Operational Innovations to Improve Malawi's HIV Sample Transportation Network

by

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Abstract

The African nation of Malawi, like other sub-Saharan countries, provides diagnostic testing to its citizens through a centralized laboratory network. Diagnostic samples are collected from patients at remote, point-of-care health facilities and diagnostic tests are performed at centralized laboratories. Sample transportation (ST) systems within these networks are crucial for timely disease diagnosis and treatment. In this thesis, I present my research regarding two operational innovations to improve the ST system, and, consequently, the diagnostic network in Malawi. I first present a report documenting the development, implementation, and testing of a novel, mobile phone-based data collection system which vastly improves the accuracy and visibility of patient sample volumes and locations across the diagnostic network. By making this logistics information available and accessible to ST system administrators, ST systems can become more flexible, limit wasted capacity, and improve the quality of care. Second, I document my work towards understanding how different strategies for deploying point-of-care (POC) diagnostic testing devices influences the performance of the network as a whole. I find allocating POC devices to facilities with the highest sample volumes can cut the average time required for a patient to receive their test results after providing a sample by 60%, from over a month to less than two weeks.

Thesis Supervisor: Jónas Oddur Jónasson
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Chapter 1

Introduction

Over twenty-five years ago, the United Nations formed the Joint United Nations Programme on HIV/AIDS (UNAIDS) to organize global action against the AIDS pandemic. Since that time, UNAIDS has continuously provided oversight to this world-wide response, establishing treatment targets, coordinating response efforts, and monitoring progress [53]. In 2014, UNAIDS established targets for HIV/AIDS treatment [50], known as the 90-90-90 goals, which were named for the targets that were set to be reached by 2020:

- that 90% of people living with HIV will know their HIV status,
- That 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy,
- That 90% of all people receiving antiretroviral therapy will have viral suppression.

In resource-limited countries with a high disease prevalence, like those in sub-Saharan Africa (over half of the people living with HIV in the world were living in sub-Saharan Africa in 2019 [52]), a desire to achieve these goals has given way to novel approaches to healthcare delivery for HIV/AIDS and other communicable diseases.

Access to diagnostic testing services is a critical element of any public health system. In the countries of sub-Saharan Africa, diagnostic services are most often provided through hierarchical networks comprised of health facilities with varying degrees of capabilities. Rural health clinics, often with poor access to infrastructure such as clean water and electricity, serve as the primary point of entry into a broader, nation-wide healthcare system. These health clinics, lacking the resources to conduct diagnostic testing on-site, refer patient samples (e.g. blood, sputum, etc.) to a relatively small number of centralized laboratories with the capacity to conduct diagnostic analysis [26]. Within these diagnostic networks, formal and/or informal delivery systems known as sample transportation (ST) systems exist to transport patient samples and test results across the difficult terrain separating health facilities and molecular laboratories (MLs) [43]. As the thread connecting the facilities in a diagnostic network together, the performance of the diagnostic network is closely related to the performance of the ST system [27]. Therefore, addressing challenges associated with ST systems can positively impact the performance of the diagnostic network as a whole and improve health outcome for the population being served [26, 20].

One challenge faced by ST systems in the region is inefficient utilization of transportation resources (i.e., a team of couriers in the ST system). Sample transportation systems in many

sub-Saharan African countries operate without accurate information regarding the quantity and location of the patient samples and test results requiring transportation [24]. Consequently, these ST systems operate in a push mode, where couriers visit facilities on fixed weekly or bi-weekly schedules [24, 6]. These fixed routes lead to unnecessary travel (when healthcare facilities do not have samples) and unnecessary delays (when samples at facilities have to wait for the next scheduled visit). A second challenge faced by these diagnostic networks due to the ST systems is transportation delays. Stated simply, transporting samples takes time and transportation is a necessity in these networks due to their centralized structure. As a result, it is often the case that these diagnostic networks experience a significant delay (also called turnaround time) between collection of samples and receipt of results at the health facility [36, 9, 23]. Recent improvements in the region's infrastructure and technological advances in diagnostic testing capabilities are creating new opportunities to address these challenges.

Improved communications infrastructure presents an opportunity to use transportation resource more efficiently. If real-time ST demand information can be collected from healthcare facilities, ST operators may be able to dynamically allocate transportation resources to adapt to daily variability in demand for ST [16]. This dynamic routing could eliminate unnecessary travel and the system delays unnecessary travel introduces. A first step toward enable this type of system is establishing a data collection system to monitor where samples are in the diagnostic network. In recent years, point-of-care (POC) testing devices designed for use in austere conditions have been tested in diagnostic networks in sub-Saharan Africa (Ganesh et al.; Nicholas et al.; Drain et al.) [15, 33, 13]. Results from these trails suggest that POC devices hold great promise towards improving diagnostic networks in the region by eliminating transportation delays. Rather than transporting samples from rural health clinics to a centralized laboratory, POC devices facilitate diagnostic sample testing at the rural health clinics. However, there is a dearth of insights into how different strategies for locating POC devices within these resource-limited diagnostic networks influences average turnaround times [12, 42].

In this thesis, I present two research papers documenting my analysis of operational innovations to improve the diagnostic network in Malawi. In chapter 2, I present a report regarding the development, implementation, and testing of a novel, mobile phone-based data collection system which vastly improves the accuracy and visibility of patient sample volumes and locations across the diagnostic network. In chapter 3, I present a working copy of a report regarding the development and initial findings of a discrete event simulation model to gain insights into how new diagnostic testing technology, known broadly as point-of-care testing devices, influence the operation of the entire diagnostic network when these new devices are placed at different points in the network.

Chapter 2

Design and Implementation of a USSD System for Daily Tracking of Patient Samples and Diagnostic Results in Malawi's Diagnostic Network

2.1 Introduction

Most populations in sub-Saharan Africa rely on rural health clinics, with poor infrastructure, as their primary point of entry to a broader healthcare system. These health clinics are often not equipped to conduct diagnostic testing but refer patient samples to a relatively small number of centralized laboratories capable of diagnostic analysis [26]. The effectiveness of programs targeting active diseases in the region, such as HIV-AIDS, Tuberculosis (TB), and Malaria, is therefore closely related to the performance of sample transportation (ST) systems, put in place to transport patient samples and test results across the difficult terrain separating health facilities and molecular laboratories (MLs) [43].

Sample transportation systems in many sub-Saharan African countries operate without accurate information regarding the quantity and location of the patient samples and test results requiring transportation [24]. Consequently, these ST systems operate in push mode, where couriers visit facilities on fixed weekly or bi-weekly schedules [24, 6]. A common result of this operating mode is empty trips: courier visits to facilities where nothing was delivered to or transported from the facility. For example, an analysis of archival 2017-2018 courier data in Malawi revealed that 31% of courier visits to clinics were empty trips. This not only results in inefficient utilization of limited resources but also contributes to delays in receiving critical test results [20], which in turn, leads to poor health-seeking behavior among the population [31] and can contribute to increased mortality rates [21].

An alternative to these ST push systems would be a pull system, in which couriers only visit facilities when patient samples or test results are ready for transport to or from that

facility. Such a pull system would limit empty trips, but would require a reliable system to track the number of patient samples and test results requiring transportation across the diagnostic network. We hypothesize that these logistics data — specifically, the location and quantity of patient samples or test results ready for transport — can be collected with a low-cost information sharing system and can be used to create an ST system which is responsive to real-time needs.

In this study, we investigated the feasibility, adoption, and accuracy of a system leveraging a communications protocol that is standard on all mobile phones, known as Unstructured Supplementary Service Data (USSD) technology [39], to gather more timely and accurate information. To conduct this investigation, we designed and developed a USSD data collection system (hereafter, the USSD System) to enable healthcare facilities in a diagnostic network to report daily sample volume data. We conducted a year-long field trial of the USSD System in Malawi from July 2019 to July 2020 to determine if our system would enable the timely collection of information.

2.2 Intervention Development and Design

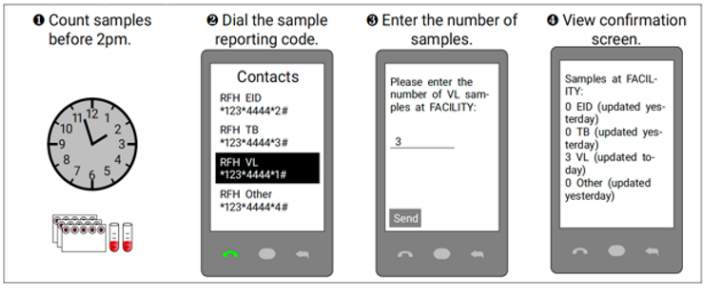
The critical design questions we faced when developing our system were:

- What technology would health workers use to submit sample volume reports?
- How would those reports would be structured?

Given the positive findings regarding the feasibility of mHealth initiatives in low- and middle-income countries [1], and the rapid growth in mobile network coverage in sub-Saharan Africa over the past decade [3, 18], we elected to design our system so that health workers could submit reports with a mobile phone. As less than half of the mobile phones in the region are smartphones [18], we based our sample volume data collection system on USSD technology – a mobile communication protocol accessible to both smartphones and less technologically advanced feature phones.

In a USSD system, users are each provided a unique numeric access code that the user can dial to access a structured menu of options. With appropriate series of key presses using the mobile phone's keypad, users can navigate through the options menu and submit information, similar to how a short message service (SMS) system conveys information through text. One advantage of USSD over SMS, especially in the context of data collection, is that USSD's built-in menu system allows for structured responses, leading to built-in data validation [39]. This also reduces the amount of effort required to leverage the data in a systematic way, which is crucial to managing the growing volume of healthcare data received through mobile phones [32].

In our USSD System, a specific USSD reporting code is assigned to every health facility operating within a diagnostic network, and each diagnostic test offered in the network is assigned a unique numeric designator. To report the number of patient samples for a specific test, a designated health worker at a designated facility can use any mobile phone to dial that facility's USSD reporting code and the numeric designator for the diagnostic test to connect to the USSD System. Once connected, they can report the number of patient samples via a text-based interface. Upon entering all the required information, the user receives a confirmation text message containing a summary of the submitted report. See Figure 2.1 for more details.



1. A health worker counts the number of samples, by sample type, that are prepared for transport.
2. The health worker dials a USSD code specifically assigned for the health worker's clinic and the type of sample (HIV early infant diagnosis (EID), HIV viral load monitoring (VLM), Tuberculosis (TB), Other) which has been saved on the health worker's phone and is displayed on a poster in the health facility.
3. The health worker enters the number of samples currently awaiting transportation at the facility.
4. The health worker views a confirmation screen which summarizes how many samples of each type have been reported for the facility.

Figure 2.1: USSD System Reporting Instructions

2.3 Methods

2.3.1 Study Setting

As of 2018, 9.2% of adults (15–49 years) in Malawi were living with HIV [51] and the country's TB incidence rate was 181 per 100,000 people [56]. The Malawi Ministry of Health (MOH) operates a diagnostic network of approximately 700 widely-distributed, community health clinics, 27 centrally located district health offices (DHOs), and 10 regionally-aligned molecular laboratories. The structure of the Malawi diagnostic network is representative of the diagnostic networks of many other countries in the region [43].

Since 2016, the Malawi branch of the nonprofit organization Riders 4 Health International (R4H) has managed the transportation of viral load (VL), early infant detection (EID) tests, and TB patient samples collected at health clinics and DHOs to the MLs. R4H maintains a team of over 70 motorcycle couriers who visit health facilities and laboratories according to fixed weekly schedules.

In collaboration with MOH and R4H, we identified three districts in Malawi to test the USSD System: Salima in the Central Region, Rumphi in the Northern Region, and Phalombe in the Southern Region. The diagnostic networks in these rural/semi-rural districts each contained between 15 and 18 facilities and relied upon one molecular laboratory to conduct the diagnostic testing for that diagnostic network, making these districts a representative sample of R4H's typical ST operations in rural and semi-rural areas.

This field trial was approved by Malawi's National Health Sciences Research Council. Evaluation by the MIT Committee on the Use of Humans as Experimental Subjects determined the trial did not constitute human subjects research as defined in Federal Regulations 45CFR46.

2.3.2 System Implementation

In early 2019, we contracted with a local vendor in Malawi to develop the user interface and information technology infrastructure. The vendor also managed the daily operation of the system, which included storing incoming data, sending reminder messages when appropriate, and contracting with the cellular network providers to enable free provision of the USSD service to health workers.

In May 2019, we asked the facility in-charge from each of the participating health facilities to nominate one or two staff members with personal mobile phones to enter data. In June 2019, we conducted three 2-hour training session (1 per study district) to train 150 health workers to use the USSD System. During the training sessions, we (i) introduced the USSD System to the participants, (ii) taught study participants how to access the system and submit reports using their personal mobile device, and (iii) provided reference posters and flyers reminding participants how to access the system for participants to display at their facilities. A field team, consisting of a local field manager and three local research assistants, monitored the implementation and addressed technical and logistical challenges through regular communication with health workers, district lab technicians, and R4H couriers via phone calls and text messages.

The USSD System was officially launched in the study districts in July 2019. Health workers were asked to report the number of patient samples waiting to be transported at the end of each day. Facilities were expected to submit a report every day, even if they had not collected any samples or prepared any new samples for transportation. Health workers and the field team were sent the following series of automated daily reminder messages to increase participation.

