Research Article

Improving Supply Chain for Essential Drugs in Low-Income Countries: Results from a Large Scale Randomized Experiment in Zambia

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Abstract—Despite increased investments in procurement of essential medicines, their availability at health facilities remains extremely low in many low- and middle-income countries. The lack of a well-functioning supply chain for essential medicines is often the cause of this poor availability. Using a randomized trial conducted in 439 health facilities and 24 districts in Zambia, this study helps understand the optimal supply chain structure for essential medicines distribution in the public sector in low-income countries. It shows that a more direct distribution system where clinics order and receive medicines supply directly from the central agency through a cross-docking arrangement significantly reduces the duration and frequency of stockouts compared to a traditional three-level drug distribution system. As an example, the frequency of stockouts for first line pediatric malaria medicines reduced from 47.9% to 13.3% and the number of days of stockout in a quarter reduced from 27 days to 5 days. The direct flow of demand and order information from health facilities to the central supply agency reduces the problem of diffuse accountability that exists in multi-tiered distribution systems. It also shifts the locus of decision making for complex supply chain functions such as scarce stock allocation and adjustment of health facility order quantities to levels in the system where staff competency is aligned with what the function needs. Even when supply chain system redesign such as the one evaluated in this paper are demonstrated to be technically robust using rigorous evidence, they often require navigating a complex political economy within the overall health system and its actors.

Keywords: health systems management, logistics, pharmaceuticals, stock-out, supply chain

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INTRODUCTION

The availability of essential medicines is a persistent challenge in developing countries. Average availability of medicines in public sector health facilities across WHO regions was as low as 29.4% (ranged from 29.4% to 54.4%). The health consequences from such low levels of medicine availability are pronounced.

Access to essential drugs is contingent upon well-functioning supply chain systems that move drugs from the manufacturer through to end use. Supply chain management in public sector health systems has received increasing attention in recent years—as both a priority and a challenge for many countries—as governments struggle to deliver an increasing number of products. With the last decade’s increases in financing for health and with much of this new funding earmarked for combating priority diseases and less for health system strengthening, many public supply chains are now in charge of delivering a larger number and volume of products yet are given limited additional resources for investments in supply chain improvements. Despite the increasing awareness about the importance of efficient logistics systems for attainment of health outcomes, systematic analysis of essential drugs distribution system and their impact on stockout rates at the point of service delivery and priority health outcomes remains limited. Few studies have investigated factors that cause stockouts of essential products at the point of service delivery. Interventions to improve supply chains have included changing procurement and financing, training and management, and system redesign.

The structure of the system used to distribute a product from the manufacturer to end-customers has been studied in vast detail in commercial sector supply chains. Due to transportation cost and lead times, it is usually necessary to have a tiered distribution network, with a few levels of storage and distribution between the manufacturer and the end customer. The optimal number of levels in a distribution system is dependent on geographical factors, demand at each service point, frequency of shipment, storage space availability, and transport cost structure. Many scholars have studied these problems and have emphasized the need of better information integration between the levels in the distribution system. Incentive problems may arise in multi-tiered distribution systems when decisions are delegated to decentralized sites that have intimate knowledge of their immediate surroundings. Decentralization of stocking decisions can lead to potential incentive misalignment between the “principal” (the central planner) and “agents” (the decentralized site managers) as each site is maximizing its own performance metric. This misalignment often manifests itself in overstocking of product at the decentralized site and provides opportunities for theft and damage due to the likelihood of storage facilities and security systems being of lower quality at smaller decentralized sites. Over time, most commercial distribution systems have reduced the number of levels in the distribution channel. Businesses have realized that more levels in the distribution system reduces the ability of planners at the higher levels in the system to make decisions without observing actual demand and as a result creates managerial accountability problems in the system.

A commonly used solution to this problem is a distribution model known as “cross-docking.” Cross-docking involves the direct transfer of ready shipments from inbound transport/truck trailers (or railroad car) and the loading of these materials either directly onto outbound trucks, trailers, or rail cars, or loading after minimal storage but in either event with no lay away inventory. This practice has been a central feature of achieving faster inventory replenishment without significantly increasing transportation costs. This concept was first used in large scale by organized retailers such as Walmart where suppliers delivered products to the retailer’s distribution centers where the product is cross docked and then delivered to individual retail stores. This change to a two-tier cross-docking system helped retailers achieve significant savings in transportation costs, inventory holding costs, and reductions in stockouts. With cross-docking, frequent deliveries are viable to a larger number of distribution points without a concomitant increase in transportation cost. However, cross-docking does not always result in gains.

Many developing county health systems, including Zambia, typically have three levels in their public sector distribution system: where the central warehouse supplies to the district or provincial warehouses which in turn send supplies to the health facilities. Two and four level models are also used in some countries. Knowing how many levels are best for a public sector run medicines distribution system in a developing country requires understanding not only the cost and technical variables but also some complex incentives issues. As health systems decentralize, it also raises questions about which decisions related to ordering, stocking and inventory control should be centralized and which decisions should be decentralized. Since the completion of this randomized trial, a few recent studies have been conducted to analyze the impact of system redesign on health product supply chain performance using simulation models or pilot implementations. However, the strength of evidence and cost effectiveness of such design changes is still questioned by country-level policy makers. As a result, very few policy changes have been made regarding redesign of the medicine supply chain. Stronger political commitment and policy action for efficient supply chain system design and its
connected accountability structures requires rigorous evidence, which is currently lacking.

This paper presents the first rigorous study that addresses this issue using a large-scale randomized trial. A randomized control trial (RCT) was carried out to examine the effectiveness of three supply chain structures, including cross-docking, as described below:

- Model A—a three-tier system with storage of product at each level (Storage at National Distribution Center, District Health Office and Health Facility)
- Model B—a two-tier system, where product is only stored as lay away inventory at the National Distribution Center and the Health Facility. The District Health Office is used as a cross-docking point without lay away inventory
- Control group—Zambia’s existing distribution system as described in the section below

Background to Zambia’s Health Product Supply Chain

The Ministry of Health (MOH) of Zambia and its development assistance partners have invested substantial amounts of money in the public-sector drug procurement and distribution system in recent years. Despite these efforts, health centers across Zambia continue to face difficulties accessing drugs and medical supplies in appropriate quantities. The nationally representative 2006 Public Expenditure Tracking Survey concluded that essential and life-saving drugs were widely unavailable in health facilities across the country. For example, ampicillin, an antibiotic, was out of stock in 86% of the urban health clinics for an average duration of 7.4 weeks.

A priority for the Zambia health sector is malaria control. Over the last five years prior to this study, the National Malaria Program has made great improvements in indicators for malaria prevention. However, malaria case management indicators, which rely on drugs being available at the point of service delivery, continued to lag behind. Artemether-Lumefantrine, the first line treatment for malaria, was out of stock in 44% of the rural health facilities for an average duration as long as 9.5 weeks. According to the results from the 2008 Malaria Indicator Survey (MIS), only 43% of children under the age of five took an antimalarial within 24 hours of onset of symptom. Of these, no more than 16.6% of children living in urban area and 11.5% of those in rural areas took Artemisinin-based combination therapy (ACT), the adopted first line treatment for malaria.

