potential effects of SF antimalarials. First, we examined a scenario with no substandard and falsified medicines, in which there is no reduction in treatment efficacy for either ACTs or other treatments due to substandard and falsified medications. In another scenario, we examined the possibility where *P. falciparum* develops drug resistance to artemisinin-based antimalarials. To simulate this, we reduced the effectiveness of both quality-assured and non-quality-assured ACTs to that of other treatments, and made artemisinin monotherapies ineffective to examine the effects.

Finally, we conducted additional scenario analyses to assess the potential impact that various interventions to improve stockouts, antimalarial quality, caregiver education, and healthcare access could have in the DRC. These intervention scenarios included the following: 1) having no antimalarial stockouts in public facilities, 2) having no antimalarial stockouts in private facilities, 3) having no antimalarial stockouts in public and private facilities, 4) replacing other treatments with ACTs such that only ACTs are present in the health system, 5) educating caregivers to select quality-assured ACTs, 6) educating caregivers to select ACTs and reject other treatments if offered, 7) removing all substandard and falsified ACTs in the health system, and 8) getting everyone to seek care. The model was presented to various experts who have worked on malaria and/or in the DRC to help validate the structure, inputs, and assumptions.

RESULTS

We assessed the health and economic burden of malaria in two regions, Kinshasa province and Katanga region, in the DRC (Table 2). Annually, we estimated approximately 1.9 million cases of malaria in children less than 5 years of age in these two regions. This resulted in 260,000 hospitalizations, 25,000 deaths, and 3 million person-weeks of annual malaria

The overall economic impact due to malaria was around \$60 million (95% CI: \$58.2–\$61.0 million) in Kinshasa and \$301 million (95% CI: \$297–\$306 million) in Katanga. Of the costs in Kinshasa, about \$981,000 were attributable to medication costs, \$8.56 million to hospitalization costs, \$181,000 to transportation, and \$30,000 to malaria diagnostic testing. The \$301 million in costs in Katanga included \$2.49 million for drug costs, \$31 million for hospitalization costs, \$2.11 million for transportation, and \$145,000 for malaria diagnostic testing. Productivity losses due to malaria cases per year amounted to \$49.9 million in Kinshasa and \$266 million in Katanga.

We estimated that the emergence of artemisinin resistance could result in 16,200 (28%) more hospitalizations, 178,000 (29%) more person-weeks of annual malaria illness, and 1180 (30%) more deaths in Kinshasa. In Katanga, 50,300 (24%) more hospitalizations, 608,000 more (25%) person-weeks of illness, and 5,100 (24%) more deaths were estimated with antimalarial resistance. Drug resistance increased the overall costs by \$17.9 million (95% CI: \$17.7–\$18.0 million; 30%) in Kinshasa and by \$73 million (95% CI: \$72.2–\$72.8 million; 24%) in Katanga compared with baseline. This included increased productivity losses of \$15.1 million (30%) and \$64 million (24%), as well as increased hospitalization costs of \$2.44 million (28%) and \$7.6 million (24%) in Kinshasa and Katanga, respectively.

Table 3 presents the impact that nine interventions which improve stockouts, antimalarial quality, caregiver education, and healthcare access can have on reducing deaths and overall costs. First, we found that removing substandard and falsified antimalarials has a substantial impact, second only to a scenario of everyone seeking care. Removing substandard and falsified ACTs makes up 55% and 65% of this impact in Kinshasa and Katanga, respectively (\$11.5 million in Kinshasa and \$85 million in Katanga), whereas the rest (\$9.4 million in Kinshasa and \$45 million in Katanga) comes

TABLE 2
Estimated annual health and economic impact of substandard and falsified antimalarials in Kinshasa and Katanga, the Democratic Republic of the Congo*

