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Optimal Supply Chain Structure for Distributing Essential Drugs in Low Income Countries: Results from a Randomized Experiment

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Abstract
Despite increased investments in health commodity procurement, the availability of essential medicines at health facilities remains very 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 experiment conducted in over 400 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 focuses on the availability of 15 essential medicines at the health facility level and compares between a cross-dock based two-tier distribution network and a three-tier network. The study shows that a two-tier "cross- dock" like system outperforms a traditional three-tier drug distribution system due to better information flow and better management accountability even though stock is positioned closer to the health facilities in the three-tier system. Results from the study advance existing knowledge in the area of public sector distribution system design in general and drug distribution systems in developing countries in particular.

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Introduction

The availability of essential medicines is a persistent challenge in developing countries. A third of the world's population, including almost half of the population on the African continent, lacks systematic access to essential drugs (WHO, 2004). The health consequences from such low levels of availability are pronounced (Yadav, 2010).

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 (JSI, 2010). With the last decade's increases in financing for health[1] 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 stock-out rates at the point of service delivery and priority health outcomes remains limited.

This paper investigates how to optimally structure public sector supply chains through an examination of three contrasting supply chain distribution models. A randomized evaluation framework is used to examine the effectiveness of the three supply chain structures, including cross-docking, a supply chain structure where warehouses function as inventory coordination points rather than inventory storage points. The study was conducted in Zambia and is the first large scale study using an experimental evaluation framework to understand how to structure the public sector supply chain for distribution of essential medicines in low income countries.

Background

The structure of the distribution network that is used to transport a product from the manufacturer to end consumers influences both the product availability to the end consumer and the cost of operating the distribution network (Simchi-Levi et al., 2003, Chopra Miendl 2007). In the field of *operations and supply chain management*, disciplines which form the operational basis for the interventions studied in this paper, a large body of literature explores the role of supply chain structure. Researchers study both the optimal number of tiers in the distribution network as well as the operating and control rules used at each tier.

For the typical health system, a single central warehouse cannot effectively supply to all the health facilities and thus it is necessary to have a tiered distribution network, with several storage and distribution levels. The optimal number of levels in a distribution system is dependent on geographical factors, demand at each health facility, frequency of shipment, storage space availability, and transport

[1] Health aid increased from USD 5 billion in 1990 31.3 billion in 2013 and a large share of this increase was through disease-specific funding from Global Health Initiative such as the Global Fund to fight AIDS TB and Malaria (GFATM) and the Vaccine Alliance GAVI (IHME, 2013).

cost structure (Ballou, 1998; Chopra Miendl 2007, Simchi-Levi et al., 2003). Many developing countries, including Zambia, typically have three tiers in their public sector distribution system; where the central warehouse supplies to the district warehouses which in turn send supplies to the health facilities. Two and four tier models are also used in some countries (Yadav, Tata and Babaley 2011).

The complexity of managing inventory increases with the number of tiers/locations where inventory resides. Empirically, for most commercial settings, the number of tiers in the distribution channel has been growing smaller in recent years (Fletcher and Wehlage 2008). Many businesses that used to have a three-tier structure earlier now have a two-tier structure and some of those with a two-tier structure are now trying to manage with a single tier channel. Increased number of tiers in the supply chain greatly reduces supply chain visibility, i.e. the ability of planners at the higher tiers to make decisions based on actual demand. It also makes each tier dependent on the operational performance of tiers that are upstream or downstream from it, thereby creating managerial accountability problems in the supply chain. For businesses that have a larger number of tiers, initiatives such as cross-docking[2] and Vendor-Managed Inventory (Simchi-Levi, et al., 2003) are increasingly becoming popular. Snyder (1995) outlines the case of Walmart where significant savings in transportation, inventory, and stock-out costs were achieved after changing their distribution system to two-tier and implementing cross-docking. Cross-docking is a process in which a warehouse function as inventory coordination point rather than inventory storage point (Simchi-Levi et al., 2003). In typical cross-docking systems, goods arrive at a warehouse from the previous tier and are delivered to the next tier as rapidly as possible without any "lay away" inventory.

With cross-docking, frequent deliveries are viable to a larger number of distribution points without a concomitant increase in transportation cost (Gue 2007). However, cross-docking does not always result in gains – Waller et al. (2006) show that when centralized information about the level of inventory and demand at each stage is not available, cross-docking may require more total inventory in the system to avoid stock-outs. Zinn and Bowersox (1988) caution that as firms implement cross-docking, they must pay careful attention to the impact of cross-docking on product availability to end-consumers. Given that the impact of cross-docking requires understanding of many context specific variables, it is unclear how well it performs in a public sector supply chain for essential medicines. This paper presents the first rigorous study that addresses this issue.

A parallel question to the issue of number of tiers in the distribution system concerns the operating /control rules that should be used to decide inventory levels at each tier in the system. A push system (an allocation system), a pull (a requisition system) or a combination, are most commonly used because both push and pull system of distribution have their own advantages and disadvantages (Yadav, Tata and Babaley 2011). To address this question, the seminal work by Clark and Scarf (1960) considers a serial multi-tiered inventory system and determines the optimal inventory control policy by taking the perspective of the central planner, who has access to the status of the inventories at all sites and makes all stocking decisions for the entire system. Since then many scholars have studied these problems and have emphasized the need of better information integration between the tiers in the distribution system. A notable example is Lee and Whang (1999) who show that incentive problems may arise in multi-tiered distribution systems when decisions are delegated to decentralized sites that have intimate knowledge of

[2] Cross docking is a distribution system where items received at the warehouse are not received into stock, but are prepared for shipment to another location or for retail stores.

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. Bossert et al. (2006) studies the impact of decentralization on logistics systems in two developing countries, Ghana and Guatemala, and finds that centralized systems may result in better performance in the area of inventory control and information systems, while decentralization may result in better planning and budgeting. They conclude that logistics systems can be effectively decentralized for some functions while others should remain centralized.

In the public health literature, a few studies have looked into factors that cause stock outs of essential products at the point of service delivery. Quick (2003) identified the following reasons for stock outs: insufficient funding to procure the needed quantities, inaccurate forecasts, long and complex procurement processes, and unreliable transportation. The performance of the in-country distribution system in the last tier as well as delivering to remote areas is also noted to be a key bottleneck to ensuring higher availability of public health products at health facilities (Yadav 2010). Similarly, an assessment of the distribution system for essential drugs in Zambia (Beer, 2007) showed that although the central to district distribution had recently improved; the district to health facility distribution had bottlenecks resulting in stock-outs. Antimalarial medicine diversion has also been reported across numerous African markets and can lead to serious stock-outs in the public sector (Bate et al 2010). Inadequate human resource capacity including the inability to select, quantify and distribute medicines, and irrational prescribing and dispensing have also been identified as reasons for stockouts of certain drugs (Waako et al 2009).