Zambia has a three-tier public sector distribution system of essential drugs. Primary distribution of drugs and other health commodities from the capital city Lusaka to approximately 120 districts stores and hospitals is managed by a parastatal agency called Medical Stores Limited (MSL). Secondary distribution of commodities from district stores to approximately 1500 health facilities falls under the responsibility of District Health Management Teams (DHMTs) reporting to the MOH. Various assessments, conducted prior to the design of this study, identified secondary distribution, from district stores to health facilities, as the main bottleneck in the distribution system. This finding was also confirmed in the baseline data for this project which revealed significantly higher stockout rates of essential drugs in health facilities compared to the district stores and hospitals; 13 of the 15 essential drugs that were tracked in the baseline survey experienced a higher probability of stockout at the health facility level rather than at the district store. The majority of these differences are statistically significant at conventional levels.

Prior to this study, a few qualitative field studies were carried out between 2006 and 2008 to assess the bottlenecks in the public sector essential medicines distribution system in Zambia. The main reasons for the elevated stockouts of essential medicines at the health facilities captured in those studies are summarized below:

- Secondary distribution from the District Medicines Store to health centers was not carried out in a uniform manner across the country and many health centers were required to travel to their district headquarters to pick up items that were not included in the health facility kits. In theory, orders were placed by health facilities once per month; in practice the frequency of order placement and delivery (or collection) was often unsystematic and unpredictable.
- Communication between the District Store and health centers was difficult and relied upon a high-frequency radio communication system and personal cell phones.
- Lack of demand data resulted in the fact that supply decisions down to district level did not take actual consumption patterns into account.
- Transport was a significant bottleneck in the secondary distribution system. There are insufficient vehicles available at the district level to complete all necessary tasks of the District Store officer, and those that existed broke down regularly because of poor roads and high usage. Some health centers were routinely cut off for months due to poor accessibility and seasonal weather patterns.
- District Health Offices did not have dedicated logistics staff available; logistics tasks such as order placement, order expediting, distribution planning and inventory monitoring were performed by pharmacy technologists alongside many other duties.
Based on these observations, the strengths and weaknesses of a number of potential different distribution models were assessed by the study team and MOH with support from bilateral and multilateral donors to the health sector. The options that were considered included: Direct distribution to health facilities, distribution through regional medical stores, contracting distribution/transport functions to private third-party companies and enhancing planning capacity at various levels in the distribution system. The nature of the road network and the vehicle fleet at MSL rendered some options such as direct distribution to health facilities infeasible. Similarly, third-party transport companies in Zambia did not have coverage in remote and rural parts of the country making the contracting out option challenging for national scale-up. Extensive consultations were conducted, and an emergent consensus centered on two proposed alternative models. The study team worked with the MOH to design a RCT to evaluate the two proposed distribution system options as compared to the existing distribution system.

Objectives
The policy objective of the RCT was to identify a nationally scalable structure for medicines distribution which leads to systematic improvements in medicine availability at the health facility level. Two alternative distribution models, Model A and Model B, were compared with the current system to evaluate which model leads to lower stockouts of tracer drugs at health facilities. Operational details of the two models are described in the Methods/Intervention section.

METHODS
Study Design and Participants
A prospective cluster randomized evaluation design with randomization of distribution models conducted at the level of the district was used to measure the comparative effectiveness of Models A and B vis-à-vis the control and with each other. 24 study districts were selected from 72 total districts in Zambia.

To maximize the generalizability of any impact estimate to the wider national context, study districts were stratified and purposively selected to test the models in a variety of settings thereby increasing the study’s external validity. Districts were first stratified by rural or peri-urban status as well as by region to ensure a geographic balance in the selected districts and to further control for possible region wide influences on stock availability such as weather patterns. Within these four strata, districts were assessed on risk factors for stock outages of Artemether-Lumefantrine (AL—one of the primary tracer drugs) and then stratified into low risk (those with 2 or fewer risk factors) or high risk districts (those with 3 or 4 these risk factors). These risk factors included high malaria incidence (a positive relationship—the greater the malaria incidence the more likely a reported AL stock outage), likelihood of phone at facility level (a negative relationship), total district population (negative relationship), and average catchment area of facility (positive relationship). Together these predictors accounted for approximately 15% of the variation in observed AL outages in the universe of districts.

Within the 24 study districts, all public sector facilities (census) and select non-profit facilities that were served by the government supply system (MSL) were enrolled in the study. A Ministry of Health official facility list dated 2008 was used as the source database, which in turn was based on facility mapping activities carried out by the Japanese International Cooperation Agency and the USAID DELIVER project. The final list of eligible facilities was confirmed by MSL and the Ministry of Health before the start of the study. 416 health centers, 23 hospitals and their corresponding District Health Offices (18) were included in the study.

To understand the expected power of the study we ran simulations on standardized variables for the specific design. Given the small number of study clusters, standard errors were corrected for downward bias through linearization methods. The simulations reveal that the selected design can identify a standardized effect size of 0.335 at a significance level of 0.05 and a power of 0.8. The study design was only moderately powered to detect small intervention effect sizes (such as an 8-percentage point decrease from a baseline stockout rate of 50%) would not have been identified with precision. However, 24 districts were the maximum study size which our partner, the Ministry of Health of Zambia, could support in terms of providing government oversight on this randomized trial.

Intervention Design
In Model A the health facilities order drugs from the district and the district store maintains the stock of drugs i.e. the district store remains a stock holding point, hence Model A continues to be a three-tier system. A new role called the Commodity Planner (CP) is introduced at the district to enhance stock planning capacity. CP is responsible for coordinating orders from the health facilities and stock management at the district. CP also ensures that requisition requests
are sent every month by each health facility to the district store and performs picking and packing operations at the district level to fulfill the order requisitions of health facilities under that district. The CP estimates the overall requirements and places orders to central stores (MSL) for the stock needed to maintain the desired inventory level at the district store. The CP estimates the overall requirements and places orders to the central store (MSL) for the stock.

Model B eliminates the intermediate storage of drugs at the district level. The district store is converted into a “cross-dock,” i.e., point of transit, wherein it receives shipments from MSL that are pre-packed for individual health facilities. Under this option, the district does not carry any stock or perform any secondary picking and packing and the supply chain becomes a two-tiered system. Order requisitions from the health facilities are directly transmitted to MSL on a monthly basis where picking, assembly and sealing of packages to individual health facilities takes place. As in Model A, a commodity planner (CP) is added to the district store under this option but her role is limited to facilitating the delivery of the packages received from MSL to the health facilities as well as ensuring the order information from the health facilities to MSL.

The role of the Commodity Planner marked the first time that a logistics specialist position had been created at district level. The tasks assigned to the commodity planner had previously been part of the role of District Pharmacy Technologist, but in practice the staff in these roles did not have the time available to manage these logistics tasks effectively. Their roles had included important areas such as dispensing, monitoring rational drug use and pharmacovigilance in addition to logistics management.

Both Models A and B share some common features. Drugs included in the system are full supply products, health center kits disaggregated into individual drugs at the central level and District Health Office (DHO)/facility orders are augmented by bulk stock available at MSL. Full supply products are defined as those products for which enough stock to supply the national need for the duration of the intervention was either already in storage at MSL or was scheduled to arrive under a fully funded supply contract. Some drugs distributed under Models A and B came from breaking down health center kits into their constituent products and supplying based on demand rather than distributing entire kits in bulk.

