5-2019

Simulating Alternative Tuberculosis Diagnosis Methods in Underdeveloped Countries

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ABSTRACT

Tuberculosis is the deadliest infectious disease in the world; it is especially rampant in underdeveloped countries because they do not have the infrastructure, technology, or funding to properly combat the infection. However, the development of portable point-of-care diagnosis machines can reverse this epidemic as they far surpass conventional laboratory identification. The question now is where to place these machines, which is a difficult decision with a lack of data. Therefore, a flexible simulation model is created to test the implementation of these machines with different countries and configurations. The simulation tests the baseline model and three proposed implementations of the machines. Initial analysis indicates these machines can reduce the average diagnosis period of patients by a factor of one-hundred. Furthermore, a fractional factorial design was conducted to test the sensitivity of each variable to determine which data needs to be collected before making any decisions. The model is built to be accessible and flexible allowing for the model to be expanded upon in future research.

1 INTRODUCTION

At the beginning of the 19th century, the understanding of the lung disease known as tuberculosis (TB) began with the work of Théophile Laennec. In 1865, Jean-Antoine Villemin further advanced the research with the demonstration of the transmissibility of Mycobacterium tuberculosis infection (Daniel, 2006). Villemin sparked the research proving the bacteria called Mycobacterium tuberculosis (Mtb) causes the highly infectious disease, tuberculosis. In response, public health measures have emerged to combat the bacterial cause. Though the spread has dramatically reduced, tuberculosis (TB) is currently the deadliest infectious disease to plague the world. A study determined TB was the cause of 1.3 million deaths in 2012 (Glaziou, 2015). Additionally, a study done by the World Health Organization estimates more than one billion people are infected with Mtb (2016). Due to advancing tuberculosis treatments, TB is being viewed less as an epidemic in wealthy areas. However, underdeveloped countries do not currently have the tools or infrastructure to fight the disease adequately.

Rapid tuberculosis diagnosis is pivotal in reducing the death rate of the disease (Nitika, 2012). A constraint with conventional laboratory identification is that the sample requires up to ten weeks to develop before an accurate diagnosis can be made. Fortunately, TB diagnosis can be made much faster with new Point-of-Care (POC) machines (Shama, 2012); these machines can produce results as quick as 90 minutes and require no time for the sample to develop. A lot of these machines are large and costly; however, portable POC machines, such as the GeneXpert Omni, have been developed, reducing the need for advanced infrastructure. Therefore, portable POC machines enable the opportunity to implement enhanced diagnosis techniques in underdeveloped countries.

Simulation can be used to determine the most cost-effective placement of these machines to reduce the average diagnosis period, thus, reducing tuberculosis-related death. The simulation model created with this project is primarily based on the research done by Amir Ghahari in his dissertation (2017). The purpose of creating a new model is to establish the framework of a more accessible simulation model, giving it the ability for other people to expand upon it in the future. Additionally, the model is made with great flexibility so it can be applied to different countries and configurations. Flexibility is especially important because of the lack of data underdeveloped countries currently collect. Many of the parameters in the model are inferred and therefore may not represent the real system as accurately as possible. A sensitivity analysis indicates which data needs to be collected most before making decisions. The ultimate goal of this research is to validate the need for improved data collection to entice the funding of advanced TB diagnosis methods. This paper will conceptually describe the system in place for TB diagnosis while evaluating some of the possible alternatives for quicker diagnosis. Then, there is an in-depth explanation of the simulation model to test the configurations. Finally, the results are examined, and the potential for future improvements is evaluated.

2 CONCEPTUAL MODEL

The current system has many steps to deliver a diagnosis. When a patient senses a tuberculosis symptom, they visit a clinic. A doctor meets with the patient to validate the symptoms, and if it is confirmed, they take the necessary swab to do further testing. At the end of the day, all samples collected are sent to a TB microscopy center. Microscopy centers are research facilities specializing in microscopic analysis. The centers conduct tests on the samples received; if the results come back positive, the patient is notified. Otherwise, the sample is sent to the hospital for further testing. Once the more detailed tests are completed at the hospital, the patient is notified whether they have tuberculosis. Figure 1 is a representation of the flow from the patient to the hospital.