There are few studies to date that rigorously measure the impact of interventions addressing supply chain improvements. Seiter (2010) provides a review of various procurement and financing related interventions that help improve the pharmaceutical supply system in developing countries. Apart from procurement and financing, training has been documented as the main intervention to improve pharmaceutical availability in public sector drug supply chains (Matowe et al 2008) but there is no clear evidence that training achieves greater availability of drugs at the health facility level. Conn et al (1996) describe the impact of a project to strengthen the basic management skills of district-level health teams in two out of the three health regions of the Gambia and find that it only leads to moderate improvements in health services delivery.[3]

The Pharmaceutical Supply Chain and Health in Zambia

With a GNI per capita, PPP (current international $)of approximately $3810 in 2013 Zambia has grown steadily over the past decade but this has not translated into significant poverty reduction. Forty two percent of the population live in extreme poverty and the absolute number of poor has increased from about 6 million in 1991 to 7.9 million in 2010, primarily due to population growth (World Bank, 2015). Providing basic health services and essential medicines to most of the population remains a challenge. The Zambian Ministry of Health (MOH) and its cooperating partners have invested substantial amounts

[3] Additional work includes the Zimbabwean Ministry of Health and Child Welfare (MOHCW), who conducted a pilot project to improve delivery of TB and malaria drugs to public health facilities using a new distribution system operating rule called the Zimbabwe Informed Push (ZIP) system. The results of this study are still to be published. Another study in Kenya (Raja et al 2008) looks at the strategic redesign of the public health distribution network using a simulation experiment.

of money in the public sector drugprocurement 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 (Picazo, and Zhao (2008)) 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 percent 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, the National Malaria Program has made great improvements in indicators for malaria prevention (Chizema-Kawesha et al, 2010). 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 percent 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)[4], only 43 percent of children under the age of five took an antimalarial within 24 hours of onset of symptom. Of these, no more than 16.6 percent of children living in urban area and 11.5 percent of those in rural areas took Artemisinin-based combination therapy (ACT), the adopted first line treatment for malaria.[5]

With regard to the existent supply chain structure, Zambia has a three-tier public sector distribution system of essential drugs. Primary distribution of drugs and other health commodities from 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 Essential Drugs Public Pilot Program (EDPPP), identified secondary distribution, from district stores to health facilities, as the main bottleneck in the distribution system (Beer, 2007, Picazo, and Zhao2008 and Yadav 2007). This finding was also confirmed in the baseline data for this project which revealed significantly higher stock-out rates of essential drugs in health facilities compared to the district stores and hospitals; thirteen of the fifteen essential drugs that were tracked in the baseline survey experienced a higher probability of stock-out at the health facility level rather than at the district store. The majority of these differences are statistically significant at conventional levels.

Secondary distribution is particularly challenging in Zambia because health clinics are geographically dispersed, off-road vehicles are often necessary to reach health facilities due to difficult roads, and certain areas are inaccessible during the rainy season. In the system that existed before EDPPP, health facilities estimated their needs for drugs (apart from antiretroviral (ARV) drugs and those drugs that were a part of the Primary Health Center Kit) and sent their requisitions to the District Health Office.[6] Often the lack of

[4] MIS 2010 Results: Thirty-four percent of febrile children took an antimalarial medicine in 2010, compared to 43% in 2008; the percentage of febrile children who took Coartem® treatment, more than doubled from 12% in 2008 to 26% in 2010.

[5] Results were similar in the 2006 Malaria Indicator Survey (MIS), where only 37 percent of children under the age of took an antimalarial within 24 hours of a fever.

[6] An additional 52 items including 20 basic medicines were delivered to the health centers in the PHC kits. Health facilities were allocated a specific number of kits each month depending on their size, service area, and past use. Consumption data on items in the kit or drugs ordered separately was not collected by the drug monitoring data system.

any communication means between the health facility and the district implied that the health facility staff would travel to the district along with their requisitions and "pick up" stock. Additional challenges also include lack of dedicated logistics staff at the district level and lack of working communication technologies.

Several 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 stock-outs of essential medicines at the health facilities captured in those studies are summarized below**:**

- Secondary distribution from the District Central 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.
- Communication between the District Central Store and health centers was difficult and relied upon a high-frequency radio 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 Central 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.

Based on these observations, the strengths and weaknesses of a number of potential different distribution models were assessed by the MOH with donor support.[7] Considered models 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 that would be contrasted with the existing system through a prospective randomized evaluation design.

Program and Intervention Design: The supply chain interventions

In April 2009, the EDPPP program was launched. The objective of the program was to *identify a cost-effective way to improve the availability of drugs through strengthening of the supply chain from MSL to districts and health facilities*. The EDPPP adopted a prospective evaluation design to assess the effectiveness of three distribution models (two alternative models, model A and model B, and the current system), which were chosen on the grounds of potential cost-effectiveness and technical feasibility as described above. The interventions were implemented over a 12 month period.

[7] Donors actively involved in these deliberations included USAID, JSI, Crown Agents, DfID, and the World Bank.

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 remains a three-tier system. A new role called the Commodity Planner (CP) is introduced at the district level to enhance stock planning capacity. This CP is responsible for coordinating orders from the health facilities and stock management at the district. The 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.[8] The CPs were trained on basic principles of inventory and stock management.

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 assembling 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 ensuring the delivery of the packages to the health facilities as well as facilitating the order information from the health facilities to MSL.

Both models A and B share common features which include drugs included in the system as 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. Table 1 summarizes the detailed features of the three delivery models.

Evaluation Design and Data

To measure the comparative effectiveness of each models A and B both vis-à-vis the control and with each other, the pilot was accompanied by a prospective cluster randomized evaluation design, with randomization of delivery models conducted at the level of the district. This relatively aggregate level of randomization is natural given the key role of the district structure, including the responsibilities of the district based CP. Randomized assignment below the district (i.e. the health facility), even if feasible from a systems perspective, would likely be subject to spillovers due to the common presence of a recently trained CP as well the general coordinating role of the DHO; therefore randomized exposure at the facility level was not pursued.

Randomization at the district level does come with potential inferential cost in the power of the analysis as the number of units of randomization is limited. In the case of the EDPPP, Models A and B were each piloted in eight districts around the country, and data was also collected from eight control districts. Besides the challenge to inferential power by the relatively few number of study units, traditional

[8] Existing pharmacy technologists carried out the CP role in districts where there was a pharmacy technologist; while new CPs were, hired directly under MSL, in districts were the pharmacy technologist position was vacant. For the 16 intervention districts, there were 12 CPs recruited and the remaining 4 districts relied on the existing pharmacy technologists.

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 (Cameron et al., 2008). To counteract this potential bias, the precision of statistical tests will be 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 assignation as the sole random variable in the data (Ernst, 2005). 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 assignations 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.

The stratified random assignation of models A and B guarantees in expectation the internal validity of any causal estimate. Researchers and policy makers also care about the generalizability of any impact estimate to the wider national context; therefore 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.[9] Within these four strata, districts were assessed on risk factors for Artemether-Lumefantrine (AL – one of the primary tracer drugs) stock outages 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 percent of the variation in observed AL outages in the universe of districts.

Within each of these eight strata, one district was randomly assigned to receive Model A, one to Model B, and one to the control group. The location of each selected district is shown in Figure 1. The 24 study districts comprise one-third of Zambia's 72 districts and study activities are represented in every region of the country.

The primary goals of the supply-chain intervention are to maintain stocking levels of key medicines and reduce both the incidence and duration of pharmaceutical stock outs. As such the primary metrics of program performance will include the incidence of drug stock-over at the time of survey as well as the inventory count of each drug. These metrics will be assessed for 15 tracer drugs deemed critical to the conduct of preventive and curative primary care in the Zambian context. Given the primacy of malaria in many rural areas of Zambia, four variants of the malaria curative drug AL, 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 (RDTs) and Sulfa-Pyramethamine (SP), a malaria preventive. Additional tracer drugs include two types of anti-biotics, a deworming medicine, and several types of contraceptives.

[9] The relatively small number of urban districts, as well as the relatively good performance of pharmaceutical supply chains in those districts, led to their exclusion from the program.

Besides inventory and stock-out incidence, other impact measures assessed include the duration of stock-outs and the condition of the primary health clinic storage facility.

Two dedicated facility surveys, qualitative interviews with Commodity Planners, and an analysis of facility stockcards provided data to evaluate the program. The baseline data collection, covering 416 health centers, 23 hospitals and 18 District Health Offices, and was conducted in Dec-Jan of 2008/09 prior to start of the pilot in April 2009.[10] The follow up data collection was conducted during the same months in 2009/10, one year after the baseline survey and 9-10 months after the start of the pilot program. Data on inventory and stock-out rates of the fifteen tracer drugs were collected at both baseline and end-line. The end-line survey was more comprehensive in design and included supplementary information on stocking history and storage conditions.