Drugs for the critical HIV and TB programs had their own program specific supply chain arrangements and were not included in this intervention. The antiretroviral medicines used in the HIV program were managed through MSL using a cross-docking system and a data driven order calculation algorithm based on consumption data and new patient enrolment data submitted by each facility. TB medicines were also distributed by MSL, but based on specific distribution allocations provided by the national TB program for each district every month based on their records of active patients under treatment.

| Model Characteristics                                      | Model A                        | Model B                        | Control                  |
|------------------------------------------------------------|--------------------------------|--------------------------------|--------------------------|
| Commodity Planner coordinates logistics at district level   | Yes                            | Yes                            | No                       |
| Entity where health facilities submit their orders         | District Store (then an aggregate order for the district is submitted to MSL) | Directly to MSL               | District Store (then an aggregate order for the district is submitted to MSL) |
| Number of tiers in the system                              | 3                              | 2                              | 3                        |
| Sealed packages earmarked for health facilities are assembled at Medical Stores Limited (MSL), the central supply and distribution center for medicine | No                             | Yes                            | No                       |
| Intended frequency of delivery from MSL to districts        | Monthly                        | Monthly                        | Monthly                  |
| Intended frequency of delivery from district store to health facilities | Monthly to facilities with adequate storage space otherwise bi-monthly | Monthly to facilities with adequate storage space otherwise bi-monthly | Monthly to facilities with adequate storage space otherwise bi-monthly. In practice ad-hoc |

**TABLE 1. Description of the Three Distribution Models**
Table 1 summarizes the detailed features of the three delivery models.

**Randomization**

Districts (clusters) were randomly assigned by the study team, on the basis of a computer-generated random number sequence, to either one of the two intervention arms or the control group within the strata identified earlier. The location of each selected district is shown in Figure 1. The selected districts were geographically balanced in terms of rural and peri-urban areas as well as regions of Zambia. Masking of participating sites was not possible as provincial, district, and health facility managers knew which distribution model they will be recovering their supplies from.

Randomizing at the district level provided relatively few number of study units. Traditional approaches to standard error estimates, notably the cluster-robust standard error, may be downward biased and thus over-reject the null hypothesis of no treatment effect. To counteract this, the precision of statistical tests was assessed through Randomization Inference (RI) which assumes all observed outcomes and covariates to be fixed and generates the reference distribution of test statistics by modeling the treatment assignment as the sole random variable in the data. RI compares the actual test statistic observed in the evaluation against the distribution of all conceivable test statistics as determined through permutation methods—where the actual statistic falls in this distribution determines the exact p-value. This one-tailed hypothesis test is considered an exact test because it does not require a large-sample approximation as randomization itself is the basis for inference and permutation methods have exhausted all possible treatment assignments across districts. An exact test has the added benefit that it does not impose distributional assumptions that are often behind approximations of reference distributions in standard hypothesis testing.

**Outcomes**

The primary metric of program performance was the incidence of drug stockouts at the time of survey defined as an instance of zero stock in the store room and dispensary of the health facility on the day of the survey visit. Stockouts (and other metrics described in the following paragraphs) were measured for 15 tracer drugs deemed critical to the conduct of preventive and curative primary care in the Zambian context. The tracer drugs used for the study evaluation provide an assortment of products with different seasonal and other demand characteristics, rather than a comprehensive list of all products needed for malaria prevention and treatment. Given the primacy of malaria in many rural areas of Zambia, four variants of the malaria curative drug Artemether/Lumefantrine, applicable to four non-overlapping age ranges, are included in the tracer list as are other malaria related drugs such as malaria Rapid Diagnostic Tests (RTDs) and Sulfadoxine/pyrimethamine (SP), used in malaria prevention for pregnant
women. Additional tracer drugs include two types of antibiotics, a deworming medicine, and several types of contraceptives. Inventory count was taken for each of the 15 drugs at each health facility at both baseline and end line and was used to validate if specific instances of stockouts observed at the time of survey tallied with explicit counts of product inventory.

Another key measure of drug availability estimated was the duration of stockouts, estimated as the number of days a drug was unavailable at the time of survey.

Two dedicated facility surveys, qualitative interviews with Commodity Planners, and an analysis of facility stock control cards provided data to evaluate the program. The baseline data collection covered all health facilities in the targeted districts, covering 416 health centers, 23 hospitals and 18 District Health Offices, and was conducted in Dec-Jan of 2008-09. The follow up data collection was conducted during the same months in 2009–10, one year after the baseline survey. Data on inventory count and stockout rates of the 15 tracer drugs were collected at both baseline and end-line. The end-line survey was more comprehensive in design and included supplementary information on stock- ing history and storage conditions. The data on duration of stockouts was collected based on a questionnaire administered during the end-line survey in Dec 2008-Jan 2009. The survey asked for days of stockout for the preceding 3 months. The reported data were validated with data regarding last receipt of stock, inventory count, and quantity in stock and receipt data from stock cards used in each facility; these cards record all receipts and consumption of stock in the health facility.

Aside from the primary outcomes relating to the availability of drugs (i.e., stockouts and stockout duration), the study also assessed pharmaceutical storage conditions at the health facilities. Table 6 lists 14 dimensions of storage conditions as judged by trained survey interviewers. These interviewers were trained by experienced public health logistics professionals from the USAID/DELIVER project using tools/methods used in similar exercises over many years in several countries. The interviewers gathered data at each health facility using a combination of standardized questions and direct observation of conditions in the health facility storage area.

**Statistical Analysis**

First, we compared key measures across the study districts at baseline. Tables 2 and 3 report the stockout probability and inventory count of the 15 tracer drugs, respectively, at the time of baseline interview for all facilities surveyed in the 24 districts in the study. For the vast majority of pair-wise comparisons with the control districts, the baseline facility outcomes in A or B districts are not significantly different. The stratified randomization process appears to have been highly successful in balancing key outcomes at baseline and thus ensuring suitable comparability between treatment and control districts.

We then estimated the effectiveness of the interventions (distribution Model A, distribution Model B) on the primary outcomes of interest at health facilities using an intention-to-treat approach. Linear regression models with district-group stratification indicators were fit using STATA version 12 to estimate the relative effectiveness of the two distribution models vis-à-vis each other and the existing system. Various measures on the post-intervention availability of selected tracer medicines are presented in tables in the following section, along with the exact p-values for the estimates of relative effectiveness.

For outcomes such as drug stockout incidence or duration, we utilized a difference-in-difference regression specification. This specification, given in equation (1) below, relates the outcome of interest (for a particular tracer drug), $O$, at facility $f$ in district $d$ at both baseline ($t = 0$) and follow-up periods ($t = 1$). The variables $A$ and $B$ are binary indicators for A and B districts, respectively. $T$ is a binary indicator for the follow-up period ($t = 1$).

$$O_{fd} = \gamma_0 + \gamma_A A_{fd} + \gamma_B B_{fd} + \gamma_1 T + \gamma_{A1} A_{fd} T + \gamma_{B1} B_{fd} T + \gamma_X X_{fd} + \epsilon_{fd}$$ (1)

The analysis also controls for the district-level stratification variables, $X$. The coefficients of interest, those that identify the causal impact of Models A and B through the interactions of A or B and T, are given by $\gamma_{A1}$ and $\gamma_{B1}$. Select coefficients from the difference-in-differences regressions that look at stockout like- lihood as the dependent outcome are included in the results section. Exact standard error for the impact estimate coefficients in equation (1), namely $\gamma_{A1}$ and $\gamma_{B1}$ are also reported in the results tables.