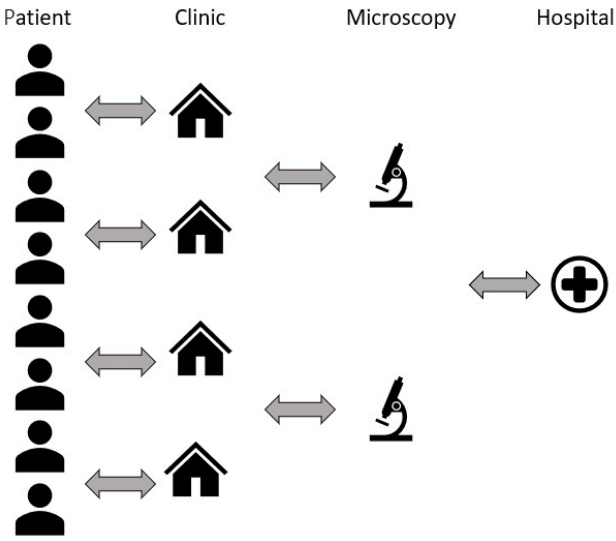


Figure 1 - Current Process of TB Diagnosis

With the creation of the new point-of-care (POC) machines, three new system configurations are proposed: putting the machines in clinics, putting the machines in existing TB microscopy centers, and putting the machines on trucks. The first two options are straightforward, and the third is the most creative. Putting the machines on trucks consists of having a fleet of medical vehicles all equipped with POC devices ready to travel to the patient's location; this configuration will be called TB-OnDemand. The base model and the three proposed system configurations will be explained further conceptually.

The current operations of the system will serve as the baseline model. Figure 2 is a flow diagram for the process of the current system. Patients are created based on the average number of people who are diagnosed with tuberculosis. Each patient goes through the system individually with shared resources.

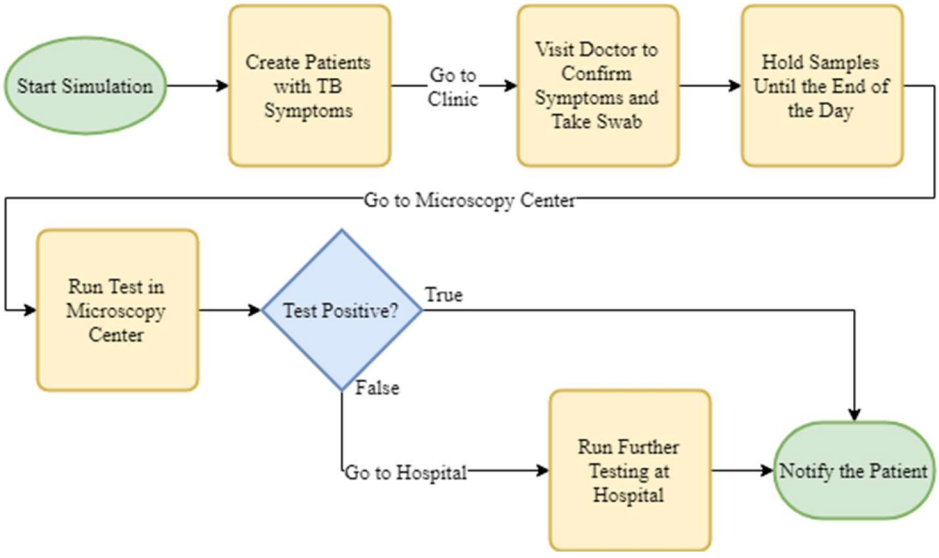


Figure 2 - Flow Diagram of the Current System

Placing the machines in the existing TB microscopy centers essentially removes the possibility of sending the machine to the hospital. Figure 3 is the flow diagram of the existing microscopy centers are equipped with POC machines. The POC machine has the capability of doing the advanced testing; therefore, if the

sample test comes back negative, the doctor can conclude with high confidence the patient does not have tuberculosis. Additionally, the time spent at the microscopy center is reduced because the sample does not require time to develop.

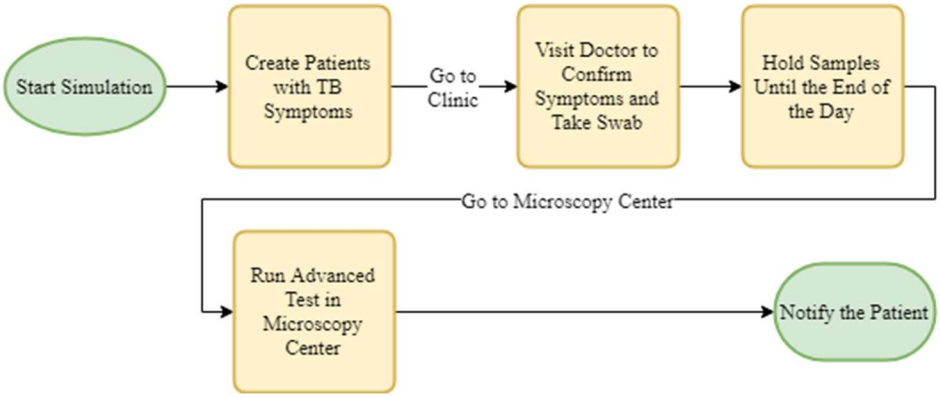


Figure 3 - Flow Diagram with POC Machines in Microscopy Centers

Putting POC machines in the clinics eliminates the need of both the hospital and microscopy center. The diagnosis can be completed with the sample never leaving the clinic. Figure 4 is the flow diagram for the configuration of the clinics were equipped with POC machines.

