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# Interventions for an Artemisinin-based Malaria Medicine Supply Chain

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Artemisinin combination therapy, the most effective malaria treatment today, is manufactured from an agriculturally derived starting material *Artemisia annua*. Artemisinin, the main ingredient in malaria medicines, is extracted from Artemisia leaves and used in the production of medicine for treating malaria. The artemisinin market has witnessed high volatility in the supply and price of artemisinin extract. A large fraction of malaria medicines for endemic countries in sub-Saharan Africa is financed by the Global Fund to Fight AIDS, TB, and Malaria and the US President's Malaria Initiative. These agencies together with the World Health Organization, UNITAID, the United Kingdom Department for International Development and the Bill and Melinda Gates Foundation are exploring ways to increase the level of artemisinin production, reduce volatility of artemisinin prices, and improve overall access to malaria medicines for the population. We develop a model of the supply chain, calibrate the model using field data, and investigate the impact of various interventions. Our model shows that initiatives aimed at improving average yield, creating a support-price for agricultural artemisinin, and a larger and carefully managed supply of semi-synthetic artemisinin have the greatest potential for improving supply and reducing price volatility of artemisinin-based malaria medicine.

*Key words:* malaria; health care; supply and demand uncertainty.
*History*: Received: November 2014; Accepted: March 2016 by Edward Anderson, after 1 revision.

## 1. Introduction

The World Health Organization (WHO) reports that there were about 219 million cases of malaria in 2012 leading to at least 660,000 deaths (WHO 2012). The vast majority of these deaths, corresponding to 90%, occur in sub-Saharan Africa, and a large fraction of them are children under five, pregnant women, and malnourished people. Malaria continues to be one of the most deadly diseases, calling for immediate attention from governments, pharmaceutical companies, and aid organizations.

Due to significant levels of resistance against the widely used drugs such as chloroquine and sulfadoxine pyrimethamine (SP), WHO has been recommending artemisinin combination therapy (ACT) as the first-line treatment for uncomplicated *Plasmodium falciparum* malaria since April 2002 (WHO 2012). Today, eighty-four countries and territories in Africa utilize ACT as its first-line treatment of the disease. Unlike previously used drugs to treat malaria such as chloroquine and SP, ACTs are manufactured from a starting material derived from a plant, *Artemisia annua*; one of the artemisinin derivatives (artemether, artesunate, or dihydroartemisinin) is combined with another antimalarial compound such as lumefantrine, amodiaquine, or piperaquine in order to obtain ACT. There are eleven companies approved by the WHO to manufacture ACTs.

Who pays for malaria treatment? Given that a large fraction of people who get malaria cannot afford to pay for the cost of treatment using ACT (which is approximately $2 per adult treatment) and there are no health insurance systems, treatments are often provided free by their governments in government-run clinics. However, most malaria-endemic countries are low-income countries and have to rely on international donor support to purchase malaria treatments for their population. The majority of ACTs are financed by international agencies, most notably the Global Fund to Fight AIDS, TB, and Malaria and the US President's Malaria Initiative. Some patients seek treatment in the private sector and pay for malaria medicines out of pocket.

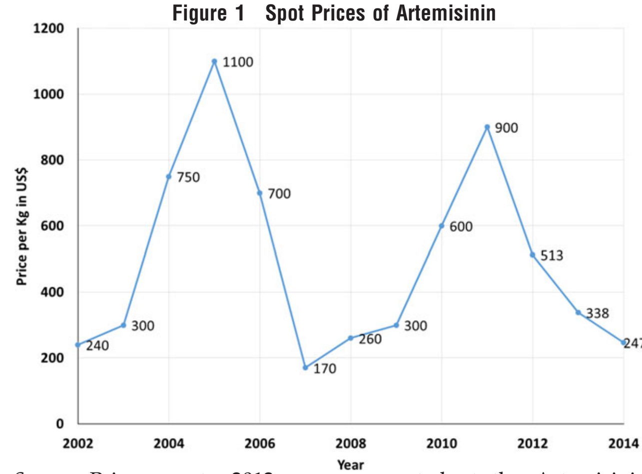
Our work responds to the needs of multilateral agencies and philanthropic organizations that are considering and pursuing interventions that affect the availability and price of ACTs and its main ingredient artemisinin. These organizations would like to know where to invest their time and effort in order to create the highest positive impact in treating malaria.

We next describe the artemisinin supply chain, and begin our discussion with supply uncertainty in the cultivation and harvesting process. Artemisia grows primarily in China, Vietnam, and East Africa due to the specific climatic conditions required for its cultivation. China and Vietnam produce over 80% of the global supply of Artemisia with the balance produced in East Africa (Shretta and Yadav 2012). Most Artemisia is grown by small farmers in plot sizes that average less than 1 hectar. It takes about eight months for the Artemisia plant to reach full growth. Upon harvest, dried Artemisia leaves are collected and sent for chemical extraction to obtain artemisinin. The per hectare yield of Artemisia leaves varies considerably from one farm plot to another, and also from year to year due to rainfall, climate, and other environmental factors. In addition, the artemisinin content in the leaves varies considerably with artemisinin content as low as 0.1% and as high as 1.2% observed in the past. Some of this depends on the variety of seeds used and also the timing of harvesting and bagging leaves relative to their flowering. Uncertainty in the yield of Artemisia leaves per hectare of cultivation and then uncertainty in the kilograms of artemisinin extracted per kilogram of dried leaves together contribute to a high level of yield uncertainty for artemisinin; and collectively, they constitute supply uncertainty in the artemisinin supply chain.

Using Coartem®, the ACT from Novartis, Spar and Delacey (2008) and Spar (2008) demonstrate that the lack of supply creates significant price increases. Kindermans et al. (2007) show that the plantation of Artemisia exhibit significant fluctuations from year to year. As demonstrated in Kindermans et al. (2007), Schoofs (2008), as well as in our Figure 1, supply fluctuations contribute to price fluctuations for the main ingredient, artemisinin, for ACT. Low supply of artemisinin in 2005 caused the bulk price to go up to \$1100/kg, and excess supply decreased the bulk price to as low as \$170/kg in 2007.

Farmers grow Artemisia if they have reasonable expectations that they will be able to sell the dried leaves at a profitable price after the harvest. In making this decision, they compare the prices obtained for Artemisia leaves with prices for other cash crops they can grow such as paddy/rice and corn. Thus, the outside option plays a crucial role in the farmers' decisions regarding whether to grow Artemisia or an alternative crop. In sum, farmers' behavior can create further supply and price fluctuations for the end-product.

**Figure 1 Spot Prices of Artemisinin**




*Source:* Prices up to 2012 are as reported at the Artemisinin Conference in Hanoi in November 2011. Prices for 2012, 2013 and 2014 are 12 month average of monthly median prices as estimated by William Davidson Institute (WDI) from data on export and import of artemisinin.

In addition to supply uncertainty, another challenge in the artemisinin supply chain is demand uncertainty. The challenges in predicting the demand for ACT have been highlighted by Kindermans et al. (2007) and Shretta and Yadav (2012). Shretta and Yadav (2012) report that Kenya experienced the worst drought in 60 years and when the rains returned it resulted in malaria outbreaks and widespread demand for malaria medicine. In addition to the natural disasters such as the one in Kenya, Steketee and Campbell (2010) and SPS (2012) report that one of the factors contributing to an increased level of uncertainty is the lack of diagnostic testing and lack of proper record keeping for diagnosis and treatment. Because the information regarding the needs are not transmitting back to the upstream in the malaria-medicine supply chain, both studies claim that the demand for ACT is extremely difficult to predict, and therefore, demand uncertainty must be incorporated into the analysis of the artemisinin supply chain.

Demand for ACTs is also influenced by price fluctuations. Despite the provision of free medicines in government-run clinics, many patients continue to seek treatment in private sector clinics, drug shops, and pharmacies due to greater convenience and higher availability. When the price of the drug is more than a patient's willingness to pay, they purchase malaria medicines that are substandard or inefficacious (Arrow et al. 2004). The overall demand for ACT is thus sensitive to the price at which the manufacturers sell the product. In recognition of this access channel, a pilot project to subsidize the cost of ACT in the private sector was implemented in 2009 (Adeyi and Atun 2010). However, this project was only carried out for a limited time and in select countries. The price in the private sector remains to be a key barrier for patients.

The uncertainties in supply and demand have created a cycle of ups and downs in the price of artemisinin and mismatches between the Artemisia cultivated and its need. A key challenge for matching supply and demand is the long lead-time (between 14 and 18 months) between the planting of Artemisia and the completion of the final manufacture of the ACTs (Shretta and Yadav 2012). In order to reduce the uncertainty associated with artemisinin prices, larger manufacturers of ACTs engage in forward contracts with extractors for a portion of their volume. These forward contracts specify a price and quantity of artemisinin they will purchase at a future point in time. Smaller manufacturers claim that demand uncertainties, lack of capital, and inability to enforce contracts limit them from engaging in forward contracts with artemisinin extractors. Rather, they purchase most of their artemisinin supplies from the spot market and continue to operate under price uncertainty. Without forward contracts, the Artemisia growers and extractors have to plan their supply based on an uncertain market demand (in addition to yield uncertainty) which is almost two years into the future.

While such ups and downs are observed in many markets with demand and supply uncertainty, the malaria-medicine market serves a larger social and public health goal where increases in consumption create a benefit externality. Because fluctuations in the artemisinin price and the uncertainty in supply and demand of artemisinin impact both the price and availability of ACTs for end patients, organizations such as the Bill and Melinda Gates Foundation, UNITAID, Clinton Health Access Initiative (CHAI), Global Fund to fight AIDS, TB and Malaria, and the UK Department for International Development have started focusing on this issue. In particular, these organizations explore if certain investments/interventions can improve outcomes in terms of availability and price.

One intervention that has been attempted focused on stabilizing prices through voluntary price agreements. In July 2008, the Clinton Foundation entered into an agreement with several Chinese and Indian manufacturers that would set price ceilings and help stabilize ACT prices (Schoofs 2008). Another intervention focused on increasing the usage of forward contracts. In 2009 UNITAID funded an initiative called Assured Artemisinin Supply Services (A2S2) based on a tripartite financing model (A2S2 2012). Under this model, extractors who had existing contracts with WHO-prequalified ACT manufacturers received loan-based pre-financing. The idea was that front-loading the financing would help increase supply and create "fair prices" on the market and would incentivize those ACT manufacturers who do not currently engage in forward contracts to start doing so. However, neither intervention has successfully stabilized prices (Shretta and Yadav 2012, UNITAID 2011). These somewhat ad hoc interventions have targeted the commonly observed symptoms and their immediate causes without addressing the underlying root causes of artemisinin price and supply volatility. Concerns about artemisinin prices soaring and supply being insufficient were again raised in 2011 (RBM/UNITAID/WHO 2011).

A third intervention, that is ongoing, targeted the development of a non-plant-based source for artemisinin. With financial support from the Bill & Melinda Gates Foundation, a research group at the University of California-Berkeley and Institute for One World Health has developed a semi-synthetic source of artemisinin that may help stabilize the price of artemisinin (Hale et al. 2007). While commercial-scale manufacturing of semi-synthetic artemisinin from this project is just beginning (Paddon and Keasling 2014, Reuters 2014), it is unlikely to resolve all the problems in the short- to medium-term because the initial capacity will only be a small fraction of the total artemisinin supply. Some argue that a larger supply of semi-synthetic artemisinin could disrupt an already volatile market as agricultural production may decrease more than the increase in semi-synthetic (Peplow 2013, Van Noordan 2010).

In this study, we develop a model of the supply chain that captures the effects of such factors as available farm space, farmer's self-interest, volatility in crop yield, volatility in demand, and the introduction of semi-synthetic artemisinin on such measures as the level and volatility of medicine price and supply. We calibrate the parameters and functions of our model, using data from the field and we investigate the impact of various interventions. Some of these interventions are under consideration by the global agencies and others are new areas of focus that are exposed through our analysis. Our main conclusions are that initiatives aimed at improving average yield, creating a support-price for agricultural artemisinin, and a larger, but carefully managed supply of semi-synthetic artemisinin have the greatest potential for improving supply and reducing price volatility of artemisinin-based malaria medicine.

## 2. Related Literature

Shretta and Yadav (2012) provide a comprehensive summary of the challenges in the artemisinin supply chain, describing the interactions between price fluctuations in artemisinin, demand uncertainty in ACT treatments. Dalrymple (2012) provides a historical account of the development and use of artemisinin-based malaria medicines and also provides an introduction to the vast array of literature available on artemisinin. Taylor and Xiao (2014) examine the merits of subsidizing retail purchases vs. retail sales in malaria medicine distribution channels, and report that donors should focus on purchase subsidies rather than sales subsidies.

Both supply and demand uncertainty have found wide examination in the operations and supply chain literature. Supply uncertainty, in the form of yield uncertainty, has received extensive consideration in the context of production planning problems. Yano and Lee (1995) provide a comprehensive review of studies that feature yield uncertainty. Rajaram and Karmarkar (2002), Galbreth and Blackburn (2006), and Gupta and Cooper (2005) examine yield uncertainty in the process industries. Tomlin and Wang (2008) and Noparumpa et al. (2016) examine co-production and pricing flexibilities under yield uncertainty.

Yield uncertainty is a widely recognized concern in agricultural supply chains. Jones et al. (2001) examine the opportunity to diversify production through the use of alternate growing seasons for a hybrid seed corn experiencing yield uncertainty in both growing regions. Burer et al. (2009) extend this work by incorporating supply chain coordination decisions. Blackburn and Scudder (2009) examine the risk of producing and distributing fresh produce. Using the olive oil industry, Kazaz (2004) introduces yield-dependent cost and revenue structure with one main supplier who experiences yield uncertainty and a contingency supplier whose price increases with lower yield. Kazaz and Webster (2011) show the negative implications of ignoring the impact of supply risk on leasing, purchasing, and pricing decisions. Li and Zheng (2006) and Tang and Yin (2007) study joint pricing and quantity decisions under supply uncertainty. Kazaz and Webster (2015) examine joint pricing and leasing decisions under supply and demand risk, and show how characteristically supply risk leads to different results than demand risk in the presence of a single source. The setting with one reliable contingency supplier is examined in Tomlin (2009), and the setting with multiple suppliers in Tomlin and Wang (2005), Dada et al. (2007), and Federgruen and Yang (2008). Huh and Lall (2013) study the impact of rainfall uncertainty on irrigation and crop choice decisions. While this literature extensively focuses on maximizing firm profits, our study differs from these publications by investigating the influence of yield uncertainty in public concerns.