Similar to the test for likelihood of stockout, a formal test of difference in stockout duration can be conducted in a single difference regression framework given by equation (2):

$$O_{fd} = \gamma_0 + \gamma_A A_{fd} + \gamma_B B_{fd} + \gamma_X X_{fd} + \epsilon_{fd}$$ (2)

where the outcome of interest, $O$, at facility $f$ in district $d$ is related to binary indicators for A and B districts, respectively. As before, the $X$ vector controls for stratification variables. The coefficients of interest, those that identify
TABLE 2. Probability of Stockout in Health Centers and Health Posts- at Baseline, by Tracer Drug (Study Balance)

| Tracer Drug                                      | Control (K) mean | Model A mean | P-value: A vs. K | Model A mean | P-value: B vs. K | P-value: B vs. A |
|--------------------------------------------------|------------------|--------------|------------------|--------------|-----------------|-----------------|
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 6 tabs | 0.423            | 0.338        | 0.113            | 0.433        | 0.923           | 0.596           |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 12 tabs | 0.380            | 0.462        | 0.133            | 0.550        | 0.725           | 0.902           |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 18 tabs | 0.338            | 0.431        | 0.049            | 0.483        | 0.904           | 0.713           |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 24 tabs | 0.338            | 0.400        | 0.893            | 0.400        | 0.734           | 0.286           |
| Amoxycillin, Oral Suspension 125 mg/5 mL, bottle of 100ml | 0.718            | 0.738        | 0.826            | 0.717        | 0.730           | 0.689           |
| Benzyl Penicillin, Inj., 5MIU/vial, 10 vials | 0.225            | 0.246        | 0.306            | 0.200        | 0.644           | 0.340           |
| Co-trimoxazole, 480 mg, tab, bottle of 1000 tabs | 0.451            | 0.415        | 0.379            | 0.400        | 0.352           | **0.038**        |
| Medroxyprogesterone acetate, 150mg/ml, injectable suspension as depot, Vial | 0.254            | 0.385        | 0.169            | 0.450        | 0.812           | 0.233           |
| Rapid Diagnostic Kit for malaria, Box of 25 tests | 0.465            | 0.462        | 0.599            | 0.433        | 0.513           | 0.375           |
| Male Latex Condoms, box of 100/144 | 0.183            | 0.262        | 0.506            | 0.317        | 0.900           | 0.166           |
| Metronidazole, 200mg, tabs, bottle of 1000 | 0.606            | 0.615        | 0.502            | 0.533        | 0.804           | 0.188           |
| Levonorgestrel and Ethinyl Estradiol Tablets, 0.15 mg/0.03 mg, tabs, 28 | 0.408            | 0.585        | 0.585            | 0.700        | 0.155           | **0.021**        |
| Quinine dihydrochloride,600 mg, Injection, 2ml ampoules | 0.338            | 0.477        | 0.157            | 0.467        | 0.629           | 0.701           |
| Quinine Sulphate, 300mg, tab, Bottle of 1000 tabs | 0.085            | 0.031        | 0.114            | 0.183        | 0.809           | 0.250           |
| Sulfadoxine+Pyrimethamine, 500mg=25mg, Tablet-FDC, Bottle of 1000 tabs | 0.535            | 0.585        | 0.413            | 0.517        | 0.806           | 0.492           |

**Note:** Estimates based on data from 196 facilities in 24 districts. Exact p-values calculated through randomization inference. P-values in **bold** significant at 10% level in a two-tailed hypothesis test.

TABLE 3. Inventory Count in Health Centers and Health posts- At Baseline, by Tracer Drug
the causal impact of Models A and B, are given by $\gamma_A$ and $\gamma_B$. The mean number of days of stockout for each of the 15 tracer drugs as well as the p-values for the regression coefficients $\gamma_A$ and $\gamma_B$ as well as a p-value of the formal direct test of Model A vs. Model B are included in the results section.

Limitations
This RCT measured the primary outcome variable i.e. medicine availability using health facility surveys conducted at baseline and end line. These surveys are a “snapshot estimate” of medicine availability and therefore may not be representative of mean availability over a month, week or any aggregate time interval. Similarly, the duration of stockout was estimated using memory recall in the health facility survey with verification from the stock control card. This study used stockouts as the main outcome measure, it did not explicitly analyze if the inventory in stock at a health facility was as per the recommended stocking policy (Tables 3 & 4 show the inventory counts).

This study only collected estimates of primary outcomes i.e. availability at two points in time (baseline and endline). If multiple observations in time either before or during the intervention period (or both) were collected, study precision could have been further increased by using ANCOVA-type analyses in addition to the difference-in-difference estimation.

Results
The summary results from the pilot program evaluation show that availability of essential medicines improved remarkably at the health facility level, particularly in districts where Model B was used to supply to the health facilities. Figures 2 and 3 show the changes in drug availability for select tracer drugs both pre- and post-intervention in health facilities under A and B districts respectively.

Although the reductions in stockout rates in health facilities under model A is apparent, the gains are far less than the gains observed in model B districts. Figure 2 shows dramatic decreases in stockout rates for the same select drugs, with

| Tracer drug                                      | Control (K) endline mean | Model A endline mean | P-value of diff-in-diff coefficient: A vs. K | Model mean |
|--------------------------------------------------|--------------------------|----------------------|---------------------------------------------|------------|
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 6 tabs | 0.479                    | 0.292                | 0.161                                       | 0          |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 12 tabs | 0.417                    | 0.246                | 0.043                                       | 0          |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 18 tabs | 0.493                    | 0.231                | 0.007                                       | 0          |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 24 tabs | 0.557                    | 0.4                  | 0.118                                       | 0          |
| Amoxycillin, Oral Suspension 125 mg/5 mL, bottle of 100ml | 0.521                    | 0.323                | 0.072                                       | 0          |
| Benzyl Penicillin, Inj., 5MIU/vial, 10 vials       | 0.028                    | 0.031                | 0.449                                       | 0          |
| Co-trimoxazole, 480 mg, tab, bottle of 1000 tabs   | 0.732                    | 0.4                  | 0.034                                       | 0          |
| Medroxyprogesterone acetate, 150mg/ml, injectable suspension as depot, Vial | 0.408                    | 0.185                | 0.026                                       | 0          |
| Rapid Diagnostic Kit for malaria, Box of 25 tests  | 0.38                     | 0.185                | 0.127                                       | 0          |
| Male Latex Condoms, box of 100/144                | 0.113                    | 0.123                | 0.243                                       | 0          |
| Metronidazole, 200mg, tabs, bottle of 1000        | 0.437                    | 0.462                | 0.544                                       | 0          |
| Levonorgestrel and Ethinyl Estradiol Tablets, 0.15 mg /0.03 mg, tabs, 28 | 0.324                    | 0.154                | 0.065                                       | 0          |
| Quinine dihydrochloride,600 mg, Injection, 2ml ampoules | 0.183                    | 0.169                | 0.147                                       | 0          |
| Quinine Sulphate, 300mg, tab, Bottle of 1000 tabs | 0.211                    | 0.077                | 0.246                                       | 0          |
| Sulfadoxine+Pyrimethamine, 500mg+25mg, Tablet-FDC, Bottle of 1000 tabs | 0.606                    | 0.484                | 0.179                                       | 0          |

Note: Estimates based on data from 196 facilities in 24 districts. Regression specification includes stratification varia region, and high-risk stockout indicator). Exact p-values calculated through randomization inference. P-values in bold one-tailed hypothesis test.

TABLE 4. Difference-In-Difference Estimate of Probability of Stockout, by Tracer Drug
decreases in stockout rates larger than 40 percentage points for Sulfadoxine/pyrimethamine, Amoxicillin and Artemether/lumefantrine for adults. (More formal tests of differential gains between intervention and control districts are included in Table 4). Overall these results show large performance improvements in the supply chain in Model B districts.

Table 4 reports stockout rates as assessed at end line. As compared to stockout rates at baseline (Table 2) we observe...
a substantially lower stockout incidence in both Model A and, especially, Model B facilities. For example, while the stockout for AL 1 6 in facilities in the control arm was 47.9%, only 29.2% of Model A districts and 13.3% of Model B districts were out of the drug at time of survey.

