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Optimising HIV drug resistance testing laboratory networks in Kenya: insights from systems engineering modelling

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ABSTRACT

Background HIV drug resistance (DR) is a growing threat to the durability of current and future HIV treatment success. DR testing (DRT) technologies are very expensive and specialised, relying on centralised laboratories in most low and middle-income countries. Modelling for laboratory network with point-of-care (POC) DRT assays to minimise turnaround time (TAT), is urgently needed to meet the growing demand.

Methods We developed a model with user-friendly interface using integer programming and queueing theory to improve the DRT system in Kisumu County, Kenya. We estimated DRT demand based on both current and idealised scenarios and evaluated a centralised laboratory-only network and an optimised POC DRT network. A one-way sensitivity analysis of key user inputs was conducted.

Results In a centralised laboratory-only network, the mean TAT ranged from 8.52 to 8.55 working days, and the system could not handle a demand proportion exceeding 1.6%. In contrast, the mean TAT for POC DRT network ranged from 1.13 to 2.11 working days, with demand proportion up to 4.8%. Sensitivity analyses showed that expanding DRT hubs reduces mean TAT substantially while increasing the processing rate at national labs had minimal effect. For instance, doubling the current service rate at national labs reduced the mean TAT by only 0.0%–1.9% in various tested scenarios, whereas doubling the current service rate at DRT hubs reduced the mean TAT by 37.5%–49.8%. In addition, faster batching modes and transportation were important factors influencing the mean TAT.

Conclusions Our model offers decision-makers an informed framework for improving the DRT system using POC in Kenya. POC DRT networks substantially reduce mean TAT and can handle a higher demand proportion than a centralised laboratory-only network, especially for children and pregnant women living with HIV, where there is an immediate push to use DRT results for patient case management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The study uses a novel combination of integer programming and queueing theory to develop a user-friendly model that is specifically designed for optimising the HIV drug resistance (DR) testing laboratory network in Kisumu County, Kenya, making it a pioneering approach in the field of HIV DR management.
⇒ It offers a comprehensive analysis by comparing a centralised laboratory-only network with an optimised point-of-care (POC) DR testing network, thereby providing evidence-based insights into how POC DRT can enhance system performance, particularly in terms of reducing turnaround time.
⇒ While the study conducts a one-way sensitivity analysis of key parameters, it may not fully capture the complex interdependencies or the impact of multiple variables changing simultaneously, which could affect the generalisability and robustness of the model under different scenarios. It also does not include costs or budget parameters.
⇒ The study focuses on Kisumu County, Kenya, and the findings might not be directly applicable to other regions or countries with different healthcare infrastructures, HIV prevalence rates, DRT guidelines or laboratory capabilities.

INTRODUCTION

HIV drug resistance (DR) is a growing threat to the durability of current and future HIV treatment success. The WHO's most recent HIV DR report in 2021 notes high concern regarding increasing pretreatment and acquired DR, especially among children and adolescents living with HIV. Three countries, Lesotho, Uganda and Zambia, who conducted systematic HIV DR surveillance among children and adolescents living with HIV with viral failure demonstrated high rates of nucleoside/nucleotide reverse transcriptase inhibitor (NRTI) (50%–80%) and non-NRTI (84%–97%) DR. Additionally, accumulation of new DR with continued viral failure has been documented in both adults and children, further limiting usable antiretroviral options.[1–4]

However, DR testing (DRT) technologies are very expensive and specialised, which render them a limited resource.[5 6] Most low and middle-income countries (LMIC) rely on centralised, highly specialised laboratories and specimen transport networks to

conduct DRT for a limited number of patients meeting certain criteria; current low access and high turnaround times, on the order of months, limit even further use of existing DRT options.[7] However, WHO endorses the need for expanded availability of DRT, including point-of-care (POC) options and acknowledges that use of new HIV treatment options will only expand this need.[8] For instance, while there is marked enthusiasm for dolutegravir-containing treatment options globally,[2 9 10] resistance to dolutegravir is already emerging, stressing the need to monitor dolutegravir DR urgently in LMIC.[11–13] Novel POC, or even near POC, assays are on the horizon to help create greater accessibility to DRT and minimise the return of results challenges often resulting from a centralised testing system.[14] Our group has been involved in the field validation of one such technology called oligonucleotide ligation assay (OLA)-Simple.[15–17] Unpublished Kenya HIV programme data suggest better HIV viral load (VL) results utilisation at POC sites than sites supported by centralised laboratory testing systems, which might have implications for POC DRT use as well.