Our study makes two main contributions to the supply chain literature. First, we examine a novel problem and develop a unique model that (1) extends the literature on uncertain yield and uncertain demand, and (2) deviates from the common performance measure of firm-level profit or utility. We analyze a public-policy problem for which multiple measures are important (e.g., social welfare, supplier welfare, manufacturer welfare). We develop and refine our model through an extensive data gathering process, including interactions with those who are actively working in this area at UNITAID, CHAI, and the Gates Foundation. Our model contains features that other researchers addressing public-policy questions may build upon.

Second, our study extends the literature by examining the impact of interventions to improve supply chain performance where a key raw material has yield uncertainty and the end product demand is uncertain. To the best of our knowledge, interventions in the artemisinin supply chain have not been explicitly analyzed before. Such analyses matter not only to the rich context considered in this study but more generally to other products such as medicinal plants. Vaccines and other such products also have uncertain yield and uncertain demand, and may benefit from a similar analysis to understand what supply chain interventions enhance social welfare the most.

## 3. Model

### 3.1. Overview

We begin with a high-level description of our artemisinin supply chain model. There are two levels in this model. Level 2 corresponds to farmers (hereinafter referred to as suppliers) and level 1 corresponds to the ACT manufacturers. While farmers and extractors are separate entities, the relevant decisions are adequately captured by treating artemisinin suppliers as a single unit.

Suppliers decide whether to produce Artemisia or the best alternative to Artemisia. The amount of farm space dedicated to Artemisia is positively influenced by the expected value of the artemisinin spot price and, due to supplier risk aversion, is negatively influenced by its variance. The volatility of the spot price is influenced by the degree of volatility in the harvest yield and in the size of the market. Price is assured for units under forward contract. The forward contract price is aligned with the expected spot price.

Artemisinin not under contract is sold in the open market, and as such, the spot price reflects the market clearing price. Accordingly, there is a negative relationship between the fraction of growing capacity dedicated to Artemisia and the expected spot price (e.g., the higher the supply, the lower the spot price).

**Figure 2 Schematic of Our Model of the Artemisinin Supply Chain**

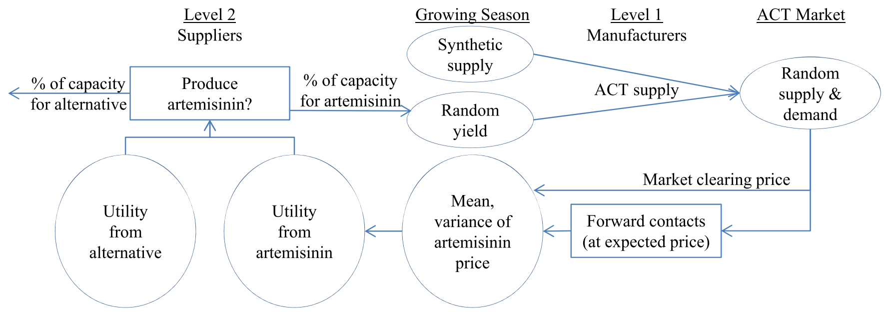



Figure 2 illustrates decisions, processes, and relationships in our model of the artemisinin supply chain.

### 3.2. Equilibrium Condition

Let $q$ denote the amount of farm space dedicated to producing artemisinin in an upcoming growing season. The random market-clearing price of artemisinin after a season's harvest of Artemisia (and prior to the next harvest) is $P(q)$ with moments denoted as

$$\bar{p}(q) = E[P(q)]$$

$$\sigma_P^2(q) = V[P(q)].$$

We abstract away the manufacturer's production cost and profit margin, so $P(q)$ is also the random price of ACT. In the next section, we introduce two models that define how the probability distribution of $P(q)$ is affected by various parameters.

Let $s$ denote the quantity of semi-synthetic artemisinin introduced to the market. Semi-synthetic artemisinin is not subject to yield uncertainty. Describing the expected yield from each unit of farm space with $\mu_2$, the random organic artemisinin yield is expressed as

$$Q = q\mu_2 Z_2, \tag{1}$$

where $Z_2$ is a positive random variable with cdf $\Phi_2$, mean 1, and variance $\sigma_2^2$. The term $q\mu_2$ is the expected amount of artemisinin from farming $q$ units of farm space. Combining equation (1) with the amount of semi-synthetic artemisinin production $s$ yields the overall random artemisinin supply $q\mu_2 Z_2 + s$. The mean artemisinin supply is $q\mu_2 + s$.

As noted in section 1, some manufacturers offer forward contracts that specify a price and quantity of artemisinin they will purchase at a future point in time. And some extractors establish forward price contracts with farmers prior to the growing season in order to obtain sufficient supply. These forward contracts specify the price for the farmer's harvested crop. Let $\alpha$ denote the fraction of farm space dedicated to producing artemisinin that is under forward contract. The forward contract price is set to match the expected spot price $\bar{p}(q)$.

Let $c$ denote the amount of farm space owned by all suppliers who could produce artemisinin. The owners of $c$ units of farm space have alternatives to producing artemisinin. Let $U_b$ denote the utility of the best alternative associated with a randomly selected unit of farm space. The cdf of $U_b$ is $\rho_b(u)$ and its mean is $\mu_b$.

We model the utility per unit of space dedicated to producing artemisinin of a representative supplier[1] as the product of two terms: (1) expected yield per unit of farm space, and (2) the utility per unit of artemisinin, which is governed by a mean-variance utility function, i.e., $u_a = \mu_2 \times \left(\bar{p}(q) - \gamma\sigma_P^2(q)\right)$.

The parameter $\gamma \geq 0$ is a measure of risk aversion, that is, the higher the value of $\gamma$, the higher the risk aversion; if $\gamma = 0$, then suppliers are risk neutral. We see that utility is increasing in average yield ($\mu_2$) and average price ($\bar{p}(q)$), and is decreasing in price variance ($\sigma_P^2(q)$) with the rate of decrease controlled by the risk-aversion parameter ($\gamma$). Note that the utility of producing artemisinin associated with a unit of space under contract is $\mu_2\bar{p}(q)$ (i.e., by the terms of the forward contract, there is no variance in the price).

Let $U_{b0}$ denote the random utility of the best alternative associated with a unit of farm space under forward contract. We define $U_{b0}$ as $U_b$ conditioned on the utility of the best alternative being less than the utility of artemisinin under contract, that is, the utilities associated with units of space under contract are representative of the population (conditioned on a preference for artemisinin over the best alternative). Accordingly, the cdf of $U_{b0} = U_b | U_b \leq \mu_2\bar{p}(q)$ is

$$\begin{aligned}\rho_{b0}(u) &= P[U_{b0} \leq u] = P[U_b \leq u | U_b \leq \mu_2\bar{p}(q)] \\ &= \frac{\rho_b(u)}{\rho_b(\mu_2\bar{p}(q))} \\ &\text{for all} \quad u \leq \mu_2\bar{p}(q).\end{aligned} \tag{2}$$

We are now ready to identify a condition for the value of $q$ in equilibrium. For a given $q$, the amount of farm space not under contract that is dedicated to producing artemisinin is

$$q - \alpha q. \tag{3}$$

And, for a given $q$, the amount of farm space not under contract with utility of the best alternative no more than the utility of producing artemisinin is

$$c\rho_b(u_a) - \alpha q \rho_{b0}(u_a) = \rho_b\left(\mu_2\left(\bar{p}(q) - \gamma\sigma_P^2(q)\right)\right)\left(c - \frac{\alpha q}{\rho_b(\mu_2 \bar{p}(q))}\right) \tag{4}$$

(see equation (2)), that is, the total farm space with $U_b \le u_a$ is reduced by the amount of farm space with $U_b \le u_a$ that is under contract. Equilibrium can be found by setting equation (3) equal to equation (4) and solving for $q$.

$$F(q^*) \equiv \frac{1-\alpha}{\frac{c}{q^*} - \frac{\alpha}{\rho_b(\mu_2 \bar{p}(q^*))}} - \rho_b\left(\mu_2\left(\bar{p}(q^*) - \gamma\sigma_P^2(q^*)\right)\right) = 0.^2 \tag{5}$$

We note that the equilibrium condition given in equation (5) has a simple interpretation when suppliers are risk neutral, that is, if $\gamma = 0$, then equation (5) reduces to

$$q^* = c\rho_b(\mu_2 \bar{p}(q^*)). \tag{6}$$

The above expression says that the farm space dedicated to producing artemisinin is the fraction of capacity with utility of the best alternative no more than the expected revenue per unit of farm space.

Figure 3 illustrates the curves associated with equations (3) and (4), and the associated equilibrium point. Note that equation (3) is increasing in $q$. For any realization of supply and demand random variables, it follows from the market-clearing property that the spot price is decreasing in $q$, which implies that the expected spot price is decreasing in $q$, that is,

$$\bar{p}'(q) < 0. \tag{7}$$

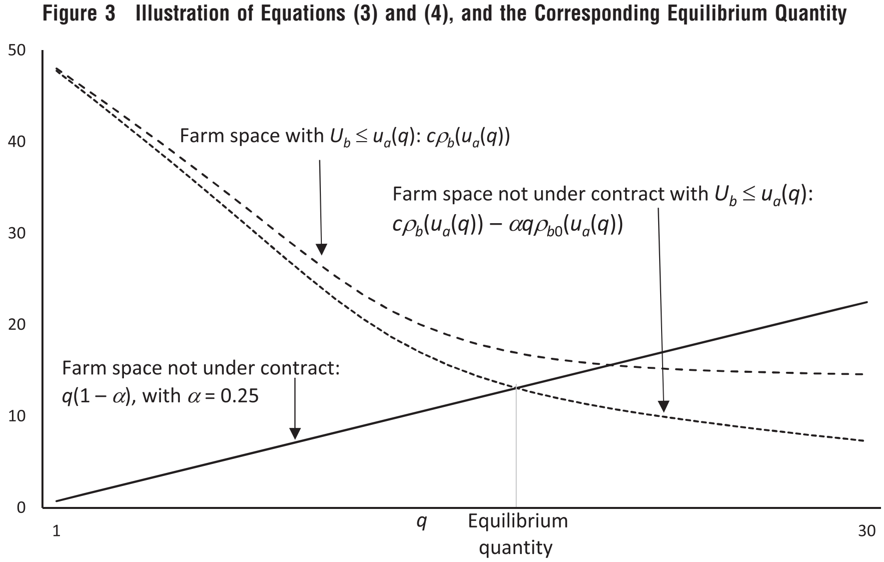
If utility $u_a$ does not increase as $q$ increases, that is,

$$\frac{d}{dq}\left(\mu_2\left(\bar{p}(q) - \gamma\sigma_P^2(q)\right)\right) \le 0, \tag{8}$$

then equation (4) is decreasing in $q$ (i.e., the right-hand side of equation (4) is the product of two positive terms that are both decreasing in $q$), and thus equation (8) is a sufficient condition for a unique equilibrium.

We emphasize that our model is static in the sense that it predicts the farm space dedicated to producing artemisinin as the system settles into equilibrium. We do not capture the dynamics of behavior in interim. Our model assumes that a supplier's decision to enter the market is based on the mean and variance of market price that suppliers are not biased in their estimates of these measures, and that suppliers, in equilibrium, do not move in and out of the market in response to random market fluctuations. As a step towards an understanding of possible interventions in the complex real-world system, our goal is to strike a balance of modeling the system with enough richness to capture the essence of how elements interact to affect performance while avoiding excess complexity that may lead to brittleness in behavior (e.g., small changes in model settings generate large changes in results). In section 5, we consider how the inclusion of dynamics and decision-making biases may affect our conclusions.

**Figure 3 Illustration of Equations (3) and (4), and the Corresponding Equilibrium Quantity**



### 3.3. Two Models of Price-Dependent Demand

The random ACT market size (e.g., number of malaria cases) is

$$M = \mu_1 Z_1,$$

where $\mu_1$ is the expected ACT market size and $Z_1$ is a positive random variable with cdf $\Phi_1$, mean 1, and variance $\sigma_1^2$. We assume that $Z_1$ is independent of the yield random variable $Z_2$. This assumption is a reasonable approximation of reality in our setting where more than 90% of *P. falciparum* malaria treated by ACTs occurs in sub-Saharan Africa and more than 80% of Artemisia growing regions are located in Asia, for example, a drought in southeast Asia is largely independent of rainfall patterns (and hence malaria) in sub-Saharan Africa. In addition, weather patterns that affect the yield at harvest time occur much earlier than when the drug from the harvest becomes available to serve market needs (influenced by much more recent weather patterns).

We consider two price-dependent demand models in our analyses:

$$M1\colon d(p) = M\rho_1(p)$$

$$M2\colon d(p) = bp^{-1}.$$

For example, $\rho_1(p)$ is the fraction of the market willing to pay price $p$ or more. The models reflect two opposing interpretations of the role of market size on demand:

M1. The fraction of the market willing to purchase at price $p$, $\rho_1(p)$, is independent of the market size $M$.
M2. The total volume purchased at price $p$ is independent of the market size $M$.

Model M1 is motivated by a setting where the market is composed of many individual buyers who purchase ACT if willing/able to pay the market price. Model M2 is motivated by a setting where the market is composed of a few buyers (e.g., NGOs and international agencies) who spend a fixed total budget, $b$, on whatever supply is available. The result is an isoelastic demand function. M1 is likely a better fit in regions where most patients seek treatment in the private sector. M2 is likely a better fit in regions where most patients seek treatment in the government or NGO-run health clinics; governments or NGOs have a fixed budget for purchasing malaria medicines for a given year. We examine measures of performance under each of these models individually. These models allow for more detailed characterizations of behavior than what could be obtained from a more complex demand model, and such characterizations are likely to span the behavior of a system with demand that is a composite of M1 and M2.