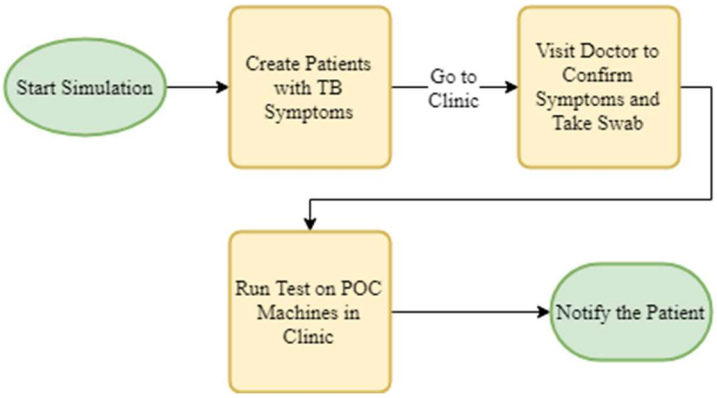


Figure 4 - Flow Diagram with POC Machines in Clinics

With TB-OnDemand, there is still the need for patients to visit the clinic. However, the system has the possibility of requiring less POC machines since one truck can service multiple clinics. Figure 5 is the flow diagram for having POC machines on medical trucks. Different routing methods can be used to determine the best paths for the trucks to take while picking up samples.

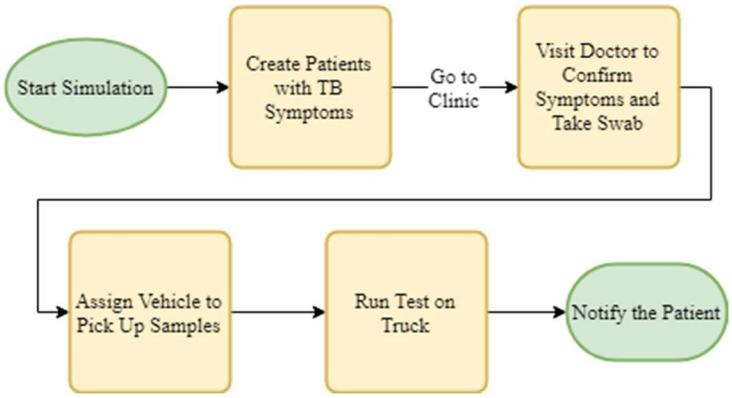


Figure 5 - Flow Diagram for TB-OnDemand

It was determined that a simulation model is an effective way to evaluate the alternative placements of POC machines. Each system configuration is modeled to enable comparative analysis. The simulation model will be explained in-depth.

3 SIMULATION MODEL

The primary goal of this research is to create a model with flexibility. Ghahari (2017) created a similar model, but it was specifically on the country of Ghana, Africa. The new model allows the user to enter different parameters to initialize the system to model different countries. Each system configuration can be tested with the same simulation model. The system configuration numbers with corresponding attributes are in Table 1. The first two subsections will describe the key inputs and outputs of the model, then an overview of the simulation model is presented.

Table 1 - Configuration Number

Configuration	Type
1	Baseline (Current System)
2	POC Machines in Microscopy Centers
3	POC Machines in Clinics
4	TB-OnDemand

3.1 INPUT PARAMETERS

Since the model was created to produce a flexible simulation, all the variables are adjustable in an Excel Interface. Flexibility allows the user to test the sensitivity of different variables; which is a necessary component with the number of assumptions required by the lack of data. Almost every number in the model is a variable to allow for the ease of manipulation.

With this model, two countries with greatly differing attributes can be tested. A design challenge when developing this model was initializing the system with the infinite input variations. The solution was to use ratios to produce a scaled model of the desired settings. For example, if the user wanted to simulate Greater Accra or Upper West in Ghana, Africa, they would enter in the facts about the two administrative regions shown in Table 2.

Table 2 - Regional Facts

Region	Surface Area	Population	Clinics	Microscopy Centers	Diagnosed TB Rate
Greater Accra	3245	3909764	123	60	0.066%
Upper West	18476	677763	21	10	0.042%

Using a ratio system, the inputs are manipulated to scale the model for the simulation. The ratios are calculated using equations (1) – (3).

$$Clinic\ to\ Microscopy\ Ratio = Clinics\ \div\ Microscopy\ Centers \quad (1)$$

$$Clinic\ to\ Population\ Ratio = \ Population\ \div Clinics \quad (2)$$

$$Population\ Density = Population\ \div Surface\ Area \quad (3)$$

One of the variables must be predetermined. In this simulation, the number of clinics in the scaled model is the single non-calculated value; this allows for the scaled variables to all stem from the same number. The remaining scaled values are calculated with equations. (4) – (6) with the previous ratios.