HIV treatment programmes in LMIC are expanding VL testing for all people living with HIV, therefore creating more opportunities to detect viral failure.[18] It is critical to determine how to create decentralised laboratory networks for DRT, possibly including POC DRT assays, to meet the anticipated increase in DRT demand. Different types of decentralised laboratory network models exist in LMIC, including for HIV VL monitoring. Example networks use hub-and-spoke or platform sharing.[19–21] Given the even more technical training and expertise needed to conduct HIV DRT compared with HIV VL testing alone, platform sharing is not a likely viable option for DRT shortly.

Given the urgent need to meet DRT demand and the specialised training required for staff, it would be beneficial to model a network optimisation for DRT using a hub-and-spoke framework, coupled with the application of queueing theory to analyse service times. The use of optimisation and queuing theory in healthcare is well documented in high-resource settings for hospital and emergency department logistics.[22–28] However, their application in resource-limited contexts, particularly for HIV care, is emerging.[29] Studies in sub-Saharan Africa highlight the prevalence of queuing issues, yet the systematic application of these models for clinical improvements is still novel.[30] Additionally, the deployment of POC devices for HIV testing and treatment in such settings is gaining attention.[31–33]

Thus, we aimed to develop a laboratory network optimisation model based on queueing theory. First, we estimated the DRT demand for two scenarios: the current scenario of repeated VL testing with adherence counselling that leads to DRT and a more idealised scenario where DRT would be implemented under more liberal guidelines. Second, we created a model for two networks: the model of using one centralised laboratory at the national level for all DRT testing for Kisumu County and an optimised network that used not only the national DRT laboratory but also the introduced additional POC DRT hubs. We hypothesised that the second scenario with POC DRT hubs would reduce turnaround time compared with the centralised laboratory model.

METHODS

Formative data collection

To gather insights into Kenyan policymakers' preferences for model function and decision-making, we conducted formative qualitative research using focus group discussions (FGDs). Demographics of FGD participants are in online supplemental table 1. Details and results can be found in part 2 of online supplemental materials. We identify the research topic as of importance to patients and service users. The policymakers we interviewed helped us better understand their needs.

Patient and public involvement statement

Our research incorporated Kenyan policymakers at the formative stage through FGDs, which informed the model's development and decision-making criteria directly relevant to patient care. These discussions were pivotal in shaping the research questions and ensuring the outcome measures reflected patient priorities and experiences.

Current DRT process and selection of POC DRT hubs

In Kisumu County's healthcare system, there are a total of 146 healthcare facilities that collect both HIV VL and DRT samples.[34] After collecting samples from patients, each facility currently sends their samples to one of three central labs (KEMRI CDC HIV/R Laboratory, AMPATH Care Laboratory and KEMRI/Walter Reed CRC Lab) for HIV VL testing. Once results are returned, patients deemed to not reach viral suppression (defined as VL <200 copies/mL per 2022 Kenya Ministry of Health (MoH) HIV treatment guidelines) undergo discussion with a multidisciplinary team at the facilities,[35] enhanced adherence counselling, including at times directly observed therapy, assessment of and addressing any other causes of viremia, and then repeat VL testing performed 3 months after the initial viremic episode detection and assurance of enhance adherence efforts.[15] If the patient still has viral non-suppression at repeat VL testing, then providers consult a national-level technical working group to seek advice on DRT. Once that working group reviews the case and approves DRT, the patient is called back to the facility to have another blood sample taken for DRT. This sample is currently sent to one facility, the National Public Health Laboratory (NPHL), to conduct DRT, which it conducts for the entire country for the public sector. While private sector DRT may occur in other facilities, it likely only represents a minority of the DRT occurring in the country. For DRT, the national-level laboratory NPHL uses Sanger 3730xl for consensus sequencing of samples, which can theoretically process up to 200 samples/day with a more

realistic throughput of 100 samples/day based on the available human resource and instrumentation available.

Currently, no POC DRT options are available commercially in Kenya. Our research team has been involved with a field validation of a novel, POC DRT option called OLA-Simple.[15–17 36] From March to June 2021, we piloted this technology at two of the facilities mentioned above, KEMRI CDC HIV/R Laboratory and NPHL. Based on the technical lessons learnt from that field validation, we have deemed that the current iteration of the POC DRT platform of OLA Simple still requires a high level of technical expertise and, therefore, can only be implemented at a limited number of sites, unlike many of the POC VL testing platforms. Thus, we have purposefully selected existing highly specialised laboratories for HIV that has pre-PCR and post-PCR rooms, that is, NPHL, the three existing HIV VL testing labs, and a fourth referral hospital laboratory to the list of potential POC DRT labs, as these facilities can maintain the technical expertise needed to run this assay. Thus, five total DRT laboratories were used to model turnaround time; from here on, we refer to the NPHL as the national laboratory and the other four as POC DRT hubs. We were also restricted to just one POC DRT machine prototype for this modelling exercise.