We now turn our attention to the form of the random spot price function $P(q)$ under these two demand models, beginning with M1. We consider the impact of a price-support intervention. For this intervention, one or more organizations such as NGOs agree to pay a minimum price of $p_0$, effectively assuring that the market-clearing price will not drop below the support-price $p_0$. We assume that the willingness-to-pay function $\rho_1(p) \in [0, 1]$ is strictly decreasing in price over the range of possible price realizations. Thus, we can invert $\rho_1(p)$ to obtain expressions for the random market-clearing price and its moments (i.e., set supply $q\mu_2 Z_2 + s$ equal to demand $\mu_1 Z_1 \rho_1$, solve for $\rho_1$, then invert $\rho_1(p)$ while accounting for the restrictions of $\rho_1 \in [0, 1]$ and $p \geq p_0$),

$$M1\colon P(q) = \max\left\{\rho_1^{-1}\left(\min\left\{\frac{q\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right), p_0\right\}, \quad (9)$$

$$\bar{p}(q) = E\left[\max\left\{\rho_1^{-1}\left(\min\left\{\frac{q\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right), p_0\right\}\right], \quad (10)$$

$$\sigma_P^2(q) = V\left[\max\left\{\rho_1^{-1}\left(\min\left\{\frac{q\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right), p_0\right\}\right].$$

For M2, we follow a similar approach,

$$M2\colon P(q) = \max\left\{\frac{b}{q\mu_2 Z_2 + s}, p_0\right\}$$

$$\bar{p}(q) = E\left[\max\left\{\frac{b}{q\mu_2 Z_2 + s}, p_0\right\}\right], \quad (11)$$

$$\sigma_P^2(q) = V\left[\max\left\{\frac{b}{q\mu_2 Z_2 + s}, p_0\right\}\right].$$

### 3.4. Performance Measures

In this section, we introduce measures of performance relevant to the manufacturer, society, and supplier. The expected artemisinin volume in equilibrium is

$$\pi_1 = E[q^*\mu_2 Z_2] + s = q^*\mu_2 + s,$$

which is a measure of the manufacturer's welfare. As an indicator of the availability of the drug for treatment, $\pi_1$ is also a measure of public health. An alternative measure of public health is the expected fraction of total need that is satisfied, or fill rate,

$$\beta = E\left[\min\left\{\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right].$$

Recall that $U_{b0} = U_b | U_b \le \mu_2 \bar{p}(q)$ and that the cdf of $U_{b0}$ is $\rho_{b0}(u) = \rho_b(u)/\rho_b(\mu_2 \bar{p}(q))$. Accordingly, the supplier surplus associated with $\alpha q^*$ units under contract at price $\bar{p}(q^*)$ is

$$\alpha q^* \int_{-\infty}^{\mu_2 \bar{p}(q^*)} (\mu_2 \bar{p}(q^*) - t) \frac{\rho_b{}'(t)}{\rho_b(\mu_2 \bar{p}(q^*))} dt = \alpha q^* \int_{-\infty}^{\mu_2 \bar{p}(q^*)} \frac{\rho_b(t)}{\rho_b(\mu_2 \bar{p}(q^*))} dt.$$

The cdf of the utility of the best alternative after units under contract are removed from the population is as follows:

$$\rho_{b\backslash 0}(u) = \begin{cases} \frac{c\rho_b(u) - \frac{\alpha q^* \rho_b(u)}{\rho_b(\mu_2 \bar{p}(q^*))}}{c - \alpha q^*}, & u \le \mu_2 \bar{p}(q^*) \\ \rho_b(u), & u \ge \mu_2 \bar{p}(q^*) \end{cases} \tag{12}$$

(obtained by dividing equation (4) by the number of units remaining in the population after removing units under contract). Thus, the supplier surplus associated with units not under contract is as follows:

$$\begin{aligned}(c - \alpha q^*) & \int_{-\infty}^{\mu_2 (\bar{p}(q^*) - \gamma \sigma^2(q^*))} \rho_{b\backslash 0}(t) dt \\ &= \left(c - \frac{\alpha q^*}{\rho_b(\mu_2 \bar{p}(q^*))}\right) \int_{-\infty}^{\mu_2 (\bar{p}(q^*) - \gamma \sigma^2(q^*))} \rho_b(t) dt \\ &= q^*(1-\alpha) \int_{-\infty}^{\mu_2 (\bar{p}(q^*) - \gamma \sigma^2(q^*))} \frac{\rho_b(t)}{\rho_b\left(\mu_2\left(\bar{p}(q^*) - \gamma \sigma_p^2(q^*)\right)\right)} dt\end{aligned}$$

(the first equality follows from equation (12); the second equality follows from equation (5)). Summing the above expressions, the total supplier surplus is

$$\begin{aligned}\pi_2 &= q^* \left[ \alpha \int_{-\infty}^{\mu_2 \bar{p}(q^*)} \frac{\rho_b(t)}{\rho_b(\mu_2 \bar{p}(q^*))} dt + (1-\alpha) \int_{-\infty}^{\mu_2 (\bar{p}(q^*) - \gamma \sigma^2(q^*))} \frac{\rho_b(t)}{\rho_b\left(\mu_2\left(\bar{p}(q^*) - \gamma \sigma_p^2(q^*)\right)\right)} dt \right] \\ &= q^* \left[ \frac{\alpha}{\rho_b(\mu_2 \bar{p}(q^*))} E\left[(\mu_2 \bar{p}(q^*) - U_b)^+\right] + \frac{1-\alpha}{\rho_b\left(\mu_2\left(\bar{p}(q^*) - \gamma \sigma_p^2(q^*)\right)\right)} E\left[\left(\mu_2 (\bar{p}(q^*) - \gamma \sigma^2(q^*)) - U_b\right)^+\right] \right].\end{aligned}$$

If $U_b$ is uniform on $[u_L, u_H]$, for example, then

$$\pi_2 = \frac{q^*}{2(u_H - u_L)} \left[ \alpha \frac{(\mu_2 \bar{p}(q^*) - u_L)^2}{\rho_b(\mu_2 \bar{p}(q^*))} + (1-\alpha) \frac{\left(\mu_2\left(\bar{p}(q^*) - \gamma \sigma_p^2(q^*)\right) - u_L\right)^2}{\rho_b\left(\mu_2\left(\bar{p}(q^*) - \gamma \sigma_p^2(q^*)\right)\right)} \right].$$

# 4. Analysis

This section presents analysis of the preceding model. The analysis proceeds along the following sequence. We first investigate the impact of changes in parameter values on measures of performance analytically (directional impact). We then conduct numerical analysis using a calibrated model. We offer interpretations of our results and discuss limitations. Section 5 summarizes the main implications of our results for policy makers.

In order to help reinforce the connection between our model, its purpose, and the real-world supply chain, we provide a few examples of interventions with changes in relevant parameters in Table 1.

### 4.1. Directional Effects of Increasing Parameter Values on $q^*$ and $\pi_1$

Table 2 contains comparative-static results for $q^*$ and $\pi_1$ given that suppliers are risk neutral (see section A3 in Appendix A for derivations and proofs). The

**Table 1 Examples of Interventions to Induce Different Types of Change**

| Example intervention | Change |
|---|---|
| Increase availability of high-yield seed varieties | Increased yield per unit of farm space ($\mu_2\uparrow$) |
| Increase supply of competing crops in regions not conducive to growing Artemisia | Reduced attractiveness of alternative crops ($\mu_b\downarrow$) |
| Increase malaria prevention efforts | Reduced market size ($\mu_1\downarrow$) |
| Assure that price will not drop below a threshold | Introduce a price support ($p_0\uparrow$) |
| Training/education/resources in regions that are underutilized yet conducive to growing Artemisia | Increased available farm space ($c\uparrow$) |
| Increase investment in semi-synthetic production | Increased semi-synthetic supply ($s\uparrow$) |
| Increase spending on ACT | Increased purchase budgets ($b\uparrow$) |
| Provide low-cost loans to farmers in the event of low yield | Reduced supplier risk aversion ($\gamma\downarrow$) |
| Increase availability of disease-resistant seed varieties | Reduced yield variability ($\sigma_2\downarrow$) |
| Improve and increase documentation in diagnostic testing and treatment | Reduced market uncertainty ($\sigma_1\downarrow$) |
| Provide low-cost loans for up-front partial payment in forward contracts | Increased usage of forward contracts ($\alpha\uparrow$) |

**Table 2 Directional Effects of Increases in Different Parameter Values When Suppliers are Risk Neutral**

| Increase in | Demand model | Change in $q^*$ | Change in $\pi_1$ |
|---|---|---|---|
| $\alpha$ | M1 | – | – |
| | M2 | – | – |
| $b$ | M1 | – | – |
| | M2 | ↑ | ↑ |
| $c$ | M1 | ↑ | ↑ |
| | M2 | ↑ | ↑ |
| $\mu_1$ | M1 | ↑ | ↑ |
| | M2 | – | – |
| $\sigma_1$ | M1 | Linear $d(p)$, ↓<br>$\text{Max}\{Z_1\} \leq 2$:<br>concave $d(p)$, ↓<br>Convex $d(p)$, ↑↓ | Linear $d(p)$, ↓<br>$\text{Max}\{Z_1\} \leq 2$:<br>concave $d(p)$, ↓<br>Convex $d(p)$, ↑↓ |
| | M2 | – | – |
| $s$ | M1 | ↓ | Linear or concave $d(p)$, ↑<br>Convex $d(p)$, ↑↓ |
| | M2 | ↓ | ↑↓ |
| $\mu_2$ | M1 | ↑↓ | ↑ |
| | M2 | ↑ | ↑ |
| $\sigma_2$ | M1 | Concave $d(p)$, ↓<br>Linear $d(p)$, –<br>Convex $d(p)$, ↑ | Concave $d(p)$, ↓<br>Linear $d(p)$, –<br>Convex $d(p)$, ↑ |
| | M2 | ↑ | ↑ |
| $\mu_b$ | M1 | ↓ | ↓ |
| | M2 | ↓ | ↓ |
| $p_0$ | M1 | ↑ | ↑ |
| | M2 | ↑ | ↑ |

↑ = increasing, ↓ = decreasing, – = no change, ↑↓ = direction depends on other parameter Values.

complexity of the model inhibits similar results for the measures $\beta$ and $\pi_2$, and for the case of risk-averse suppliers.

The results in Table 2 generally align with intuition: (1) the increased use of forward contracts ($\alpha$) has no impact (given suppliers are risk neutral), (2) the spend budget ($b$) does not play a role under M1, but increases in the budget lead to increases in supply under M2, (3) an increase in farm space with potential to produce artemisinin ($c$) leads to increases in supply, (4) an increase in market size ($\mu_1$) leads to increases in supply under M1, (5) an increase in either market size ($\mu_1$) or market volatility ($\sigma_1$) has no effect on supply under M2, (6) an increase in the attractiveness of the best alternative to artemisinin ($\mu_b$) leads to decreases in supply, and (7) an increase in the support-price ($p_0$) leads to an increase in supply.

Increases in the remaining parameters exhibit less intuitive effects. Let us begin with the impact of an increase in the coefficient of variation of organic yield ($\sigma_2$). Suppliers are risk-neutral and thus are not concerned about price volatility, so we may expect that changes in yield volatility will have no effect on supply. We see this result under M1 when demand is linear. However, changes in yield uncertainty affect supply when the demand function is nonlinear. The reason is that the equilibrium condition includes an expected value of a function of random variables (e.g., see equation (10) and equation (11)). If the function is nonlinear, as is the case of M1 with a nonlinear demand function and M2, then upside deviations from the mean are either amplified or compressed relative to downside deviations. This distortion from nonlinearity is what drives the directional arrows in Table 2. A convex demand function, for example, means that the increase in price from a unit decrease in supply is greater than the decrease in price from a unit increase in supply. Consequently, an increase in yield uncertainty exerts an upward pressure on the expected price, which in turn leads to a higher equilibrium quantity. The behavior is reversed if the demand function is such that a unit increase in supply causes a larger change in price than a unit decrease in supply (i.e., if the demand function is concave).

The changes in supply in response to increases in the coefficient of variation of market size ($\sigma_1$) under M1 are similar, but not identical, to what we see for $\sigma_2$. There is similarity because the directional arrows are caused by nonlinearities. However, note that a linear demand function means that the fraction of the market willing to pay price $p$ is proportional to supply but is *inversely* proportional to market size (see equation (9)), that is, if price is linear in supply, then it is nonlinear in market size. In particular, the decrease in price from a unit decrease in market size (or need for the drug) is greater than the increase in price from a unit increase in market size. This puts downward pressure on the expected price as market uncertainty increases, and leads to a lower equilibrium quantity. In the next section, we will see that this structural difference between the roles of random yield and market size contributes to meaningful differences in sensitivities to changes in these parameters.

While an increase in semi-synthetic artemisinin ($s$) generally leads to an increase in supply, it is possible that supply could decrease if demand is sufficiently convex in price. The convexity of the demand curve can lead to a steep drop in price in response to an increase in semi-synthetic supply resulting in a large exit of suppliers from the market and lower total supply (see Figure 8 for an example). The main driver of the result is nonlinearity as discussed above, and is particularly related to the comparative-static results for $\sigma_2$. There is no uncertainty in semi-synthetic yield, and thus as the production of semi-synthetic increases, the coefficient of variation of total yield—the sum of organic and semi-synthetic—decreases. If the demand function is convex, then a reduction in the coefficient of variation of total yield puts a downward pressure on supply (as shown in Table 2 for $\sigma_2$)

that can more than offset the increase in semi-synthetic artemisinin.