Although the selection of districts followed stratified random sampling and hence districts are balanced across rural and peri-urban areas as well as region, the data allows a check of balance of key stock measures at baseline. Tables 2 and 3 report the mean stock-out 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. Each table reports the means separately for the A, B, and control groups as well as the exact p-value of the difference tests between all pair-wise comparisons of A, B, and control. Pairwise comparisons significantly different from each other at the 10% level are indicated in bold.

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. In fact only one of the stock-out rates across the 15 drugs observed in Model A districts is significantly different from that found in the control district facilities. In the Model B district facilities, none of the stock-out rates are significantly different from control district facilities and only two are different from those in Model A districts. In terms of the inventory count for the same 15 drugs, in only one pair-wise comparison (a Model A versus Control district) is the stock level 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.

Results

The summary results from the pilot program evaluation show that availability of essential drugs improved remarkably at the health facility level, particularly in districts where Model B was implemented. Figures 1 and 2 show the changes in drug availability of the pilot program for select tracer drugs both pre- and post-pilot implementation in A and B districts respectively. Taking one example from Model A, during the baseline period 38 percent of health facilities were stocked out of DepoProvera, while the stock out rate in the follow up period was reduced to 17 percent. Reductions in the probability of stock out rates in the same magnitude are observed for Amoxicillin and ACT for adults. Although the reductions in stock out rates in model A districts is apparent, the gains are far less than the gains observed in model B districts. Figure 2 shows dramatic decreases in stock out rates for the same select drugs; with decreases in stock out

[10] Health centers, health posts that carry pharmaceutical stock, as well as district hospitals were all included in the data collection efforts. Since the primary goal of the interventions considered is to improve drug availability at the primary clinic level, most of the analysis will focus on primary health clinics and health posts.

rates larger than 40 percentage points for SP, DepoProvera, Amoxicillin and AL for adults. Overall these results show large performance improvements in the supply chain in model B districts whereas the A districts perform somewhat better with respect to baseline stock-out rates.

While the information presented in Figures 1 and 2 is suggestive, more formal tests of differential gains between intervention and control districts are presented in Tables 4 and 5. This analytic framework takes into account the relative difference between baseline and endline values in both the treatment and control areas through 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).

$$(1) \qquad O_{fd} = \gamma_0 + \gamma_{A0} A_{fd} + \gamma_{B0} B_{fd} + \gamma_1 T + \gamma_{A1} A_{fd} T + \gamma_{B1} B_{fd} T + \gamma_X X_d + \varepsilon_{fd}$$

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 γ_{A1} and γ_{B1}.

Table 4 reports select coefficients from the difference-in-differences regressions that look at stock-out likelihood as the dependent outcome. The table first reports mean stock-out rates as assessed at endline. In contrast with the stock-out rates at baseline (Table 2) these mean values suggest substantially lower stock-out incidence in both Model A and, especially, Model B facilities. For example, while the stock-out likelihood for AL 1x6 in control district facilities stood at 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 baseline stock-out rates were much more similar in magnitude across the treatment and control arms. Table 4 also reports the exact standard error for the impact estimate coefficients in equation (1), namely γ_{A1} and γ_{B1}.

The likelihood of stock-outs is significantly lower in Model A facilities than control facilities for 6 of the 15 tracer drugs – AL 2x6, AL 3x6, Amoxicillin, CTX, Depoprovera, and OralconF. Model B performed even more impressively – all but 3 of the 15 tracer drugs experienced significantly lower rates of stock-out 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 also presents the p-value for the difference-in-difference impact 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 AL, Depoprovera, and SP – and nearly significant reductions for 3 additional drugs – Amoxicillin, OralconF, and Quinine. The number of significant or nearly significant findings for Model B along with greater reductions in mean stock-out rates indicates Model B performed relatively better than Model A in reducing the likelihood of stock-out. 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 but both models but, especially, Model B.

A similar difference-in-difference analysis looking at drug inventory levels at time of survey is presented in Table 5 and the same general pattern is apparent – Model B performs significantly better than either

Model A or controls. Model B facilities hold significantly higher stocking levels for nine of the 15 tracer drugs when compared with controls, and 11 of 15 tracer drugs when compared with Model A. Taken together with the results on stock outs it is clear that Model B performs substantively better in terms of availability of drugs and inventory levels than either control or Model A districts for the majority of drugs studied.

Another key measure of drug availability is the duration of stock-outs, measured here as the number of days a drug was unavailable over the common reference period of the fourth quarter of 2009. Figure 3 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 stock outs compared to comparison district for DepoProvera, and the difference between comparison districts (37 days) and A districts (36 days) for SP is negligible.

A formal test of difference in stock-out duration can be conducted in a single difference regression framework given by equation (2):

$$(2) \quad O_{fd} = \gamma_0 + \gamma_A A_{fd} + \gamma_B B_{fd} + \gamma_X X_d + \varepsilon_{fd}$$

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 the causal impact of Models A and B, are given by γ_A and γ_B. Table 6 conveys the mean number of days of stock-out for each of the 15 tracer drugs as well as the p-values for the regression coefficients γ_A and γ_B as well as a p-value of the formal direct test of Model A vs. Model B. In general, i.e. for 11 of the 15 tracer drugs, Model A experiences less drug stock-out 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 stock-out 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 stock-out 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

Aside from the primary outcomes relating to the availability of drugs, the study assessed additional measures of supply chain effectiveness, notably pharmaceutical storage conditions at point of service. Table 7 lists 14 dimensions of storage conditions as judged by trained survey interviewers. The exact p-values from regressions similar to the specification in equation (2) yield the precision of each pair-wise comparison. 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 interviewer assessed adequate storage conditions. 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 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, Models A and, especially, B were effective in increasing drug availability and storage conditions when compared to the "business-as-usual" distribution system. Presumably these gains in pharmaceutical availability will also impact population health for the better, although this dimension of impact was not assessed in the available data. An exercise in Appendix I attempts to translate these increases in tracer drug availability to improvements in health using both data from the randomized evaluation along with available published data on treatment seeking for malaria. This analysis posits a nationwide scale-up of Model B and suggests substantial health gains even when the benefits are restricted to this one disease.

Discussion of Results

While the previous analysis clear demonstrates the effectiveness of the two interventions, especially Model B, it has not yet highlighted the casual mechanisms behind the improved performance.

Based on intuition one would argue that Model A would function better compared to Model B for drugs with higher demand variability. In Model A the district stores hold some "un-allocated" stock from which any unanticipated demand at the health facility level can be met. In Model B the district does not hold any stock and only has pre-packs earmarked for health facilities based on the quantities they ordered. If a health facility under-orders and then runs out of stock during the month, they would have to obtain supply all the way from MSL. Similarly, it appears that for items with lower demand variability Model B would function better because it reduces the health facility's risk of stocking on account of poor ordering and allocation practices followed at the district i.e. if the district did not order the right quantities from MSL to fulfill health facility demand. Which of these factors will supersede the other depends on many behavioral and health systems aspects.

The results from this evaluation indicate that availability at the health facility is higher under Model B as compared to Model A for almost all the drugs including those with high demand variability such as malaria medicines and those with low demand variability such as condoms. We argue that health facilities ordering directly from MSL with help from the Commodity Planner at the district can reasonably estimate the quantity they need to order for each month and this direct flow of demand information from the health facility to MSL is a key performance enhancing attribute of Model B. In Model A on the other hand (and also in the control districts), the demand at the health facility level is opaque both to MSL and often also to the district due to "order inflation" by the health facilities. Health facilities, knowing that district "rations" stock to them, tend to over order and the district loses its ability to robustly estimate the overall demand for the health facilities it serves in order to maintain the right amount of inventory. This leads to higher stock outs in Model A and in the control districts compared to Model B districts. Such behavior is witnessed in a number of industries, including consumer packaged goods and hi-tech electronics (Sterman 2000) and its existence is attributed to both operational (Lee *et al.* 1997) and behavioral factors (Croson and Donohue 2006). A system where stock levels for many drugs have to be maintained at the district to serve the demand for multiple health facilities under a district faces multiple behavioral challenges such

as 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 decisions (Sterman 1989), and the tendency to mistrust and develop counteracting strategies for the actions of decision makers at the higher (or lower) tier in the supply chain (Croson *et al.* 2004). This randomized pilot allows us to understand the combined impact in our setting of these intricate operational and behavioral issues which are difficult to model analytical or through simulation.