	Burden of malaria				Difference with better quality antimalarials				Additional costs with antimicrobial resistance				
	Kinshasa province		Katanga region		Kinshasa province		Katanga region		Kinshasa province		Katanga region		
					% Diff	P-value	% Diff	P-value	% Diff	P-value	% Diff	P-value	
Health impact	Malaria cases	412,000	1,500,000		68	0	0.65	0	0.91	-320	0	0.98	0
	Malaria deaths	3,900	21,000		-1,270	-33	< 0.01†	-9,100	-43	1,180	30	< 0.01†	24
	Malaria hospitalizations	57,000	206,000		-35,800	-63	< 0.01†	-128,000	-62	16,200	28	< 0.01†	24
Economic impact	Malaria days of illness	4,310,000	5,600,000		-1,055,000	-24	< 0.01†	-4,890,000	-28	1,250,000	29	< 0.01†	25
	Malaria person-weeks	616,000	2,480,000		-151,000	-24	< 0.01†	-699,000	-28	178,000	29	< 0.01†	25
	Medication costs	\$981,000	\$2,490,000		\$464,000	47	< 0.01†	\$741,000	30	\$282,000	29	< 0.01†	24
	Hospitalization costs	\$8,560,000	\$31,000,000		-\$5,380,000	-63	< 0.01†	-\$19,200,000	-62	\$2,440,000	28	< 0.01†	24
	Healthcare transportation costs	\$181,000	\$2,110,000		-\$44,900	-25	< 0.01†	-\$598,000	-28	\$51,300	28	< 0.01†	24
	Diagnostic costs	\$30,300	\$145,000		-\$7,800	-26	< 0.01†	-\$42,000	-29	\$8,440	28	< 0.01†	24
	Short-term productivity losses	\$5,360,000	\$21,500,000		-\$1,310,000	-24	< 0.01†	-\$6,040,000	-28	\$1,550,000	29	< 0.01†	25
	Long-term productivity losses	\$44,500,000	\$244,000,000		-14,700,000	-33	< 0.01†	-\$105,000,000	-43	\$13,500,000	30	< 0.01†	24
	All productivity losses	\$49,900,000	\$266,000,000		-16,000,000	-32	< 0.01†	-\$111,000,000	-42	\$15,100,000	30	< 0.01†	24
	Total costs	\$59,600,000	\$301,000,000		-\$20,900,000	-35	< 0.01†	-\$130,000,000	-43	\$17,900,000	30	< 0.01†	24

* All estimates are rounded to the nearest three digits. All costs are presented in 2017 US dollars.

+ *P*-value < 0.05.

† P -value < 0.05 .

FIGURE 2. Model snapshot in Netlogo. This figure appears in color at www.ajtmh.org.

from improving the quality of other treatments. If we were able to educate all caregivers to choose quality-assured ACTs or to choose ACTs over other treatments, this reduced the economic impact by \$7.1–\$9.9 million in Kinshasa and by \$82.5–\$97.2 million in Katanga. Following the WHO treatment guidelines of only using ACTs for treatment was estimated to reduce deaths by 759 in Kinshasa and 7,100 in Katanga annually, while decreasing costs by \$7.4 million and \$96.3 million in Kinshasa and Katanga, respectively. Improving stockouts at public and/or private facilities was less effective in reducing the burden of malaria, but still saved substantial costs, especially in Katanga.

DISCUSSION

Substandard and falsified antimalarials threaten the progress made in combatting malaria, as seen in the significant health and economic impact of poor-quality antimalarials in the DRC. We found that providing access to quality-assured ACTs and quality antimalarial treatments could reduce the economic impact of malaria by about 35–43% ($P < 0.01$) and decrease deaths by 33–43% ($P < 0.01$). The emergence of artemisinin resistance, on the other hand, could increase both the number of deaths and overall costs by as much as 24–30% ($P < 0.01$). Such potential costs are important to consider, as resistance to artemisinin-based therapies has already been observed in Asia and could bring significant harm if it develops in parts of Africa, including in the DRC.^{39,40}

Although we based the substandard and falsified antimalarial prevalence at 19.1% based on a meta-analysis specific to antimalarials,¹ a number of studies have examined the quality of medicines in the DRC,⁴¹ including a recent study that found the prevalence of poor-quality antimalarials in Kinshasa to be as high as 62%.⁴² Our estimate on the impact of substandard and falsified antimalarials may therefore be conservative.