Lastly, while it is not surprising that supply is increasing in average yield ($\mu_2$), it is noteworthy that the amount of farm space dedicated to producing artemisinin ($q^*$) can increase as well. This behavior is assured under M2, and depending on the demand function, can occur under M1. This is noteworthy because the system is governed by a negative feedback loop (stemming from the inverse relationship between supply and price) that, in general, works to mute the impact of interventions. If $q^*$ is held fixed and $\mu_2$ increases, then organic supply will increase proportionally. The effect of an increase in $\mu_2$ on supply is amplified when it also leads to an increase in $q^*$. The result hints that $\mu_2$ is a potentially powerful lever, and we present an illustration of its power in the next section.

### 4.2. Numerical Analysis of Effects of Changes in Parameter Values

The comparative statics in the previous section are limited to the case of risk-neutral suppliers. In this section, we use numerical methods to investigate the sensitivity of system performance to changes in parameters. Using the limited available historical data as a guide, we develop a set of parameter values and functions for our base-case model (see Table 3). Parameters $\sigma_1$, $\sigma_2$, $s$, $\alpha$, $\mu_1$, $\mu_2$, and $b$ are estimated using historical data related to these values.[3] We estimate the risk aversion parameter as $\gamma = 0.008$.[4] We assume uniformly distributed willingness-to-pay and utility of the best alternative on the basis of the principle of insufficient reason proposed by Pierre Laplace in the 1700s (Luce and Raiffa 1957); if all that is known about a random variable is that it can take on values over a finite range, then any distribution other than uniform implies that something else is known. We use the symmetric triangular distribution for $Z_1$ and $Z_2$ in order to capture a central tendency (that is not present in the uniform distribution) about the mean of 1. Finally, we use historical data on price, annual supply, need, and fill rates as a guide, finding values of $\mu_b$, $\sigma_b$, $c$, and coefficients of linear function $\rho_1(p)$ that lead to equilibrium results that are generally consistent with observed results.

We use stochastic optimization with 10,000 trials per simulation via Analytic Solver Platform from Frontline Systems to identify the equilibrium quantity. Table 4 lists statistics from the base-case model.

We compute the sensitivity of performance to changes in each of the 11 parameters listed in Table 2. With the exception of support-price $p_0$, each parameter is varied between −50% and +50% of its base-case value ($p_0 = 0$ in the base-case). We find that the relative sensitivity of performance to changes in different parameter values is reflected in the grouping of parameters in Table 1. Performance is more sensitive to changes in parameters listed near the top of Table 1 and is less sensitive to changes in parameters listed near the bottom of the table. We categorize the parameters into three groups—high, moderate, and low sensitivity:

High-sensitivity: average yield ($\mu_2$), average utility of the best alternative ($\mu_b$), average market size ($\mu_1$)
Moderate-sensitivity: available farm space ($c$), semi-synthetic supply ($s$), spend budget ($b$)
Low-sensitivity: risk aversion ($\gamma$), yield variability ($\sigma_2$), demand variability ($\sigma_1$), forward contract % ($\alpha$)

While the boundaries of these categories are subjective (due to multiple performance measures and nonlinearities), the parameters in each category exhibit some commonality that may help explain observed differences in sensitivity. In particular, the high category can be viewed as *first-moment* parameters, the low category can be viewed as *second-moment*

**Table 3 Units, Functions, Random Variables, and Parameters in our Base-Case Model**

| | | |
|---|---|---|
| Units | | |
| Space unit = 1000 hectares (H) | Artemisinin unit = 1000 kgs (K) | Currency unit = \$1000 (D) |
| Functions and random variables | | |
| $\rho_1(p) = 2 - 0.0032p$ | $Z_1, Z_2 \sim$ symmetric triangular $\sigma_1 = 0.1$ K, $\sigma_2 = 0.3$ K/H | $U_b \sim$ uniform $\mu_b = 4800$ D, $\sigma_b = 1500$ D |
| Parameters | | |
| Potential farm space ($c$) = 80 H | Semi-synthetic supply ($s$) = 60 K | Forward contract % ($\alpha$) = 25% |
| Risk aversion ($\gamma$) = 0.008 | Mean demand ($\mu_1$) = 240 K | Mean yield ($\mu_2$) = 10 K/H |
| Purchase budget ($b$) = 75,000 D | | |

**Table 4 Statistics from the Base-Case Model in Equilibrium**

| | Demand model | |
|---|---|---|
| | M1 | M2 |
| Hectares producing artemisinin in 000s ($q^*$) | 17 | 15 |
| Average total supply in metric tons ($\pi_1$) | 235 | 212 |
| Average semi-synthetic production as fraction of total (%) | 26 | 28 |
| Average fill rate ($\beta$) (%) | 89 | 85 |
| Average supplier surplus in \$000,000s ($\pi_2$) | \$10 | \$8 |
| Average total spend in \$000,000s | \$73 | \$75 |
| Average artemisinin price in \$ per kg ($\bar{p}$) | \$345 | \$373 |
| Standard deviation in artemisinin price ($\sigma_P$) | 46 | 90 |
| Min and max price per kg (in 10,000 trials) | \$313, \$505 | \$232, \$740 |

parameters, and the moderate category can be viewed as *quantity* parameters. In other words, in the high category, we have parameters that specify the averages of random variables whereas in the low category we have parameters that are closely linked to volatility. Parameters $\sigma_1$ and $\sigma_2$ are direct measures of volatility, whereas parameters $\gamma$ and $\alpha$ control the importance of volatility in supplier decision making. Parameter $\gamma$ measures the degree to which suppliers care about volatility in the market and parameter $\alpha$ controls the fraction of suppliers that are immune to market volatility (via a forward contract). The moderate category contains the remaining parameters that are not closely linked to moments of the random variables. We do not categorize the support-price parameter ($p_0$) because its base-case value is 0 (i.e., no price support currently in effect).

In what follows, we present and discuss results for one parameter within each category; figures illustrating the sensitivity of performance measures to changes in other parameters are available in an Appendix S1.

Figures 4–6 show the sensitivity of total supply ($\pi_1$), fill rate ($\beta$), and supplier surplus ($\pi_2$) to changes in one parameter from each category—forward contract percentage (low), semi-synthetic supply (moderate), and average yield (high). For all of the sensitivity figures, we divide $\pi_1$ and $\pi_2$ by constants (635 and 85,500, respectively) so that all measures take on values between 0 and 1.

Recall that a tripartite financing model was introduced in 2009, in part to encourage increased use of forward contracts and thereby increase supply. Our results in Figure 4 indicate that increased use of forward contracts have minimal impact on supply and other measures. To assess the robustness of this observation, we increased the risk aversion parameter by an order of magnitude (from $\gamma = 0.008$ to $\gamma = 0.08$), and we find little difference in sensitivity. Greater sensitivity can arise in an alternative calibration with higher variation in utility ($\sigma_b$) and risk aversion ($\gamma$), but these higher values are not reasonable in the current market for artemisinin.

Figure 7 augments Figure 3 to illustrate how the base-case equilibrium shifts in response to the extreme of no forward contracts ($\alpha = 0$). Both Figures 3 and 7 are created using the base-case model under M1 (the behavior is similar under M2). We see that a reduction from $\alpha = 0.25$ to $\alpha = 0$ creates an upward shift in equation (3) that puts pressure to decrease equilibrium, and creates an upward shift in equation (4) that puts pressure to increase equilibrium. The result of these offsetting pressures is a very narrow band of equilibrium quantities for $\alpha \in [0, 0.25]$. In contrast, equation (3) is unaffected by changes in $s$ or $\mu_2$, and we find similar or larger shifts in equation (4) as $s$ or $\mu_2$ change, leading to larger changes in equilibrium. As discussed in section 4.1, increases in average yield ($\mu_2$) positively affect the supplier's utility per unit of farm space as well as supply. However, increases in semi-synthetic supply ($s$) positively affect supply only. This difference helps explain the differences in observed sensitivities to changes in $s$ and $\mu_2$.

Recall from Table 2 that it is possible for total supply to be decreasing in semi-synthetic production when demand is convex in price, as is the case with demand model M2. Figure 5 shows that supply is increasing in semi-synthetic production. However, while we suspect this to be the dominant behavior in

**Figure 4 Sensitivity of Total Supply, Fill Rate, and Supplier Surplus to Changes in the Forward Contract Percentage ($\alpha$)**

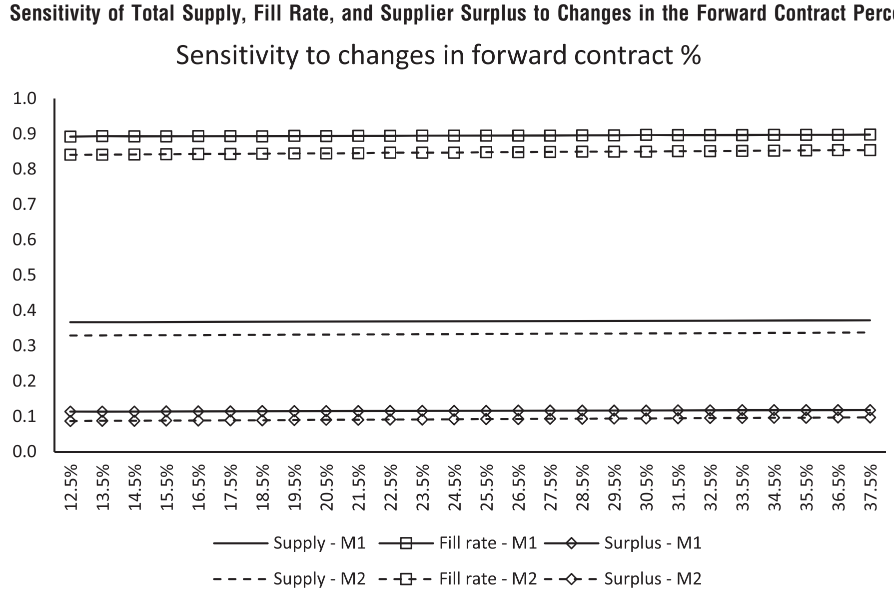


**Figure 5 Sensitivity of Total Supply, Fill Rate, and Supplier Surplus to Changes in Semi-Synthetic Production ($s$). The figure also includes semi-synthetic production as a fraction of the total ($s/(s + q^*)$)**

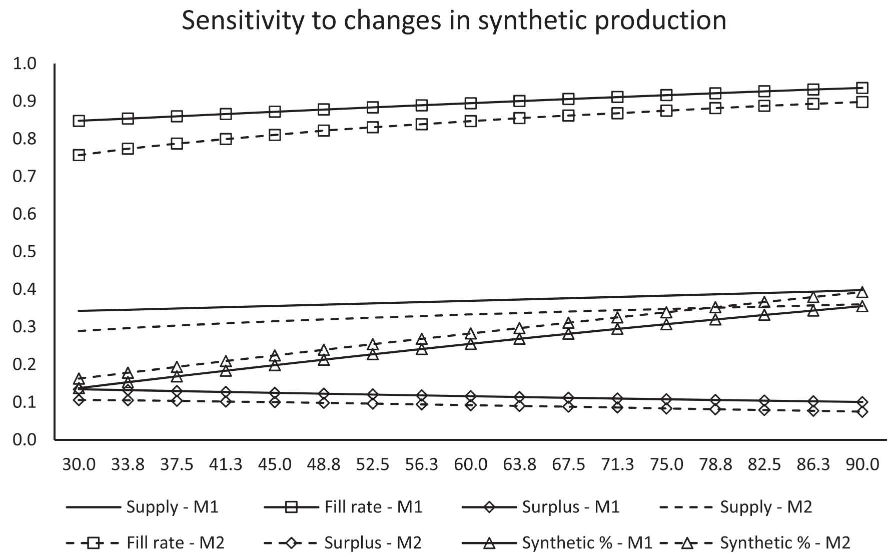
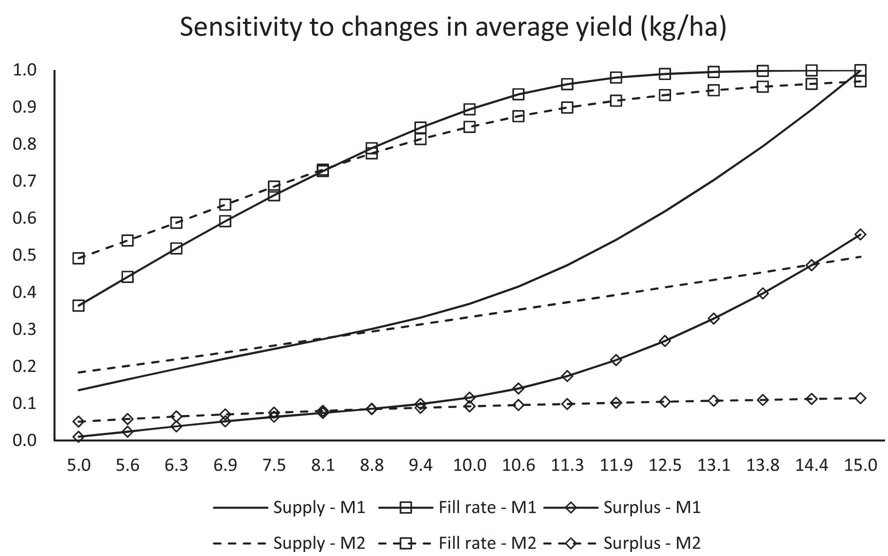



**Figure 6 Sensitivity of Total Supply, Fill Rate, and Supplier Surplus to Changes in Expected Yield Per Hectare ($\mu_2$)**




real-world settings, it does not take much of a change in the base-case model to yield a decreasing supply function. Figure 8 is based on two changes to the base-case model: suppliers are risk neutral and yield uncertainty is increased by one-third (i.e., $\gamma$ is decreased from 0.008 to 0 and $\sigma_2$ is increased from 0.3 to 0.4).

### 4.3. Effects of Changes in Parameter Values on Price Volatility

Price volatility influences a supplier's decision on whether or not to produce artemisinin, and in this sense, the effects of price volatility are captured in the summary performance measures reported above. That said, the impact of interventions on price volatility is a measure of interest in its own right among policy makers. As one may expect, the sensitivity of price volatility to changes in parameters is consistent with the sensitivity of other performance measures, that is, parameters that exhibit low (high) sensitivity with respect to supply, fill rate, and supplier surplus tend to exhibit low (high) sensitivity with respect to price volatility.