- 8:00 am - Health workers at each facility are sent a message notifying them whether or not a courier will visit their facility later that day and a reminder to report sample volumes.
- Noon - Health workers at each facility are sent a second reminder to report sample volumes.
- 1:30 pm - Members of the field team are sent a summary of the facilities for which a report has or hasn't been submitted.
- 2:15 pm - Health workers at facilities missing all or part of a complete daily report are reminded to report sample volumes.
- 3:00 pm - Members of the field team are sent an updated summary of the facilities for which a report has or hasn't been submitted, and a comparison of each facility's current report with their previous report (as an unusual increase/decrease from the previous report may indicate that the facility is reporting incorrectly).
- 4:15 pm - Members of the field team are sent a notification informing them whether couriers submitted reports to the Courier Database. Reports submitted to the Courier Database are summarized by facility, compared to that facility's most recent USSD report, and sent to members of the field team to assess facility reporting accuracy.

- 7:00 pm - Members of the field team are sent an updated list of the couriers who have or haven't submitted reports to the Courier Database. A summary of reports submitted to the Courier Database by facility are recompiled to capture any updates, re-compared to that facility's most recent USSD report, and sent to members of the field team to assess facility reporting accuracy.

Based on notifications received from health facilities, the field team sought out any unusual participation patterns such as intermittent, erratic, and/or extended periods of no participation. Upon detection of unusual participation patterns, the field team was authorized to address these patterns directly with the participant. In situations where an ordinarily reliable participant simply forgot to report, or health workers in the same facility failed to properly delegate reporting responsibilities, the field team could contact the designated staff member at the facility to remind them to submit their daily report or to delegate reporting responsibilities to a different health worker when the primary contact was not at the facility. If the field team identified intermittent network coverage as the cause of a missed report, the field team could delegate reporting responsibility to someone with a network connection. In addition, the field team could also ask the courier to hand-deliver a message to the responsible health worker, to identify someone else at the facility to accept reporting responsibilities, or to request escalation to a higher authority at the non-reporting facility in email notifications regarding their facility's participation.

The field team also monitored accuracy of reports and intervened directly with participants if they observed a pattern of low accuracy reports. As in the case of poor participation, the field team could use combination of phone calls, text messages, and hand-delivered messages to identify the root causes of data inaccuracies and address them. The preferred approach for improving accuracy of reports was to provide additional instructions to the non-compliant participant. If a training update failed to address the situation, more drastic measures (e.g., requesting transfer of reporting to another staff member) could be adopted.

2.3.3 Evaluation Framework

As part of the USSD System implementation plan, we elected to evaluate the feasibility, adoption, and accuracy of the USSD System using relevant descriptive statistics. Feasibility and adoption are common evaluation domains in intervention assessment literature [41, 40]. Accuracy, while not a common evaluation domain regarding health interventions, is relevant in the context of mobile-device based data collection systems [38]. Table 2.1 lists the guiding questions and associated metrics for assessing system performance within the three domains. The feasibility of the USSD System depended on whether each facility had access to the technology required to participate in the system. Therefore, we identified the number of facilities employing someone with a mobile device who was willing to participate in the study and the number of facilities in the field trial districts receiving service from a wireless network provider.

To assess adoption of the USSD System, we monitored specific participation-related metrics: percent of facilities reporting by day, individual facility participation over the course of the field trial, and the longest period each facility went without participating.

Table 2.1: Evaluation Framework

Domain	Guiding Question	Metric
Feasibility	Do facilities have access to mobile devices?	The fraction of facilities for which a personal mobile phone was registered.
	Do facilities receive a mobile network signal?	The fraction of facilities where insufficient network connection never prevented that facility from submitting a report.
		The fraction of facilities where staff members at that facility submitted a daily report for at least seven consecutive days.
Adoption	Are facilities participating?	The fraction of facilities that reported/failed to report each day by sample type.
		The fraction of total reporting days over the trial period when each facility reported/fail to report.
		The largest number of consecutive days a facility has failed to report.
	Which operational factors influenced facility participation?	The fraction of facilities where an insufficient understanding of the USSD System on the part of health workers prevented USSD participation.
		The fraction of facilities where hardware limitations prevented USSD participation.
		The fraction of facilities where health worker work-load prevented USSD participation.
		The fraction of facilities where health worker absences prevented USSD participation.
		The fraction of facilities where health worker forgetfulness prevented USSD participation.
Accuracy	How accurate is the data reported by participating facilities?	The average and variance of the difference between reported and actual sample volumes.

We determined the accuracy of the USSD System by comparing submitted USSD reports to program data. A data report was deemed accurate if the reported number of patient samples of a given type ready for delivery and the actual number of patient samples ready for delivery, as determined by the Courier Database, were identical.

2.3.4 Data

We used data from four distinct sources to calculate the metrics listed in Table 2.1: the USSD System Database, the Courier Database, a survey administered to members of the field team, and the attendance roster from the USSD System training sessions.

Every data report submitted through the USSD System over the field trial was archived in the USSD System Database. This database included the facility name, the date and time, the

user's mobile device number, the sample type, and the number of patient samples reported by the user for every data report.

The Courier Database contained sample-specific information submitted by the courier upon completion of the courier's daily route to a data collection system operated by R4H. The sample data captured in the Courier Database consisted of the sample's identification code, the name of the facility the sample originated from, the date of sample collection, and the date of sample pick-up from the originating facility.

Upon completion of the study, we administered a survey to the research assistants to assess barriers to system participation. For each of the 51 facilities included in the field trial, the research assistants were asked to answer the following inquiries:

1. Estimate the number of times a particular event, including poor network reception, caused each facility in the research assistant's district to fail to report.

2. Rate the effectiveness of the following techniques on participation by facilities in their district:

    - SMS messages.
    - individual messages via a popular internet messaging platform.
    - phone calls.
    - asking a courier to deliver a message.
    - in-person facility visits.
    - group messages via a popular internet messaging platform.

We compiled a master attendance roster by combining the individual attendance rosters that were recorded at each of the three USSD System training sessions. These rosters included the name of each training participant, the facility the participant represented, the participant's staff position, and the participant's contact information.

2.3.5 Analysis

To calculate the percent of facilities for which a personal mobile phone was registered, we reviewed the master training attendance roster. Attendance at a training event by an employee from a given facility indicated that the employee owned a mobile phone and was willing to use their device to submit data reports to the USSD System. To calculate the percent of facilities with a sufficient network connection, we summarized the survey responses regarding the frequency with which poor network connectivity prevented each facility from participating.

To determine the number of facilities for which a USSD report was submitted for at least seven consecutive days, we analyzed the facility name and date of every report submitted to the USSD System Database. Aggregation and/or summarization of data in the USSD System Database also allowed us to measure all three metrics listed associated with the first guiding question in the Acceptability Domain in Table 2.1.

We calculated the accuracy of the reported data by comparing the reported data in the USSD System Database to the courier reports in the Courier Database, which captured the number of patient samples collected from the healthcare facilities.

All data analysis was conducted with R (v 4.0.0) and RStudio (v 1.2.5042). Reported p-values were calculated using one-sided non-parametric Mann-Whitney tests (unless otherwise noted).

2.4 Results

2.4.1 Descriptive Statistics

Over the study duration (July 2019 - July 2020), participating facilities submitted 37,771 reports to the USSD System, accounting for 48,852 patient samples. The majority of these patient samples (83.8%) were VL samples (n = 40,952), while 6.1% were EID samples (2,979), 5.9% were TB samples (2,859), and 4.2% were classified as "Other" (2,056). Of the samples reported, 43.7% of them (21,355) originated in Phalombe, 35.1% (17,155) originated in Salima, and 21.1% (10,342) originated in Rumphi. The table included in (Multimedia Appendix 1) contains sample volume statistics by district.

2.4.2 Feasibility

All participating facilities employed at least one individual willing to submit reports to the USSD System with a personal mobile device. Research assistants reported that an insufficient network connection never prevented 47% of the participating facilities from submitting a report to the USSD System, caused occasional submission problems in 24% of facilities, and caused frequent problems in 29% of facilities. Our analysis of the USSD Database data also revealed that each facility had at least one seven-day period where the facility submitted a daily report every day.

2.4.3 Adoption

Figure 2.2 illustrates the daily sample reporting rates and the 7-day moving average of daily sample reporting rates for the three patient samples types between July 2019 and July 2020. At the beginning of the study, only 10-20% of facilities participated each day. However, after three weeks, daily participation rates rose and remained between 53% and 98% for VL, between 51% and 98% for EID samples, and between 43% and 96% for TB samples. Between, August 2019 and January 2020, the average participate rate increased gradually for VL (63% to 87%), EID (60% to 85%) and TB (54% to 79%) samples with notable but temporary declines during the second half of November and December. For the final six months of the trial (February 2020 to July 2020), the average participation rate remained at or above 75% for all three sample types.

The distribution of facility participation rates across all districts and by individual districts, where facility participation rate is calculated as the percent days out of total possible reporting days for which a facility reported, is shown in Figure 2.3. On average, facilities provided a report 79% of the time (198 days out of the total 251 possible reporting days, $\sigma = 32.6$ days). The median number of days a facility reported was 204 days (81%), with a range from 121 days (48%) up to 245 days (98%). Facilities in Phalombe reported less frequently than facilities in Salima (P = .003) and Rumphi (P =.01) on average.

Figure 2.2: Facility Participation by Sample Type, shown as Daily Participation Percentages and as a 7-day Moving Average

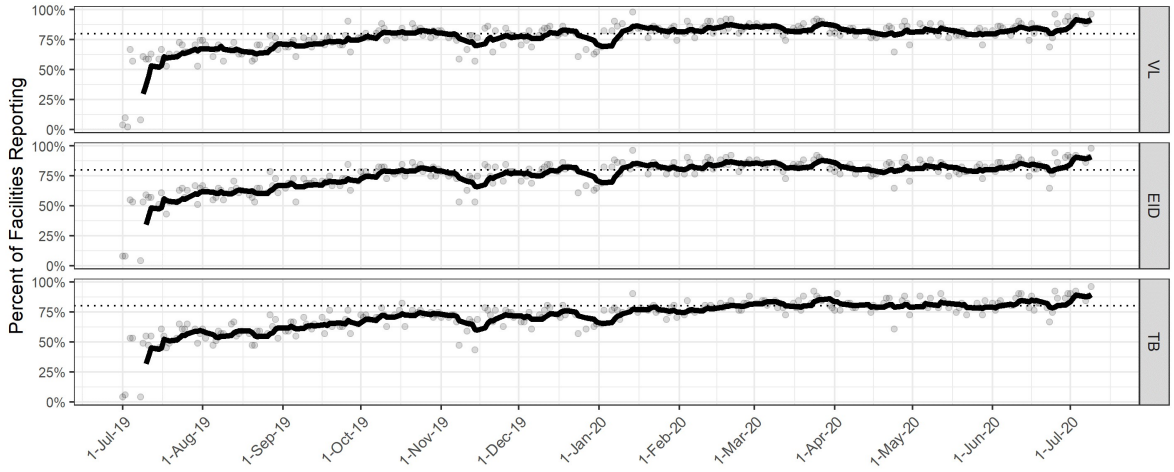
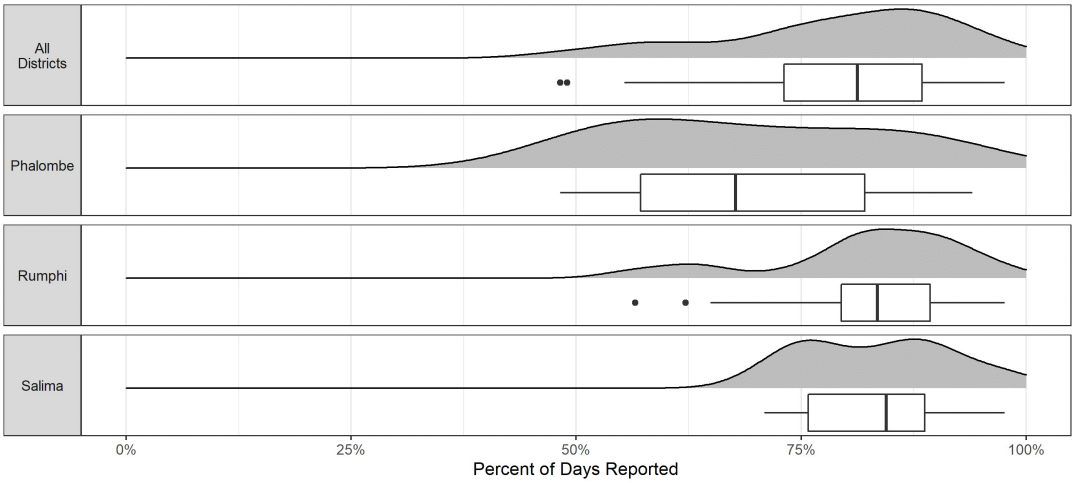


Figure 2.3: Distribution of Facility Reporting Frequency



Of the 51 health facilities, 45% of facilities (n = 23) never went more than one business week (5 days) without submitting a report, and the longest any facility went without providing a report was 30 days. On average, the longest period a facility went without submitting a report was 8.65 days ($\sigma = 6.33$).

Table 2.2 shows the frequency of participation challenges faced by health facilities according to the three local research assistants. Each cell shows the number and percent of facilities reported to experience a specific concern to the given extent. Recurring compliance issues were most often due to poor network reception, while the occasional non-compliance issue was most likely due to forgetfulness on the part of the health worker. Staff absence at participating facilities also caused reporting issues at a majority (60%) of the participating facilities. These research assistant survey results also suggest that health workers had an adequate understanding of the system; poor staff training did not cause any reporting problems in over 80% of the facilities.