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 incentives for reporting. Figure 5 underscores reporting compliance from CPs in both models where, in a matter of months, reporting achieved almost universal compliance. Linking ordering and information reporting as a requirement for receiving drug supplies incentivized health workers to report and order on a timely basis. As a result increased reporting rates were found in both Model A and Model B districts. The higher reporting rates in turn contributed to better visibility of health facility level demand at MSL leading to better planning and lower stock-outs.

The direct ordering from Health Facilities to a well-managed Logistics Management Unit based at MSL was also an important factor in the performance of Model B. There is reduced fragmentation and less possibility for communication errors. The well-trained logistics staff at MSL is dedicated to logistics management and provided improved supervision and management. In the current logistic system, the district health management teams have many competing tasks and responsibilities and not the same level of logistic capacity. Sealed packaging for the health facilities is likely to have made a difference in ensuring leakage in the supply chain during transportation and temporary storage is reduced. It also prevents district managers from making drug allocation decisions based on most immediate and visible needs in the system (District Hospital) without a full overview of the district wide demand for drugs.

In both Model A and B district a commodity planner was recruited and trained as a dedicated logistics officer. The results of the study suggest that the role of the commodity planner alone was not the determining factor in the success of the study, although it could have possibly contributed to some of the improvements seen between the current system and model A.

Future research

This is the first large scale study to understand how to structure the public sector supply chain for distribution of essential medicines in low income countries. While this pilot and paper rigorously address the question of how to best structurally organize an essential drugs supply chain, it does not analyze operational issues such as the optimal inventory control policy at each level in the system. An analysis of health facility stock cards that was made possible through the pilot program shows that further improvements in availability of essential drugs at the health facility level are possible if a better inventory control system is run across supply chain (Gallien, Leung and Yadav 2011). Under the current system each health facility relies on the average monthly consumption of drugs over the past three months in computing its order quantity for the next month. This leads to stock outs for products with highly seasonal demand such as malaria drugs. Similarly, the current system fails to systematically anticipate any upcoming predictable changes in delivery lead-times and relies on a rather ad-hoc and subjective way for

allocating stocks to health facilities when inventory levels at MSL are not sufficient to cover all orders**.** Understanding the role of better inventory control systems and how they impact each supply chain structure requires further research, some of which is ongoing.

References

Ballou, R. H. "Business Logistics Management: planning, organizing and controlling the supply chain", 4th ed., Upper Saddle River, NJ : Prentice Hall, (1998).

Bate R., K. Hess, L. Mooney 2010. Antimalarial Medicine Diversion Stock-Outs and Other Public Health Problems, *Research and Reports in Tropical Medicine* , September 02, 2010

Beer, K. (2007), "Zambia Malaria Commodity Security Assessment", unpublished report to the World Bank.

Bossert T. J, D M Bowserand J K Amenyah 2006. Is decentralization good for logistics systems? Evidence on essential medicine logistics in Ghana and Guatemala, *Health Policy and Planning* 22 (2). 73-82.

Cameron, A. C., Gelbach, J. B., & Miller, D. L. (2008). Bootstrap-based improvements for inference with clustered errors. *The Review of Economics and Statistics*, *90*(3), 414-427.

Clark, A. and H. Scarf. 1960. Optimal Policies for a Multi-echelon Inventory Problem. *Management Science.* 6. 475-490

Chizema-Kawesha E, Miller JM, Steketee RW, Mukonka VM, Mukuka C, Mohamed AD, Miti SK, Campbell CC. Scaling up malaria control in Zambia: progress and impact 2005-2008. A*m J Trop Med Hyg*. 2010 Sep;83(3):480-8

Chopra S , Meindl P (2007), Supply Chain Management: Strategy, Planning and Operation, 2nd Edition, New Jersey: Pearson Prentice Hall.

Conn CP, Jenkins P, Touray SO. Strengthening health management: experience of district teams in the Gambia. *Health Policy and Planning* 1996;11:64-71.

Croson R, K Donohue Behavioral causes of the bullwhip effect and the observed value of inventory information. - *Management Science* 2006

Croson, R. T., Donohue, K. L., Katok, E., & Sterman, J. (2004). Order stability in supply chains: Coordination risk and the role of coordination stock. MIT Sloan School, Working Paper 2004

Ernst, M. D. (2004). Permutation methods: a basis for exact inference. *Statistical Science*, *19*(4), 676-685.

Fletcher C., C.J. Wehlage, Multi-Tier Distribution Channels: Moving From Three Tier to Two Tier, Wednesday, December 17, 2008 , AMR Technical report

Leung Z, Chen A, P Yadav, Gallien J, The Impact of Inventory Management on Stock-outs of Essential Drugs in Sub-Saharan Africa: Secondary Analysis of a Field Experiment in Zambia. LBS Working Paper 2014

Gue, K R. (2007), "Warehouse without Inventory," International Commerce Review, Vol. 7, No. 2, pp. 124-132.

Institute for Health Metrics and Evaluation. *Financing Global Health 2013:Transition in an Age of Austerity*. Seattle, WA: IHME, 2014.

JSI and USAID | DELIVER PROJECT, Task Order 1. 2010. Emerging Trends in Supply Chain Management: Outsourcing Public Health Logistics in Developing Countries. Arlington, Va.: USAID | DELIVER PROJECT, Task Order 1.

Lee, H. L. and Whang, S.(1999).Decentralized multi-echelon supply chain: incentives and information. Management Science, 45(5), pp. 633-640.

Lee, H. L., Padmanabhan, V. and Whang, S.(1997).Information distortion in a supply chain: the bullwhip effect. Management Science, 43, pp.546-558.

Matowe L, Waako P, Adome RO, Kibwage I, Minzi O, Bienvenu E.A strategy to improve skills in pharmaceutical supply management in East Africa: the regional technical resource collaboration for pharmaceutical management. *Hum Resour Health*. 2008 Dec 23;6:30.

Picazo, O and F. Zhao (2008). Zambia Health Sector Public Expenditure Review. Washington, DC: The World Bank Group.

Quick, J. D., J. R. Rankin, R. O. Laing, R. W. O'Connor, H. V. Hogerzeil, M. N. G. Dukes, and A. Garnett, eds. 1997. *Managing Drug Supply*. 2nd ed. Management Sciences for Health.West Hartford, CT: Kumarian Press.

Seiter, Andreas. *A practical approach to pharmaceutical policy*. World Bank Publications, 2010.

Simchi-Levi, D., Kaminsky, P. and Simchi-Levi, E. (2003).Designing and Managing the Supply Chain: Concepts, Strategies and Case Studies. New York: McGraw-Hill.

Sterman, J. (2000) Business Dynamics: Systems Thinking and Modeling for a Complex World. Boston: Irwin/McGraw-Hill.

Sterman, J. (1989a) Modeling managerial behavior: Misperceptions of feedback in a dynamic decision making experiment, Management Science 35(3), 321-339.

Yadav P, H Tata , M. Babaley (2011) Storage and Supply Chain Management. The World Medicines Situation 2011, Geneva WHO

Yadav P, Focus on In-Country Supply Chains. Global Health Magazine, 2010

Yadav P. Analysis of the public, private and mission sector supply chains for essential drugs in Zambia (a study conducted for DFID Health Resource Center under the aegis of the META project), 2007. http://apps.who.int/medicinedocs/en/d/Js18001en/

Waako PJ, Odoi-adome R, Obua C, Owino E, Tumwikirize W, Ogwal-Okeng J, Anokbonggo WW, Matowe L, Aupont O. Existing capacity to manage pharmaceuticals and related commodities in East Africa: an assessment with specific reference to antiretroviral therapy. *Hum Resour Health*. 2009 Mar 9;7:21.