While direct comparisons with other models are difficult to make, our results are similar to estimates made by Lubell and

others who modeled the global impact of artemisinin resistance on populations affected by *P. falciparum* malaria.⁴³ Their results showed total direct medical costs for malaria treatment increased by 28% across malaria-endemic countries, whereas our model estimated increases in direct medical treatment costs between 24% in Katanga to 29% in Kinshasa. Although Lubell and others assumed 30% treatment failure based on a study on artesunate resistance in Cambodia,^{43,44} our model used a conservative estimate between 7% and 35% decreased treatment efficacy with artemisinin resistance.

Quality-assured ACTs are the WHO-recommended first-line regimen for treating *P. falciparum* malaria, and national guidelines in the DRC include ACTs (artesunate-amodiaquine) as first-line treatment options for uncomplicated malaria.¹³ Our results illustrate that greater focus should be given to increasing demand and reliable provision of quality-assured ACTs, where non-quality-assured ACTs comprised between 3% and 17% of antimalarials in public facilities, 17% and 31% in private practices, and 28% and 43% in pharmacy and drug stores in Katanga and Kinshasa, respectively.¹⁶ This presents a major opportunity for government and international stakeholders to increase access to quality-assured ACTs. Our results also support the idea that cost differences between quality-assured and non-quality-assured ACTs would likely be offset by the economic impact of having quality ACTs.

The MOPH of the DRC presently contracts out some services to private health facilities to help alleviate the burden on the public healthcare system. Previous studies have reported lower rates of private provider knowledge on appropriate treatment for malaria as compared with public providers.⁴⁵ Our model scenarios in which caregivers are educated to choose quality-assured ACTs or to choose ACTs over other treatments illustrate that this could be effective in reducing the burden of malaria. In addition, our scenario analysis of improving care-seeking shows that educating caregivers of young children with malaria to seek care could significantly decrease the burden and costs of malaria. Although the

TABLE 3
Impact of intervention scenarios to improve health and economic outcomes

Interventions	Kinshasa province					Katanga region				
	Deaths*		Economic impact (in \$ millions)			Deaths*		Economic impact (in \$ millions)		
	No.	P-value	Estimate	95% CI	P-value	No.	P-value	Estimate	95% CI	P-value
Base case	3,860	–	\$59.6	[58.2, 61.0]	–	21,200	–	\$301	[297, 306]	–
Difference from base case										
Drug resistance	1,170	< 0.01†	\$17.9	[17.7, 18.0]	< 0.01†	5,100	< 0.01†	\$73	[72.2, 72.8]	< 0.01†
No public stockouts	44	0.65‡	\$0.5	[0.42, 0.49]	0.66	–177	0.50	–\$2.3	[–2.28, –2.41]	0.44
No public or private stockouts	–422	< 0.01†	–\$5.5	[–5.34, –5.59]	< 0.01†	–5,030	< 0.01†	–\$63.8	[–63.3, –64.3]	< 0.01†
No private stockouts	–487	< 0.01†	–\$6.2	[–6.36, –6.1]	< 0.01†	–4,750	< 0.01†	–\$60.2	[–59.7, –60.7]	< 0.01†
Only ACTs	–759	< 0.01†	–\$7.4	[–7.29, –7.44]	< 0.01†	–7,100	< 0.01†	–\$96.3	[–95.5, –97.1]	< 0.01†
Reject substandard/falsified ACTs	–468	< 0.01†	–\$7.1	[–7.05, –7.23]	< 0.01†	–6,120	< 0.01†	–\$82.5	[–81.9, –83.1]	< 0.01†
Reject other treatments	–750	< 0.01†	–\$9.9	[–9.79, –9.98]	< 0.01†	–7,140	< 0.01†	–\$97.2	[–96.3, –98.0]	< 0.01†
No substandard/falsified ACTs	–1,690	< 0.01†	–\$11.5	[–11.4, –11.7]	< 0.01†	–6,240	< 0.01†	–\$85.0	[–84.2, –85.9]	< 0.01†
No substandard/falsified antimalarials	–1,270	< 0.01†	–\$20.9	[–20.7, –21.2]	< 0.01†	–9,120	< 0.01†	–\$130.0	[–129, –131]	< 0.01†
Everyone seeks care	–578	< 0.01†	–\$20.3	[–20.0, –20.6]	< 0.01†	–13,500	< 0.01†	–\$163.0	[–161, –165]	< 0.01†

ACTs = artemisinin-based combination therapies; CI = confidence intervals.