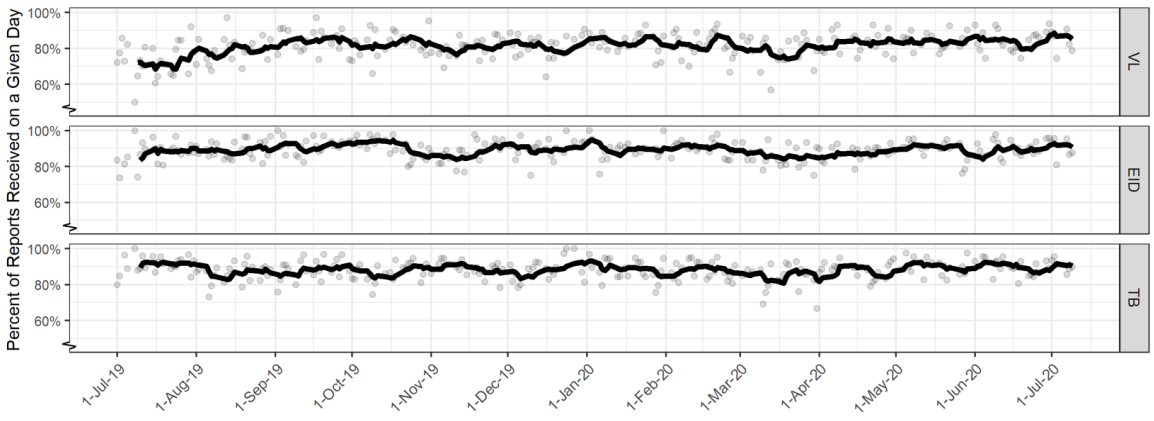
Table 2.2: Survey Results Regarding the Causes of Reporting Issues at each of the 51 Participating Facilities

Reason for No Report	No Problems	Occasional Problems	Frequent Problems
Insufficient Mobile Network Reception	24 (47%)	12 (24%)	15 (29%)
Phone Issues (e.g., low battery, broken phone)	29 (57%)	18 (35%)	4 (8%)
Staff are Absent	20 (39%)	21 (41%)	10 (20%)
Staff are Too Busy	26 (59%)	15 (29%)	6 (12%)
Staff Do Not Understand How to Use the System	43 (84%)	8 (16%)	0 (0%)
Staff Forgot to Report	4 (8%)	39 (76%)	8 (16%)

2.4.4 Accuracy

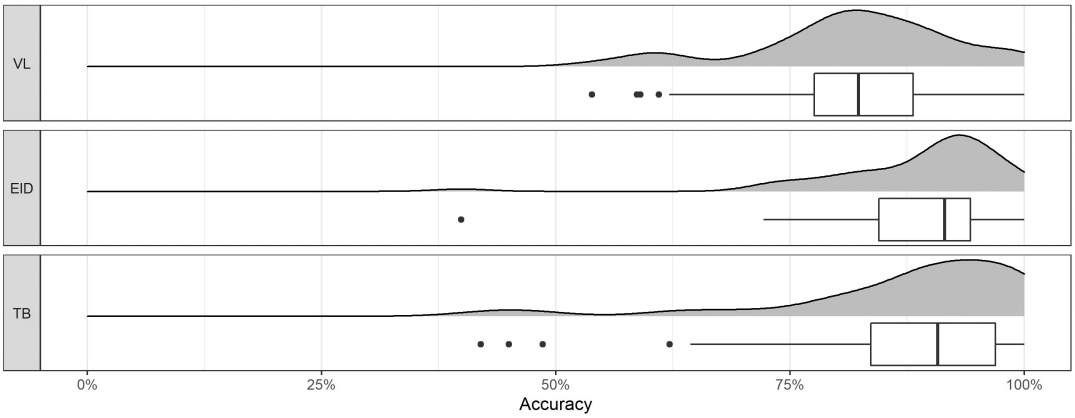
Figure 2.4 illustrates the daily percentage accuracy of reports for each sample type, and its 7-day moving average. The daily accuracy for VL reports slowly improved over the first two months of the field trial and settled at around 80% for the remainder of the trial. Unlike VL reports, the daily accuracy of EID and TB reports did not change substantially throughout the trial, with the daily accuracy of VL reports exhibiting greater variance ($\sigma = 7.23$) than both EID daily reporting accuracy ($\sigma = 5.25$; P ¡ .001; Levene's Test) and TB daily reporting accuracy ($\sigma = 5.38$; P ¡ .001; Levene's Test) . On average, 81% of the daily VL reports, 89.2% of the daily EID reports, and 88.2% of the daily TB reports were accurate.

Figure 2.4: The Number of Accurate Reports by Sample Type, shown as Daily Accuracy Percentages and as a 7-day Moving Average



The distribution of data accuracy by sample type across facilities is displayed in Figure 2.5. The accuracy of EID reports exhibited the least variation ($\sigma = 0.01$), followed by VL reports ($\sigma = 0.11$), and then TB reports ($\sigma = 0.14$). Median facility reporting accuracy were 82% for VL, which was lower than that for EID (91%; P = .001; Paired Mann-Whitney) for TB (91%; P = .001; Paired Mann-Whitney). For each sample type, over half of the facilities submitted accurate reports on more than 80% of the days in the field trial.

Figure 2.5: Distribution of Facility Reporting Accuracy by Sample Type



2.5 Discussion

2.5.1 Summary of Findings

We designed a system whereby staff members in geographically dispersed healthcare facilities could report, via any mobile device, the number of patient samples prepared for delivery to a diagnostic test facility. Between July 2019 and July 2020, we conducted a field trial of the system in 3 districts in Malawi to assess the system's feasibility, adoption, and accuracy. The results from our field trial suggest that the USSD System is a feasible, adoptable, and accurate tool for assembling accurate daily reports on the quantity and location of transportation-ready patient samples and diagnostic test results.

Feasibility

The feasibility of the USSD System is driven by the ease with which facilities can access it for report submission with a mobile network connection and a mobile device. While mobile network coverage varies by country, our findings with respect to the number of facilities able to submit a report through the system illustrate the potential of using mHealth systems to link rural health facilities to central operations managers in sub-Saharan Africa – especially as mobile network coverage continues to improve across the region [18]. We also found at least one person at each facility with a mobile phone - a significant result as less than half of the population in the region owns a mobile phone [2]. While prior work in the region regarding mHealth initiatives among the general population has, at times, found poor eligibility rates among potential participants driven by low mobile phone ownership [4, 54], our findings suggest that mHealth efforts requiring ownership among health workers may be more feasible than those requiring ownership among the general population (see also [45]). Additionally, it is likely that the use of USSD in a region where smartphones constitute less than 40% of all mobile phones with lower-tier connections (i.e., 1G/2G as against 4G/5G) also contributed to system feasibility [18]. The use of health workers' personal phones avoided the additional cost for deploying new devices in the field and leveraged familiarity with their devices to enhance system usability and transfer maintenance responsibilities to them [5].

Adoption

Adoption of the USSD System improved consistently over the course of the study and peaked near 90% toward the end, with the exception of small and temporary declines coinciding with personnel transitions (i.e., staff reallocations and annual training sessions) and holiday seasons. These findings are comparable to results from similar mHealth studies conducted in the region [45, 5], despite our study requiring more frequent reporting than other studies and doing so without monetarily compensating participation. Based on the calculated descriptive statistics, we attribute the wide adoption of the USSD System to close collaboration with MOH representatives. This collaboration secured the support of senior government officials who encouraged participation by health workers at the facilities. Additionally, this collaboration improved the chances that that the system's design complemented health workers' existing responsibilities rather than adding to them, which is known to increase the likelihood of system adoption [4, 45, 22]. The efforts of the field team in their role as real-time participation monitors and problem solvers may have also influenced the observed participation rate.

Accuracy

The existence of the Courier Database, and our ability to access that data, played a significant role in ensuring high accuracy of records (greater than 80%). In contrast with prior mHealth initiatives [5, 30], the Courier Database allowed us to assess the accuracy of every report submitted through our system with minimal delay and to provide feedback, via the field team, to correct improper reporting behavior daily. Providing timely and relevant feedback to a health worker regarding their reporting behavior likely contributed to the overall reporting accuracy achieved in the field trial [19].

2.5.2 Study Strengths and Limitations

The scope of our study is limited to establishing the feasibility, adoption, and report accuracy of a USSD system for collecting information on the quantity and location of patient samples and test results prepared for delivery in the diagnostic network. Therefore, the impact of making this data available on subsequent operational decisions or patient care remains undetermined. It is expected that this information is useful for avoiding unnecessary health facility visits, but the rigorous quantification of this effect on ST operations requires future research. In addition, the results presented in Table 2.2 regarding the operational factors affecting facility participation are based on data collected indirectly through a survey administered to the three research assistants in the field. Ideally, this data should have been collected directly from each facility, as this would provide more granular information about the operational drivers for participation. However, collecting operational data on a daily basis was beyond the scope of this effort and the constant rotation of health workers into and out of facilities over the course of the study made it infeasible to conduct an end-of-study survey at each facility. We believe that the use of research assistants was the next best solution since they were in regular contact with multiple health workers from each facility and were aware of their experiences with the USSD system. Regardless of this limitation, the main objective of the study was to assess the feasibility, adoption, and accuracy

of collecting information using the USSD system, all of which can be evaluated using primary data sources.

While our study exhibits numerous strengths – including the fact that the structure of the system allowed us to determine the accuracy of every submitted report and a sustained field implementation for a year – a notable strength of our study is that it demonstrates a novel use of mHealth technology to significantly improve information sharing in diagnostic networks, which have a similar structure in many in low- and middle-income countries. Previous mHealth studies have investigated how mHealth technology can improve healthcare delivery through the wide dissemination of health-related information [1], providing patient-specific reminders and/or results to patients [49, 25], connecting healthcare providers at different levels in the healthcare network [6, 28], and monitor medical supply stock levels [45, 5, 28], among other applications [4, 10]. This study, to the best of the authors' knowledge, represents the first application of mHealth technology track the location of samples and results in a large-scale diagnostic network.

2.5.3 Scalability

The USSD System is extremely scalable from a technological perspective, as there is no requirement to purchase a specific mobile phone, mobile phone airtime, or any other system-specific technology. Expanding the system to operate with new facilities and/or new diagnostic tests simply requires assigning USSD identification codes and training new users, which itself is not very onerous due to familiarity of mobile users in the region with USSD technology through other applications [39]. Scalability of the USSD System is further enhanced as it does not require purchase of new hardware or software. The system operates with a mobile network signal that is increasingly available across most of the region and uses technology universally embedded on all mobile devices.

As explained earlier, the USSD system was designed to minimize its impact of the workload of health workers, which should positively affect adoption in other health facilities without disrupting their routines [35, 46]. Further, health workers who currently use the USSD system can share their experiences in the training sessions for new facilities thereby further speeding up adoption. However, scalability may be adversely affected with continued reliance on the field team for data monitoring and supervision. As we work on developing scale-up plans, in collaboration with R4H and MOH, we believe that incorporating these tasks into the roles of senior personnel within the ST systems such as the regional ST coordinators who oversee ST operations within the districts can help overcome this problem and facilitate scalability.

2.6 Conclusion

Malawi's diagnostic network, both in terms of the network's structure and the challenges present, is representative of many diagnostic networks operated in sub-Saharan Africa [43]. The descriptive results of our study suggest that a USSD-based system is a feasible, adoptable, and accurate solution to the challenge of untimely, inaccurate, or incomplete data present in these diagnostic networks. There are many ways to incorporate the information provided by the USSD system into a courier routing system aimed at reducing empty trips and delays. As one example, a

recent report from Gibson et al. [16] indicates that this information, along with a sophisticated routing system, can reduce empty trips by at least 55%. The scalability of the USSD System, along with the promising results of our study, suggest that system implementation at the national level in many sub-Saharan nations is feasible and worthwhile.

2.7 Acknowledgements

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Chapter 3

Where to Locate Point-of-Care Testing Devices

3.1 Introduction

As of 2019, over half of people living with HIV in the world, are living in sub-Saharan Africa [52]). To combat this high disease prevalence many countries in sub-Saharan Africa have initialized viral load (VL) monitoring and early infant diagnosis (EID) testing programs. These programs typically involve a diagnostic network of community-level health clinics where patients are seen and diagnostic samples such as blood or sputum collected, centralized health offices which register diagnostic samples, and regionally-aligned molecular laboratories where diagnostic samples are processed [20, 43]. Diagnostic samples are transported through the network via a combination of formal and informal courier systems, referred to as sample transportation (ST) systems [16]. Unfortunately, ST systems within these networks are often inefficient, leading to poorer health outcomes among the population being served [20, 26].

In recent years, point-of-care (POC) testing devices, which facilitate diagnostic sample testing outside of the typical laboratory environment, have been tested in diagnostic networks in sub-Saharan Africa [13, 15, 33]. Results from these trails suggest that POC devices hold great promise towards improving diagnostic networks in low- and middle-income countries (LMICs) by reducing transportation requirements and easing the burden on formal molecular laboratories. The belief is that incorporating POC devices into these LMIC diagnostic networks will reduce the average time between a patient submitting a sample for testing and the patient receiving their test result, known as the system turn-around time (TAT) [15, 42]. Reduced TAT has been shown to have many positive benefits including an increase in patient return probability, initiating treatment more quickly, and more rapidly identifying when a patient's treatment regime requires modification [13, 33].