We present selected price volatility sensitivity results below. In order to highlight how relative price volatility changes as parameters change, we report the price coefficient of variation (CV = SD/mean).

**Figure 7 Illustration of Equations (3) and (4), and the Corresponding Equilibrium Quantities for $\alpha = 0$ and $\alpha = 0.25$**

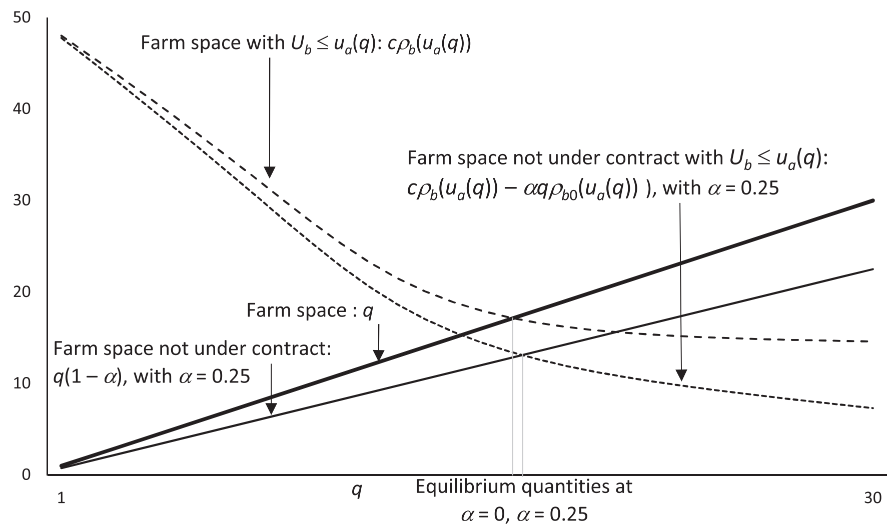



**Figure 8 Sensitivity of Total Supply to Changes in Semi-Synthetic Production ($s$) with Risk Neutral Suppliers ($\gamma = 0$) and Higher Yield Uncertainty ($\sigma_2 = 0.4$) Under Demand Model M2**

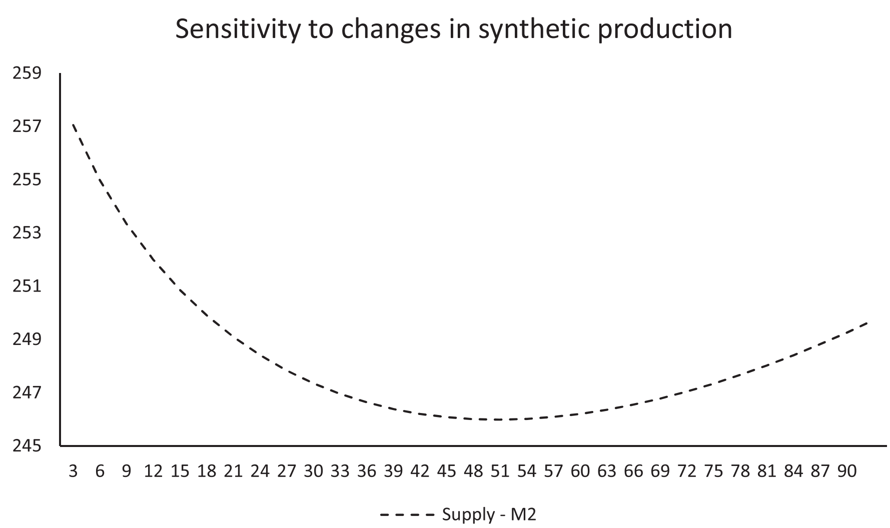



Figure 9 illustrates that changes in demand uncertainty have little effect on price volatility, whereas reductions in yield uncertainty translate into noticeable reductions in price volatility. The reason for the difference, in part, is due to the greater degree of yield uncertainty than demand uncertainty in the base-case model (e.g., $\sigma_2 = 3\sigma_1 = 0.3$, so a 50% increase in $\sigma_1$ is comparable to a 17% increase in $\sigma_2$), though a difference in sensitivity remains when $\sigma_2 = \sigma_1 = 0.1$. As discussed in section 4.1, there is a structural difference in the price function equation (9) that explains this result—the fraction of the market willing to pay price $p$ is proportional to supply but is inversely proportional to market size. This nonlinearity acts to soften the effects of changing volatility in market size on the volatility of price.

While we find the supply, fill rate, and surplus measures to be relatively insensitive to changes in $\sigma_1$ and $\sigma_2$, there is an important lesson for policy makers if interventions to impact $\sigma_1$ and $\sigma_2$ are being considered. Our analysis points to greater impact from changes in $\sigma_2$ than $\sigma_1$ for two reasons. The first reason is the structural difference explained above. A second reason is that changes in $\sigma_1$ have no effect of on performance under M2; the sensitivity of performance to changes in $\sigma_1$ is further diminished by the extent that reality reflects M2 over M1.

**Figure 9 Sensitivity of Price Coefficient of Variation to Changes in Demand Uncertainty ($\sigma_1$) and Yield Uncertainty ($\sigma_2$). The sensitivity to yield uncertainty is illustrated at the base-case value $\sigma_2$ = 0.3, and at $\sigma_2$ = 0.1 = $\sigma_1$. Sensitivity results are not reported for demand model M2 because demand uncertainty does not affect the system**

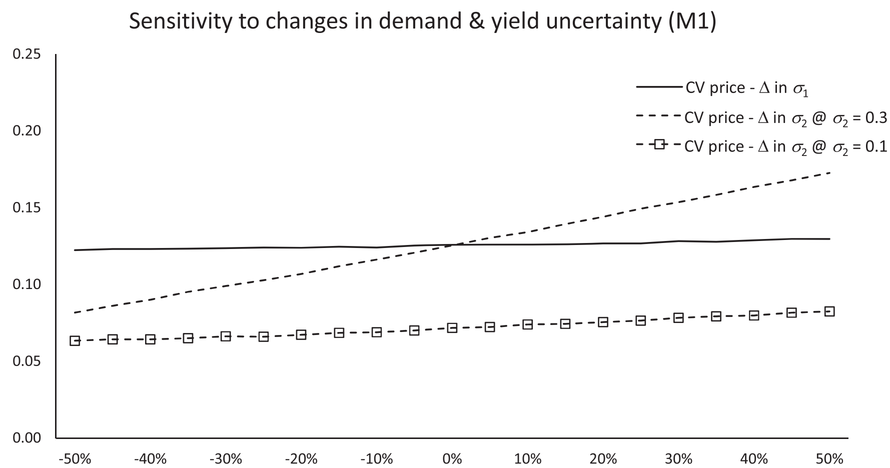
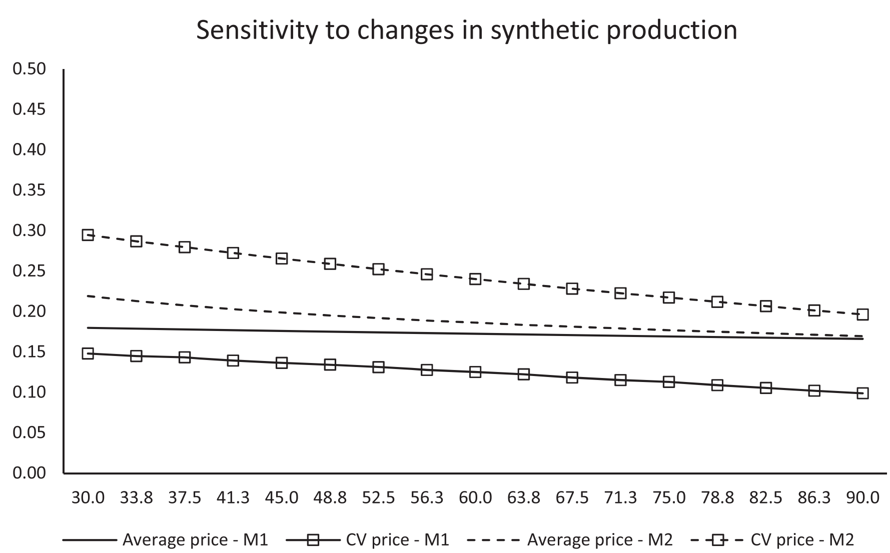



**Figure 10 Sensitivity of Average Price (Divided by $2000) and Price Coefficient of Variation to Changes in Semi-Synthetic Production (*s*)**

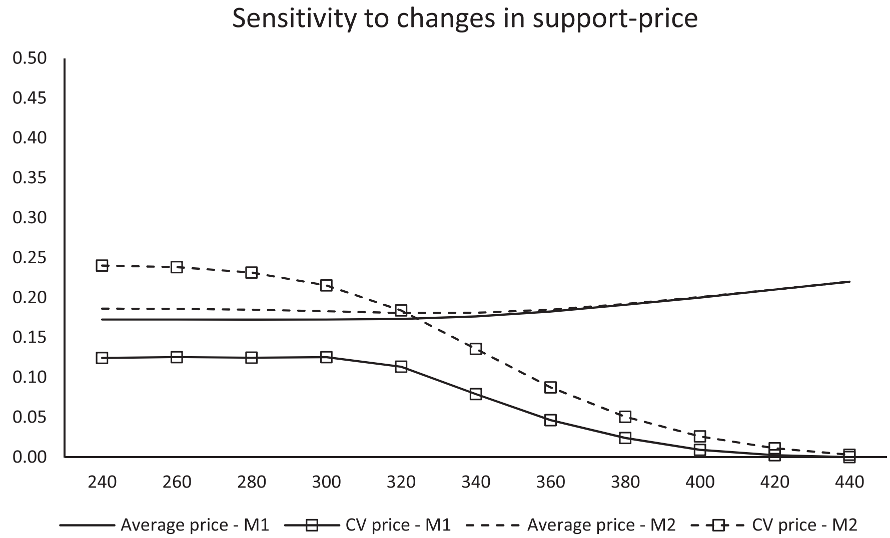



Figures 10 and 11 illustrate the sensitivity of price volatility to changes in semi-synthetic production and to the support-price. These figures also report the average price in order to expose the relationship between average price and its relative volatility. We rescale the average price by dividing by $2000. (Average price is virtually unchanged as $\sigma_1$ and $\sigma_2$ are varied, so the average price curves are excluded from Figure 9.)

One advantage of increasing semi-synthetic production with its deterministic yield is that it translates into lower supply uncertainty, and as a consequence, lower price volatility. We see this effect in Figure 10. A 50% increase in semi-synthetic production reduces price volatility by 20% for both M1 and M2. The figure also illustrates the downward pressure on price from semi-synthetic production. A 50% increase in semi-synthetic production reduces average price by about 5%, slightly less for M1 and slightly more for M2.

Similar to an increase in semi-synthetic production, the introduction of a support-price has a direct effect on price volatility (i.e., by restricting the downward range of price). Figure 11 illustrates this effect. The support-price does not affect the system until it reaches about $300 (i.e., the price rarely drops below

**Figure 11 Sensitivity of Average Price (Divided by \$2000) and Price Coefficient of Variation to Changes in the Support-Price ($p_0$)**




\$300), and price volatility nearly disappears once the support-price reaches \$440.

### 4.4. Limitations

There are limitations in our model that should be taken into account when interpreting our results. Our model is static, ignoring dynamics that arise from an intervention that causes the system to move towards a new equilibrium. Thus, interventions that are found to be especially impactful in our model may have a negative side effect of inducing a greater degree of dynamic instability in the system, both in terms of the magnitude of supply–demand imbalance in response to the intervention and the time to settle into a new equilibrium. We come back to this point in the next section.

As a related point, our model considers a single-period problem where excess inventory from one year is not used/sold in the following years. The over three-year shelf life of artemisinin allows holding inventory from one year and using it in the following years. While suppliers do not necessarily have the capital to invest in holding inventory, ACT manufacturers do hold inventory. We have conducted numerical tests of a model that includes random leftover inventory from the prior period, and we find no differences in our sensitivity conclusions. This is not unexpected in light of our numerical results in section 4.2 where we find that the system is insensitive to changes in volatility measures. This muted behavior is influenced by the static nature of our model, that is, that suppliers do not move in and out of the market in response to random market fluctuations and instead decide what to produce based on the mean and variance of market price. The system will be more erratic than our model predicts if there are many suppliers who move in and out of the market based on current conditions. There is a dearth of information on the extent to which suppliers move in and out of the market, and thus represents a potential area for future investigation.

Our model assumes full and symmetric information between suppliers, manufacturers, and purchasers/financiers. Suppliers do not under- or over-react to market signals. In practice, suppliers may have poor knowledge of market demand compared to the financiers and purchasers (Levine et al. 2008). Forecasting helps in resolving this information asymmetry more than reducing the intrinsic demand uncertainty.

Finally, the attractiveness of an intervention is based on both its impact and cost, including ease and speed of implementation. There are likely many possible approaches for influencing the value of each parameter in our model, each with its own cost and implementation challenges. The identification and cost assessment of alternative approaches to affect different types of desired change is left to those with specialized expertise, and is outside the scope of this study.

## 5. Summary of Implications for Policy Makers

Although a number of results developed in the previous section are valuable in developing a better understanding of the market, we discuss the impact of the interventions that have either been implemented in this market in the past or are being actively considered by policy makers. We explain in greater detail the most significant and the most surprising results.

### 5.1. Increasing Forward Contracting has Marginal Impact

As noted above, the A2S2 initiative was created in 2009 to increase artemisinin supply to meet the projected ACT demand. A2S2 was based on a tripartite financing model where extractors who had existing contracts with WHO-prequalified ACT manufacturers received financing at subsidized rates. The underlying premise was that offering lower interest capital would incentivize more forward contracts with farmers and increase artemisinin supply. An independent review estimated the impact to be 35% below expectations, though the team was not able to identify specific reasons for the shortfall (UNITAID 2011). The program has since been terminated. While our results are consistent with that outcome, we caution that our analysis may understate the impact of forward contracts. In particular, the beneficial impact of increased forward contracts, as well as improvements in other second-moment parameters and a support price, are likely to be greater than predicted by our model if there are many suppliers who move in and out of the market based on current conditions.