The likelihood of stockouts is significantly lower in Model A facilities than control group facilities for 6 of the 15 tracer drugs—AL 2x6, AL 3x6, Amoxicillin, Cotrimoxazole, Depot medroxyprogesterone acetate (DMPA), and Ethinylestradiol/Levonorgestrel tablets. Model B performed even more impressively—all but 3 of the 15 tracer drugs experienced significantly lower rates of stockout as a result of the Model B activities. Given the inferential challenges of the small number of districts in the study, the magnitude and precision of the gains are especially striking. The final column in Table 4 also presents the p-value for the difference-in-difference estimate comparing Models A and B directly. This shows that Model B also attains significantly lower stockouts when compared with Model A for 6 drugs—all four forms of Artemether/Lumefantrine, Depot medroxyprogesterone acetate (DMPA), and Sulfadoxine/Pirimethamine—and nearly significant reductions for 3 additional drugs—Amoxicillin, Ethinylestradiol/Levonorgestrel tablets, and Quinine. The number of significant or nearly significant findings for Model B along with greater reductions in stockout rates indicates Model B performed relatively better than Model A in reducing the likelihood of stockout. Given the aggregate nature of this systems intervention, the ability to identify statistically significant impacts under the conservative approach of Randomization Inference speaks to the magnitude of gains achieved in both models but, especially, Model B.

Another key measure of drug availability is the duration of stockouts, measured here as the number of days a drug was unavailable over the common reference period of the fourth quarter of 2009 captured during the end line survey. Figure 4 shows the average number of days of stocks-outs of selected drugs in health facilities for the fourth quarter of 2009 across the different study arms (A, B, and control). Model B facilities experienced much reduced lengths of drug unavailability while A districts performed only marginally better than control districts. For pediatric AL 1x6, the drug was stocked out an average of 27 days out of a maximum of 92 days in control districts while this number was 18 days in Model A facilities and 5 days in Model B facilities. A similar pattern occurs for AL 4x6 for adults, Amoxicillin, and CTX. Districts where Model A was implemented had more days of stockouts compared to comparison districts for DMPA, and the difference between comparison districts (37 days) and A districts (36 days) for SP is negligible.

Table 5 conveys the number of days of stockout for each of the 15 tracer drugs as well as the p-values for the estimated statistical models. In general, for 11 of the 15 tracer drugs, Model A experiences less drug stockout days than control facilities. However, for only one drug, AL 2x6, is this reduction significant. In contrast Model B yields far fewer
days of drug stockout for virtually all drugs (14 of the 15) and for 11 of these drugs the reductions are statistically significant. Model B facilities also experience significantly less stockout days than Model A facilities for six of the tracer drugs. Overall, Model B results in significantly greater drug availability than either the existing distribution system in the control districts or that found in Model A.

In addition to the primary outcome relating to the availability of drugs, the study compared pharmaceutical storage conditions at point of service. Table 6 lists the 14 storage condition categories for health facilities in Model A, Model B and control group. Select storage conditions are significantly higher at endline in both Models A and B than in the control facilities. Both Models A and B stock-rooms have significantly higher rates of separated damaged or expired medicines, appropriate fire safety equipment, and storage conditions assessed adequate by the interviewer. Model A stock-rooms also score significantly higher on 4 additional conditions and Model B scores higher on two further conditions. Comparing A and B directly, Model B facilities exhibit significantly higher rates of commodities stored and organized according to First to Expire, First Out (FEFO) principles, storage kept at appropriate temperature, appropriate fire safety, and products stored on pallets and shelves. It is clear that the presence of CPs introduced in both models resulted in not only increased drug availability (especially in Model B districts) but also safer drug storage conditions.

In conclusion, a more streamlined distribution model (Model B) was highly effective in increasing drug availability and storage conditions when compared to the “business-as-usual” distribution system or a system with increased district technical capacity. Appendix 1 provides a preliminary modelling based comparative effectiveness and cost-effectiveness of the interventions in this study.

DISCUSSION

The preceding analysis clearly demonstrates the effectiveness of the two interventions, especially Model B. While this study was not explicitly designed to understand the causal mechanism, we present some ideas for what contributes to remarkable improvements in medicine availability under the interventions that were evaluated.

Both Model A and B perform better than the control districts because information flow and stock visibility are higher in Models A and B due to the presence of clear

| Tracer drug | Control (K) endline mean | Model A endline mean | P-value of diff-in-diff coefficient: A vs. K | Model B mean | P-value of diff-in-diff coefficient: B vs. K | P-value of diff-in-diff coefficient: B vs. A |
|-------------|--------------------------|----------------------|---------------------------------------------|--------------|---------------------------------------------|---------------------------------------------|
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 6 tabs | 69.28 | 76.56 | 0.363 | 139.50 | 0.052 | 0.021 |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 12 tabs | 97.68 | 81.86 | 0.570 | 177.93 | 0.068 | 0.001 |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 18 tabs | 89.93 | 72.97 | 0.566 | 152.67 | 0.125 | 0.003 |
| Artemether-lumefantrine, 20mg/120mg, FDC, Blister 24 tabs | 62.60 | 56.30 | 0.617 | 161.33 | 0.044 | 0.002 |
| Amoxycillin, Oral Suspension 125 mg/5 mL, bottle of 100ml | 9.00 | 19.31 | 0.130 | 68.47 | 0.001 | 0.001 |
| Benzyl Penicillin, Inj., 5MIU/vial, 10 vials | 48.56 | 31.55 | 0.925 | 58.03 | 0.193 | 0.004 |
| Co-trimoxazole, 480 mg, tab, bottle of 1000 tabs | 1.45 | 3.10 | 0.115 | 4.59 | 0.173 | 0.494 |
| Medroxyprogesterone acetate, 150mg/ml, injectable suspension as depot, Vial | 46.19 | 93.66 | 0.044 | 262.45 | 0.000 | 0.002 |
| Rapid Diagnostic Kit for malaria, Box of 25 tests | 14.03 | 7.84 | 0.997 | 9.63 | 0.577 | 0.005 |
| Male Latex Condoms, box of 100/144 | 28.51 | 12.05 | 0.777 | 28.19 | 0.362 | 0.033 |
| Metronidazole, 200mg, tabs, bottle of 1000 | 1.22 | 2.39 | 0.139 | 2.28 | 0.082 | 0.551 |
| Levonorgestrel and Ethinyl Estradiol Tablets, 0.15 mg/0.03 mg, tabs, 28 | 144.94 | 390.82 | 0.102 | 269.55 | 0.100 | 0.621 |
| Quinine dihydrochloride,600 mg, Injection, 2ml ampoules | 76.53 | 37.03 | 0.641 | 157.95 | 0.000 | 0.000 |
| Quinine Sulphate, 300mg, tab, Bottle of 1000 tabs | 50.69 | 3.52 | 0.703 | 5.49 | 0.593 | 0.118 |
| Sulfadoxine+Pyrimethamine, 500mg+25mg, Tablet-FDC, Bottle of 1000 tabs | 0.48 | 0.73 | 0.229 | 2.06 | 0.002 | 0.004 |

Note: Estimates based on data from 196 facilities in 24 districts. Regression specification includes stratification variables (rural or peri-urban, region, and high-risk stockout indicator). Exact p-values calculated through randomization inference. P-values in **bold** significant at 10% level in a one-tailed hypothesis test.