Ideally, every facility which sees patients in the diagnostic network would be outfitted with a POC device. However, the limited processing capacity of POC devices and their upfront investment means that purchasing and operating the necessary quantity of POC devices to meet demand can prohibitively expensive in countries already operating a centralized laboratory diagnostic network [48, 11]. For this reason, many experts suggest that POC devices should be seen as an extension of a countries pre-existing centralize laboratory network rather than as a

complete replacement [12, 42].

The question then is, where in these resource-limited diagnostic network should POC devices be located to reduce TAT? As stated by Diallo et al. [12], "for optimal usage in the greatest impact on patient care, these new instruments require proper placement within the existing efficient laboratory network." To address the challenge of POC device location in an existing centralized laboratory network, we developed a discrete event simulation model to determine the effect of various location policies on the TAT of patient samples within Malawi's diagnostic network.

3.2 Study Setting and Point-of-Care Testing Devices

3.2.1 Study Setting

As of 2018, 9.2% of adults (15–49 years) in Malawi were living with HIV [51]. Like many other countries in the region, the Malawi Ministry of Health (MOH) operates a diagnostic network of health clinics and laboratories to provide access to HIV viral load (VL) and early infant detection (EID) testing to its citizens [43]. The Malawi diagnostic network contains approximately 700 widely-distributed, community health clinics, 27 centrally located district health offices (DHOs), and 10 regionally-aligned molecular laboratories. Figure 3.1 shows the locations of Malawi's health clinics, DHOs, and molecular laboratories.

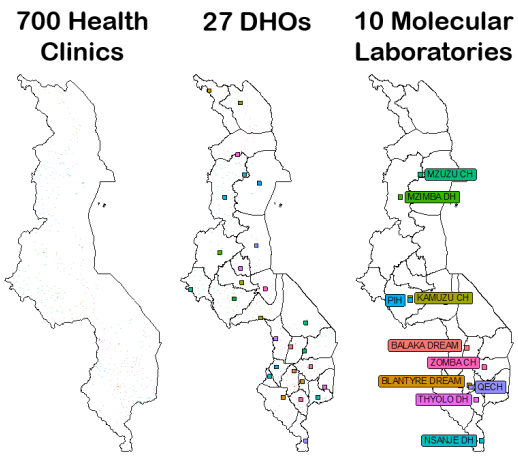

Figure 3.1: Health Facility Locations

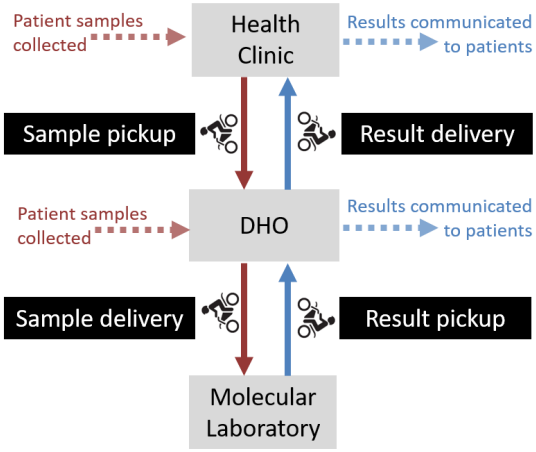

Figure 3.2: The Malawi Diagnostic Network and R4H ST System

The Malawi diagnostic network and ST system is depicted in Figure 3.2. As shown in the figure, patient samples are collected at the health clinics and DHOs. Samples collected at a health clinic wait to be transported to the specific DHO that has been assigned to that specific health clinic. Once the health clinic samples have been transported to the DHO, these samples, along with those collected directly at the DHO, are registered by the DHO staff into the country's national sample database. After registration at the DHO, samples are then transported to the specific molecular laboratory aligned with that specific DHO. Samples then wait at the molecular lab until they can be batch tested. After testing, the test results are printed and then transported back to the correct DHO. The test results are registered into the

national sample database by the DHO staff, and are then transported to the correct health clinic where they are passed along to the patient's physician. If the patient receives treatment directly at the DHO, that patient's test results forgo delivery to a health clinic.

Since 2016, the Malawi branch of the nonprofit organization Riders 4 Health International (R4H) has managed the ST system within the Malawi diagnostic network. R4H maintains a team of over 70 motorcycle couriers to transport diagnostic samples collected at health clinics and DHOs to the MLs according to fixed weekly schedules. Couriers are stationed at DHOs and visit clinics and molecular labs according to fixed weekly schedules specifying the facilities to be visited each day, and the order in which to complete these visits.

3.2.2 Point-of-Care Testing Devices

Schito et al. [42] define POC testing as "diagnostic testing that is performed near the patient or treatment facility, has a fast turnaround time, and may lead to change in patient management", choosing also to specify that POC testing "should not require trained laboratory personnel or clinical laboratory or other infrastructural support." For the purposes of this paper, POC testing refers to testing conducted at a community-based health clinic, and near-POC testing refers to testing conducted at a centrally-located district health office.

Malawi currently operates 117 POC/near-POC testing devices. These devices are able to conduct both VL and EID tests, as well as other diagnostic tests. The estimated daily testing capacity of these devices is 21 samples per day [7]. The deployment of POC testing devices in Malawi has been gradual and ad-hoc, without consideration for how POC devices may integrate with other aspects of the networks, such as ST. Most POC devices have been deployed to provide near-POC testing (i.e., POC devices have been placed at district hospitals, not at rural clinics).

3.3 Methods

3.3.1 Discrete Event Simulation Model

To explore the impact of POC device placement within Malawi's centralized laboratory network, we created a day-based discrete event simulation model of the Malawi diagnostic network as it existed in 2018 and included functionality to simulate POC testing at user-specified health facilities. The model's structure, including this POC testing functionality, is graphically depicted in Figure 3.3.

The simulation model simulates the daily operation of a network containing health clinics, C, DHOs, D, molecular laboratories, M, and which is designed to provided diagnostic test(s) of type T.

Following the "Main Path" in Figure 3.3 (denoted by the bold arrows), on day d, at clinic C, a random number of patient samples for a specific type of test, $SA_{C,T,D}$ enter the simulation, or "arrive". $SA_{C,T,D}$ is drawn from a Poisson distribution with arrival rate, $AR_{C,T}$. Upon arrival in the system, these samples are immediately available to be transported to DHO D. Transportation capacity is limited by the number of couriers. Therefore, if the samples cannot be transported immediately, samples enter the clinic's sample pickup queue, SPQ_C, joining

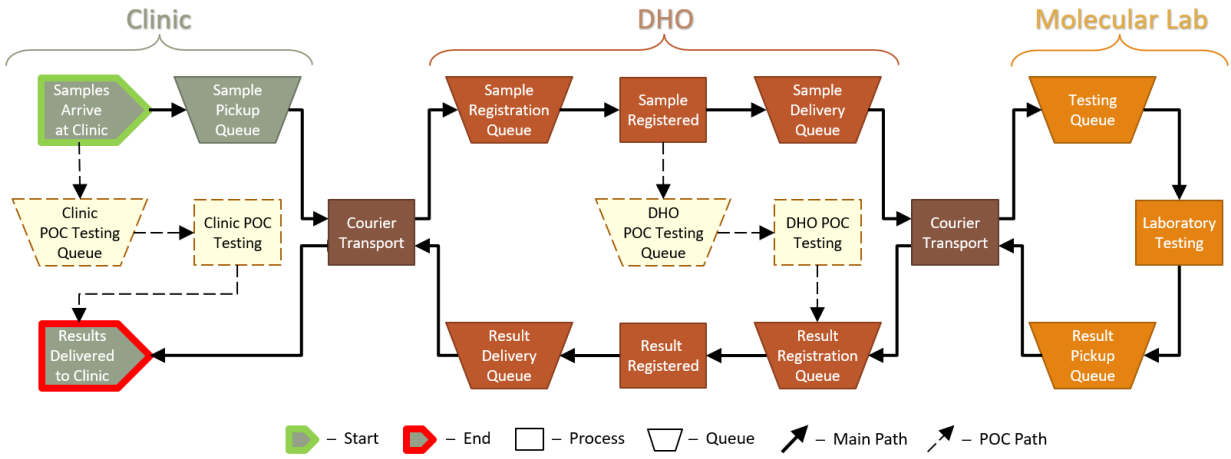

Figure 3.3: Malawi Diagnostic Network Simulation Model Structure

other samples awaiting pickup from clinic C. Samples remain in SPQ_C until a courier visits clinic C.

Whether or not a facility is visited by a courier is controlled by courier routes, $Route_{D,w(d),i}$, where $w(d)$ denotes the weekday of day d, and i represents a specific courier and ranges from 1 to the total number of couriers at DHO D.

When a courier visits clinic C, all of the samples in SPQ_C on the day of the courier's visit, and any samples that arrived at clinic C that day, are transported to DHO D. Once at DHO D, samples are ready to be registered. DHO staff have a stochastic daily sample registration capacity so newly arrived samples enter the DHO's sample registration queue, $SRQ_{D,T}$ to await registration. The daily sample registration capacity at DHO D on day d, $SR\_Cap_{D,T,d}$ is simulated by randomly sampling from a registration capacity distribution, $SRdist_{D,T}(\cdot)$. On day d, the number of samples at DHO D of type T that are pulled from $SRQ_{D,T}$ and registered, $SR_{D,T,d}$, is the minimum of $SR\_Cap_{D,T,d}$ and $SRQ_{D,T}$. After registration at DHO D, samples are ready to be transported to the molecular laboratory. Samples cannot be transported to the laboratory on the same day that they have been registered so registered samples enter the DHO's sample delivery queue, SDQ_D to wait for a courier. As with the transportation from clinic C to DHO D, samples remain in SDQ_D until $Route_{D,w(d),i}$ includes a visit to molecular laboratory M.

After being delivered from DHO D to molecular laboratory M, samples are ready to be batch tested. The number of batches of size b_T varies each day, so newly arrived samples enter testing queue $TestQ_{M,T}$. The capacity of batches that can be tested at lab M on day d for samples of type T, $Test\_Cap_{M,T,d}$, is simulated by randomly sampling from a testing capacity distribution, $Testdist_{M,T}(\cdot)$. The number of samples are drawn from $TQ_{M,T}$ and tested on day d, $Test_{M,T,d}$, is the minimum of $(b_T * Test\_Cap_{M,T,d})$ and $\lfloor TQ_{M,T}/b_T \rfloor$. After testing, the test results enter the molecular laboratory's result pickup queue RPQ_M. Test results destined for DHO D remain in RPQ_M until $Route_{D,w(d),i}$ includes a visit to molecular laboratory M.

Test results of type T arriving at DHO D must be registered. Daily DHO result registration capacity is limited, so results enter the DHO's result registration queue $RRQ_{D,T}$. The daily result registration capacity at DHO D on day d, $RR_cap_{D,T,d}$, is simulated by randomly sampling

from a result registration capacity distribution $RRdist_{D,T}(\cdot)$. The number of results registered at DHO D on day d, $RR_{D,T,d}$, is the minimum of $RR\_Cap_{D,T,d}$ and $RRQ_{D,T}$. Registered results then enter the DHO's results delivery queue RDQ_D. Test results destined for clinic C remain in RDQ_D until $Route_{D,w(d),i}$ includes a visit to clinic C.

Introducing POC testing devices, either at a clinic or a DHO, causes a sample to deviate from the "Main Path" in Figure 3.3 and follow a "POC Path". POC paths, denoted in Figure 3.3 with the dashed lines, are activated at the clinic C or DHO D when C or D operate a POC testing device with daily testing capacity $TPOC\_Cap_C$ or $TPOC\_Cap_D$. When a sample arrives at a clinic equipped with a POC device, that sample is immediately added to that clinic's POC testing queue, $POCQ_C$. Note that $POCQ_C$ is not sample type-specific, as the same POC testing device is capable of conducting multiple types of tests. On day d, $TPOC_{C,d}$ samples are removed from $POCQ_C$ and are tested. $TPOC_{C,d}$ is the minimum of $TPOC\_Cap_C$ and $POCQ_C$. After testing, the test result is immediately delivered to clinic C.

POC testing at a POC testing-enabled DHO follows a similar path to POC testing at the clinic level. Samples arriving at DHO D when D is equipped with a POC device, wait to be registered in $SRQ_{D,T}$ and on day d, $SR_{D,T,d}$ samples are registered. After registration, samples (again regardless of type) are added to the DHO's POC testing queue, $POCQ_D$. On day d, $TPOC_{D,d}$ samples from $POCQ_D$ are tested, where $TPOC_{D,d}$ is the minimum of $TPOC\_Cap_D$ and $POCQ_D$. After POC testing, the results enter the DHO's result registration queue $RRQ_{D,T}$ and continue through the system as described above.

Model Parameters

The simulation model operates with the following parameters:

- Facility Master List – A list of all health clinics, DHOs, and molecular laboratories indicating the health clinics assigned to each DHO, and all of the DHOs assigned to each molecular laboratory.
- Distance Matrix – The pairwise distances, in km, between all health clinics and the DHO in each district and between each DHO and the molecular laboratory serving that DHO.
- $Route_{D,w(d),i}$ – The scheduled routes driven by the couriers.
- $AR_{C,T}$ – The arrival rate of samples of type T at every health clinic.
- $SRdist_{D,T}(\cdot)$ – The distribution used to simulate $SR\_Cap_{D,T,d}$.
- b_T – The batch testing size for samples of type T.
- $Testdist_{M,T}(\cdot)$ – The distribution used to simulate $Test\_Cap_{M,T,d}$.
- $RRdist_{D,T}(\cdot)$ – The distribution used to simulate $RR\_Cap_{D,T,d}$.
- $TPOC\_Cap_C$ – The testing capacity of POC devices at clinic C.
- $TPOC\_Cap_D$ – The testing capacity of POC devices at DHO D.