### 5.2. Reducing Demand Uncertainty has Marginal Impact

The model shows that attempts to decrease market uncertainty through better disease forecasting also have limited impact. Understandably, when the overall budget for purchasing malaria medicines is fixed and known to all actors in the system, reductions in demand uncertainty do not impact the market outcomes. More interestingly, even when the overall budget is not fixed and the total quantity purchased depends upon the price offered, reductions in demand uncertainty through better epidemiological forecasting result in only small increases in overall supply. This result, which is similar to impact of forward contracts noted above, is a reflection of the more general phenomenon observed in numerical results of our calibrated model: equilibrium is relatively insensitive to changes in measures that relate to volatility.

### 5.3. Increasing the Production of Semi-Synthetic Artemisinin has a Moderate Impact, and the Transition Period Requires Careful Management of the Two Sources of Supply

A greater production of semi-synthetic artemisinin increases overall supply, increases fill rate, and decreases price volatility. This is notable because of the debate surrounding the value of this intervention (Peplow 2013, Van Noordan 2010). On the surface, one might view increasing semi-synthetic as a very significant and positive tool to improve overall supply and decrease price volatility. However, we see that a 50% increase in semi-synthetic production translates into approximately an 8% increase in supply and a 5% increase in fill rate (for both demand models). In addition, supplier surplus drops by about 15%. We also observe some risk that overall artemisinin supply could decrease (see Figure 8). This results from the semi-synthetic supply not being able to offset the decrease in agricultural artemisinin production as suppliers exit the market. However, beyond a certain threshold volume of semi-synthetic production, overall output increases as semi-synthetic increases. This highlights that, while semi-synthetic may increase overall supply unconditionally as its capacity nears the total demand, in the interim, it is important to manage the two sources of supply carefully in order to avoid decreases in overall supply. In addition, increasing semi-synthetic production has its own challenges. For example, the use of semi-synthetic in an ACT production process requires that the producer go through an FDA-type approval process that takes time and money. In addition, there is resistance to purchasing semi-synthetic by some ACT manufacturers because the semi-synthetic producer is also a competitor in the ACT market.

### 5.4. Increasing Agricultural Yield has Significant Impact

The overall supply of artemisinin increases with increases in average yield due to two positive effects – the output per hectare planted increases but additionally the farmer's utility for producing artemisinin increases. Other interventions are one-dimensional in the sense of exerting a single force on the system. The supply chain has a negative feedback loop that dampens the sensitivity of performance to interventions. For example, the positive effect of increased output per hectare is mitigated by the negative relationship between supply and price, i.e., supply up → price down → reduced supplier interest → supply down. However, the increased productivity increases both output and farmer utility that, compared to other interventions, diminishes the strength of the negative feedback loop in the system. Figure 6 shows that the impact of yield improvements is less under M2 than M1. This is because the fixed total spend under M2 leads to larger reductions in price with improved efficiency.

Changes in planting methods, and other agricultural practices can lead to some improvements in yield. Radical improvements can only come from the use of higher-yielding varieties of Artemisia. Such high-yielding seed varieties may also lead to slight reductions in yield uncertainty, but a large part of the yield uncertainty depends on rainfall and weather in the growing regions. Years with excessive rainfall tend to have lower yields.

While increasing yield is an impactful intervention, there are challenges and risks. There has been work on the development of new high-yield seed varieties that show promise (Dalrymple 2012). However, reports from agencies promoting the seed indicate some resistance to switching to these seed varieties in Asia, perhaps in part due to a long and successful history with the strain of Artemisia that is grown there. Increasing agricultural yield requires extensive support from the governments of the main growing region (China, Vietnam) and has high transaction costs associated with implementing it. In addition, there is some risk that a large increase in average yield could exacerbate market volatility. As noted earlier, our analysis is based on a static model that predicts equilibrium, but does not account for dynamics in the interim. While increasing yield is impactful in our model, this very impact may lead to a period of higher price volatility, for example, the promise of high yield induces many suppliers to enter the market, only to exit a short time later due to low prices.

### 5.5. A Price Support has Significant Impact

The demand and supply of artemisinin is matched at a certain price that is determined by the market. In many agricultural markets if the market price is too low, few farmers grow that crop. So in such cases governments often intervene in the market by offering a minimum support-price, that is, when the market price is lower than the support-price, government purchases from the farmers at the support-price and sells in years when the price is high. A similar market intervention can be used for increasing the supply of agricultural artemisinin and reducing price volatility. As an example, under M2, a budget increase of \$25 million translates into a 20% increase in supply. By comparison, a support-price set at \$360 requires an average investment of \$25 million and increases supply by 30%. Furthermore, price volatility (coefficient of variation) decreases by 60%, whereas a budget increase of \$25 million increases price volatility (by 7%). Note, however, that the budget is in terms of spend on artemisinin, which constitutes about 30% of the total ACT spend. ACT spend would have to increase by approximately \$80 million to generate a 20% increase in supply.

While a price support shows potential for impact, there are barriers to implementation. Most notably is the determination of a support price that improves price stability while being sustainable (e.g., not so high that it leads to excess supply with support price consistently higher than the natural market price; not so low that there is no meaningful effect). In addition, artemisinin is not a pure commodity. There are some differences in quality, which leads to a simple but crude single support price or the complexity of a quality-dependent support price.

### 5.6. Other High Sensitivity Interventions

Expanding the cultivation of Artemisia to viable regions where the crop has traditionally not been considered and initiatives that make competing crops less attractive to farmers also yield positive outcomes. However, influencing the attractiveness of rice, corn, and other competing crops is a more difficult policy intervention. Outcomes are also sensitive to decreases in the overall incidence of malaria. Several initiatives for malaria control and eradication are already being implemented in malaria-endemic countries.

## 6. Conclusion

Using a parsimonious model to capture the effects of factors such as available farm space, manufacturer capacity, farmer's incentive to plant Artemisia, volatility in Artemisia yield, supply of semi-synthetic artemisinin, and demand uncertainty in the malaria medicine market, this paper estimates the directional impact of various supply chain interventions on overall supply, fill rate, and price volatility in the market. The model is calibrated with field data to the extent available, and a sensitivity analysis is conducted based on this information.

The analysis shows that analytical modeling can help illuminate impactful interventions to mitigate market shortcomings. In the absence of analytical modeling or other rigorous analysis, interventions with only marginal benefits may be selected. Tight budgets and resource constraints require implementing only those interventions which have the highest potential to stabilize the market and increase overall supply. While this study does not include the costs of implementing each intervention, and thus cannot comment on the cost effectiveness, it provides a strong basis for understanding the likely impact from each intervention. We find that a support-price for agricultural artemisinin, improved average yield, and a larger and carefully managed supply of semi-synthetic artemisinin have the greatest potential for improving the supply of artemisinin-based malaria medicine.

This study also highlights the application of modeling and analytical tools to address policy-relevant problems faced by developing-country governments. Further research should seek to understand the dynamic behavior of the system in response to an intervention and the role of information asymmetry in this supply chain. In addition, future research may model extractors as a separate entity in order to assess the impact of extractor strategic behavior such as price gouging or constraining supply.

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## Appendix

### A.1. Notation

$q$ = units of farm space dedicated to producing artemisinin
$s$ = units of semi-synthetic artemisinin supply introduced to the market
$Z_2$ = positive supply random variable; $E[Z_2] = 1$, $\sigma_2{}^2 = V[Z_2]$
$\Phi_2(\cdot)$ = cdf of $Z_2$
$\mu_2$ = expected yield per unit of farm space
$Q$ = random organic artemisinin supply; $Q = q\mu_2 Z_2$
$U_b$ = random supplier utility from dedicating farm space to best alternative to producing artemisinin; $\mu_b = E[U_b]$, $\sigma_b{}^2 = V[U_b]$
$\rho_b(u)$ = cdf of $U_b$
$P(q)$ = random artemisinin spot price (and ACT price); $\bar{p}(q) = E[P(q)]$, $\sigma_P^2(q) = V[P(q)]$
$\gamma$ = supplier risk aversion parameter; $\gamma \geq 0$
$Z_1$ = positive and normalized ACT market size random variable; $E[Z_1] = 1$, $\sigma_1{}^2 = V[Z_1]$
$\Phi_1(\cdot)$ = cdf of $Z_1$
$\mu_1$ = expected value of the ACT market size
$M$ = random size of the ACT market; $M = \mu_1 Z_1$
$\alpha$ = fraction of farm space dedicated to producing artemisinin under forward contract
$c$ = units of farm space owned by all suppliers who could produce artemisinin
$p_0$ = artemisinin support-price
$q^*$ = equilibrium units of farm space dedicated to producing artemisinin
$\rho_1(p)$ = fraction of consumers willing to purchase ACT at price $p$; $\rho_1{}'(p) < 0$; applicable to demand model M1, $d(p) = M\rho_1(p)$
$b$ = budget for the purchase of ACT; applicable to demand model M2, $d(p) = bp^{-1}$
$\pi_1$ = expected artemisinin volume in equilibrium; $\pi_1 = q^*\mu_2 + s$
$\beta$ = expected availability of ACT as a percent of the total need (market size)
$\pi_2$ = supplier surplus

## A.2. Lemma 1A

Let $g(x, y)$ and $h(x)$ be continuous, differentiable functions, and let $X$ and $Y$ be independent random variables with pdfs $\phi_X$, $\phi_Y$. The following lemma is used in derivations of comparative-static results.

LEMMA A1. $A \equiv E[g(X, Y)h(X)] - E[g(X, Y)]E[h(X)]$.

| | $g$ | $g_x$ | $h'$ | $A$ |
|---|---|---|---|---|
| 1 | | =0 | | =0 |
| 2 | >0 | >0 | >0 | >0 |
| 3 | >0 | >0 | <0 | <0 |
| 4 | >0 | <0 | >0 | <0 |
| 5 | >0 | <0 | <0 | >0 |
| 6 | <0 | >0 | >0 | >0 |
| 7 | <0 | >0 | <0 | <0 |
| 8 | <0 | <0 | >0 | <0 |
| 9 | <0 | <0 | <0 | >0 |

PROOF. A1-1: If $g_x = 0$, then $g(x, y) = a + k(y)$ for some function $k(y)$, and $E[g(X, Y)h(X)] = E[(a + k(Y))h(X)] = E[a + k(Y)]E[h(X)]$.

A1-2:

$$E[g(X, Y)h(X)] = E[g(X, Y)] \int h(x)f(x)dx,$$

where

$$f(x) = \left(\frac{E[g(x, Y)]}{E[g(X, Y)]}\right)\phi_X(x).$$

Note that $f(x)$ is a valid pdf (i.e., non-negative and integrates to 1). From $g_x > 0$, it follows that distribution $f(x)$ has first-order stochastic dominance over distribution $\phi_X(x)$, i.e.,

$$\int_x^\infty f(t)dt \geq \int_x^\infty \phi_X(t)dt \tag{A.1}$$

and the inequality is strict for some $y$ (e.g., for any $x$ such that $\phi_X(z) > 0$ for some $z \geq x$). From $h' > 0$ and equation (A.1) it follows that

$$\int h(x)f(x)dx > \int h(x)\phi_X(x)dx = E[h(X)]. \tag{A.2}$$

A1-3: The proof parallels the proof of A1-2, except the sign of $h'$ is reversed, which causes the sign of $A$ to be reversed.

A1-4: The proof parallels the proof of A1-2, except that $g_x < 0$ causes inequality equation (A.1) to be reversed, which causes the sign of $A$ to be reversed.

A1-5: The proof parallels the proof of A1-4, except the sign of $h'$ is reversed, which causes the sign of $A$ in A1-4 to be reversed.

A1-6 through A1-9: Let $\hat{g} = -g$ and $\hat{g}_x = -g_x$. From

$$\begin{aligned} A &= -(E[-g(X, Y)h(X)] - E[-g(X, Y)]E[h(X)]) \\ &= -(E[\hat{g}(X, Y)h(X)] - E[\hat{g}(X, Y)]E[h(X)]) \end{aligned}$$

it follows that the signs of $A$ in A1-6 and A1-7 are obtained from A1-4 and A1-5 (for which $\hat{g}_x = -g_x < 0$) but with the signs reversed. Similarly, the signs of $A$ in A1-8 and A1-9 are obtained from A1-2 and A1-3 but with the signs reversed. □

## A.3. Derivation of Results in Table 2

For given parameter $y \in \{\alpha, b, c, \mu_1, \sigma_1, s, \mu_2, \sigma_2, \mu_b\}$

$$q^{*\prime}(y) = \frac{-F_y(q^*, y)}{F_{q^*}(q^*, y)}$$

(obtained by taking the total derivative of both sides of the equilibrium condition $F(q^*, y) = 0$ with respect to $y$ and solving for $q^{*\prime}(y)$). Note that $\bar{p}'(q) < 0$

$$\rho_b{}'(u) > 0.$$

From the preceding inequalities, it follows that

$$F_{q^*}(q^*, y) > 0,$$

and thus the sign of $q^{*\prime}(y)$ is determined by the sign of $-F_y(q^*, y)$.

Defining $F(\cdot)$ in accordance with the risk-neutral equilibrium condition (6),

$$M1: F(q^*, y) = q^* - c\rho_b \left(\mu_2 E\left[\max\left\{\rho_1{}^{-1}\left(\min\left\{\frac{q\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right), p_0\right\}\right]\right)$$

$$M2: F(q^*, y) = q^* - c\rho_b\left(\mu_2 E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right]\right).$$

Note that the truncation functions, $\max\{\cdot, \cdot\}$ and $\min\{\cdot, \cdot\}$, affect the sensitivity of

$$\rho_b\left(\mu_2 E\left[\max\left\{\rho_1{}^{-1}\left(\min\left\{\frac{q\mu_2 Z_2 + s}{\mu_1 Z_1}, 1\right\}\right), p_0\right\}\right]\right) \quad (A.3)$$

to changes in parameter values relative to

$$\rho_b\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right]\right), \quad (A.4)$$

but not the direction of change. Thus, to simplify the presentation of analysis, we predominantly use equation (A.4) in place of equation (A.3). We use the form given in equation (A.3) only when the truncation functions play a role in the results.