**TABLE 5.** Difference-In-Difference Estimate of Inventory Counts, by Tracer Drug
The direct flow of demand and order information from health facilities to MSL under Model B reduced the problem of diffuse accountability. In Model A and the current system, the district was holding stock and district managers made allocation decisions about how much of the order from each clinic to fill. They did this without a full overview of the district-wide demand for drugs and alongside with managing many other competing tasks and responsibilities. In Model A (and also in the control districts), the demand at the health facility is opaque to MSL and often also to the district due to “order inflation” by the health facilities. Health facilities, knowing that the district “rations” stock to them, tend to engage in “order inflation” i.e. over order. As a result the district loses its ability to robustly estimate the actual demand at the health facilities it serves. Such behavior is witnessed in several industries, including consumer packaged goods and hi-tech electronics and its existence is attributed to both operational and behavioral factors. A system where stock levels for many drugs have to be maintained at the district to serve the demand for multiple health facilities faces multiple behavioral challenges, including: the cognitive limitation of the district level decision maker to manage the underlying complexity, the tendency of the health facility and district not to fully account for what is on-order but still not delivered when making ordering decision, and the tendency to mistrust and develop counter-acting strategies for the actions of decision makers at the higher (or lower) tier in the supply chain.

Also, pre-packaged supplies earmarked for each health facility ensured there is no leakage or product diversion in the supply chain during transportation and storage at the district. The direct flow of demand information from the health facility to MSL and pre-packaged supplies for health facility were the key performance-enhancing attributes of Model B. And, importantly, by removing some of the burden from the non-specialist staff at the District Health Offices, Model B allowed for the centralization of a greater portion of the supply chain functions within MSL, a specialist supply chain organization. The specialist staff at MSL are better trained to pick up on inflated or miscalculated order quantities than district staff and are more objective in their choice of adjusted replenishment quantities to health facilities as compared to district level staff. In theory, district staff should have closer communication with the health facilities in their district and as a result have better information and ability to adjust over ordering or under ordering by health facilities. In practice, the cultural, political and economic context within which district and health facility relationships operate often prevents such careful stock allocation outcomes at the district. Enabling better incentive design for district health managers and the health facilities

| Storage condition                                      | Control (K) mean | Model A mean | P-value: A vs. K | Model B mean | P-value: B vs. K | P-value: B vs. A |
|-------------------------------------------------------|------------------|--------------|------------------|--------------|-----------------|-----------------|
| Commodities stored and organized according to FEFO     | 0.59             | 0.75         | 0.163            | 0.85         | **0.008**       | 0.013           |
| Separated damaged or expired medicines                 | 0.77             | 0.96         | **0.011**        | 0.94         | **0.010**       | 0.331           |
| Medicines separated from insecticides and chemicals    | 0.82             | 0.92         | **0.098**        | 0.91         | 0.104           | 0.418           |
| Sufficient current storage space                       | 0.62             | 0.64         | 0.306            | 0.66         | 0.354           | 0.408           |
| Storage area free of rodents or insects                | 0.66             | 0.77         | 0.114            | 0.67         | 0.425           | 0.384           |
| Storage secured by lock and key                        | 0.95             | 0.95         | 0.481            | 1.00         | **0.031**       | 0.116           |
| Protection from direct sunlight                        | 0.91             | 0.97         | **0.065**        | 0.93         | 0.485           | 0.995           |
| Storage area kept at appropriate temperature           | 0.74             | 0.67         | 0.826            | 0.73         | 0.626           | **0.017**       |
| Supplies protected from water penetration              | 0.82             | 0.77         | 0.768            | 0.90         | 0.178           | 0.138           |
| Appropriate fire safety equipment                      | 0.23             | 0.48         | **0.043**        | 0.51         | **0.014**       | **0.040**       |
| Products stored on pallets/shelves                     | 0.74             | 0.78         | 0.448            | 0.87         | 0.137           | **0.039**       |
| Products stored away from outer wall                   | 0.55             | 0.67         | **0.095**        | 0.55         | 0.448           | 0.856           |
| Interviewer assessed adequate storage conditions        | 0.59             | 0.77         | **0.055**        | 0.78         | **0.052**       | 0.216           |
| Interviewer assessed facility maximized storage potential | 0.73             | 0.88         | **0.021**        | 0.75         | 0.550           | 0.943           |

Note: Estimates based on data from 196 facilities in 24 districts. Regression specification includes stratification variables (rural or peri-urban, region, and high-risk stockout indicator). Exact p-values calculated through randomization inference. P-values in bold significant at 10% level in a one-tailed hypothesis test.

**TABLE 6.** Likelihood of Satisfying Select Storage Conditions Observed at Time of Interview
contained in the district so that they are jointly held accountable for outcomes, is an important area of future research which this study doesn’t delve into.

The results of this study have been used by the Ministry of Health of Zambia to inform and improve the design of the public sector health supply chain in recent years. MSL now operates four distribution hubs outside of Lusaka (located in Eastern, Southern, Western and Copperbelt provinces) which operate as cross docking-points for health facilities in those regions. MSL has also expanded and reconfigured its national distribution center in Lusaka to support its shift from picking relatively few large, bulk orders for district health offices to picking larger numbers of small orders for individual health facilities. Orders processed through MSL per month have increased from 300 to more than 2,000 and the number of distribution routes has increased from 34 to 71. A supply chain assessment carried out by USAID in 2017 shows that frequency of stockouts at health centers was 12% (average across a list of 10 health products with some overlap with the tracer drugs included this study) and average stockout duration was 14.5 days over a 6-month period from December 2016 through May 2017. As stated earlier this study was focused on improving distribution for selected products which were in full supply at the national procurement agency level. Any comparisons with stock availability over time would also have to take into account any discrepancies or delays in product procurement.

In summary, this RCT has allowed us to understand the impact of intricate operational, behavioral and political issues which are difficult to model analytically or through simulation. Reorganization of stock ordering and stock keeping roles and reduction in the commonly accepted hierarchical structure of the medicine supply chain is fraught with a complex political economy. Streamlining flows and skipping storage at districts or provinces causes unease among provincial or district health managers who may view this change as a loss of authority and control. Moving the locus of decision making about order quantities farther from the district health teams can also be seen as contradictory to health system decentralization in which district is the management unit responsible for primary care. Supply chain design and decision-making structures which are technically optimal in some cases lead to conflict between district and federal level health officials over which party is truly responsible for health system performance. Rigorous empirical studies which more explicitly capture the political and behavioral dimensions of supply chain reform are needed to create policy acceptance and action.

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APPENDIX 1 COMPARATIVE EFFECTIVENESS AND COST-EFFECTIVENESS OF THE SUPPLY-CHAIN INTERVENTIONS

The evaluation directly measures the gains in drug availability as a result of the supply-chain interventions. Translating these increases in availability to gains in health—an important step necessary to compare the effectiveness of these interventions in relation to other potential uses of health resources— requires a modeling exercise that leverages household survey estimates of health behavior as well as epidemiological estimates of disease burden.

There is no standard methodology for estimating the health outcome impact of stockouts. The key health outcome investigated in this exercise is malaria-related mortality and a decision tree framework was used to estimate the impact on mortality and morbidity of reduced stockouts rates of the first-line malaria treatment in A, B and comparison districts. A patient centered decision-tree framework was adopted to describe the decision alternatives that may be chosen by a patient/care giver who encounters a stockout in a public health facility. The consequences for each pathway the patient can take in terms of full recovery, partial recovery, deaths, and days of illness were then measured. Appendix 2 presents the full decision tree framework for both under-five and over-five malaria infections.