Data

Our primary sources of data were our partners with R4H and the Malawi Ministry of Health (MoH). Data sources included:

(1) 2018 R4H Routes – R4H provided the scheduled routes each courier was expected to follow each weekday in 2018. Each route included the DHO where the route began and ended, the day of the week the route was to be completed (Monday-Friday), and the facilities visited, listed in the order they were to be visited. R4H provided data for 315 routes, in total.

(2) 2018 Facility Locations – R4H provided a list of all the facilities R4H couriers visited in 2018 along with the latitude and longitude of each facility. This list contained 10 molecular laboratories, 27 DHOs, and 667 health clinics.

(3) Laboratory Information Management System (LIMS) – MoH's official source for information regarding medical laboratory and diagnostic services across Malawi (Malawi Ministry of Health, 2015). LIMS contains the date of diagnostic sample collection, type of diagnostic test requested, sample collection location, the date the sample arrived at a test location, sample test date, testing location, and the test result, among other data fields not relevant to this analysis. We limited our queries of LIMS for VL and EID samples collected at facilities listed in the 2018 Facility Locations data. Our query of LIMS for samples collected in 2018 yielded 411,228 complete record, of which 90% (368,539) were designated as VL samples, and 10% (42,689) were EID samples. Our query of LIMS for VL and EID samples collected during the first quarter of 2019 which yield 122,080 (73%) complete records for VL samples, and 46,109 (27%) complete records for EID samples (168,189 samples total).

Parameter Estimation

Facility Master List We compiled the Facility Master List by extracting a list of all facilities from the 2018 Facility Locations data and then determining each clinic's primary DHO, and each DHO's primary laboratory by analyzing the route assignments in the 2018 R4H Routes data.

Distance Matrix We manually compiled the Distance Matrix using a combination of courier input and an open source GIS routing program. This program accepted the GPS coordinates provided in the 2018 Facility Locations data and provided a route using known roadways. These routes were reviewed by couriers to confirm that each route was acceptable and travel distances, in km, were recorded for each route.

Courier Routes The courier routes were provided by R4H in the 2018 R4H Routes data.

Sample Arrival Distributions Analysis of the arrivals in the 2018 LIMS data suggested that the day of the week and the month of the year both influenced the number of samples

arriving on a given day. To simulate the arrival process, we calculated the average number of arrivals by sample type at each facility for every combination of weekday (Sunday, Monday, etc.) and month. These average arrival rates were then used as the input parameters to Poisson distributions. The number of arrivals each day was then randomly sampled from the Poisson distribution using the arrival rate who's month and weekday matched the current simulation day.

Daily Sample Registration Distributions Ideally, we would have estimated the Daily Sample Registration Distribution by fitting a distribution to the actual number of samples registered at each DHO each day in 2018. However, the date a sample is registered is not recorded in LIMS and no alternate data set containing this information exists. As an alternate approach, we used the 2018 R4H Routes data and the date of sample collection and date of receiving at the molecular lab, which are recorded in LIMS, to estimate the date each sample arrived at and then departed a DHO. From these estimated DHO arrival and departure dates, we were able to estimate the amount of time each sample spent at the DHO with the understanding that at some point during this time period, the sample was registered.

We then constructed a simple queue model featuring a single process representing DHO sample registration. Samples arrived in this simple queue model according to their estimated 2018 DHO arrival date and the number of samples processed each day was determining by randomly sampling from a user-defined distribution. The average amount of time samples spent in the simple queuing model was then compared against the average of our estimate of the actual amount of time spent by samples at a DHO. Using this simple queuing model and an objective to minimize the difference between the simulated DHO duration and the real-world DHO duration, we conducted tuning exercises with both a Poisson distribution and a Negative Binomial distribution. We identified the distribution parameters for a Poisson distribution and a Negative Binomial distribution which yielded DHO durations most closely matching the real-world 2018 data. We then evaluated these two models using the estimated DHO arrivals and DHO durations for samples in the first-quarter 2019 data. The simulated durations for the 2019 most closely match the real-world durations when the number of samples to register each day was drawn from a Negative Binomial distribution in 24 of the 27 DHOs we simulated. For simplicity, we elected to estimate the Daily Sample Registration Distribution for each DHO using a Negative Binomial distribution and the parameters identified through the tuning exercise.

Batch Size and Daily Batches Tested Estimates for Batch Size were provided by R4H personnel with knowledge of the testing equipment operated at each laboratory and cross-referenced with the 2018 LIMS data. The subject matter experts (SMEs) stated that both VL and EID samples were tested in batches of 93 samples. Our analysis of the LIMS data confirmed that batches of 93 samples were standard for VL sample testing. Regarding EID testing, our analysis revealed that EID samples were often times tested in amount below the full batch amount, likely due to the fact that, in 2018, there were almost 9 VL samples for every 1 EID sample. To account for the testing of EID samples in batches below the full batch size of 93, we calibrated the model using an EID batch size of 48.

To estimate the Daily Batches Tested Distribution, we followed a procedure similar to that

described for estimating the Daily Sample Registration Distributions described above. We constructed a simple queue model, this time with a batch processing requirement, to model laboratory testing. Samples arrived on the same days they arrived according to the 2018 LIMS data, and the number of batches to test on a given day was drawn from a distribution specified by the user. We evaluated both Poisson and Negative Binomial distributions and calibrated the parameters for both of these distributions by identifying those parameters which yielded lab wait times most closely matching the real-world 2018 data. We evaluated both distributions using the lab arrival dates and lab wait times for samples in the first quarter 2019 data. The simulated wait times for the 2019 mostly closely match the real-world durations when the number of batches to test each day was drawn from a Negative Binomial distribution in 6 of the 10 molecular labs we simulated. For simplicity, we elected to estimate the Daily Batches Tested Distribution for each laboratory using a Negative Binomial distribution and the calibrated parameters.

Daily Result Registration Distribution LIMS does not contain any data regarding when a result was registered at the DHO. Additionally, LIMS also contains no data regarding when a registered result was delivered to a health clinic. Without any useful data, we relied upon the input of SMEs to estimate the Daily Results Registration Distribution. SMEs with R4H indicated that result registration is relatively easy and that it would be safe to assume that all results are registered after being at the DHO for one day.

POC Testing Device Capacity The majority of POC testing devices currently operated by MoH are GeneXpert© IV devices produced by Cepheid Corporation. As advertised by Cepheid, these devices have an 8-hour testing capacity of 21 samples [7]. We assume one 8-hour shift per weekday for POC devices placed at clinics or DHOs, and zero shifts on weekends.

Model Meta-Parameters

For our analysis, we used the simulation model to simulate the Malawi Diagnostic Network for one year, beginning 1 January 2018. Preliminary model testing indicated that a 6-month model warm-up period was sufficient. Therefore, all model runs simulated a total of 547 (365+182) day and all output statistics were calculated using only those samples which arrived in the simulated after the first 182 days.

Measures

The following metrics are calculated for every simulation run completed in the simulation model:

(1) Average Turnaround Time (TAT) – The average number of days that elapse between when a patient sample is collected and when the diagnostic test results arrive at the facility from which the patient sample originated.

(2) Travel Distance – The total distance traveled by all couriers.

(3) Number of Empty Trips – The number of empty trips completed by all couriers, where an empty trip is defined as a facility visit where the courier transported no patient samples and no test results to/from the visited facility.

(4) Lab/POC Utilization – The theoretical utilization of the Lab/POC testing device based on the expected sample volumes and the average capacity of the Lab/POC testing device.

(5) Positive to Negative Result Ratio – The average ratio of positive results to negative results across all POC devices or all molecular laboratories.

3.3.2 Experiments

Thirty simulations were completed for each of the policies below and reported statistics were calculated as an average of the 30 model runs.

We also sought to explore the robustness of these strategies to increased sample volumes. We conducted 30 model runs for each of the policies below under the conditions that arrivals were increased by 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 35, 40, 45, and 50 percent from the 2018 arrival volumes. We assume POC devices are reallocated across clincs under the different increases in arrival volume to ensure any clinics that have at least one POC device have enough devices to keep device utilization below 1. Additionally, we assume that DHO processing capacity scales linearly with the increase in sample volumes. This is done to highlight utilization changes at the molecular laboratories absent of any effect due to DHO utilization.

Status Quo

The Status Quo policy serves as both a validation of the simulation model and as a baseline against which POC deployment policies can be compared. This policy mimics the operation of the Malawi Diagnostic Network in 2018, meaning that no POC testing devices are deployed.

Greedy Sample Volume

Under the Greedy Sample Volume policy, POC testing devices are deployed to the health clinics collecting the most patient samples. The motivation for this policy is that placing POC devices at high volume facilities promotes a high POC device utilization and has a maximum impact on reducing the Diagnostic Network's average TAT. However, one critique of this type of deployment policy is that high-volume facilities are often based in urban areas where frequent and reliable access to the centralized laboratories is common. Therefore, TATs for samples originating at high-volume facilities may already be below-average for the diagnostic network and the effect of this deployment strategy on average TAT may be marginal at best. An analysis of the 2018 Malawi LIMS data revealed that while this critique makes logical sense, it may not be valid. In Malawi, the top 20% of facilities by sample volume are, on average, 28 km away from their assigned DHO but the average TAT across these facilities was only half a day faster than the national average TAT.

Greedy Distance

The Greedy Distance deployment policy involves deploying POC devices at the facilities which are located the furthest distance from their assigned DHO. The logic motivating this strategy is that facilities which are the hardest facilities for the couriers to visit presumably have above-average TATs as a result. Supporters of this type of strategy may claim that placing POC devices at these location will yield significant reductions in TATs at these facilities, which will have a noteworthy effect on the Network's average TAT. Conversely, critics of this strategy might claim that facilities which are the most difficult to reach are often located in sparsely populated areas. As a result of their locations, these facilities experience less-than-average sample volumes meaning POC testing devices would be under-utilized and any effect of reducing TATs at these facilities would have a negligible effect on the network-wide average TAT.

Greedy Prevalence

Facilities with the highest proportion of positive to negative test results receive POC devices under a Greedy Prevalence POC deployment strategy. This strategy is motivated by the belief that, from a health outcomes perspective, it is more important for patients with positive test results to receive their test results quickly, than it is for patients with negative test results to receive their results quickly. Therefore, in an effort to devote more POC device capacity to testing samples that are more likely to be positive, POC devices are located in facilities which have historically high disease prevalence. A critique of this strategy is that facilities with above-average disease prevalence may be located in less populated areas, leading to below-average sample volumes and thus low utilization of the POC device.

3.4 Results

3.4.1 TAT Results

The TAT results are presented in Figures 3.4 and 3.5. Figure 3.4 shows the average TAT across the entire system, the average TAT for samples tested at a molecular lab, and the average TAT for samples tested on a POC testing device, under the Status Quo and for each of the three POC device allocation policies. As shown in the figure, the average system TAT was 34 days, 12 days, 28 days, and 25 days under the Status Quo, Greedy Sample Volume, Greedy Distance, and Greedy Prevalence policies, respectively. Considering only the Greedy Sample Volume, Greedy Distance, and Greedy Prevalence policies, the average TAT for samples tested at a molecular lab was 19 day, 30 days, and 28 days, and the average TAT for samples tested with a POC testing device was 2.6 days, 2.4 days, and 2.3 days, respectively. Figure 3.5 contains the same statistics as Figure 3.4, but with an added dimension capturing the diagnostic test completed.

Keys observations from these figures are:

- Figure 3.4

  (1) Under the Greedy Volume policy, System-wide and Laboratory-only TAT is the lowest among all policies, but POC-only TAT is the highest among the three POC device

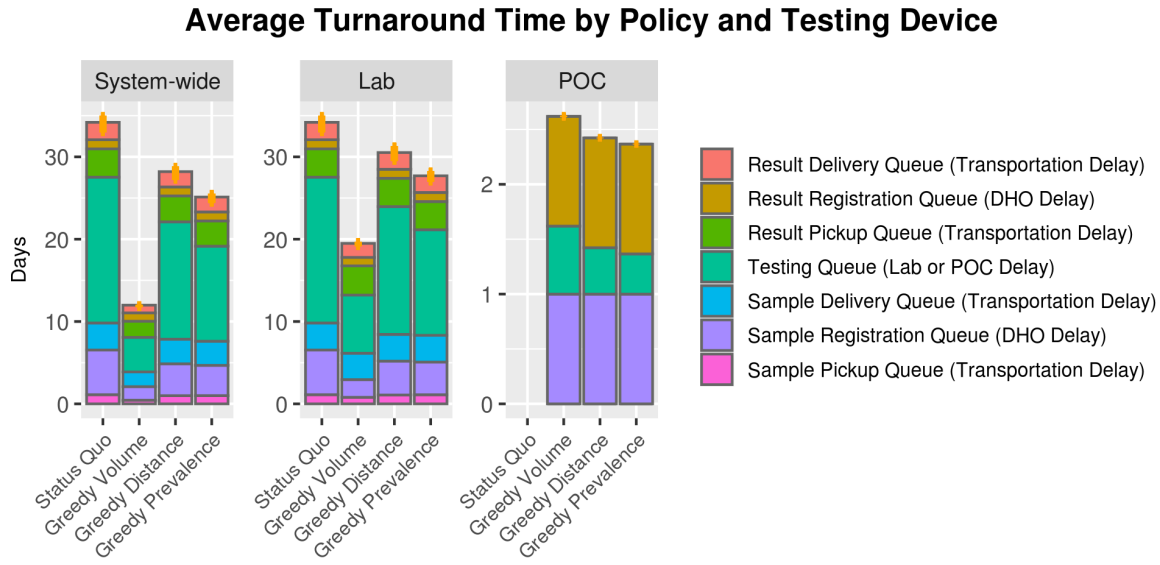

Figure 3.4: System-wide, Lab Only, and POC Only Average TATs

allocation strategies. By the definition of the Greedy Volume policy, POC devices are placed where they can test the most samples. As such, the total volume of samples directed to the molecular labs is reduced by 39%, leading to a 60% reduction in the average amount of time samples being tested at the molecular labs wait to be tested. Conversely, 360% and 251% more samples are sent to POC devices under the Greedy Volume strategy than the Greedy Distance and Greedy Prevalence strategies, respectively, increasing the amount of time POC-tested sampled waited to be tested by 47% and 69% when compared to the other two strategies.