$$Scaled\ Population = Scaled\ Clinics\ \times Clinic\ to\ Population\ Ratio \quad (4)$$

$$Scaled\ Surface\ Area = Scaled\ Population\ \div Population\ Density \quad (5)$$

$$Scaled\ Microscopy = Scaled\ Clinics\ Clinic\ to\ Microscopy\ Ratio \quad (6)$$

The incident rate is the rate at which patients get TB symptoms. Equation (7) depicts how the incident rate is calculated. The TB diagnosis rate is the percentage of the population of those who are diagnosed with TB in a year. Health agencies report these statistics, and therefore can be accurately represented in the model. The incident magnifier is used to increase the number of patients who appear to have tuberculosis since the diagnosis rate only represents patients who were officially diagnosed; agencies do not report the number of samples tested for TB in a year.

$$Incident\ Rate = TB\ Diagnosis\ Rate\ \times Population\ \times Incident\ Magnifier \quad (7)$$

Essentially, the model takes a sample of a random part of the defined country and uses the reduced data for the simulation. The variables used to initialize the scaled model for the two regions are shown in Table 3.

Table 3 - Emulated Regions

Region	Surface Area	Population	Clinics	Microscopy Centers	Incident Rate
Greater Accra	264	317867	10	5	0.0744
Upper West	8798	322744	10	5	0.0122

Beyond the factual data about the country, the dashboard has other inputs to initialize the system. First, there is information needed for each specific building. The user can input the coordinates for the locations of the clinics, microscopy centers, and truck home. The user can specify the resource levels at each location such as the number of doctors or POC machines. The clinics also need the portion of the population it serves, and the microscopy center assigned to each clinic.

Additionally, the model allows the user to input different distributions. With the lack of research over underdeveloped countries, a lot of the distributions are guesswork. For example, there is no indication of how many samples must be sent to the hospital for further testing from the microscopy centers; therefore, it is worth testing the sensitivity of this probability. Having flexible distributions allows the user to test more "what if" scenarios easily. Uniform distributions include the average travel speed, doctor diagnosis time, microscopy diagnosis time, and hospital diagnosis time.

Another benefit of having an Excel Interface is an opportunity for error checking and data validation. Each value has a recommended setting and Excel will produce a warning if there is a substantial variation. For example, the recommended incident magnifier is five; if it goes below three, a warning will be displayed on how the figure is small. If the incident magnifier is zero, there will be an error message because the simulation would produce zero TB patients. Another example is how interface makes sure the buildings are on the coordinate plane. With the calculated surface area for the system, Excel calculates the boundary to ensure every clinic and microscopy center is within the perimeter.

3.2 Performance Measures

Assign and Record modules are used throughout the model to record different performance measures. The two key performance measures are the average diagnosis period (ADP) and the number of diagnosed patients (NDP). The ADP is the time between the patient arriving at the clinic and the patient being notified of the diagnosis. In the model, the possible communications barriers are ignored, and it is assumed the patient is immediately notified. The NDP is the total number of patients processed throughout the simulation.

Throughout the model, additional statistics are recorded. These include the average times spent on each step of the process. The average time in the clinic is from when the patient steps foot in the clinic until the sample is sent to the microscopy center. The average time in the microscopy center is from when the sample arrives at the microscopy center until it leaves the center. The average hospital time is the average time the specimen spends in the hospital. The average transportation time is the average time each specimen spends being relocated. For each of these steps, the average number of patients or samples in each step at one time is also recorded.

3.3 Model Overview

The model was built with Arena Simulation software by Rockwell Animation. In Arena, the simulation uses objects called entities to flow through the system. Most of the entities in this simulation represent the patients. Entities representing patients with symptoms of tuberculosis are created with an exponential distribution of one divided by the incident rate. The incident rate is calculated with equation (7).

Figure 6 is an overview of the patients entering the system. Once created, the entity is assigned the necessary attributes. Patients are then immediately routed to a clinic. The model determines which clinic to send the patient to from a discrete distribution based on the portion of the population each clinic serves. The travel time from the location of the patient to the clinic is considered negligible and the diagnosis period starts once the patient reaches the clinic.

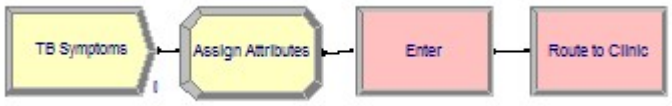


Figure 6 - Enter System Modules

Sets are heavily used in the model to keep the modules as concise as possible. Figure 7 is an overview of the modules when the patient first enters the clinic. Once at the clinic, a doctor must diagnose the patient. For this model, the doctor is considered a resource and the time spent with the doctor is a uniform

distribution. The doctor confirms if the symptoms are worth testing for tuberculosis; if the doctor determines the patient does not have TB symptoms, the patient is disposed from the system. The confirmation is determined by a 2-way-chance decide module. Other patients without tuberculosis symptoms are also created at this time to accurately represent congestion in the clinics and the queue to receive attention from the doctor. These patients are filtered out from the system and are disposed after seeing the doctor. A level of calibration was required to achieve the desired level of resource utilization.