We provide a flowchart of the POC DRT system as online supplemental figure 1.

DRT rate estimation

Estimating the demand data for DRT has proven challenging due to the structure of publicly accessible routine data and the difficulties associated with individual-level data, including issues with patient identity tracking. In addition, missing data and inconsistencies were observed to varying degrees depending on the characteristic.[37] As a result, there are no established standards in the literature for such estimations at the country level or within smaller geographic areas.[38] It is necessary to use estimated proportion of receiving DRT among people living with HIV to approximate the DRT demand.

To incorporate a range of possibilities for the demand of DRT, we considered the following two scenarios based on the overall Kenya MoH HIV treatment guidelines (figure 1).[35] For Scenario 1, we model the current DRT demand based on existing data on high VLs from the available data for Kisumu County from the Kenya MoH HIV VL dashboard.[39] We propose a range of demand values that includes an upper estimate based on the assumption of perfect adherence to the 2022 Kenyan guidelines. This approach is motivated by the observation that the current demand for DRT may underestimate the true need for the service. In the figure, the blocks coloured blue represent the chain leading to DRT, with the green blocks showing variable rates. We computed the DRT proportion with combinations of the two varying parameters of (1) percentage of the second VL being conducted (range 25%–100%) and (2) the second VL being >1000 copies/mL (range 25%–75%). The estimated proportion of receiving DRT under scenario 1 ranges from

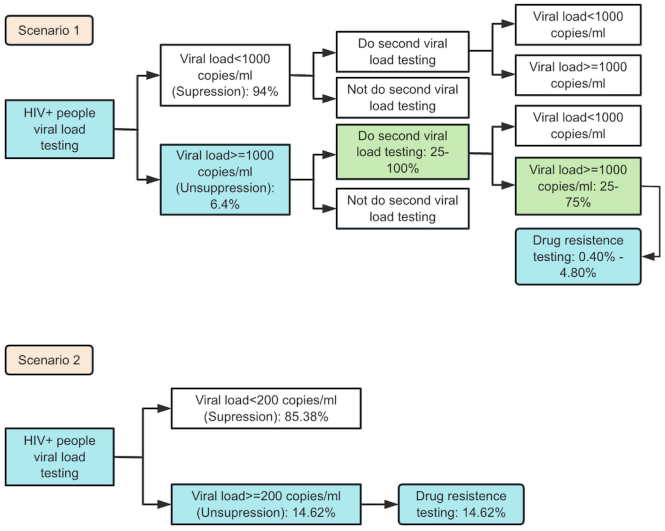

Figure 1 Scenario 1 (current DRT based on existing VL data from 2019) and 2 (more idealised DRT) flowchart for DRT demand estimation for Kisumu County, Kenya. Colour Schematic: In both scenarios 1 and 2, blue coloured blocks are used to illustrate the trajectory of HIV samples that lead to DRT at the final stage, in accordance with various guidelines. In scenario 1, green coloured blocks are employed to signify the consideration of various rates for conducting a second VL test and the suppressing rate for the second VL. Data source: NASCOP VL database[11]. Details of data used can be found in online supplemental table 3. DRT, drug resistance testing; VL, viral load.

0.40% to 4.80%. Details of the calculation process are found in online supplemental table 2. For scenario 2, we consider a more idealised case scenario where DRT is recommended earlier in algorithm management and, therefore, chose a lower VL level and earlier step in VL monitoring to conduct DRT, akin to high-income country settings, where DRT is done at first detection of viremia (eg, DRT requested at first VL >200 copies/mL). This scenario has no variable rates. Of note, while the most recent Kenya MoH HIV treatment guidelines generally recommend using a VL cut-off threshold of >200 copies/mL as non-suppression, unfortunately, estimates of DRT demand are only available for VL as low as 400 copies/mL. The estimated proportion of receiving DRT under scenario 2 is 14.62%.

Data acquisition

Our team collected model parameter information through collaboration with Kenyan policymakers and laboratory specialists. Table 1 lists all model parameters we used in the model, base case values, and their data sources. Note that in the table, we considered two scenarios of DRT rate. The operational parameters that can be varied for sensitivity analysis include transportation and batching parameters, queueing parameters in national laboratory and POC DRT hubs. As a base case, we assumed that samples are sent once a week to the national laboratory and daily to other POC DRT hubs