(2) System-wide TAT and Lab-only TATs are more similar under the Greedy Distance and Greedy Prevalence policies than they are under the Greedy Volume policy. On average, 8.5% (31,689) and 10.6% (39,398) of all samples tested were tested on POC devices under the Greedy Distance and Greedy Prevalence strategies, respectively. Comparing this to the fact that 44.9% (177,504) of all samples tested were tested on POC devices under the Greedy Volume strategy. While the Greedy Distance and Greedy Prevalence strategies certainly ease the burden of testing at the molecular labs, as seen by the fact that average TATs for samples tested at the molecular labs under the Greedy Distance and Greedy Prevalence strategies are below the Status Quo Lab TAT, it is not surprising that Lab TAT has such a significant influence on the System-wide TAT.

- Figure 3.5

(1) System-wide TAT are decreased by a larger magnitude for VL samples than for EID samples under the Greedy Volume policy. VL samples experience a TAT decrease of 66.8% (23 days) under the Greedy Volume policy, while EID samples experience a TAT decrease of 46.3% (12 days). The larger decrease in the TAT for VL samples is that more VL samples are tested on POC devices than EID samples, due to the system-wide VL to EID ratio. While the VL and EID TAT for POC-tested samples

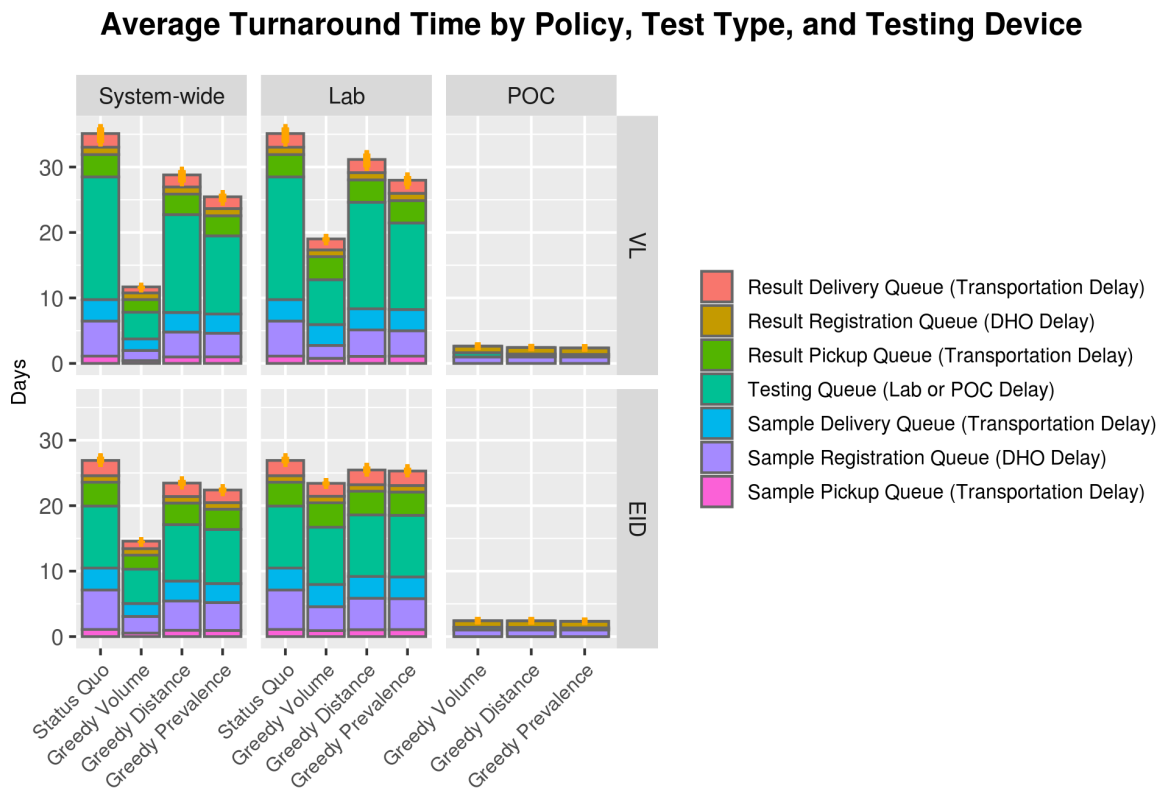

Figure 3.5: System-wide, Lab Only, and POC Only Average TATs by Sample Type

are very similar (14.5 days vs 11.6 days), a higher proportion of those POC-tested samples are VL samples, causing the effect on system-wide VL TATs to be more pronounced than the effect on system-wide EID TATs.

3.4.2 Transportation-Related Results

The total distance traveled in one year under the specified policy and the total number of trips made, colored based on the proportion of total trips that were empty trips, are shown in Figures 3.6 and 3.7, respectively.

Keys observations regarding these transportation-related figures are as follow:

- Figures 3.6 and 3.7

  (1) Couriers travel the fewest kilometers per year and complete the fewest empty trips under the Greedy Distance strategy. Under the Greedy Strategy, couriers no longer travel to those facilities that are located the furthest distances from the DHO assigned to those facilities. These far-away facilities also tend to have some of the lowest average sample volumes among all facilities. The top 30.2% (200) of all clinics, by distance, account for only 17.9% of all the samples collected in the system. Consequently, removing visits to these facilities eliminates the empty trips that were associated with these facilities.

  (2) The Greedy Volume strategy only reduces the number of empty trips by 543 trips, compared to 4,397 fewer empty trips under the Greedy Distance strategy. High

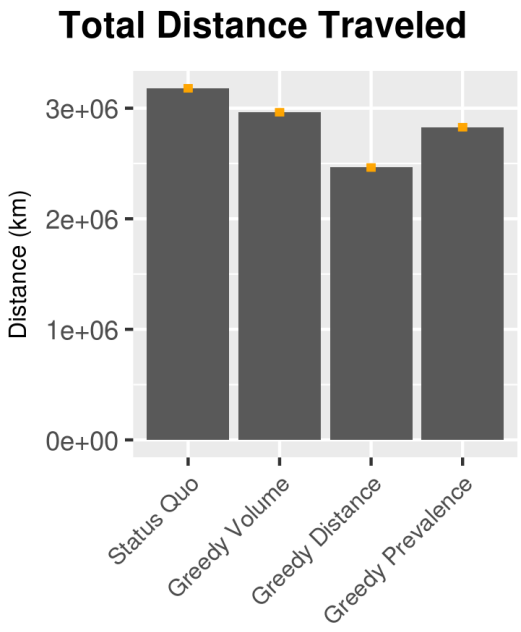

Figure 3.6: Travel Distance by Policy

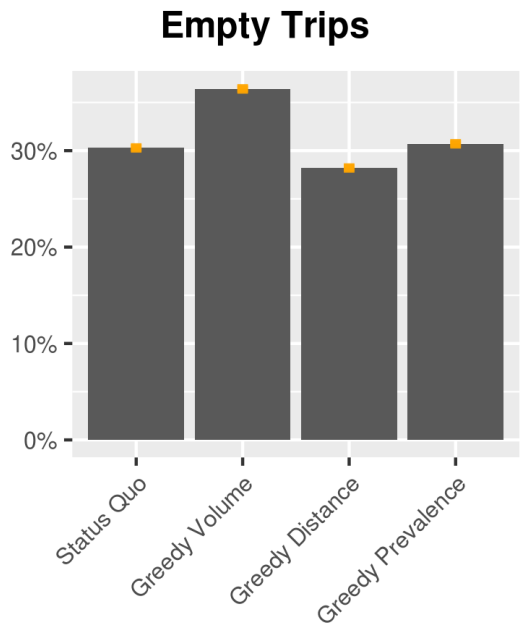

Figure 3.7: Empty Trips - % of All Trips by Policy

volume facilities, by their nature, almost always have samples that need to be retrieve or results that need to be delivered. Thus, high volume facilities have very few empty trips associated with them – under the Status Quo, the top 116 clinics by sample volume (17.5%) accounted for 2.7% of all empty trips. Therefore, placing POC devices at the highest volume facilities eliminates only a small fraction of the empty trips made under the Status Quo scenario.

3.4.3 Utilization Results

The average utilization of the molecular laboratories under each strategy, and the average utilization of the POC testing devices under the three POC device deployment strategies, are show in Figure 3.8.

Key observations from Figure 3.8 are:

- Figure 3.8

  (1) Average POC device utilization is the lowest under the Greedy Distance Strategy (0.05), with average POC device utilization under the Greedy Prevalence Strategy (0.06) being only slightly higher. The facilities allocated POC devices under the Greedy Distance Strategy account for 10% (35,554) of all samples collected in 2018. Similarly, the facilities allocated POC devices under the Greedy Prevalence Strategy account for 11% (38,698) of all samples collected in 2018.

3.4.4 Test Result Proportion Results

The average proportions of tests at the molecular lab or on POC devices that tested positive and negative are shown in Figure 3.9. The average TAT displayed along the same dimension of Figure 3.9 are shown in Figure 3.10. Key observations from Figures 3.9 and 3.10 are:

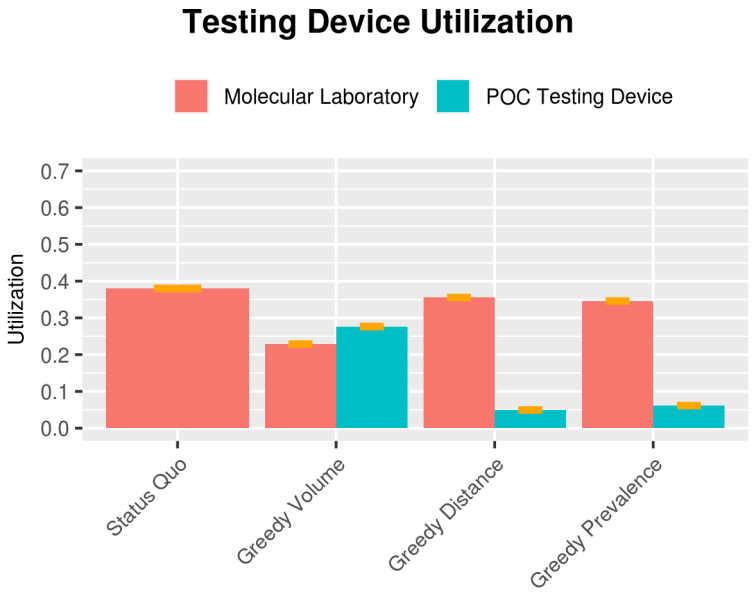

Figure 3.8: Utilization by Testing Location and Policy

- Figures 3.9 and 3.10

  (1) The average percent of all samples tested on a POC device that tested positive was highest under the Greedy Prevalence strategy (18.5%). Explicitly placing POC devices at health clinics based on the prevalence of HIV among the population served by that health clinic ensures that a higher proportion of the samples tested on the POC device have a positive test result.