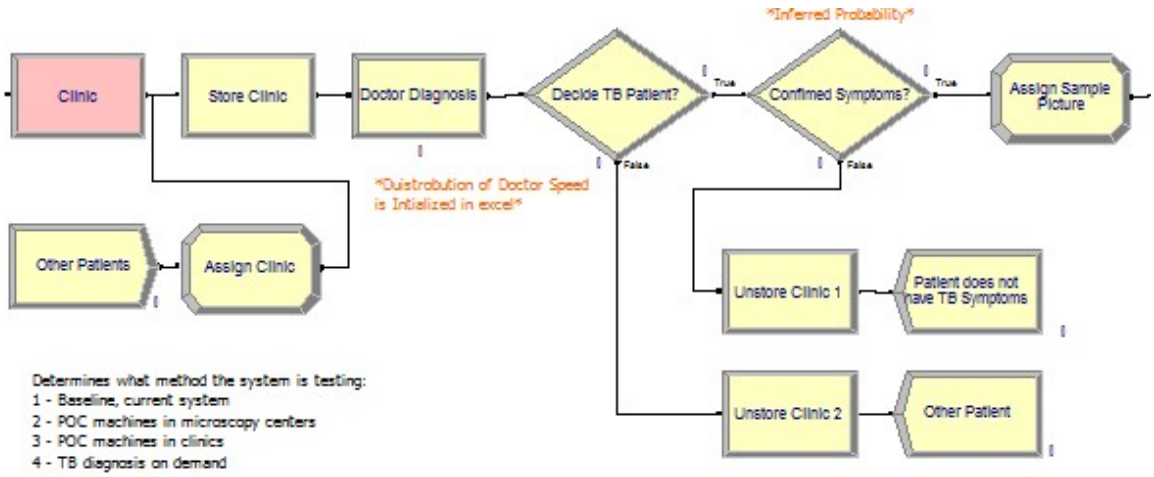


Figure 7 - Clinic Start Modules

After the doctor confirms the symptoms, the entity is split based on the current method being tested. Figure 8 shows where the differing modules for each method start in the model. The split is done with a Decide module based on the current value of the method variable. If the POC machines are placed at the clinics (method three), the samples are placed in a queue to be tested by the machine. Each POC machine at each clinic is a separate resource. With the current technology, each sample takes a constant 90 minutes to test; this is still an input variable in case new technology further reduces the time. Once the test is complete, the machine immediately starts testing the next sample in the queue, key performance measures are recorded, and the patient is notified.

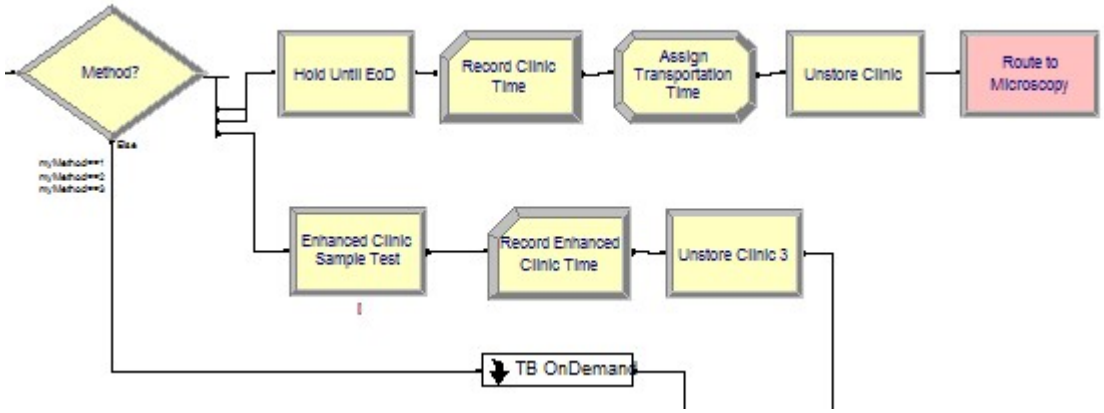


Figure 8 - Clinic End Modules

If the method one or two is being tested, the samples momentarily follows the same path. The samples wait in a hold queue until the end of the day to be sent to the assigned microscopy center. The clock entity ticks at the end of each day and signals the release of the samples. The clinics, microscopy centers, and hospital are represented on an (X, Y) coordinate grid. The distance formula and a uniform distribution for the travel

speed are used to determine the travel time from each clinic to microscopy center. The entity is sent with a Route module and arrives at a Station module based on a station set of microscopy centers. Figure 9 is an overview of the modules representing the microscopy center. If the POC machines are at the microscopy centers (configuration 2), the samples follow the same procedure used for configuration three. If the baseline configuration is still being tested (configuration one), the samples are delayed based on distribution developed from the average time samples spend in microscopy centers. If the diagnosis is positive, the patient is notified; otherwise, the sample must be sent to a Hospital for further testing.