Table 1 Model parameters, assumptions and data sources

Parameter	Base case value	Note
HIV VL test demand (per working day)		
HIV VL testing demand in 146 facilities	Ranges from 0 to 37 (per working day) for different facilities	The quantity of VL samples from each facility is determined through the HIV client volume data from 2019 in Kisumu County's DHIS II. This was necessary because of the COVID-19 pandemic-related interruptions in 2020 and the subsequent nationwide interruptions in VL testing. Details of these estimations can be found in our related work on HIV VL testing.[31] Data Source: http://kmhfl.health.go.ke/ and https://dhis2.org/
DRT rate		
Scenario 1	0.40%~4.80%	Proportion of valid VL tests unsuppressed at VL≥1000 copies/ml threshold * Percentage completing second VL testing * Percentage of second VL≥1000 copies/mL. Calculation process with parameter combinations can be found in online supplemental table 2 and details of the data source can be found in online supplemental table 3. Data Source: https://viralload.nascop.org/
Scenario 2	14.62%	Proportion of valid VL tests unsuppressed at VL≥200 copies/mL threshold. Of note, we changed the threshold from newly recommended 200–400 copies/mL since the data provided does not enumerate values at the 200 copies/mL threshold.[35]
HIV DR test demand (per working day)		
HIV DRT demand in 146 facilities under Scenario 1	Minimum demand is 0; maximum demand ranges from 0 to 2	HIV VL test demand * DRT rate
HIV DRT demand in 146 facilities under Scenario 2	Ranges from 0 to 5	
Transportation		
Distance between all facilities to the national laboratory and POC DRT hubs (km)	0–370	We used Google Map API to collect the distance and time data given the name of facilities in Kisumu, Kenya and the locations of the national laboratory and hubs. (https://developers.google.com/maps)
Speed: (km/hour)	5 (walk), 20 (bike), 40 (motorbike), 50 (car)	To calculate the transportation time, we provided different types of transportation modes and allowed the user to decide which one to use and estimated the average speed for each transportation mode.
Road condition adjustment coefficient	0.8 (good), 1 (average), 1.2 (bad)	We considered different weather and road conditions and allowed users to change these conditions based on their needs. The weather and road conditions are 'good', 'average' or 'bad', and the time needed for transportation could be less given better weather and road conditions.
Weather condition adjustment coefficient	0.8 (good), 1 (average), 1.2 (bad)	
Batching delay (min):(frequency with which samples are transported to testing facility (hub or national laboratory))		
Immediately	0	If the samples are sent immediately once received at the facility due to the scarcity of the demand, we would simply remove the aspect of batching. We assumed that each working day has 7 hours. If the samples are sent daily, the average delay time is half of the working day, which is 3.5 (hours), i.e., 210 min. If the samples are sent two times a week, the average delay is a whole day and a working day, which is 24+7 = 31 hours, that is, 1860 minutes. If the samples are sent only once a week, the average delay is half of 4 whole days and a working day, which is (24*4+7)/2=51.5 hours, that is, 3090 min. As a base case, we assume that the samples are sent daily to DRT hubs and once a week to the national laboratory.
Daily*	210	
Two times a week	1860	
Once a week†	3090	
National laboratory (NPHL) queueing parameters		
Entering process		

Continued

Table 1 Continued

Parameter	Base case value	Note
Mean service rate (test per day)	100	Mean service rate refers to the average number of DR samples received at one central laboratory given current staffing and process steps. Number of servers refers to the number of workers processing the entering of samples. We assume that there are two workers in each central laboratory working on entering the samples into the system.
Number of servers	2	
Machine process		
Mean service rate (test per day)	100	We assume each central laboratory can handle up to 500 samples per week, which in turns to be 100 samples per working day. Estimates based on personal communication with central laboratory managers. Users can adjust the service rate to account for machine downtimes due to maintenance, failure, etc.
Number of machines at each central lab	1	Estimates based on personal communication with central laboratory managers.
Percentage of capacity for DRT	100%	It is possible that a POC DRT assay could be used as a multi-disease or multi-diagnostic tool, such as those that exist for HIV VL, tuberculosis, and other infectious disease testing (eg, GeneXpert platforms). While set at 100%, the percentage allocation of service for HIV DRT vs another disease or diagnostic use can be modified here.
Percentage of DRT samples from Kisumu	7.9%	For 2021, 89 of 1123 DRT samples (7.925%) were from Kisumu County per personal communication with central laboratory managers.
POC DRT hub queueing parameters		
Entering process		
Mean service rate (test per day)	100	Mean service rate refers to the average number of DR samples received at DRT hubs given current staffing and process steps. We assume that there is only one worker in each hub working on entering the samples into the system.
Number of servers	1	
Machine process		
Mean service rate (tests per day)	2	Data source: personal communication with implementing partner director for HIV programmes in Kisumu County. OLA DR assay can only do two samples per working day.
Number of servers		
Hub 1: KEMRI CDC	2	Number of servers refers to the number of POC DRT machines assigned for each hub.
Hub 2: AMPATH	2	
Hub 3: Walter Reed CDC	2	
Hub 4: JOORTH	2	
Percentage of samples from Kisumu		
KEMRI CDC	100%	Given that the POC DRT hubs conduct POC DRT, we assumed all samples coming to these hubs are from facilities within Kisumu County. Of note, because POC DRT will likely be based on point mutation detection, and not full genome sequencing, some of the samples with positive findings on POC DRT may need full genomic sequencing via consensus sequencing at the national, central laboratory. Our DRT demand estimates, and modelling parameters do not account for these few additional DRT samples that may be needed at the national, central laboratory.
AMPATH	100%	
Walter Reed CDC	100%	
JOOTRH	100%	