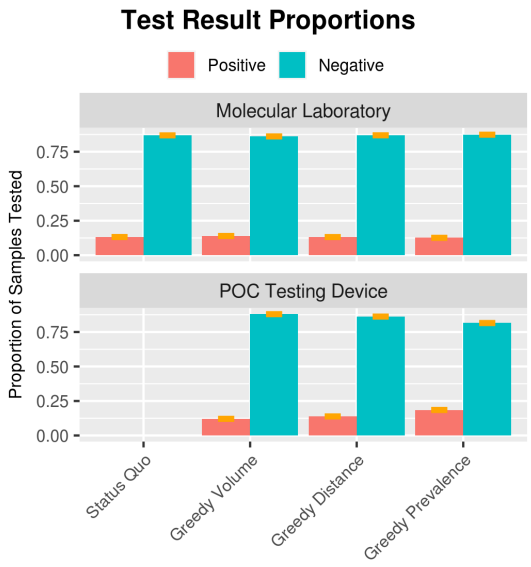

Figure 3.9: Test Results of Samples Tested

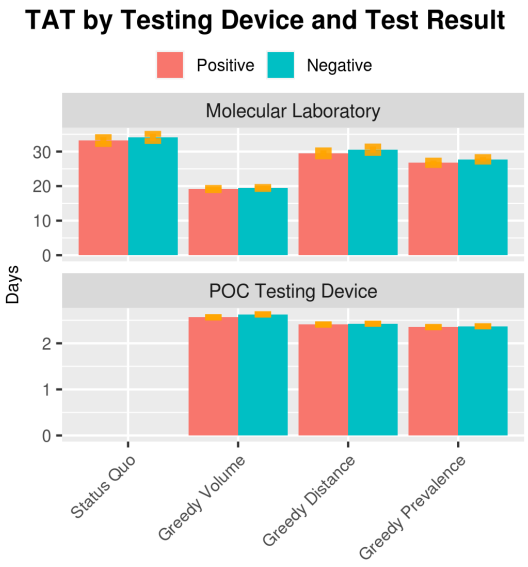

Figure 3.10: TAT of Samples by Test Result

3.4.5 Robustness Results

The results from the robustness experiments are shown in Figures 3.12, 3.13, and 3.14. Figure 3.12 shows how average TAT changes for all samples (System-wide), for samples test at molecular laboratories, and for samples tested with POC testing devices as the annual number of samples arriving in the system is increased by certain percentages. Figure 3.13 shows how the proportion of courier trips that were empty changes under each policy as annual arrival volume is increased. Figure 3.14 show how the average utilization of molecular laboratories and POC testing devices varies as annual arrival volume is increased. The key observations for the robustness experiment results are as follows:

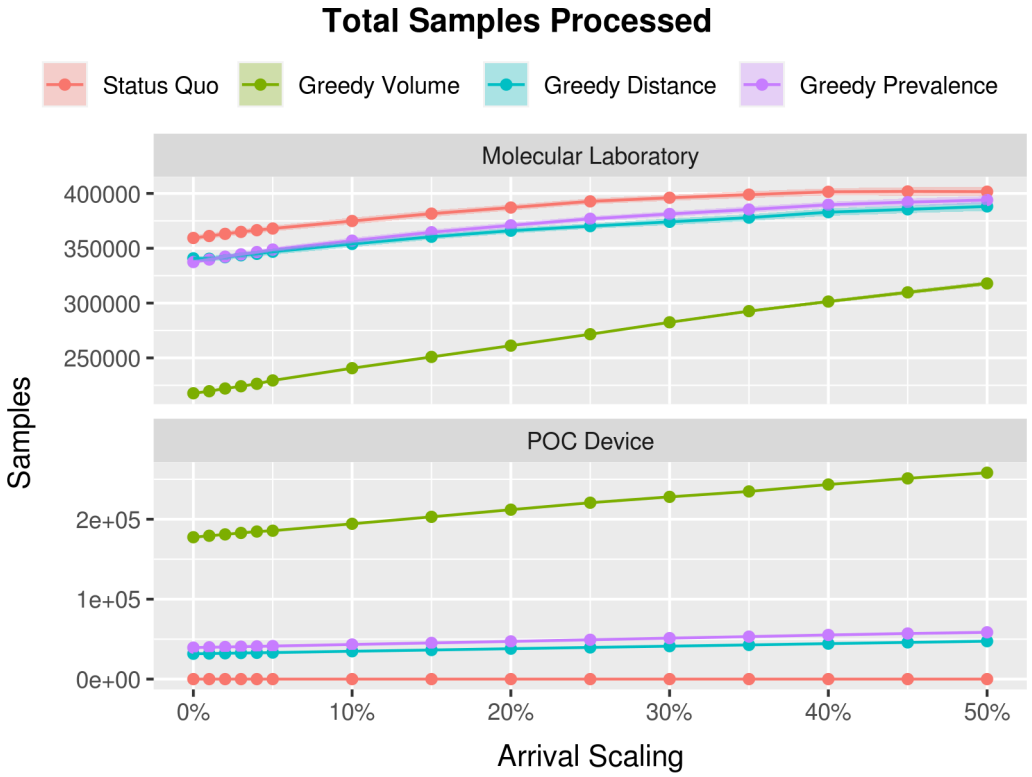

Figure 3.11: Samples Tested Under Increased Arrivals

- Figure 3.11

  (1) The molecular laboratories appear to approach a processing threshold when samples volumes are increased by 30% under the Status Quo, and Greedy Distance and Greedy Prevalence strategies. As the volume of samples sent to the molecular laboratories increases, utilization of the labs increases until the labs are no longer able to keep pace with the increased sample volume.

  (2) The number of samples processed at the molecular laboratories under the Greedy Volume policy does not appear to have reached a processing limit and the number of samples processed on POC devices increases at a faster rate for the Greedy Volume policy than the other policies. As discussed in Section 3.4.1, the fraction of all samples that are tested using POC devices is the highest under the Greedy Volume policy. As

the total volume of arrivals is increased, the difference between the number of samples tested using POC devices under the Greedy Volume policy and the Greedy Distance and Greedy Prevalence policies grows. Then, because more samples are tested with POC devices, fewer samples need to be tested at the molecular labs, preventing the arrival rate of samples at the labs from exceeding the testing capacity.

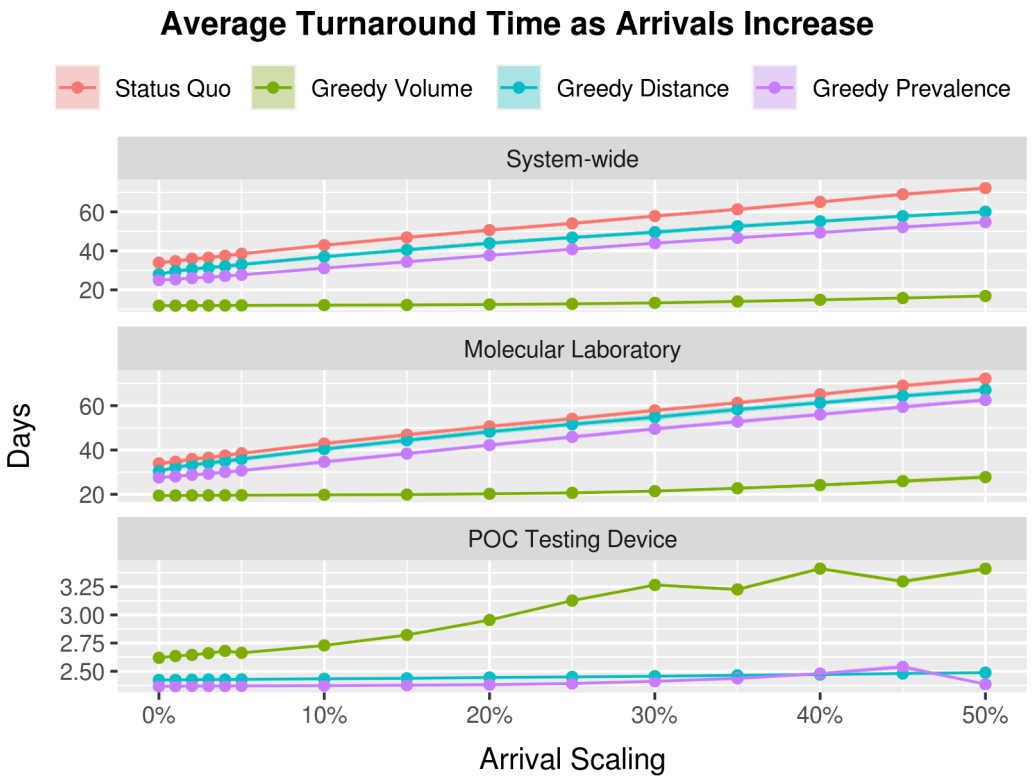

Figure 3.12: TAT By Testing Device Under Increased Arrivals

- Figure 3.12

  (1) System-wide average TAT remains stable under the Greedy Volume policy, (relative to the changes experienced under the Status Quo, Greedy Distance, and Greedy Prevalence policies) but the average TAT for samples tested with POC devices grows at a higher rate as arrivals increase. As discussed in Section 3.4.1, the fraction of all samples that are tested using POC devices is the highest under the Greedy Volume policy. As the total volume of arrivals is increased, the difference between the number of samples tested using POC devices under the Greedy Volume policy and the Greedy Distance and Greedy Prevalence policies grows. This causes TAT times for POC-tested samples to increase as POC testing delays increase due to this increase in sample volume. However, because a higher proportion of total samples are tested with POC devices, there are fewer samples to test at the molecular laboratories. The lower volumes of samples to test at the molecular laboratories under the Greedy Volume policy, compared to the other policies, results in relatively slow growth in average TATs for laboratory-tested samples are the total arrival volume grows. It is

this stability in the average TAT of laboratory samples that leads to stability in the system-wide average TAT.

(2) The average TAT for samples tested on POC devices does not increase monotonically under the Greedy Volume and Greedy Prevalence policies. As explained in Section 3.3.2, POC devices are allocated to different clinics within a deployment strategy based on the arrival scaling. This reallocation within deployment strategies causes the average TAT of samples tested on POC devices to "jump" under certain strategies as arrivals are increased.

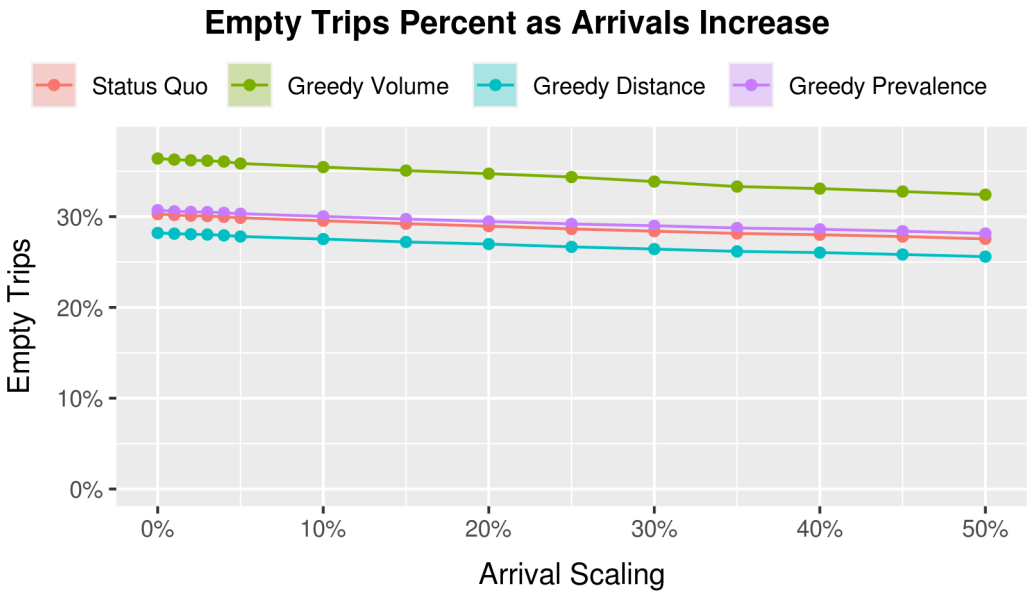

Figure 3.13: Percent of All Trips that were Empty Under Increased Arrivals

- Figure 3.13

  (1) The proportion of all trips that were empty trips decrease at the same rate for all strategies as arrival volume increases. As the total arrival volume increases, the number of arrivals at each facility increases proportionally. This increased arrival at each facility leads to fewer occasions where that facility does not have any sample that need to be tested or results that need to be delivered. Consequently, the proportion of trips that are classified as "empty" decreases.

- Figure 3.14

  (1) The average utilization of POC testing devices increases at a higher rate under the Greedy Volume policy, than it increases under the Greedy Distance and Greedy Prevalence policies. As discussed in Key Observation (1) for Figure 3.11, more samples are tested with POC devices under the Greedy Volume strategy than are tested under the Greedy Distance and Greedy Prevalence strategies, and the difference only grows as the total sample volume increases. This larger volume of samples tested on POC devices corresponds directly with the average POC utilization.

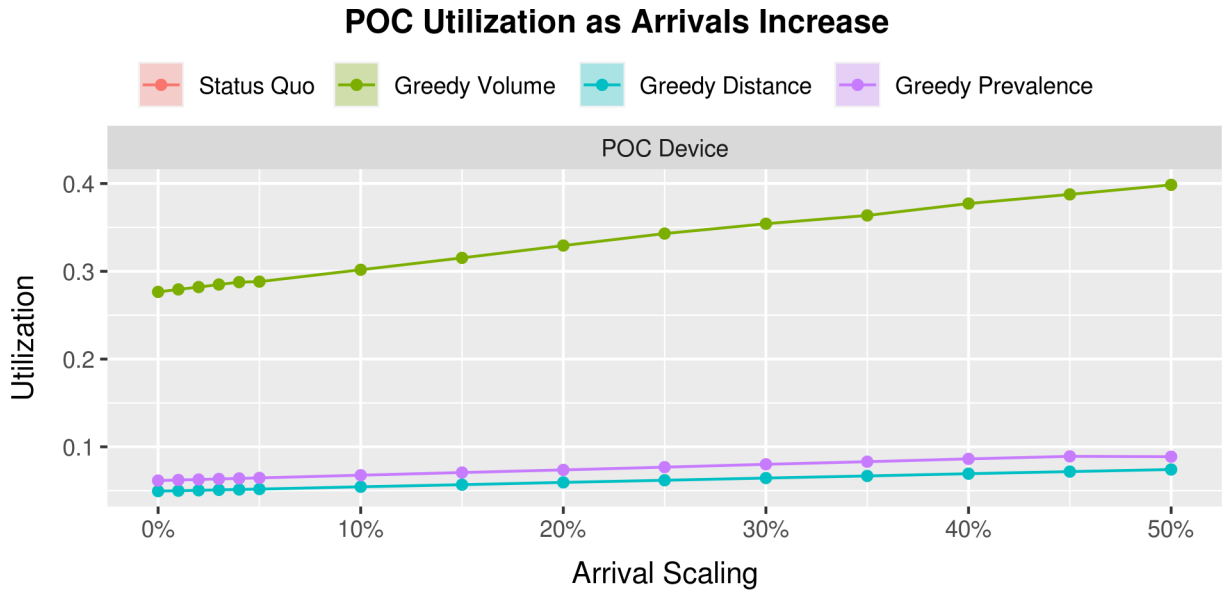

Figure 3.14: POC Device Utilization Under Increased Arrivals

3.5 Discussion

Malawi's diagnostic network and those like it in operation all across sub-Saharan Africa have not been able to reach their potential in terms of quality of care because of long TATs driven in part by transportation and testing delays [55, 8, 43]. Malawi's diagnostic network and those like it in operation all across sub-Saharan Africa eliminating the need to outsource sample testing to a separate health facility. Samples can be tested almost as soon as they are collected and the transportation delays associated with outsourcing testing are eliminated. Furthermore, POC testing devices are self-contained, meaning a skilled workforce is not required to operate the device. The self-contained nature of POC devices vastly expands the pool of potential testing personnel, freeing the diagnostic network from any limitations associated with a limited availability of classically trained laboratory technicians [37, 12, 42, 29]. Given the numerous benefits often cited regarding the effect of introducing POC testing devices into pre-existing diagnostic networks, there is surprisingly little academic evidence providing insight into where these POC devices should be deployed. Most of the academic works published with respect to POC testing devices are related to the technical performance of the devices (a literature review by Drain et al. [14] cites numerous examples of these types of studies). The body of work related to the operational aspects of POC devices is much sparser. Several studies have highlighted the need for comprehensive analysis to compare and contrast different deployment options, but forego suggesting what analysis could be conducted to inform decision-makers [12, 42]. Other studies have focused on the costs associated with POC device deployment strategies [34, 44, 47, 17], and the effect of POC device use on patient treatment decisions [33]. We are aware of only one report where the focus of the report was specifically on comparing different POC deployment strategies and estimating the effects of these strategies on nation-wide performance metrics [11]. This work differs from that of Deo and Sohoni [11] in that, Deo and Sohoni considered a simplified version of a diagnostic network, with a single lab serving multiple