### A.3.1. Demand Model M1

#### A.3.1.1. Increasing $\alpha$.

$$F_\alpha(q^*, \alpha) = 0 \Rightarrow q^{*\prime}(\alpha) = 0, \pi_1{}'(\alpha) = 0$$

#### A.3.1.2. Increasing $c$.

$$F_c(q^*, c) = -\rho_b\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right]\right) < 0 \Rightarrow q^{*\prime}(c) > 0, \pi_1{}'(c) > 0$$

#### A.3.1.3. Increasing $\mu_1$.

$$\frac{\partial \rho_1{}^{-1}\left(\frac{q^*\mu_2 z_2 + s}{\mu_1 z_1}\right)}{\partial \mu_1} > 0 \text{ for any realization}$$

$$(z_1, z_2) \Rightarrow \frac{\partial E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right]}{\partial \mu_1} > 0$$
$$\Rightarrow F_{\mu_1}(q^*, \mu_1) < 0$$
$$\Rightarrow q^{*\prime}(\mu_1) > 0, \pi_1{}'(\mu_1) > 0$$

#### A.3.1.3. Increasing $\sigma_1$.

$$F_{\sigma_1}(q^*, \sigma_1) = -c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right]\right) \times \frac{\partial}{\partial \sigma_1}\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right]$$

We write $Z_1$ in terms of a standardized random variable $\zeta$ with pdf $\varphi_\zeta$ as follows: $Z_1 = 1 + \sigma_1\zeta$, where $E[\zeta] = 0, V[\zeta] = 1$, and $\zeta > -1/\sigma_1$ (to assure positive $Z_1$).

If $\rho_1^{-1\prime\prime}(x) = 0$ (linear demand), then $\rho_1{}^{-1\prime}(x) = -a$ with $a > 0$ ($a$ is the slope of $\rho_1{}^{-1}$), and

$$\frac{\partial}{\partial \sigma_1} E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right] = \frac{a(q^*\mu_2 + s)}{\mu_1} E\left[\left(\frac{1}{1 + \sigma_1\zeta}\right)^2 \zeta\right].$$

Letting $g(x) = \left(\frac{1}{1+\sigma_1 x}\right)^2$ and $h(x) = x$, we have $g > 0$, $g_x < 0$, and $h' > 0$. Thus, from Lemma A1-4,

$$E\left[\left(\frac{1}{1 + \sigma_1\zeta}\right)^2 \zeta\right] < E\left[\left(\frac{1}{1 + \sigma_1\zeta}\right)^2\right] E[\zeta] = 0 \quad (A.5)$$

and

$$\frac{\partial}{\partial \sigma_1} E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2 + s}{\mu_1 Z_1}\right)\right] = \frac{a(q^*\mu_2 + s)}{\mu_1} E\left[\left(\frac{1}{1 + \sigma_1\zeta}\right)^2 \zeta\right] < 0,$$

which implies $F_{\sigma_1}(q^*, \sigma_1) > 0, q^{*\prime}(\sigma_1) < 0$, and $\pi_1{}'(\sigma_1) < 0$.

Assume that the right endpoint of the support of $Z_1 = 1 + \sigma_1\zeta$ is not more than 2, i.e., the realized market size is assured to be no more than 100% more than the mean:

$$\max\{1 + \sigma_1\zeta\} \leq 2. \quad (A.6)$$

Note that

$$\frac{\partial}{\partial\sigma_1}E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]$$
$$=E\left[\left(\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2 Z_2+s}{\mu_1}\right)\right)\left(\frac{-\zeta}{(1+\sigma_1\zeta)^2}\right)\right]$$

Let $g(x,y)=\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{q^*\mu_2 y+s}{\mu_1}\right)$ and $h(x)=\frac{-x}{(1+\sigma_1 x)^2}$. Note that $1+\sigma_1 x>0$ for any realization $x$ of $\zeta$ (due to positive $Z_1$) and $h'(x)=\frac{\sigma_1 x-1}{(1+\sigma_1 x)^3}\le 0$ (due to equation (A.6)) and the inequality is strict for any $x$ inside the support of $\zeta$. Therefore, if $\rho_1^{-1\prime\prime}(x)<0$ (concave demand), then $g<0, g_x=\rho_1^{-1\prime\prime}(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)})(\frac{q^*\mu_2 y+s}{\mu_1})^2(\frac{-\sigma_1}{\mu_1(1+\sigma_1 x)^2})>0$, and $h'<0$. Thus, from Lemma A1-7,

$$E\left[\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2 Z_2+s}{\mu_1}\right)\left(\frac{-\zeta}{(1+\sigma_1\zeta)^2}\right)\right]$$
$$<E\left[\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2 Z_2+s}{\mu_1}\right)\right]$$
$$\times E\left[\frac{-\zeta}{(1+\sigma_1\zeta)^2}\right]<0 \text{ (due to equation (A.5) and } \rho_1{}^{-1\prime}(x)<0),$$

which implies $F_{\sigma_1}(q^*,\sigma_1)>0, q^{*\prime}(\sigma_1)<0$, and $\pi_1{}'(\sigma_1)<0$.

If $\rho_1^{-1\prime\prime}(x)>0$ (convex demand), then the sign of $F_{\sigma_1}(q^*,\sigma_1)$ can be positive or negative depending on parameters. To gain some sense into the determinants of the sign, we let $g(x,y)=\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)^2}\right)$ and $h(x)=-x$, for which $g<0$ and $h'<0$. Note that

$$g_x=\rho_1^{-1\prime\prime}\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{q^*\mu_2 y+s}{\mu_1}\right)^2\left(\frac{-\sigma_1}{(1+\sigma_1 x)^4}\right)$$
$$-2\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{q^*\mu_2 y+s}{\mu_1}\right)\left(\frac{\sigma_1}{(1+\sigma_1 x)^3}\right)$$
$$=-2\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\left(\frac{\sigma_1}{(1+\sigma_1 x)^3}\right)$$
$$\left(1-0.5\varepsilon\left(\frac{q^*\mu_2 y+s}{\mu_1(1+\sigma_1 x)}\right)\right),$$

Where $\varepsilon(u)=\frac{-u\rho_1^{-1\prime\prime}(u)}{\rho_1^{-1\prime}(u)}$ is a measure of the degree of convexity of $\rho_1{}^{-1}$ (more formally, $\varepsilon(u)$ is the elasticity of function $\rho_1{}^{-1\prime}(u)$). For example, if $\varepsilon>0.5$ for all realizations of $\zeta$ and $Z_2$, then $g_x<0$, and by Lemma A1-9,

$$E\left[\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2 Z_2+s}{\mu_1(1+\sigma_1\zeta)^2}\right)(-\zeta)\right]$$
$$>E\left[\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2 Z_2+s}{\mu_1(1+\sigma_1\zeta)^2}\right)\right]E[-\zeta]=0,$$

and $F_{\sigma_1}(q^*,\sigma_1)<0, q^{*\prime}(\sigma_1)>0$, and $\pi_1{}'(\sigma_1)>0$. Similarly, if $\varepsilon<0.5$ for all realizations of $\zeta$ and $Z_2$, then $g_x<0$, which implies $F_{\sigma_1}(q^*,\sigma_1)>0, q^{*\prime}(\sigma_1)<0$, and $\pi_1{}'(\sigma_1)<0$.

**A.3.1.4. Increasing** ***s*****.** Note that $\frac{\partial\rho_1{}^{-1}\left(\frac{q^*\mu_2 z_2+s}{\mu_1 z_1}\right)}{\partial s}<0$ for any realization $(z_1, z_2)$ of $(Z_1, Z_2)$ $\Rightarrow$ $\frac{\partial E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]}{\partial s}<0 \Rightarrow F_s(q^*,s)>0 \Rightarrow q^{*\prime}(s)<0$.

Now consider the sign of $\pi_1{}'(s)=1+\mu_2 q^{*\prime}(s)=1+\mu_2\left(\frac{-F_s(q^*,s)}{F_{q^*}(q^*,s)}\right)$.

$$F_s(q^*,s)=-c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right]$$
$$F_{q^*}(q^*,s)=1-c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[\left(\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right)(\mu_2 Z_2)\right]$$

If $\rho_1^{-1\prime\prime}(x)=0$ (linear demand), then by Lemma 1A-1,

$$F_s(q^*,s)=c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[\left(-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right)\left(\frac{1}{\mu_1 Z_1}\right)\right]$$
$$=c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]E\left[\frac{1}{\mu_1 Z_1}\right]$$
$$F_{q^*}(q^*,s)=1+c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{\mu_2}{\mu_1 Z_1}\right)\right]E[Z_2]$$
$$=1+c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)$$
$$\times\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{\mu_2}{\mu_1 Z_1}\right)\right].$$

Therefore,

$$\pi_1{}'(s) = 1 + \frac{-F_s(q^*, s)}{F_{q^*}(q^*, s)/\mu_2} = 1 - \frac{c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]E\left[\frac{1}{\mu_1 Z_1}\right]}{\frac{1}{\mu_2} + c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]E\left[\frac{1}{\mu_1 Z_1}\right]} > 0.$$

If $\rho_1^{-1\prime\prime}(x) < 0$ (concave demand), then $-\rho_1^{-1\prime\prime}(x) < 0$ and by Lemma A1-2

$$E\left[\left(-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right)(\mu_2 Z_2)\right] > E\left[\left(-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right)\right]\mu_2, \quad \text{(A.7)}$$

(i.e., $g(x, y) = \left(-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 x+s}{\mu_1 y}\right)\left(\frac{1}{\mu_1 y}\right)\right)$ and $h(x) = \mu_2 x$ in the notation of Lemma A1) which implies

$$\begin{aligned}\pi_1{}'(s) = 1 + \frac{-F_s(q^*, s)}{F_{q^*}(q^*, s)/\mu_2} &= 1 - \frac{c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right]}{\frac{1}{\mu_2} + c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]} \\ &> 1 - \frac{c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right]}{\frac{1}{\mu_2} + c\rho_b{}'\left(\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right]} > 0.\end{aligned}$$

If $\rho_1^{-1\prime\prime}(x) > 0$ (convex demand), then inequality equation (A.7) is reversed, i.e.,

$$\Delta \equiv E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{\mu_1 Z_1}\right)\right] - E\left[-\rho_1{}^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]\frac{1}{\mu_2} > 0,$$

and both $\pi_1{}'(s) > 0$ and $\pi_1{}'(s) < 0$ are possible.

From the fact that $\pi_1{}'(s) > 0$ for linear demand, it is clear that there exist convex demand functions for which $\pi_1{}'(s) > 0$ occurs (e.g., introduce a slight degree of convexity to a linear demand function). As a simple example of $\pi_1{}'(s) < 0$, suppose $\rho_1 = 1/p$, $\sigma_1 = 0$, $\mu_1 = \mu_2 = 1$, $s = s_1 = 1$, $Z_2$ is uniform on [0.5, 1.5], and other parameters and functions are such that the equilibrium quantity is $q_1{}^* = 5$. Then the expected price in equilibrium is

$$\bar{p}_1 = E\left[\rho_1{}^{-1}\left(\frac{q_1^*\mu_2 Z_2+s_1}{\mu_1 Z_1}\right)\right] = E\left[\frac{1}{q_1^*\mu_2 Z_2+s_1}\right] = E\left[\frac{1}{5Z_2+1}\right] \approx 0.18$$

and at this price, fraction $\rho_b(\bar{p}_1)$ of farm space is dedicated to producing artemisinin leading to a total supply of $\pi_1(s_1) = c\rho_b(\bar{p}_1)\mu_2 + s_1 = q_1{}^*\mu_2 + s_1 = 5 + 1 = 6$. Now suppose that $s = s_2 = 3$. Let $q_2 = q_1{}^* - (s_2 - s_1)/\mu_2 = 3$, which yields the same expected total supply, i.e., $q_2\mu_2 + s_2 = q_1{}^*\mu_2 + s_1 = 6$. However, the expected price at this quantity is

$$p_2 = E\left[\rho_1{}^{-1}\left(\frac{q_2\mu_2 Z_2+s_2}{\mu_1 Z_1}\right)\right] = E\left[\frac{1}{3Z_2+3}\right] \approx 0.17 < \bar{p}_1.$$

If $c\rho_b(p_2) < q_2 = 3$, then more suppliers will exit the market leading to equilibrium quantity $q_2{}^* < q_2 = 3$, and a reduction in total supply, i.e.,

$q_2{}^*\mu_2 + s_2 < q_1{}^*\mu_2 + s_1$ if and only if $\rho_b(p_2) < 0.6\,\rho_b(\bar{p}_1)$.

In other words, if the slope of $\rho_b(\cdot)$ in the neighborhood of $\bar{p}_1$ is sufficiently steep, then total supply at $s_2 = 3$ is less than total supply at $s_1 = 1$; otherwise total supply increases.

#### A.3.1.5. Increasing $\mu_2$.

Note that $F_{\mu_2}(q^*, \mu_2) < 0$ and $q^{*\prime}(\mu_2) > 0 \Leftrightarrow \frac{\partial}{\partial \mu_2}\mu_2 E\left[\rho_1{}^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right] = \frac{\partial}{\partial \mu_2}\mu_2 \bar{p}(q^*, \mu_2) > 0$

$$\frac{\partial}{\partial \mu_2}\mu_2 \bar{p}(q^*, \mu_2) = \bar{p}(q^*, \mu_2)\left(1 - \frac{-\mu_2 \bar{p}_{\mu_2}(q^*, \mu_2)}{\bar{p}(q^*, \mu_2)}\right),$$

where $\frac{-\mu_2 \bar{p}_{\mu_2}(q^*, \mu_2)}{\bar{p}(q^*, \mu_2)}$ is the yield-elasticity of expected price, which is positive, i.e., $\frac{\partial}{\partial \mu_2}\rho_1{}^{-1}\left(\frac{q^*\mu_2 z_2+s}{\mu_1 z_1}\right) < 0$ for any realization $(z_1, z_2)$ of $(Z_1, Z_2)$.