* Deaths are rounded to the nearest three digits.

† P-value < 0.05.

‡ Because of the low probability of stockouts (1.5%) at public facilities in Kinshasa, we did not observe a statistically significant impact by removing public stockouts.

scenario of getting everyone to seek care may be unrealistic, a large impact could still be observed by incrementally improving care-seeking rates.

Improving stockouts at public or private facilities provided some cost savings, but the benefits were much smaller than other interventions examined. This could be due to the low probability of stockouts at public facilities (1.5%) and low level of care-seeking at public facilities in our model, particularly in Kinshasa (5.28%).²⁶ Records from ACTwatch illustrate that stockouts have improved in these regions of the DRC in recent years.²⁶ However, stockouts due to ineffective stock management were noted as a problem in the past and the occurrence of a large stockout in the future could have much graver health and economic impacts than what these scenarios demonstrate.

This study is a novel first attempt at an ABM to examine the country-level impacts of substandard and falsified antimalarials in a LMIC. With this model, we are able to contribute a baseline assessment of the impact of substandard and falsified antimalarials in two geographic areas of the DRC. As new data become available and as interventions are carried out and evaluated, we will be able to provide updated analyses and better estimates of the impact. However, our model is presently limited by the quality of available data in the DRC, which had several implications. First, although we conducted a rigorous literature search to identify publications to inform our model inputs and also consulted multiple experts, nationally representative data were often unavailable for the DRC. Therefore, our findings represent two regions in the DRC and not for the entire country. Second, this model is not able to capture the heterogeneity in the population because of limited data availability. Each agent in the model has the same malaria incidence, care-seeking rate, and chance of hospitalization and death, where further analysis cannot be conducted to examine the variation within a heterogeneous population. Future research should examine the heterogeneous impact within the population. Third, economic impact presented is from the patient perspective as we were unable to obtain costs

for the health sector. We also assumed the same transportation costs for urban and rural areas because of limited data availability. In addition, the economic impact is likely a conservative estimate, as a high proportion of children in the DRC receive concomitant prescriptions with antimalarials, which was not accounted for in our model.⁴⁶ Fourth, our disease model is based on symptomatic recovery rather than parasite clearance, which may affect transmission patterns and overall health outcomes.⁴⁷ We were also not able to estimate the impact of treatment adherence, as there was little recent data available.⁴⁸ Fifth, our analysis does not distinguish which drugs may have resulted from poor manufacturing versus from product degradation or improper cold-chain management. Rather, drug quality was factored into efficacy stated in the literature, where substandard and falsified antimalarials were assumed not to be effective. Finally, this analysis focused on the benefits of improving the quality of antimalarials and did not estimate the costs of interventions. Future research could examine the costs of these interventions to estimate the return on investment.

Results from this study should be used to help inform policymakers to ensure investments are made in the most effective and efficient ways to decrease the burden of malaria. Interventions may succeed in reducing the health and economic impact of malaria on Congolese families if they focus on providing good quality, efficacious antimalarial regimens in addition to encouraging people to seek good quality treatment and care. Donors and implementation agencies should continue to work with the local government on alleviating barriers to access quality-assured ACTs. The DRC government, including the MOPH, Department of Pharmacy and Medicine (DPM), the National Medicine Supply Program (PNAM), and donors working on reducing, eliminating, and eradicating malaria must invest in improving access to high-quality antimalarial medications. Novel approaches to engage the private sector and improve the quality of antimalarials in the market could help to alleviate malaria burden and associated costs. More data are

needed to improve modeled estimates and examine the impact of substandard and falsified antimalarials for the entire country.

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