clinics, while this work looks to expand on the insights of Deo and Sohoni by considering the operational insights gained from using a full-scale, validated diagnostic network model. To the best of our knowledge, there has not been any work published where a validate country-specific simulation model has been used to quantify the effect of common POC deployment strategies on system-wide TATs. Using a discrete event simulation to model the 2018 diagnostic network of Malawi, we quantify the trade-offs between three commonly proposed POC testing device deployment strategies. We consider a Greedy Sample Volume strategy, where POC devices are located within the highest volume health clinics, a Greedy Distance strategy, where POC devices are located at health clinics which required the couriers to travel the furthest, and a Greedy Prevalence strategy, where POC devices are located at health clinics with above-average rates of positive test results. We compare these strategies along the dimensions of sample TATs, courier travel distances, POC device utilization, and the percent of samples test on a POC device which tested positive. We then conduct a sensitivity analysis to understand the sensitivity of the model results to increases in patient arrivals in the system. We find that a Greedy Sample Volume strategy out-performs both the Greedy Distance and Greedy Prevalence strategies in terms of the reduction in system-wide TAT and the average utilization of POC testing devices. Additionally, the Greedy Sample Volume strategy is more robust to increases in the rate of patient arrivals than either of the other two strategies considered. We also find that the Greedy Distance strategy outperforms all other strategies in terms of the reduction in total distance traveled by the couriers in the ST system and the proportion all of trips made by the couriers that are unnecessary (i.e., empty trips). However, the Greedy Distance strategy is less robust to increases in the arrival rate. The clinics allocated POC devices have below-average sample arrival rates. This causing POC device utilization to remain low (even under a 50% increase in the patient arrival rate from 2018 levels) and the molecular laboratories to reach a processing threshold. In this case, it is expected that administrators of the diagnostic network would need to intervene to reallocate or reinforce laboratory testing capacity. The Greedy Prevalence strategy did outperform the Greedy Sample Volume and Greedy Distance in terms of the proportion of samples that, when tested with POC devices, yielded positive test results. However, low sample volumes at facilities with above-average disease prevalence and robustness issues similar to those for the Greedy Distance strategy are drawbacks of the Greedy Prevalence strategy. There is one consideration for both the Greedy Distance and Greedy Prevalence strategies that is not captured in this report and which should be highlighted. Our findings indicate that all three of the of the considered POC deployment strategies reduce the total distance traveled by the couriers compared to the Status Quo, with the Greedy Distance strategy yielding the largest decrease in travel distance. Decreasing travel distances can be important as less distance traveled means a reduction in fuel costs and vehicle maintenance costs among other cost savings. However, the real benefit of reducing travel distances is that it allows transportation capacity to be reallocated. In our analysis, we have not considered transportation capacity reallocation (e.g., scheduling more frequent visits to facilities without POC devices) and thus the second-order effect that a reduction in travel distance has on sample TAT is not captured. Extending our model to incorporate transportation capacity reallocation strategies would provide additional insight into the system-wide effects of POC device allocation. There are additional avenues for expanding this work. First, we only consider pure strategies (i.e.,

strategies with only a single considerations). In future work, we intend to consider hybridizations of the three strategies we considered, such as a strategy where both facility distance and sample volume are used to determine where to place POC devices, and how TATs vary under these strategies. Second, we consider only POC deployment strategies, as opposed to near-POC deployment strategies. In near-POC strategies, POC devices are located at DHOs where they can be used to serve an entire district (since all the clinics in a given district first send their samples to a district hospital, before they are shipped on to a centralized molecular laboratory). Near-POC deployment strategies do not achieve the main objective of POC deployment, which is to allow for timely diagnosis of patients' samples at their primary contact point with the healthcare system. However, near-POC deployment does result in POC devices being shared across facilities which likely has a different effect on TATs than the deployment strategies we have considered.

3.6 Conclusion

POC testing devices developed for use in austere environments have the potential to great improve the quality of care for for patients seeking HIV/AIDS treatment in Malawi, and other LMICs in sub-Saharan Africa. To maximize the impact of these devices, diagnostic network administrators must first understand how different strategies for locating POC devices in the network effect the network's performance. Through the development and use of a simulation model calibrated to represent Malawi's actual diagnostic network, this study illuminates the quantitative difference between three common POC allocation strategies. Our findings highlight the robustness of the Greedy Sample Volume policy to changes in patient volumes, and the reduction in the required transportation capacity under the Greedy Distance and Greedy Prevalence strategies. These results should prove useful to diagnostic network administrators considering the benefits and consequences of POC testing device deployment strategies.

Appendix A

Abbreviations

AIDS Acquired Immunodeficiency Syndrome

DHO District Health Office

EID Early Infant HIV Diagnosis

GIS Geographic Information System

GPS Global Positioning System

HIV Human Immunodeficiency Virus

LIMS Laboratory Information Management System

LMIC Low- and Middle- Income Country

ML Molecular Laboratory

MOH Malawi Ministry of Health

POC Point-of-Care

R4H Riders 4 Health International

SME Subject-Matter Expert

SMS Short Message Service

ST Sample Transportation

TAT Turnaround Time

TB Tuberculosis

TUT Time until Tested

USSD Unstructured Supplementary Service Data

VL Viral Load

Appendix B

Summarized Sample Volumes

	VL	EID	TB	Other	Total
Phalombe	**19,354**	**1,405**	**569**	**27**	**21,355**
Nambazo Health Center	2,317	67	62	5	2,451
Kalinde Dispensary	1,946	177	16	0	2,139
Holy Family	1,966	95	61	0	2,122
Phalombe District Hospital	1,730	163	0	0	1,893
Sukasanje Health Center	1,659	71	7	0	1,737
Chitekesa Health Center	1,529	146	21	0	1,696
Migowi Health Center	1,432	6	220	0	1,658
Mkhwayi Health Center	1,217	150	127	0	1,494
Nkhulambe Health Center	1,324	50	8	4	1,386
Mpasa Health Center	1,190	111	9	2	1,312
Gogo Nazombe Health Center	1,209	86	0	1	1,296
Mwanga Health Center	687	51	1	0	739
Chiringa Maternity	501	98	3	5	607
Mulungu Alinafe	394	106	0	8	508
Chiringa Dispensary	253	28	34	2	317
Salima	14,947	1,091	466	651	17,155
Salima District Hospital	3,720	294	0	0	4,014
Khombedza Health Center	1,553	81	43	0	1,677
Chipoka Health Center	1,465	59	24	18	1,566
Lifeline Health Center	1,407	48	58	14	1,527
Thavite Health Center	1,049	69	27	93	1,238
Lifuwu Health Center	1,073	122	10	11	1,216
Maganga Health Center	746	67	12	15	840
Mchoka Health Center	704	60	31	45	840
Senga Bay Baptist Dispensary	715	58	10	0	783
Makiyoni Health Center	458	23	64	124	669
Ngodzi Health Center	364	49	17	149	579
Mafco Health Center	579	19	28	7	633

	VL	EID	TB	Other	Total
Chinguluwe Health Center	336	31	24	28	419
Katawa Health Center	282	32	60	25	399
Chitala Health Center	190	20	29	0	239
Parachute Health Centre	92	5	0	93	190
Chagunda Health Center	113	18	21	18	170
Kaphatenga Health Center	101	36	8	11	156
Rumphi	**6,657**	**483**	**1,824**	**1,378**	**10,342**
Rumphi District Hospital	1,804	66	341	5	2,216
Bolero Health Center	1,847	125	155	29	2,156
Lura Health Center	506	19	83	319	927
Mhuju Hospital	533	52	51	49	685
Katowo Rural Hospital	518	43	41	73	675
Jalawe Health Center	3	4	257	244	508
Chitsimuka Health Center	0	0	465	3	468
Nthenje Dispensary	156	10	55	176	397
DGM Livingstonia Hospital	212	22	66	67	367
Mwazisi Health Center	244	29	57	8	338
Chitimba Health Center	226	26	0	62	314
Ngonga Health Center	128	15	78	68	289
Mzokoto Health Center	238	38	1	1	278
Luwuchi Health Center	121	14	3	92	230
Mlowe Health Center	41	5	67	45	158
Mphopha Health Center	35	6	62	42	145
Tcharo Dispensary	1	0	5	94	100
Eva Demaya	44	9	37	1	91
Grand Total	**40,958**	**2,979**	**2,859**	**2,056**	**48,852**

Table B.1: Summarized Sample Volumes

Appendix C

Simulation Model Validation

To validate the simulation model, we used the model to simulate operations during the year 2018 thirty times, and compared the simulation results for sample volume, average time until tested (TUT), and average TAT. TUT refers to the number of days that elapse between when a patient sample is collected and when the diagnostic testing of that sample is conducted. This metric is reported as part of the validation exercise, in addition to TAT, since the average TAT in 2018 cannot be calculated from the 2018 LIMS data, but the average TUT can be calculated. The validation results are shown in Figure C.1. Notice that these validation results indicate that our model overestimate TUT by approximately 1 day, and TAT by approximately 2 days.

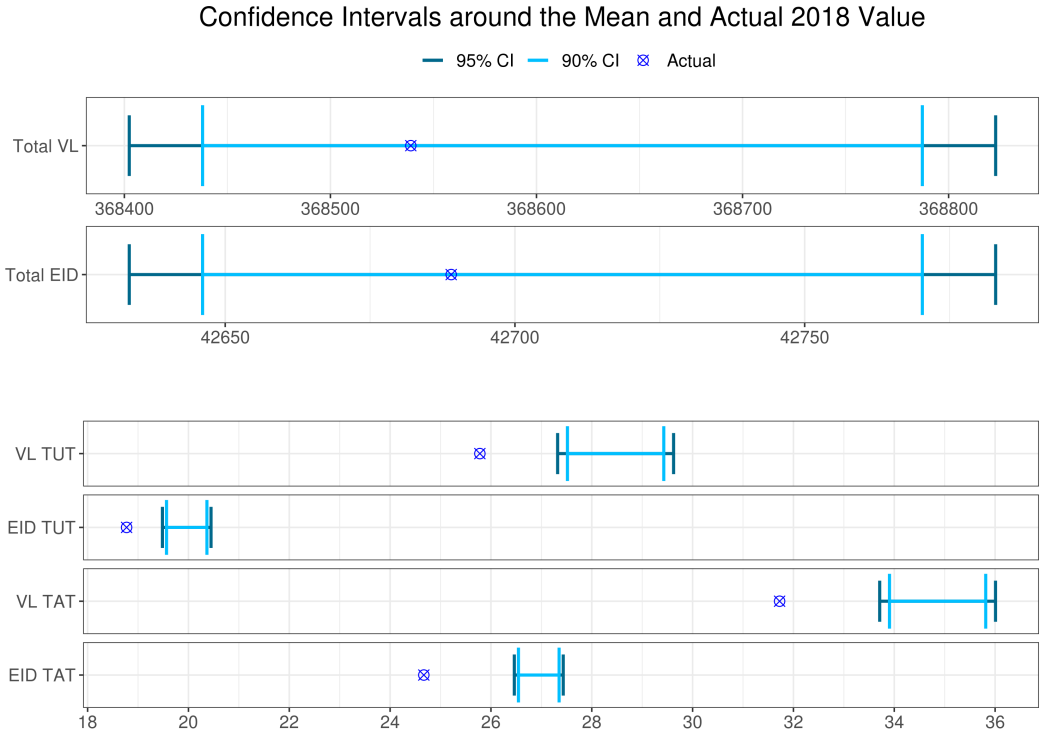

Figure C.1: Simulation Model Validation Results

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