The estimates presented focus only on the health outcome improvements from a reduction in the stockouts of Artemether Lumefantrine (AL) used for the treatment of uncomplicated malaria. Because the pilot program had a positive impact on the access to all essential drugs that are supplied to the health facilities, these estimated health gains are highly conservative in their focus on one drug—there is no additional attempt to estimate health gains from increased availability of the 52 medicines and medical supplies in the Primary Health Center (PHC) Kit and over 50 other medicines in various pack forms that are available in the MSL catalogue and are ordered by health facilities.

Under Model B the probability that not one of the ACT packages is available at a given clinic is only 1 percent. Given that stockouts are substantially higher in Model A and control districts, the health gains should be significant. This decision-tree approach deliberately takes conservative estimates of key behavioral parameters. The results suggest that if Model B were scaled-up nationwide, under-five and over-five mortality due to malaria would decrease by 21 percent and 25 percent respectively.

Appendix Table 1 presents a comparison of the current system (the control), Model A and Model B in terms of actual cases of uncured malaria, severe malaria, and deaths due to malaria for under-five and over-five children respectively should these different models be scaled up nationwide. Translating the information in the table to averted deaths, if Model B were scaled up nationwide, an additional 3,320 under-five deaths and 448 over-five deaths due to malaria would be averted each year. This implies a reduction of 21.4 percent and 25.4 percent in under-five and over-five mortality attributable to malaria respectively.

An episode of illness also has a significant economic cost to the household due to the productive time lost per episode for a sick adult and also for an adult caring for sick children. Often times, the economic burden of an illness episode on a household can be devastating enough to bring a household into extreme poverty, debt and the sale of assets, which jeopardizes a household's future earnings potential. Again with a focus on untreated or ineffectively treated malaria, and using the concept of foregone income (i.e. calculating the value of lost workdays as a result of malaria based on estimated wages) a national scale-up of model B should result average direct savings of over $1,629,312. Appendix Table 2 summarizes the benefit from national scale-up of Model.

Although Models A and B are effective to various degrees, another important consideration for health policy makers is the relative cost of each option. A comprehensive costing exercise covered both recurrent costs such as salaries and transport as well as fixed initial costs such as staff recruitment and training. In order to estimate a per district average monthly cost the fixed initial cost was distributed over a 5 year period. As costs will be compared across versions A, B, and control areas, future costs were neither adjusted for expected inflation nor were they discounted (this is equivalent to setting the discount rate to equal the expected inflation rate). All costs were measured in 2010 Zambian Kwacha and cost aggregates then converted to US dollars at the 2010 exchange rate of 4500 Kwacha to one dollar.

The estimated additional costs to the supply chain per district per month are presented in Appendix Table 3. These costs are estimated to be $3479 for intervention A and $3971 for B (including recurrent costs and fixed costs). The monthly recurrent costs for Model A and Model B are $2832 and $3120 respectively.
and $3325 respectively. The cost difference between the two interventions is due to the additional transport costs captured under B as well as higher personnel costs at central stores for picking and packing activities. The estimate cost differential implies that the additional cost of B is 17 percent greater than the additional cost of A. Given the relative performance of version B, this cost differential may well be worth the investment.

When comparing the average distribution cost in pilot areas to the equivalent for the average district in Zambia, it is important to keep in mind that the pilot was implemented in remote districts with higher transport costs. In many ways the more pertinent cost comparison is with regards to the per district monthly cost of the existing distribution system. This cost, determined by dividing the total system cost by the number of districts in Zambia, is $3878.

How do these intervention costs relate to the gains observed by models A and B? Cost-effectiveness interventions of the two models are presented in two ways—first in terms of the cost per day of essential medicine and $3325 respectively. The cost difference between the two interventions is due to the additional transport costs captured under B as well as higher personnel costs at central stores for picking and packing activities. The estimate cost differential implies that the additional cost of B is 17 percent greater than the additional cost of A. Given the relative performance of version B, this cost differential may well be worth the investment.

When comparing the average distribution cost in pilot areas to the equivalent for the average district in Zambia, it is important to keep in mind that the pilot was implemented in remote districts with higher transport costs. In many ways the more pertinent cost comparison is with regards to the per district monthly cost of the existing distribution system. This cost, determined by dividing the total system cost by the number of districts in Zambia, is $3878. This cost estimate includes the distribution of all drugs, not only essential medicines, although essential medicines make up the vast majority of staff time, storage space, picking activity, and transport volumes. This estimate is the average for all districts in Zambia, including centrally located and relatively accessible districts, where the average cost is undoubtedly lower due to lower transport costs. Hence a comparison of the additional costs of A or B, which have been measured in the more remote districts of Zambia, against the distributional costs in an average Zambian district may somewhat overstate the cost differential and this should be born in mind when comparing the relative costs of various delivery options.

APPENDIX TABLE 3. Estimated District Average Monthly Incremental Costs ($) of Versions A and B, by Cost Category

| Cost category                                  | Model A | Model B |
|-----------------------------------------------|---------|---------|
| **Recurrent cost—staff related**              |         |         |
| Salaries                                      | 1693    | 1867    |
| Travel Expenses by CPs, Project Manager, Supervisors etc to Piloted Districts | 87      | 87      |
| Telephone/Cellphone Accessories and Expenses  | 106     | 106     |
| Staff Welfare expenses-Accomodation for CPs, Refreshments etc | 90      | 90      |
| Group Life Assurance Premium                  | 8       | 8       |
| Gratuities                                    | 476     | 537     |
| Medical Expenses                              | 8       | 8       |
| **Recurrent cost—other categories**           |         |         |
| Packaging Material for Repackaging of Drugs   | 8       | 33      |
| Fuel & Lubricants—Travel by Project Manager to Piloted Districts & Entitlements | 33      | 33      |
| Extra fuel for distribution trips             | 78      | 311     |
| Canteen Expenses                              | 96      | 96      |
| Stationery & office Supplies                  | 87      | 87      |
| Bank Charges                                  | 14      | 14      |
| Postage                                       | 4       | 4       |
| Repairs & Maintenance General-Computers       | 44      | 44      |
| **Fixed cost**                                |         |         |
| Recruitment Expenses                          | 11      | 11      |
| Subscription & Licenses (Medical Council of Zambia—Pharmacist CP’s) | 1       | 1       |
| Protective Clothing for Warehouse WBP Staff   | 0       | 0       |
| Computer & Computer Accessories               | 26      | 26      |
| Pallet Jacks for Warehouse                    | 6       | 6       |
| Office Equipment-Aircon, Solar Panels etc     | 3       | 3       |
| Furniture,Fixture & Fittings                  | 5       | 5       |
| Computer Software                             | 7       | 7       |
| Training Materials                            | 65      | 65      |
| District Personnel Training Costs             | 454     | 454     |
| Monitoring and Evaluation Costs               | 67      | 67      |
| **Total**                                     | 3,479   | 3,971   |

Note: Exchange rate = 4500 Kwacha/dollar
stockout averted (weighting all tracer drugs equally) and then in terms of cost per Year of Life Lost (YLL) averted as a result of the increased availability of one essential anti-malarial drug, AL. To estimate the cost per stockout day averted, assume a district of average size with 18 health facilities. The evaluation results suggest that in the fourth quarter of 2009 there was an average of 1704 stockout days per month across all 15 tracer drugs in the control districts. This total reduces to 1464 in Model A and 756 in Model B. Thus by this metric, Model A reduces a stockout day of one tracer drug at a cost of $14.5 in additional operating costs. Model B, on the other hand, achieves the same stockout reduction at a cost of $4.2. With regards to this particular measure of stock availability, Model B is three and a half times as cost-effective as Model A.