*Represents base case batching delay mode of sending samples to DRT hubs.
†Represents base case batching delay mode of sending samples to national laboratory.
DRT, drug resistance testing; POC, point-of-care; VL, viral load.

by each facility, using motorbikes as the transportation mode, under average road and weather conditions.

Model: optimisation and queueing model

This section outlines the formulation of our optimisation model, including decision variables, constraints and objectives. The primary goal of the model is to improve the total turnaround time of the whole testing system by reorganising the referral network. Further information about the mathematical expressions used in the model can be found in the part 3 of online supplemental materials.

The decision variable is a binary referral indicator (ie, 0 or 1), which connects each facility with testing demand and a potential service site. If their referral indicator is equal to 1, it means the corresponding facility sends their testing samples to that service site. Two constraints are considered for both demand and supply sides. For the demand side, there is one constraint ensuring that each testing demand is met, and the samples are assigned to only one testing facility. For the supply side, the total number of accepted samples for the national laboratory and POC DRT hubs should not exceed its capacity.

The objective of the model is to minimise the overall time it takes to process the DR testing samples across all 146 facilities. This time is made up of three parts: the time it takes for a facility to prepare and send the samples (batching delay), the time it takes for the samples to be transported to the testing site (transportation time), and the time it takes for the samples to be processed at the testing site (processing time).

The processing time in the DRT laboratories was analysed using queueing models, which are used to represent systems that involve waiting lines. The M/M/s queueing model, one of the most widely studied models, was used to model the arrival and processing of DRT samples at each selected laboratory.[40] Two separate queues were built to reflect the processes: entering samples into the computer system and sample preparation and testing process. The processing time in the system is the sum of these two queueing times.

For practical use, we focused on optimising two factors—batching delay time and transportation time—in the objective function. Since we do not optimise over processing time, we have introduced a predetermined and adjustable maximum utilisation rate to avoid excessively large service times. Layout of Excel Decision Support Tool is found in online supplemental figure 2 and details are found in part 4 of online supplemental materials.

RESULTS

In the results section, we compare two networks: the first solely comprises the national laboratory, and the second incorporates four POC DRT hubs alongside the national laboratory. Both networks were evaluated against two DRT rate scenarios—scenario 1 with rates ranging from 0.4% to 4.8%, and scenario 2 with a fixed rate of 14.62%. We report the mean turnaround time for each scenario under optimised network conditions. The maximum utilisation rate is heuristically set at 0.9 for the national laboratory and 0.7 for the hub.

The section is further organised as follows: section 3.1 provides a statistical summary of the performance of the system in turnaround time under varying DRT rates (scenario parameter); in section 3.2, we visualise the facilities and referral networks on a map; and section 3.3 focuses on the sensitivity analyses for several key operational parameters.

Turnaround time

Under the national laboratory-only network, when DRT rate ranges from 0.4% to 1.2%, the mean turnaround time across all 146 facilities is about 9 working days, which is consistent with the current observed turnaround time (per unpublished, internal data from NPHL). However, as the DRT rate increases and reaches 1.6%, demand exceeds capacity and waiting times become excessively long, rendering the model infeasible. By contrast, when the four POC DRT hubs are added to the network, the mean turnaround time reduces between 1.13 and 2.11 working days, substantially improving system efficiency. The POC DRT hub network remains feasible until the DRT rate reaches 4.8%, at which point the addition of more POC machines or improvements to the capacity of the national laboratory would be needed to meet the DRT demand. Of note, our results show that as the DRT rate increases, the mean turnaround time exhibits a monotonically increasing trend for both networks. In the POC DRT hub model, when POC DRT hub capacity is insufficient to meet demand, samples are rerouted to national laboratory. As presented in table 2, the increase in the DRT rate to 2.4% is associated with a marked surge in the SD of turnaround time from 0.05 to 0.87 working days as well as an escalation in the maximum of turnaround time from 1.71 to 8.56 working days.