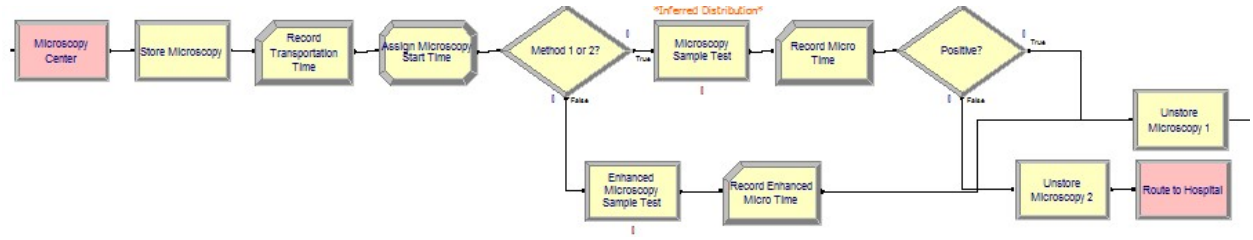


Figure 9 - Microscopy Center Modules

The travel time between the microscopy center and the hospital is modeled with the same calculation for the time between the clinic and microscopy center. Figure 10 is an overview of the modules used to represent the hospital. At the hospital, the sample is delayed once again on a uniform distribution based on the average time it takes the hospital to do advanced tests. Whether the sample is positive or negative, the key performance measures are recorded, and the entity is disposed from the system.

Figure 10 - Hospital Modules

Configuration number four tests TB-OnDemand. Once the doctor takes the sample from the patient, it goes into an indefinite hold module to be picked up from a medical truck. At the beginning of the simulation, an entity is created to represent the truck driver. Figure 11 is an overview of the beginning modules the truck driver follows. The driver starts at its home location and is placed in a hold queue until it has a sample to go pick-up. If multiple clinics have samples ready to be picked up, the driver goes to the clinic with the most samples using a PickStation module.

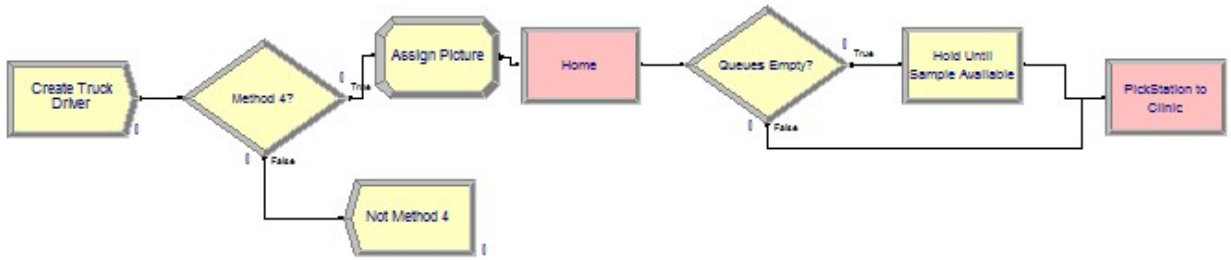


Figure 11 - TB-OnDemand Start Modules

Figure 12 presents the modules needed once the driver reaches a location with samples to test. The driver uses a Pickup module to retrieve all the entities in the hold at the clinic the driver is visiting. Using a Dropoff module, the samples are put in a queue to use the POC as the driver returns to its home location. After the

sample is processed, performance measures are recorded, and the patient is notified. The truck driver entity continues to repeat the same process. The travel times between each location are determined with an array of linked stations and a uniformly distributed travel time.

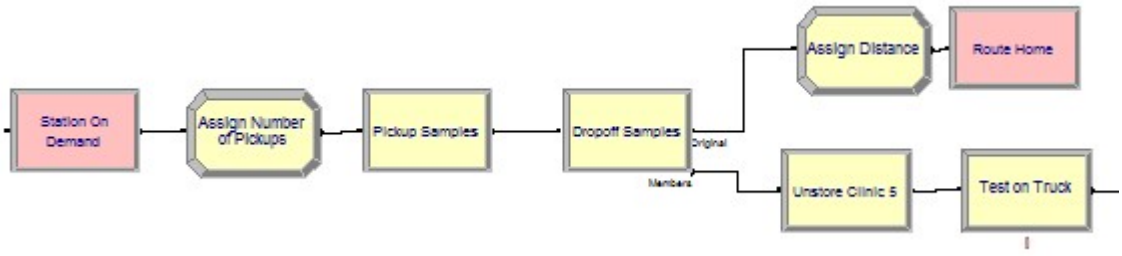


Figure 12 - TB-OnDemand End Modules

3.4 EVENT HORIZON

The system does not have a defined start and end; it more closely follows a continuous process. The concern is not the ADP for each day, but rather the ADP over a long period of time. Therefore, it is a steady-state simulation.