To express cost-effectiveness in terms of health gains, focus on malaria deaths averted due to increase availability of ACT at the facility level. As expressed earlier, a national scale-up of Model B may result in 3320 fewer under-five deaths and 448 over-five deaths annually. In 2008, the life expectancy in Zambia (World Bank WDI, 2008) was estimated at 45.4 years. In terms of years of life lost averted, this translates into 720,440 YLLs averted from the reduction in under-five deaths, and 50,175 from the reduction in over five deaths (assuming the median age of Zambians over 5 is 22 years as per the 2011 CIA World Factbook). This implies a monetary value of $22 per YLL averted for a national scale-up of Version B operating over a 5 year period.

In addition, the cost estimates above do not take into account possible savings such as the discontinuation of picking and packing services at the district level, or the saved local transport costs from the district store to the facility. A scale-up may also involve further savings such as the ability to reassign the district-level store keeper to other duties as that position is no longer necessary. By including these savings, the net additional monthly operating costs of Model B falls to a maximum of $2992 and perhaps even less depending on the current transport costs incurred at the district level. If these additional savings are included in the analysis the additional cost for Model B will less and hence the cost-effectiveness estimates even greater.

It is difficult to find benchmark comparisons for this estimate of cost-effectiveness since it is a marginal investment into an active health system. However one contextual comparison is the estimated cost-effectiveness of antiretroviral therapy where one estimate for Sub-Saharan Africa stands at $350/DALY averted (Marseille et al. 2002). This comparison cost-effectiveness includes additional inputs such as medical staff as well as pharmaceutical costs. Other benchmarks include the cost-effectiveness of a global ACT subsidy at approximately $43/YLL averted (Marseille et al. 2002). However one contextual comparison is the estimated cost-effectiveness of antiretroviral therapy where one estimate for Sub-Saharan Africa stands at $350/DALY averted (Marseille et al. 2002). This comparison cost-effectiveness includes additional inputs such as medical staff as well as pharmaceutical costs.

While the additional cost of A or B is large in proportional terms—a national scale up of Model B would increase the supply chain operational cost from 4.1 percent to 8.5 percent of the total pharmaceutical budget in Zambia—the cost implications should be understood in light of international comparisons. Benchmarks of the distribution cost in relation to drug cost show that the equivalent number for less-developed and geographically challenged states (e.g. Tanzania, Malawi and Rwanda) is between 20–25 percent and for more developed states between 12–20 percent (USAID, 2009). The equivalent number for the ARV system in Zambia is about 10 percent in urban areas and 16 percent in rural areas (ibid). In general, logistics costs tend to decline with increased efficiency in the economy (e.g. improved infrastructure). Therefore distribution costs are generally higher in developing countries compared to developed countries. The current distribution cost of 4.1 percent in Zambia is even lower than typical logistic costs of US pharmaceutical companies which are around 4.5 percent (ibid). These data and the poor performance of the supply chain system suggest that Zambia is currently under-investing in its supply chain and the cost for scaling up Model B would still keep distribution costs below benchmarks in countries with similar level of development.

APPENDIX 2 THE IMPACT OF REDUCED STOCKOUTS OF ACTS ON UNDER- AND OVER-FIVE MORTALITY

1,508,448 cases of malaria were reported amongst children less than 5 years old in Zambia in 2008 (World Malaria report 2009). Of these, approximately 61.8 percent (LCMS 2006) sought any form of formal consultation for malaria like fevers. Approximately 28.6 percent self-administered medicines purchased primarily (95 percent) in non-public sites. Among those who sought formal consultation, 93 percent seek care at a public sector facility and 62 percent of those who use drugs for the treatment of malaria like fevers obtain them in a public sector facility.

The market share of ACTs in the non-public sector at the time of the intervention stands at 8.0 percent based on multiple earlier studies on the private anti-malarial market in Zambia. The remaining 92 percent of those who obtain drugs in the private sector use primarily SP (Fansidar).

Chanda et al. (2007) suggests the current efficacy of AL is 98.2 percent as compared to 68.4 percent for SP. In accordance with the longer length of AL treatment relative to SP/Fansidar the compliance of ACTs is set at 75.2 percent and of SP at 85 percent. These figures are also from Chanda et al. (2007) but tie closely with other studies on malaria interventions notably (Saving Lives Buying Time, Arrow et al, IOM 2004). A further assumption posits that 50 percent of patients who do not comply with the complete dosage of AL are still cured whereas non-compliance with SP full dosage leads to a 0 percent cure rate. These parameters are widely accepted in numerous cost-effectiveness studies on malaria treatment due to the shorter treatment course of SP and its mechanism of parasite elimination.

Currently those who seek treatment in the control public facilities find any dosage form of AL available only 59 percent of the time. Upon encountering a stockout, the caregivers have to resort to seeking treatment in the non-public sector where the share of AL was extremely low at the time of study. In a fraction of cases (10 percent) these caregivers do not seek any formal treatment at all once they cannot find drugs in the public sector health facility. The result being that a larger number of care givers obtain ineffective SP treatment in the private sector. This translates into 621,526 of the total 1,508,448 under five malaria cases not being effectively treated. 5 percent of these ineffectively treated cases translate into severe malaria with a 50 percent chance of death resulting from it.

One caveat is that those presenting for consultation at a public sector clinic and encountering a stockout might in some cases travel to other health facilities. However, given the acute nature of malaria symptoms for children under five and the lack of patient transport systems in most primary care health centers, such instances are assumed to be rare and thus not have a significant effect. Also, when stockouts occur, the duration is several days (average duration in the current as-is system is 22 days for all forms of AL) thereby not allowing repeat visits to the health facility. The decision and flow pathway which brought about the numbers quoted above are illustrated in Appendix Figure 1.

The reduction in ineffectively treated cases, complicated cases and mortality for patients over five years or older is estimated using a similar approach as described above. The only significant difference in the computation is the proportion of those who seek any form of treatment is slightly lower for the over-five population. Also, a more stringent assumption of 30 percent of those over five years old who seek treatment in the public sector health facilities and encounter a
drug stockout on the day of their visit do not obtain any treatment at all. This fraction is higher as compared to the 10 percent for under-five. Multiple earlier studies have documented such behavior among adults with malaria. The higher developed immunity in the population over 5 leads to fewer cases of complicated malaria (1 percent) and fewer of the complicated cases resulting in death (25 percent) even when malaria was not treated effectively. Appendix Figure 2 depicts the decision and flow pathway for the over-five population.

Notes
a We assume full substitutability between the 4 different weight bands for Artemether Lumefantrine for under-five patients implying that a health facility will dispense fewer tablets from a strip of 24, 18 or 12 tabs rather than not fulfilling the demand for a strip of 6 for a children less than five years old. Admittedly, some health facilities may not engage in such a practice but this assumption allows us to obtain the most conservative estimates for the reduction in mortality and morbidity.
b We assume the average additional time lost per episode of malaria that is not effectively treated to be 2 days for a sick adult and also 2 days for an adult caring for sick children. Admittedly, apart from the direct short term economic consequences due to wages lost, there are also likely to be significant indirect effects and long term effects such as income lost due to death/increased mortality and cognitive loss due to malaria related anemia in young children. The estimation of such long term consequences of treating a larger fraction of the population with effective drugs is beyond the scope of this study.
c This value is estimated based on 2010 MOH salaries.
d In the case of malaria DALY and YLL are not equal but similar given that effects of malaria on disability are small. Correspondingly, the bulk of HIV related DALY’s derive from YLLs.
APPENDIX FIGURE 2. A Model of Patient Flow and Treatment Seeking to Estimate the Impact of Stockout Reductions on the Over-5 Population