Referral network maps

We present a visualisation of the referral network, highlighting both national laboratory and POC DRT hubs in figure 2. The visualisations are organised into different levels of DRT rate (0.4%, 1.2%, 3.6%), each with one plot displaying the complete map encompassing all facilities in Kisumu County. When DRT rate is 3.6%, we provide an additional plot zooming into facilities surrounding Kisumu city to reflect the involvement of the national lab when DRT rate grows. The figure does not contain a panel showing the national laboratory-only network, since all samples are directed to that laboratory. Typically, facilities forward samples to the POC DRT hub closest to their location, with exceptions arising due to limited capacity at the nearest testing hub. At DRT rates of 0.4% and 1.2%, the referral network is similar, with demand for DRT largely being handled by three POC DRT hubs (KEMRI CDC HIV/R Laboratory, KEMRI/Walter Reed CRC Laboratory and JOOTRH). At these

Table 2 Statistics summary of mean turnaround time for two networks under various DRT demand proportion

Scenarios	DRT proportion	National laboratory only		National laboratory and POC DRT hubs	
		Turnaround time, working days mean (SD)	Turnaround time, working days min, max	Turnaround time, working days mean (SD)	Turnaround time, working days min, max
Scenario 1	0.4%	8.52 (0.09)	8.33, 8.70	1.13 (0.07)	1.03, 1.30
	0.8%	8.53 (0.09)	8.33, 8.71	1.35 (0.2)	1.04, 1.65
	1.2%	8.55 (0.09)	8.36, 8.73	1.44 (0.15)	1.16, 1.70
	1.6%	Infeasible		1.53 (0.05)	1.46, 1.71
	2.4%	Infeasible		1.69 (0.87)	1.48, 8.56
	3.2%	Infeasible		1.90 (1.49)	1.48, 8.60
	3.6%	Infeasible		2.11 (1.81)	1.49, 8.67
	4.8%	Infeasible		Infeasible	
Scenario 2	14.62%	Infeasible		Infeasible	

DRT, drug resistance testing; POC, point-of-care.

two levels of DRT rate, the AMPATH Care Laboratory and the national laboratory do not receive any samples from Kisumu County, presumably due to high transportation times. When the DRT rate increases to 3.6%, the referral network expands to incorporate both the AMPATH Care Laboratory and the national laboratory. More specifically, when the DRT demand proportion ranges from 0.4% to 1.6%, no facilities send samples to the national lab. However, when the proportions are 2.4%, 3.2% and 3.6%, 2, 6 and 9 facilities out of 146, respectively, send samples to the national lab. Those facilities sending their samples to NPHL face substantially longer turnaround times due to the extended transportation and batching times.

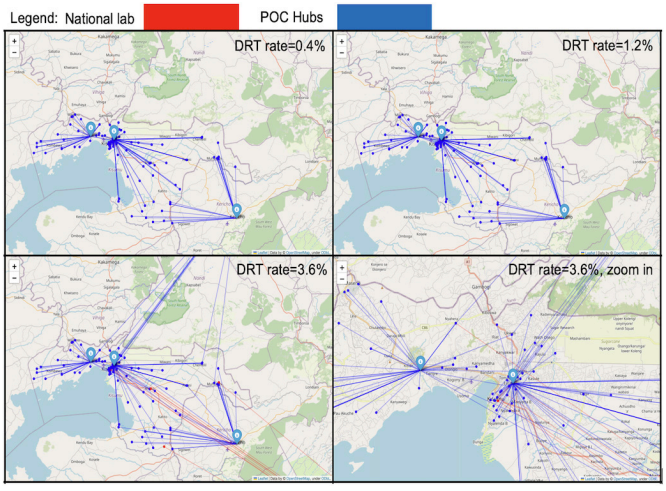

Figure 2 Referral network when POC DRT hubs are included in the testing network, with varying DRT rates and zoom levels. The markers with colours of red and blue correspond to national and four POC DRT hubs, respectively. Additionally, blue dots are used to represent 146 facilities. The network is shown through links between facilities and selected DRT laboratories. DRT, drug resistance testing; POC point-of-care.

One-way sensitivity analyses

Table 3 outlines the mean turnaround time of all facilities under three different settings for each parameter as well as their percentage change compared with the base case results. We ground these changes at a DRT rate of 1.2% with the national-laboratory only model, 1.2% with adding four POC DRT hubs model and 3.6% with the latter model. For quick visualisation, a grey scale captures the magnitude of change from base case.