The simulation takes time to populate with patients; therefore, a Welch analysis was necessary to determine the warm-up period for the simulation. Figure 13 shows the Welch Plot for the average diagnosis period. The left of the black line is the warm-up period, and the right is when the statistics start to record.

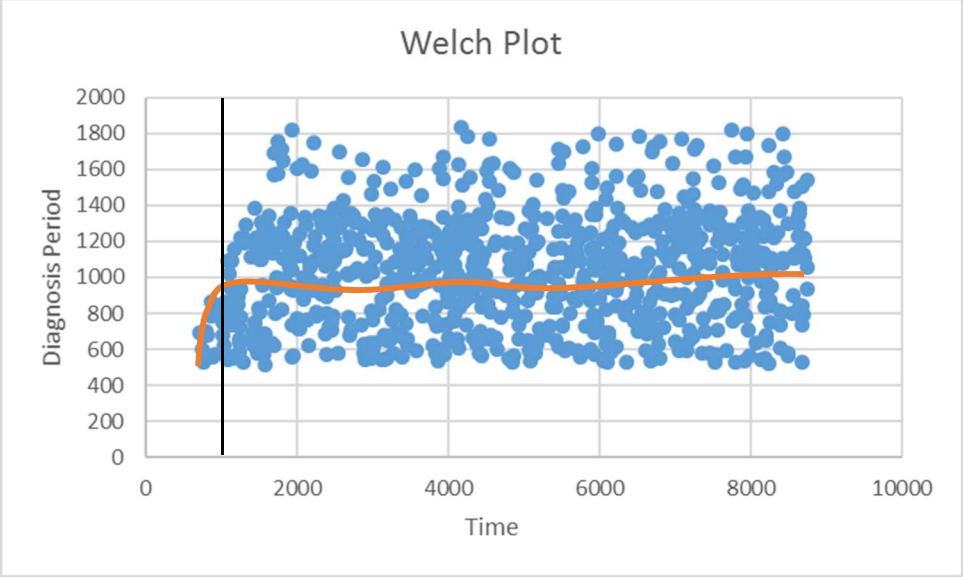


Figure 13 - Welch Plot based on Average Diagnosis Period

The Welch Plot was done with method one because it takes the longest time to populate. It was determined the warm-up period should 38 days because it is clear on the plot the data reaches a steady state. However, the simulation run parameters can be manipulated on the Excel interface. Table 4 is the default run parameters by giving the simulation appropriate half-widths.

Table 4 - Simulation Run Parameters

Parameter	Value
Warm-Up Period	38 days
Replication Length	365 days
Number of Replications	10

3.5 VERIFICATION AND VALIDATION

The model was first built independently for each method. Having a separate model allowed for each method to be verified with ease. Once the code was confirmed to be working as intended, the four models were meshed into one model. Furthermore, the animation aided greatly in the verification process. The simulation can be observed as it is running, ensuring the entities are flowing as intended.

The model was partially validated by comparing results to Amir's research (2017). Additionally, different statistics were recorded in the model to confirm different metrics. For example, a calculation can be done by hand to determine an estimate for the number of patients; then this calculated number can be compared to the number of patients the model produces.

3.6 ANIMATION

The primary purpose of the animation is to show the location and flow of entities. Spatially speaking, the animation does not accurately represent the system under study. Since the user can change the size and location of buildings with every replication, doing so would be difficult. However, the animation suffices in getting a feel for how everything flows, and the time spent at each step.

The animation supports all four methods. Figure 14 shows the layout of the animation. Since a single queue does not represent the entire time a patient spends in a building, Store and Unstore Modules are used to show who is at which building. The flow from each building uses the animation capabilities from the Route and Station models. When an entity is traveling to another building in the model, it can be observed moving in the animation. The animation shows both normal patients and TB patients in the clinic. The normal patients are red, and the TB patients are yellow. Once the doctor takes the sample from the patient, the entity's picture changes of a vial; this is accomplished with an Assign module. The dot on the top left the "home" for the medical truck in method four. The samples waiting to be picked up by TB-OnDemand are in the same clinic holds as the rest of the model. The mobile laboratory entity is represented by a truck.