Thus, the sign of $q^{*\prime}(\mu_2)$ depends on whether the yield-elasticity of expected price is more or less than 1. We require $\frac{-\mu_2 \bar{p}_{\mu_2}(q^*, \mu_2)}{\bar{p}(q^*, \mu_2)} > 1$ (e.g., average equilibrium price is relatively sensitive to increases in average yield) for $q^*$ to be decreasing in $\mu_2$, which we suspect to be unusual in practice. However, in general, both $q^{*\prime}(\mu_2) < 0$ and $q^{*\prime}(\mu_2) > 0$ are possible.

Note that $\pi_1'(\mu_2) = q^*\left(1 - \frac{-\mu_2 q^{*\prime}(\mu_2)}{q^*}\right)$, and thus

$$\pi_1'(\mu_2) > 0 \Leftrightarrow \frac{-\mu_2 q^{*\prime}(\mu_2)}{q^*} < 1,$$

where $\frac{-\mu_2 q^{*\prime}(\mu_2)}{q^*}$ is the yield-elasticity of the equilibrium quantity. Note that

$$\begin{aligned}\frac{-\mu_2 q^{*\prime}(\mu_2)}{q^*} &=, \frac{\mu_2 F_{\mu_2}(q^*,\mu_2)}{q^* F_{q^*}(q^*,\mu_2)} = \frac{c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]}{\frac{1}{\mu_2} + c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]} \\ &\quad - \frac{c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right) E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{1}{q^*}\right)\right]}{\frac{1}{\mu_2} + c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]} \\ &< \frac{c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]}{\frac{1}{\mu_2} + c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right)\mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\left(\frac{Z_2}{\mu_1 Z_1}\right)\right]} < 1 \\ &\Rightarrow \pi_1'(\mu_2) > 0.\end{aligned}$$

**A.3.1.6. Increasing $\sigma_2$.** We write $Z_2$ in terms of its standardized random variable, i.e.,

$Z_2 = 1 + \sigma_2\zeta$,

where $E[\zeta] = 0$, $V[\zeta] = 1$, and $\zeta > -1/\sigma_2$ (to assure positive $Z_2$). Accordingly,

$$F_{\sigma_2}(q^*,\sigma_2) = c\rho_b'\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2(1+\sigma_2\zeta)+s}{\mu_1 Z_1}\right)\right]\right) \times \mu_2 E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2(1+\sigma_2\zeta)+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2\zeta}{\mu_1 Z_1}\right)\right]$$

If $\rho_1^{-1\prime\prime}(x) = 0$ (linear demand), then $-\rho_1^{-1\prime}(x) = a > 0$ and

$$E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2(1+\sigma_2\zeta)+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2\zeta}{\mu_1 Z_1}\right)\right] = \frac{q^*\mu_2 a}{\mu_1}E\left[\frac{1}{Z_1}\right]E[\zeta] = 0,$$

which implies $q^{*\prime}(\sigma_2) = \pi_1'(\sigma_2) = 0$.

If $\rho_1^{-1\prime\prime}(x) > 0$ (convex demand), then $-\rho_1^{-1\prime\prime}(x) < 0$ and by Lemma 1A-4,

$$E\left[\left(-\rho_1^{-1\prime}\left(\frac{q^*\mu_2(1+\sigma_2\zeta)+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2}{\mu_1 Z_1}\right)\right)(\zeta)\right] < E\left[-\rho_1^{-1\prime}\left(\frac{q^*\mu_2(1+\sigma_2\zeta)+s}{\mu_1 Z_1}\right)\left(\frac{q^*\mu_2}{\mu_1 Z_1}\right)\right]E[\zeta] = 0,$$

(i.e., $g(x,\ y) = -\rho_1^{-1\prime}\left(\frac{q^*\mu_2(1+\sigma_2 x)+s}{\mu_1 y}\right)\left(\frac{q^*\mu_2}{\mu_1 y}\right)$ and $h(x) = x$ in the notation of Lemma A1) which implies $F_{\sigma_2}(q^*,\sigma_2) < 0$, $q^{*\prime}(\sigma_2) > 0$, and $\pi_1'(\sigma_2) > 0$.

The same approach may be used to conclude that a concave demand function implies $q^{*\prime}(\sigma_2) < 0$ and $\pi_1'(\sigma_2) < 0$.

**A.3.1.7. Increasing $\mu_b$.** Assume that $U_b$ is a nonnegative random variable that is based on either of the following two models:

$U_b = \mu_b + Z_b$, where $E[Z_b] = 0$, $V[Z_b] = \sigma_b^2$
$U_b = \mu_b Z_b$, where $E[Z_b] = 1$, $V[Z_b] = \sigma_b^2$.

We make this assumption so that we can isolate the effect of changing mean while keeping a measure of variation fixed. For example, if $U_b = \mu_b + Z_b$, then $V[U_b] = V[Z_b] = \sigma_b^2$ remains fixed as $\mu_b$ increases. If $U_b = \mu_b Z_b$, then the coefficient of variation of $U_b$ is $[\mu_b\sigma_b]/\mu_b = \sigma_b$, which remains fixed as $\mu_b$ increases. For the above two models of $U_b$,

$$\frac{\partial\rho_b(u)}{\partial\mu_b} = \frac{\partial}{\partial\mu_b}P[\mu_b + \sigma_b Z_b \le u] = \frac{\partial}{\partial\mu_b}P\left[Z_b \le \frac{u-\mu_b}{\sigma_b}\right] < 0$$

$$\frac{\partial\rho_b(u)}{\partial\mu_b} = \frac{\partial}{\partial\mu_b}P[\mu_b Z_b \le u] = \frac{\partial}{\partial\mu_b}P\left[Z_b \le \frac{u}{\mu_b}\right] < 0.$$

Therefore,

$$F_{\mu_b}(q^*,\mu_b) = -c\frac{\partial}{\partial\mu_b}\rho_b\left(\mu_2 E\left[\rho_1^{-1}\left(\frac{q^*\mu_2 Z_2+s}{\mu_1 Z_1}\right)\right]\right) > 0,$$

which implies $q^{*\prime}(\mu_b) < 0$ and $\pi_1'(\mu_b) < 0$.

**A.3.1.8. Increasing $p_0$.**
From

$$\bar{p}(q) = E\left[\max\left\{\rho_1^{-1}\left(\min\left\{\frac{q\mu_2 Z_2+s}{\mu_1 Z_1},1\right\}\right),p_0\right\}\right],$$

it is clear that $\bar{p}(q)$ is non-decreasing in $p_0$, and thus $F(q^*,p_0) = q^* - c\rho_b(\mu_2\bar{p}(q))$ is non-increasing in $p_0$, which implies $q^{*\prime}(p_0)(0$ and $\pi_1'(p_0) \ge 0$.

**A.3.2. Demand Model M2**

**A.3.2.1. Increasing $\alpha$.**

$$F_\alpha(q^*, \alpha) = 0 \Rightarrow q^{*\prime}(\alpha) = 0, \pi_1{}'(\alpha) = 0$$

**A.3.2.2. Increasing $b$.**

$$F_b(q^*, b) = -c\rho_b{}'\left(\mu_2 E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right]\right) \times \mu_2 E\left[\frac{1}{q^*\mu_2 Z_2 + s}\right] < 0$$
$$\Rightarrow q^{*\prime}(b) > 0, \pi_1{}'(b) > 0$$

**A.3.2.3. Increasing $c$.**

$$F_c(q^*, c) = -\rho_b\left(\mu_2 E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right]\right) < 0$$
$$\Rightarrow q^{*\prime}(c) > 0, \pi_1{}'(c) > 0$$

**A.3.2.4. Increasing $\mu_1$ and $\sigma_1$.** $F$ does not depend on market parameters, and thus $q^{*\prime}(\mu_1) = 0$, $\pi_1{}'(\mu_1) = 0, q^{*\prime}(\sigma_1) = 0, \pi_1{}'(\sigma_1) = 0$.

**A.3.2.5. Increasing $s$.** Note that $\frac{\partial}{\partial s}\left(\frac{b}{q^*\mu_2 z_2 + s}\right) < 0$ for any realization $z_2$ of $Z_2$. Thus, $\frac{\partial}{\partial s}E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right] < 0$ and $q^{*\prime}(s) < 0$.

However, $\pi_1{}'(s) > 0$ and $\pi_1{}'(s) < 0$ are possible. One example of positive and negative slopes of $\pi_1(s)$ can be found in section A.3.1.4, wherein $b = 1$, and another example is illustrated in Figure 8.

**A.3.2.6. Increasing $\mu_2$.**

$$\frac{\partial}{\partial \mu_2}\mu_2 E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right] = E\left[\frac{b(q^*\mu_2 Z_2 + s) - b\mu_2 q^* Z_2}{(q^*\mu_2 Z_2 + s)^2}\right]$$
$$= E\left[\frac{bs}{(q^*\mu_2 Z_2 + s)^2}\right] > 0$$
$$\Rightarrow F_{\mu_2}(q^*, \mu_2) < 0 \text{ and } q^{*\prime}(\mu_2) > 0$$
$$\Rightarrow \pi_1{}'(\mu_2) = q^* - \mu_2\left[-q^{*\prime}(\mu_2)\right] > 0.$$

**A.3.2.7. Increasing $\sigma_2$.** We write $Z_2$ in terms of its standardized random variable, i.e.,

$Z_2 = 1 + \sigma_2\zeta$,

where $E[\zeta] = 0$, $V[\zeta] = 1$, and $\zeta > -1/\sigma_2$ (to assure positive $Z_2$). Accordingly,

$$F_{\sigma_2}(q^*, \sigma_2) = c\rho_b{}'\left(\mu_2 E\left[\frac{b}{q^*\mu_2(1 + \sigma_2\zeta) + s}\right]\right) \times \mu_2 E\left[\frac{bq^*\mu_2\zeta}{(q^*\mu_2(1 + \sigma_2\zeta) + s)^2}\right]$$

$$E\left[\frac{bq^*\mu_2\zeta}{(q^*\mu_2(1 + \sigma_2\zeta) + s)^2}\right] < bq^*\mu_2 E\left[(q^*\mu_2(1 + \sigma_2\zeta) + s)^{-2}\zeta\right]E[\zeta] = 0$$

(due to Lemma A1-4)
$\Rightarrow q^{*\prime}(\sigma_2) > 0$ and $\pi_1{}'(\sigma_2) > 0$.

**A.3.2.7. Increasing $\mu_b$.** As in section A.3.1.7, assume that $U_b$ is a nonnegative random variable that is based on either of the following two models:

$U_b = \mu_b + Z_b$, where $E[Z_b] = 0$, $V[Z_b] = \sigma_b{}^2$
$U_b = \mu_b Z_b$, where $E[Z_b] = 1$, $V[Z_b] = \sigma_b{}^2$.

Then

$$\frac{\partial \rho_b(u)}{\partial \mu_b} = \frac{\partial}{\partial \mu_b}P[\mu_b + \sigma_b Z_b \le u] = \frac{\partial}{\partial \mu_b}P\left[Z_b \le \frac{u - \mu_b}{\sigma_b}\right] < 0$$

$$\frac{\partial \rho_b(u)}{\partial \mu_b} = \frac{\partial}{\partial \mu_b}P[\mu_b Z_b \le u] = \frac{\partial}{\partial \mu_b}P\left[Z_b \le \frac{u}{\mu_b}\right] < 0.$$

Therefore,

$$F_{\mu_b}(q^*, \mu_b) = -c\frac{\partial}{\partial \mu_b}\rho_b\left(E\left[\frac{b}{q^*\mu_2 Z_2 + s}\right]\right) > 0,$$

which implies $q^{*\prime}(\mu_b) < 0$ and $\pi_1{}'(\mu_b) < 0$.

**A.3.2.8. Increasing $p_0$.**

From $\bar{p}(q) = E\left[\max\left\{\frac{b}{q\mu_2 Z_2 + s}, p_0\right\}\right]$, it is clear that $\bar{p}(q)$ is non-decreasing in $p_0$, and thus $F(q^*, p_0) = q^* - c\rho_b(\mu_2\bar{p}(q))$ is nonincreasing in $p_0$, which implies $q^{*\prime}(p_0) \ge 0$ *and* $\pi_1{}'(p_0) \ge 0$.

# Notes

[1]A representative supplier has utility that is equal to the average utility, $u_a$, among the population of suppliers. To simplify notation, we use random variable $U_b$ to capture all of the randomness associated with the difference in utilities from the best alternative and artemisinin. For example, letting $U_B = \mu_b + \varepsilon_B$ and $U_a = u_a + \varepsilon_a$ denote the respective utilities from a randomly selected unit of farm space where $E[\varepsilon_B] = E[\varepsilon_a] = 0$, we define $U_b = \mu_b + \varepsilon_B - \varepsilon_a$, and thus the fraction of suppliers who prefer to produce artemisinin is $P[U_B \le U_a] = P[U_b \le u_a] = \rho_b(u_a)$.

[2]Note if $q^* < 0$, then no artemisinin is grown/produced, or if $q^* > c$, then all capacity is dedicated to producing artemisinin. We assume parameters are such that these extreme solutions are excluded.

[3]Data sources on historical prices and supply can be found in A2S2 (2012) and in Figure 1. Other (non-public) data on market size, yield, and usage of forward contracts are

collected and provided by UNITAID and WDI as part of multiple projects under the A2S2 initiative.

[4]A risk aversion parameter of $\gamma = 0.008$ is consistent with a threshold value for participation in 50/50 gamble of winning $0.5/\gamma$ = \$62,500 and losing $0.25/\gamma$ = \$31,125 (Howard 1988), for example, a supplier is willing to enter a 50/50 gamble of winning \$60K and losing \$30K, but not a 50/50 gamble of winning \$70K and losing \$35K.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article:

**Appendix S1.** Derivations and Proofs.