Waller, M A., C. R Cassady, and J Ozment (2006), "Impact of Cross-docking on Inventory in a Decentralized Retail Supply Chain," *Transportation Research*. Part E, Logistics & Transportation Review, Vol. 42, No. 5, pp. 359-382.

World Health Organization (2004) The World Medicines Situation, Geneva WHO, 2004 chapter 7.

World Bank (2015). Zambia country overview available at: http://www.worldbank.org/en/country/zambia/overview

Zinn W, DJ Bowersox. Planning physical distribution with the principle of postponement. Journal of Business Logistics 9 (2) . 1988

Table 1. Description of the three distribution models

Model Characteristics	**Model A**	**Model B**	**Control**
Commodity Planner coordinates logistics at district level	Yes	Yes	No
Storage of drugs at district level	Yes	No	Yes
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 individual packages to health facilities are assembled at MSL	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

Table 2. Probability of stock-out in health centers and health posts at time of baseline interview, by tracer drug

Tracer drug	Control (K) mean	Model A mean	Exact P-value: A vs. K	Model B mean	Exact P-value: B vs. K	Exact P-value: B vs. A
AL 1x6 (strip of 6 tabs)	0.423	0.338	0.113	0.433	0.923	0.596
AL 2x6 (strip of 12 tabs)	0.380	0.462	0.133	0.550	0.725	0.902
AL 3x6 (strip of 18 tabs)	0.338	0.431	**0.049**	0.483	0.904	0.713
AL 4x6 (strip of 24 tabs)	0.338	0.400	0.893	0.400	0.734	0.286
Amoxicillin Suspension (bottle of 100ml)	0.718	0.738	0.826	0.717	0.730	0.689
Benzyl Penicillin Inj. (5ML 10ml vials)	0.225	0.246	0.306	0.200	0.644	0.340
CTX 480mg (bottle of 1000 tabs)	0.451	0.415	0.379	0.400	0.352	**0.038**
DepoProvera (vial)	0.254	0.385	0.169	0.450	0.812	0.233
Malaria RDTs (box of 25 tests)	0.465	0.462	0.599	0.433	0.513	0.375
Male 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
OralconF (Levonorgestre/Ethinylestradio)	0.408	0.585	0.585	0.700	0.155	**0.021**
Quinine Injection (2ml ampoules)	0.338	0.477	0.157	0.467	0.629	0.701
Quinine Tabs (bottle of 1000 tabs)	0.085	0.031	0.114	0.183	0.809	0.250
SP (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 time of baseline interview, by tracer drug

Tracer drug	Control (K) mean	Model A mean	Exact P-value: A vs. K	Model B mean	Exact P-value: B vs. K	Exact P-value: B vs. A
AL 1x6 (strip of 6 tabs)	48.72	38.95	0.355	46.33	0.316	0.596
AL 2x6 (strip of 12 tabs)	34.80	36.51	0.358	32.65	0.177	0.676
AL 3x6 (strip of 18 tabs)	48.57	47.00	**0.039**	45.22	0.514	0.084
AL 4x6 (strip of 24 tabs)	39.45	54.72	0.174	35.35	0.089	0.085
Amoxicillin Suspension (bottle of 100ml)	1.61	6.51	0.691	2.87	0.733	0.012
Benzyl Penicillin Inj. (5ML 10ml vials)	27.18	32.91	0.234	23.18	0.158	0.097
CTX 480mg (bottle of 1000 tabs)	1.88	1.58	0.339	3.04	0.323	0.261
DepoProvera (vial)	55.35	33.11	0.196	35.28	0.181	0.563
Malaria RDTs (box of 25 tests)	4.10	18.06	0.590	4.80	0.154	0.794
Male Condoms (box of 100/144)	13.99	8.11	0.790	8.58	0.436	0.635
Metronidazole 200mg tabs (bottle of 1000)	0.63	0.98	0.454	0.97	0.399	0.691
OralconF (Levonorgestre/Ethinylestradio)	118.93	40.17	0.396	36.32	0.167	0.051
Quinine Injection (2ml ampoules)	73.57	55.65	0.057	21.58	0.118	0.034
Quinine Tabs (bottle of 1000 tabs)	2.24	3.95	0.405	2.65	0.458	0.422
SP (bottle of 1000 tabs)	0.59	0.62	0.823	0.63	0.201	0.500

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 4. Difference-in-difference estimate of probability of stock-out, by tracer drug

Tracer drug	Control (K) endline mean	Model A endline mean	Exact P-value of dif-n-dif coefficient: A vs. K	Model B mean	Exact P-value of dif-n-dif coefficient: B vs. K	Exact P-value of dif-n-dif coefficient: B vs. A
AL 1x6 (strip of 6 tabs)	0.479	0.292	0.161	0.133	**0.015**	**0.037**
AL 2x6 (strip of 12 tabs)	0.417	0.246	**0.043**	0.083	**0.002**	**0.037**
AL 3x6 (strip of 18 tabs)	0.493	0.231	**0.007**	0.050	**0.000**	**0.031**
AL 4x6 (strip of 24 tabs)	0.557	0.400	0.118	0.117	**0.009**	**0.026**
Amoxicillin Suspension (bottle of 100ml)	0.521	0.323	**0.072**	0.167	**0.023**	0.124
Benzyl Penicillin Inj. (5ML 10ml vials)	0.028	0.031	0.449	0.033	0.572	0.768
CTX 480mg (bottle of 1000 tabs)	0.732	0.400	**0.034**	0.350	**0.034**	0.414
DepoProvera (vial)	0.408	0.185	**0.026**	0.000	**0.002**	**0.085**
Malaria RDTs (box of 25 tests)	0.380	0.185	0.127	0.183	0.217	0.559
Male Condoms (box of 100/144)	0.113	0.123	0.243	0.067	**0.031**	0.161
Metronidazole 200mg tabs (bottle of 1000)	0.437	0.462	0.544	0.417	0.646	0.615
OralconF (Levonorgestre/Ethinylestradio)	0.324	0.154	**0.065**	0.067	**0.008**	0.103
Quinine Injection (2ml ampoules)	0.183	0.169	0.147	0.033	**0.051**	0.165
Quinine Tabs (bottle of 1000 tabs)	0.211	0.077	0.246	0.117	**0.073**	0.106
SP (bottle of 1000 tabs)	0.606	0.484	0.179	0.167	**0.027**	**0.090**

Note: Estimates based on data from 196 facilities in 24 districts. Regression specification includes stratification variables (rural or peri-urban, region, and high-risk stock out 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

Tracer drug	Control (K) endline mean	Model A endline mean	Exact P-value of dif-n-dif coefficient: A vs. K	Model B mean	Exact P-value of dif-n-dif coefficient: B vs. K	Exact P-value of dif-n-dif coefficient: B vs. A
AL 1x6 (strip of 6 tabs)	69.28	76.56	0.363	139.50	**0.052**	**0.021**
AL 2x6 (strip of 12 tabs)	97.68	81.86	0.570	177.93	**0.068**	**0.001**
AL 3x6 (strip of 18 tabs)	89.93	72.97	0.566	152.67	0.125	**0.003**
AL 4x6 (strip of 24 tabs)	62.60	56.30	0.617	161.33	**0.044**	**0.002**
Amoxicillin Suspension (bottle of 100ml)	9.00	19.31	0.130	68.47	**0.001**	**0.001**
Benzyl Penicillin Inj. (5ML 10ml vials)	48.56	31.55	0.925	58.03	0.193	**0.004**
CTX 480mg (bottle of 1000 tabs)	1.45	3.10	0.115	4.59	0.173	0.494
DepoProvera (vial)	46.19	93.66	0.044	262.45	**0.000**	**0.002**
Malaria RDTs (box of 25 tests)	14.03	7.84	0.997	9.63	0.577	**0.005**
Male 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
OralconF (Levonorgestre/Ethinylestradio)	144.94	390.82	0.102	269.55	**0.100**	0.621
Quinine Injection (2ml ampoules)	76.53	37.03	0.641	157.95	**0.000**	**0.000**
Quinine Tabs (bottle of 1000 tabs)	50.69	3.52	0.703	5.49	0.593	0.118
SP (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 stock out indicator). Exact p-values calculated through randomization inference. P-values in **bold** significant at 10% level in a one-tailed hypothesis test.