We further conducted one-way sensitivity analyses on key operational parameters. Our goal was to perform these analyses using both the national laboratory-only model and the optimised model with POC hubs, selecting different DRT rates that are feasible. Batching delay mode had the most substantial impact on the mean turnaround time in the national laboratory-only network. Specifically, when transitioning from a weekly to a twice-a-week or daily batching delay mode, the mean turnaround time decreased by 34.3% or 80.1%, respectively. In both the national laboratory and POC DRT hub networks, we observed that adding POC DRT machines or improving the service rate also improved the system's efficiency. For example, the addition of two machines for all existing hubs led to a 40.8% reduction in turnaround time. On the other hand, increasing the operational capacity of national laboratory had a minor impact on the mean turnaround time under all settings, suggesting that expanding the capacity of the national laboratory (eg, by adding more machines or human resources) would not substantially improve the system's efficiency. In addition, road and weather conditions had negligible effects on the mean turnaround time in all scenarios, while transportation mode had a more substantial impact on the turnaround time, particularly with walking sample delivery—an unlikely scenario—compared with a base case of motorbike transport (93.5% slower). However, car transport was not meaningfully better (only 2.7% faster) compared with motorbike transport.

Table 3 Results for one-way sensitivity analyses, with mean and SD of turnaround time in working days and the percentage change from the base case parameter

	National laboratory-only (DRT rate: 1.2%)	National laboratory and POC DRT hubs (DRT rate: 1.2%)	National laboratory and POC DRT hubs (DRT rate: 3.6%)
Capacity Improvement			
Improving operation capacity of the national lab			
Current service rate *	8.55 (0.09)	1.44 (0.15)	2.11 (1.81)
1.5 times current service rate	8.52 (0.09),%–0.4%	1.44 (0.15), 0.0%	2.07 (1.81),%–1.9%
2 times current service rate	8.52 (0.09),%–0.4%	1.44 (0.15), 0.0%	2.07 (1.80),%–1.9%
Add POC DRT machines in hubs			
No additional machines *	**	1.44 (0.15)	2.11 (1.81)
Add 1 server for all existing hubs	**	1.23 (0.12),%–14.6%	1.47 (0.90),%–30.3%
Add 2 servers for all existing hubs	**	1.12 (0.07),%–22.2%	1.25 (0.05),%–40.8%
Improving operation capacity of hubs			
Current service rate*	**	1.44 (0.15)	2.11 (1.81)
2 times current service rate	**	0.90 (0.07),%–37.5%	1.06 (0.05),%–49.8%
4 times current service rate	**	0.73 (0.06),%–49.3%	0.79 (0.08),%–62.6%
Batching delay of sending samples to the national lab			
Daily	1.70 (0.09),%–80.1%	1.44 (0.15), 0.0%	1.61 (0.11),%–23.7%
Two times a week	5.62 (0.09),%–34.3%	1.44 (0.15), 0.0%	1.89 (1.06),%–10.4%
Once a week*	8.55 (0.09)	1.44 (0.15)	2.11 (1.81)
Transportation parameters			
Road/weather condition			
Good	8.32 (0.07),%–2.7%	1.43 (0.15),%–0.7%	2.06 (1.76),%–2.4%
Average *	8.55 (0.09)	1.44 (0.15)	2.11 (1.81)
Bad	8.78 (0.11), 2.7%	1.46 (0.15), 1.4%	2.13 (1.87), 0.9%
Transportation mode			
Walk	16.54 (0.73), 93.5%	2.04 (0.48), 41.7%	3.38 (3.73), 60.2%
Bike	9.69 (0.18), 13.3%	1.53 (0.17), 6.3%	2.29 (2.08), 8.5%
Motorbike *	8.55 (0.09)	1.44 (0.15)	2.11 (1.81)
Car	8.32 (0.07),%–2.7%	1.43 (0.15),%–0.7%	2.06 (1.76),%–2.4%

The legend of the gray scale plot: , 0~2; , 2~4; ,4~6; ,6~8; , 8~10; , ≥ 10.
*Represents base case parameter settings.
DRT, drug resistance testing; POC, point-of-care.

DISCUSSION

Our modelling study, employing systems engineering methodologies, reveals that POC DRT is likely to be required in addition to centralised laboratory testing to realise the demand for DRT in LMICs in the upcoming years. The existing strategy, in which a solitary national laboratory is responsible for conducting DRT for the entire laboratory network, will rapidly encounter capacity limitations if the DRT demand was to merely triple from 0.4% to 1.2%. The new configuration of a POC DRT network is designed to accommodate up to a ninefold escalation in the current rate, from 0.4% to 3.6%. As noted previously, despite marked enthusiasm for dolutegravir-containing regimen use in LMICs, DR will be an enduring concern. DR to dolutegravir is already emerging,[9 41–45] and because it remains unclear what regimens should be used in cases of dolutegravir resistance, the use of DRT is only going to increase as surveillance for dolutegravir resistance intensifies in LMICs. Though the maximum potential DRT demand rate (14.6%) modelled in our scenario 2 is highly improbable to occur in LMICs in the foreseeable future, there is a pressing need for a substantial increase in centralised and POC DRT capacity to cope with the likely upsurge in DRT demand. This increase in capacity will be critical to ensuring that LMICs are able to effectively manage the growing need for HIV DR test especially among the children and pregnant women living with HIV that are more sensitive to return of results.