Table 6. Total days of stock-out in the 4th quarter 2009, by tracer drug

Tracer drug	Control (K) mean	Model A mean	Exact P-value: A vs. K	Model B mean	Exact P-value: B vs. K	Exact P-value: B vs. A
AL 1x6 (strip of 6 tabs)	27.3	17.9	0.268	4.9	**0.030**	**0.044**
AL 2x6 (strip of 12 tabs)	15.2	12.2	**0.069**	0.3	**0.073**	0.165
AL 3x6 (strip of 18 tabs)	18.5	16.2	0.920	2.3	0.370	0.129
AL 4x6 (strip of 24 tabs)	23.7	13.6	0.391	1.2	**0.079**	**0.020**
Amoxicillin Suspension (bottle of 100ml)	27.4	21.3	0.368	8.0	0.105	0.137
Benzyl Penicillin Inj. (5ML 10ml vials)	3.2	3.7	0.143	1.9	**0.011**	**0.068**
CTX 480mg (bottle of 1000 tabs)	35.2	33.3	0.349	23.2	**0.016**	0.436
DepoProvera (vial)	10.6	15.3	0.160	3.6	**0.084**	**0.097**
Malaria RDTs (box of 25 tests)	12.4	11.7	0.541	9.1	**0.054**	0.114
Male Condoms (box of 100/144)	9.5	7.7	0.161	4.4	0.148	0.737
Metronidazole 200mg tabs (bottle of 1000)	31.7	34.5	0.561	32.3	0.166	0.385
OralconF (Levonorgestre/Ethinylestradio)	10.2	13.6	0.486	22.5	**0.008**	0.553
Quinine Injection (2ml ampoules)	4.2	3.6	0.363	0.0	**0.013**	**0.093**
Quinine Tabs (bottle of 1000 tabs)	5.4	5.1	0.855	3.2	**0.012**	**0.085**
SP (bottle of 1000 tabs)	37.4	35.9	0.915	14.1	**0.059**	0.315

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

Table 7. Likelihood of satisfying select storage conditions observed at time of interview

Storage condition	Control (K) mean	Model A mean	Exact P-value: A vs. K	Model B mean	Exact P-value: B vs. K	Exact 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 stock out indicator). Exact p-values calculated through randomization inference. P-values in **bold** significant at 10% level in a one-tailed hypothesis test.

Figure 1. Participating study districts by treatment arm

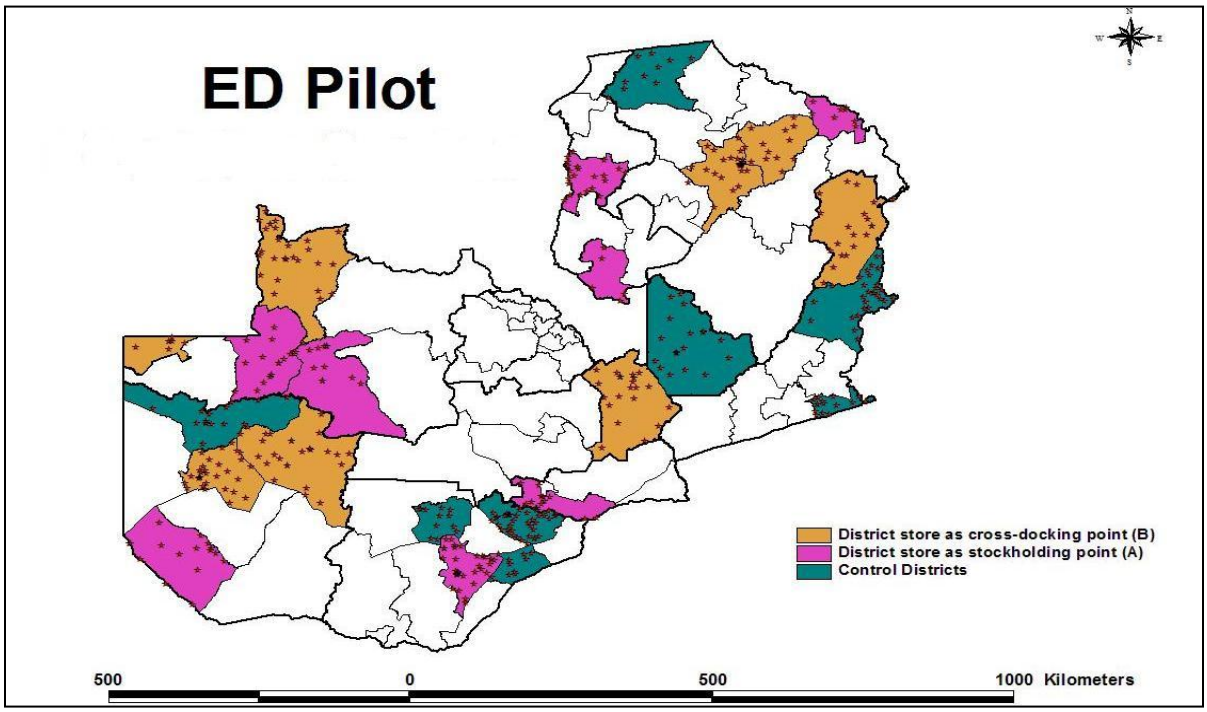


Figure 2: Comparison of baseline and endline stock-out rates in model A district health facilities, select tracer drugs

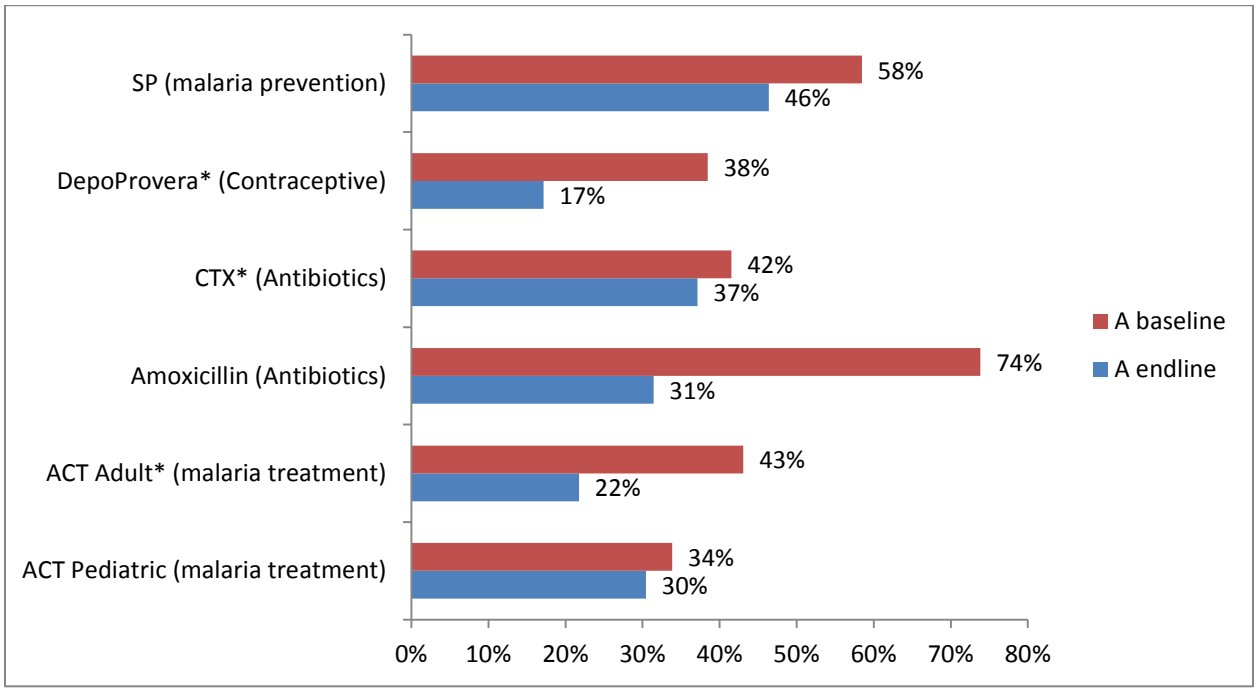


Figure 3: Comparison of baseline and endline stock-out rates in model B district health facilities, select tracer drugs