One of the largest determinants of turnaround time was the batching delay. For instance, increasing the

sample transportation frequency from a weekly to a twice-weekly basis could potentially halve the turnaround time. Furthermore, if samples were transported daily, the turnaround time could be halved once again, potentially resulting in more efficient and timely processing of samples. Of course, a trade-off between the cost and labour of frequent shipment against economies of scale of batching needs to be considered when determining the batching delay for transport of samples from a spoke to a hub facility. By having closer POC DRT facilities to the spoke facilities than the national laboratory, this issue of batching delay is overcome by a network that includes POC DRT hubs. Since direct data about the impact of POC DRT testing on results utilisation have not been studied, parallels with POC VL testing may be useful: although POC VL testing has not necessarily consistently improved viral suppression,[21 46–48] improved turnaround times are highly motivating for providers and patients[49] and result utilisation appears to improve as well.[20 47 50]

Another important factor influencing turnaround time is the service rate or operational capacity of POC machines. This expansion of POC machines may lead to very efficient and timely delivery of test results (possibly within 1 day). However, our study suggests that augmenting the operational capacity of the national laboratory does not have a substantial impact on reducing the mean turnaround time for DRT. This is because facilities continue to experience substantial delays due to the long transport and batching delays involved in sending samples to the national laboratory. Furthermore, since the national laboratory has a limited capacity share reserved for Kisumu County to process samples from other parts of the country, it is fundamentally limited in improving turnaround times for the region. While we did not explicitly model the additive improvements in both increasing the operational capacity at the centralised laboratory and reducing the batching delays, were those factors more easily modifiable for a given national laboratory, it is possible that a national laboratory network could be responsive to the increasing needs of increasing DRT demand over time. Therefore, decision-makers should consider focusing on optimising POC machine capacity as a potentially more effective approach to improve the overall performance of the DRT network.

Given our findings, we suggest that decision-makers should prioritise the introduction of POC DRT machines to meet the current and anticipated demand for DRT in Kisumu County.[51] This would effectively reduce the turnaround time and offer several programmatic advantages. POC has been shown to increase patient satisfaction and adherence,[52] reducing healthcare costs by minimising multiple clinic visits for result inquiries.[53] Implementing POC DRT hubs may address access disparities for marginalised communities facing limited investments, as we have shown with POC VL hubs.[31] It also ensures proper chain of custody, mitigating specimen rejection and errors in centralised referral networks.[54 55] Onsite POC testing significantly reduces the risk of poor results, enhancing clinical follow-up and confidence in laboratory systems. Additionally, it may be beneficial for decision-makers to explore the possibility of improving the frequency of batching samples to the national laboratory and substantially increasing the service rate of POC machines as potential next steps to further enhance the system's performance.

Despite unique insights yielded by our model, there are several limitations to this work. First, one of the biggest challenges in selecting POC DRT hubs for DRT is the intrinsic laboratory capacity for that hub to handle the more technical elements related to HIV DR versus VL testing. This immediately limits the pool of candidate hubs to a few select facilities already functioning at a relatively high laboratory capacity. Second, the model uses VL demand data from 2019, as more recent data may be affected by COVID-19-related VL testing reagent shortages. Third, we emphasise only time delays; however, the budget of machine instalment, staff training and development programmes have not been considered in this model, necessitating a further cost-effectiveness analysis. Fourth, future models could model clinical decision-making parameters, such as results utilisation, to better demonstrate utility of such models. Fifth, this model is limited to the service delivery level of Kisumu County and would require expansion for it to be applicable in other counties. Finally, our formative work was limited to two focus groups with 12 total participants. On face value, this may have failed to reach thematic saturation or identify other model inputs or attributes that were desirable to decision-makers. However, the source population of individuals who make the types of resource allocation decisions targeted by this model is reasonably small. We elected to have a smaller sample size that included individuals whose scope of work is directly related to the model question.

CONCLUSIONS

In conclusion, our findings provide a valuable framework for improving the current DRT laboratory network system in Kenya, offering decision-makers an opportunity to identify ways forward for DRT demand estimation, optimal referral networks and identifying key factors like transportation delays and operational capacity of POC DRT hubs. As the demand for DRT is expected to increase, we recommend the inclusion of POC DRT hubs to handle a larger volume of samples within an acceptable turnaround time.

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