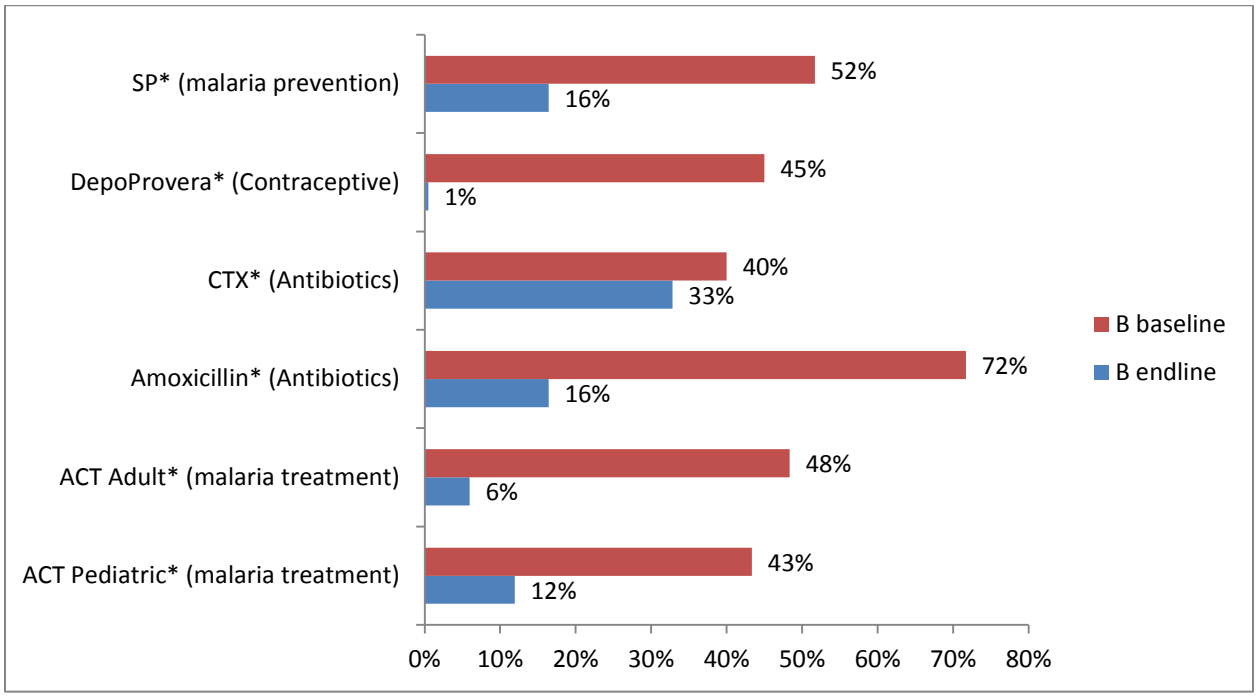


Figure 4: Number of days of stock outs in Q4 2009 of select tracer drugs by treatment arm

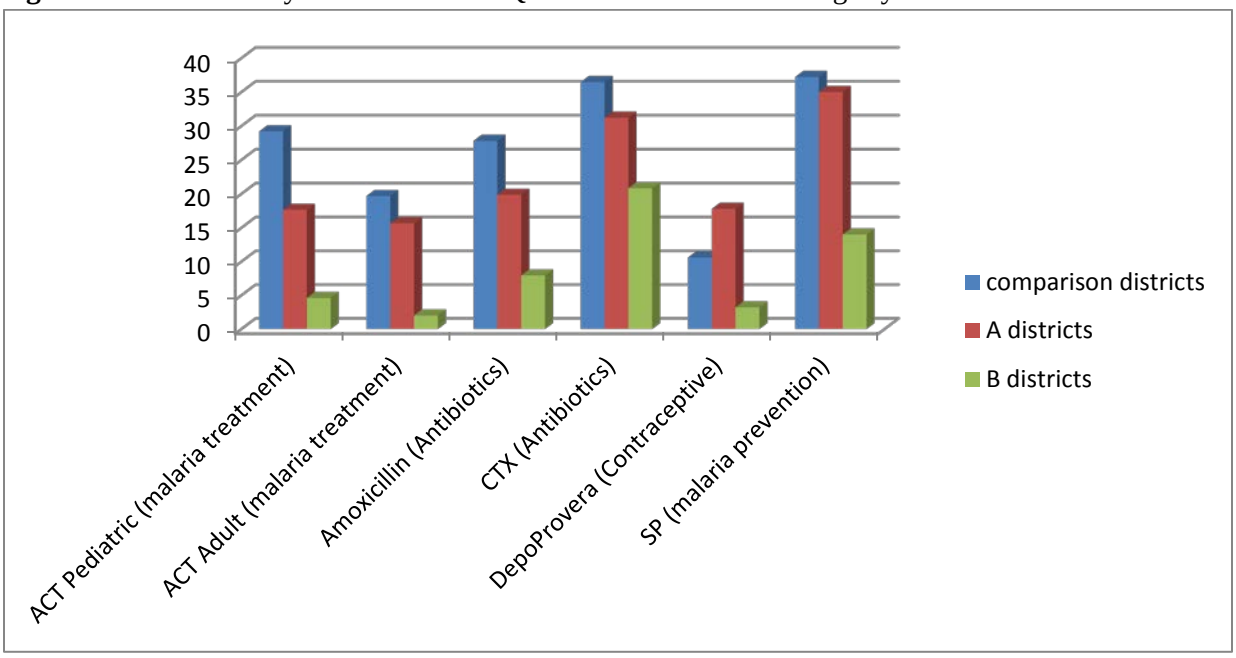
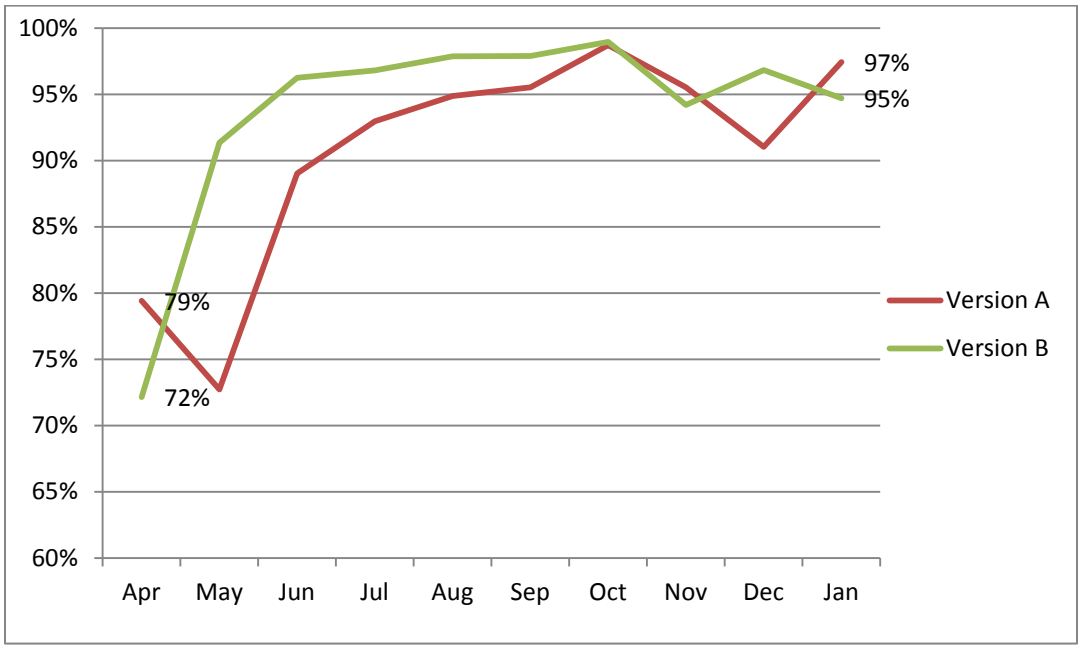


Figure 5: Average reporting rate to MSL by A and B districts by month of implementation



Source: Data from MSL

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 stock-outs. 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 stock-outs 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 stock out 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 stock outs of Artemether Lumefantrine (AL) used for the treatment of uncomplicated malaria.[11] 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 stock-outs 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.

[11] 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.

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.[12] 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 $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 **i**n Zambia, it is important to keep in mind that the pilot was implemented in remote districts with higher transportation 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.[13] 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.

[12] 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.

[13] This value is estimated based on 2010 MOH salaries.

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 stock-out 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 stock-out 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 stock-out 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 stock-out day of one tracer drug at a cost of $14.5 in additional operating costs. Model B, on the other hand, achieves the same stock-out 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 inclduing 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).[14] 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 (assuming full subsidy of one dollar per treatment course of ACT and the life expectancy for Zambia) (Laxminarayan et al. 2006) and the cost effectiveness of intermittent preventive treatment for malaria in pregnant women with Sulfadoxine-Pyrimethamine (SP) of $19/DALY averted (Yadav, 2010). Whichever benchmark that is being used, it is clear from this analysis that investments in the supply chain are cost-effective compared to other common public health

[14] 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 DALYs derive from YLLs.

interventions. In addition, this supply chain estimate only concerns malaria deaths averted and not the possible other numerous health benefits from increased availability of other essential drugs.

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 Table 1. Estimates of annual cases of uncured malaria cases, severe malaria cases and deaths by population groups for as-is (the current system), Option A and Option B (assuming nationwide coverage of each system)

	Under-five population			Over-five population (1)	
	Control	Option A	Option B	As-is	Option B
Uncured malaria cases	621,526	614,885	488,711	706,242	527,043
Severe malaria cases	31,076	30,744	24,436	7,062	5,270
Deaths	15,538	15,372	12,218	1,766	1,318

Note: (1) Only the results of Option B are presented because in this case Option A leads to a slight increase in the probability of stock out as compared to the "as-is" case for adult bands of ACT. As before, this increase is however statistically insignificant and therefore not included in the table.

Appendix Table 2. Annual benefits from national scale-up of Model B at-a-glance (compared to the current system)

Reduction in uncured malaria cases per year	Reduction in Severe malaria cases per year	Under 5 Deaths averted per year	Over 5 Deaths averted per year	Total deaths averted	Aggregate average direct household income loss saved
312,014	8,433	3,320	448	3758	$ 1,629,312

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

Appendix 2 - *The impact of reduced stock-outs 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.

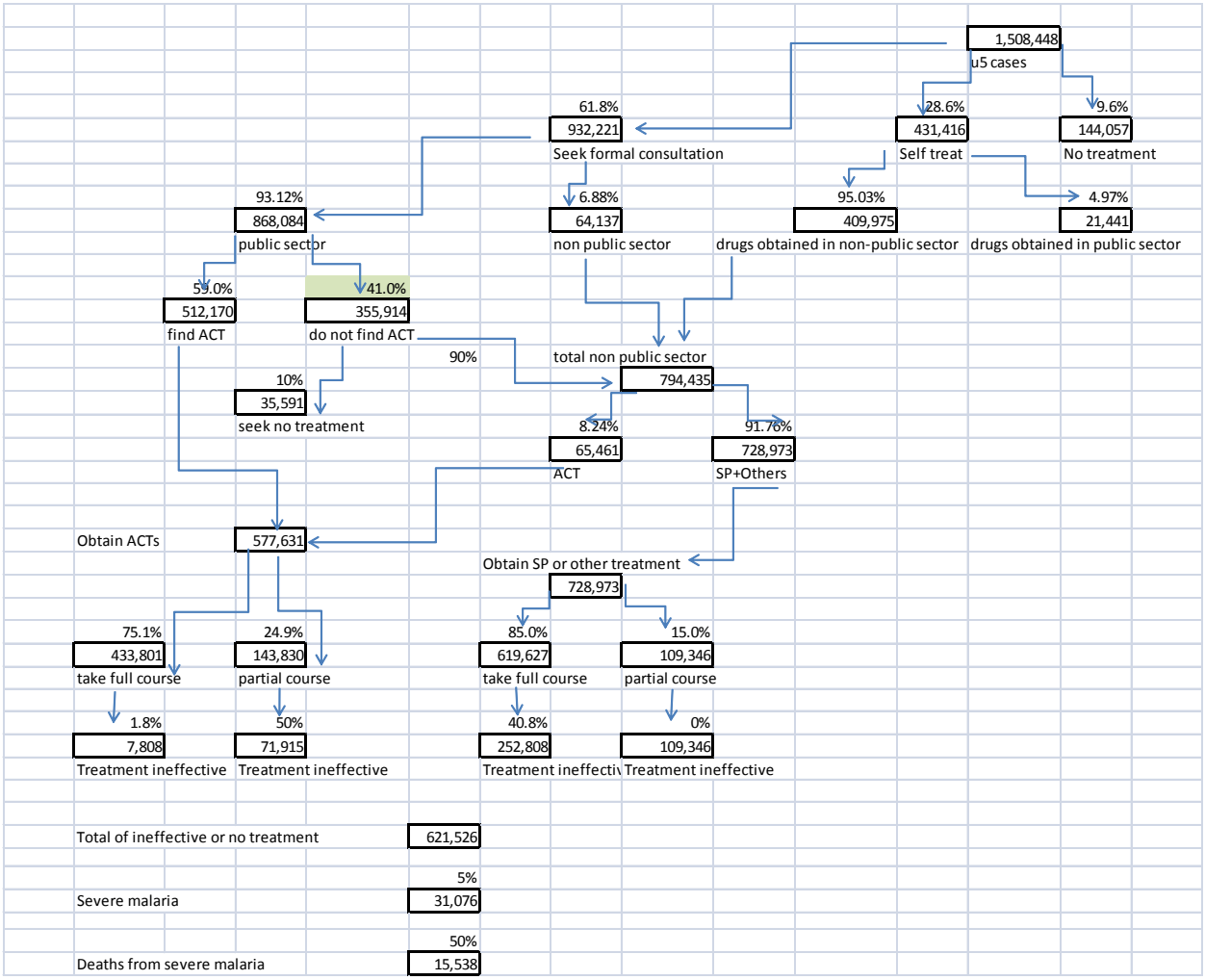
Currently those who seek treatment in the control public facilities find any dosage form of AL available only 59 percent of the time. Upon encountering a stock out, the caregivers have to resort to seeking treatment in the non-public sector where the share of AL was extremely low at the time of study. 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 stock out 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 stock outs 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 stock out 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.

Appendix Figure 1. A model of patient flow and treatment seeking to estimate the impact of stock-out reductions on the under-5 population



Appendix Figure 2. A model of patient flow and treatment seeking to estimate the impact of stock-out reductions on the over-5 population