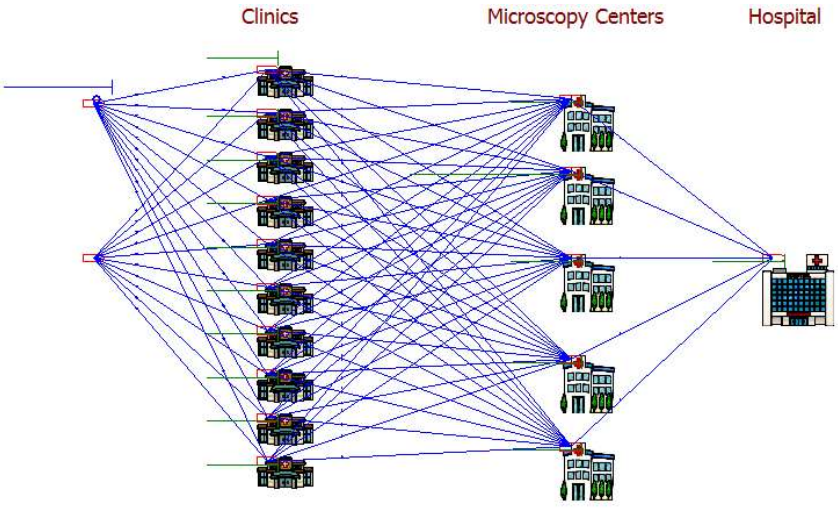


Figure 14 - Animation Layout

Additionally, the animation has a dashboard pane of all performance measures. The dashboard allows the user to monitor the measures in simulated-time. Every value stated in the performance measures section is viewable on the dashboard.

4 RESULTS

With the possible variation in the system, different parameters can have significant effects on the results. The results presented will be using the emulated Greater Accra seen in Table 3. Additionally, the other essential system parameters used in the test are in Table 5; these are the recommended parameters for the model.

Table 5 - Testing Parameters

Parameter	Value
Incident Magnifier	5
Doctor Diagnosis Speed	[10, 20] min
Travel Speed	[35,45] Km/h
Confirmed Symptoms	95%
Further Testing	75%
Time in Microscopy	[21, 56] days
Time in Hospital	[14,21] days
Other Patent Arrivals	20 per hour

There was one doctor at each clinic and one POC machine at each building when testing the corresponding method. For method four, one truck equipped with one POC machine was used. Equal portions of the population were assigned to each clinic, and each microscopy location was assigned the two closest clinics. Using this parameter set, the average diagnosis periods can be observed in Figure 15.

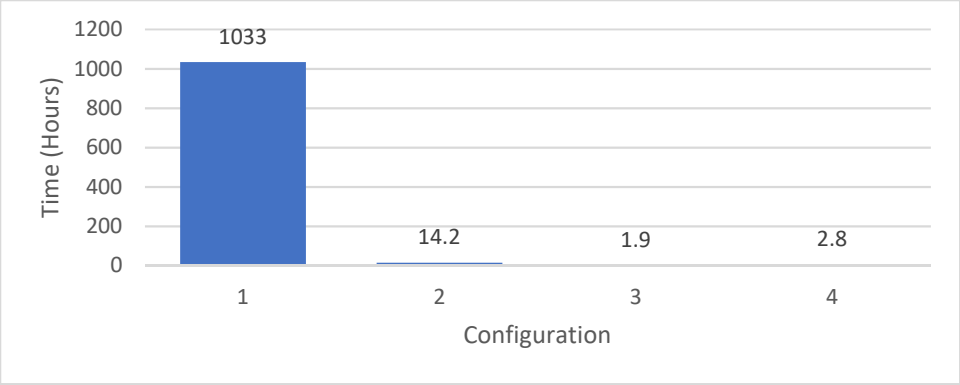


Figure 15 - Average Diagnosis Period per Method

Any of the methods are superior to traditional diagnosis methods. Method three was the best in terms of diagnosis time with this parameter set, but the cost is still something to consider. Method three requires ten POC machines, and method two only requires five; it may not sound like much, but when it is scaled to the real size of Greater Accra it is 123 machines versus 60.

Furthermore, experiments were conducted to test the sensitivity of different variables. With the lack of data, it is important to test because most variables in the system are guesstimates. Eight variables in the system were tested for sensitivity. These variables are the percent of patients with confirmed symptoms at the clinics, percent of samples sent to the hospital for further testing, the incident magnifier, the arrival rate of patients without tuberculosis to the clinics, the doctor speed, the travel speed, the microscopy processing time, and the hospital. For the variables regularly determined by a distribution, a shift variable was used to change the mode of a triangular distribution where the limits remained constant. For example, the doctor travel time was tested with a triangular distribution where the limits are 5 minutes and 40 minutes, the minimum test makes the mode 5 minutes and the maximum test makes the mode 40 minutes. The average diagnosis period was evaluated as the primary response.

To prevent having to run the experiment with 256 different configurations for method one, an 2_{IV}^{8-4} fractional factorial design was conducted to produce results with level IV resolution. Each configuration was tested with ten replications. A graphical representation of the results is shown in Figure 16. As defined in the fractional factorial design, negative one represents the minimum possible value and the positive one represents the maximum possible value. Setting up the variables in this manner allows the analysis of these variables on the same scale of change. The test was run with each different method, but they yielded very similar results.

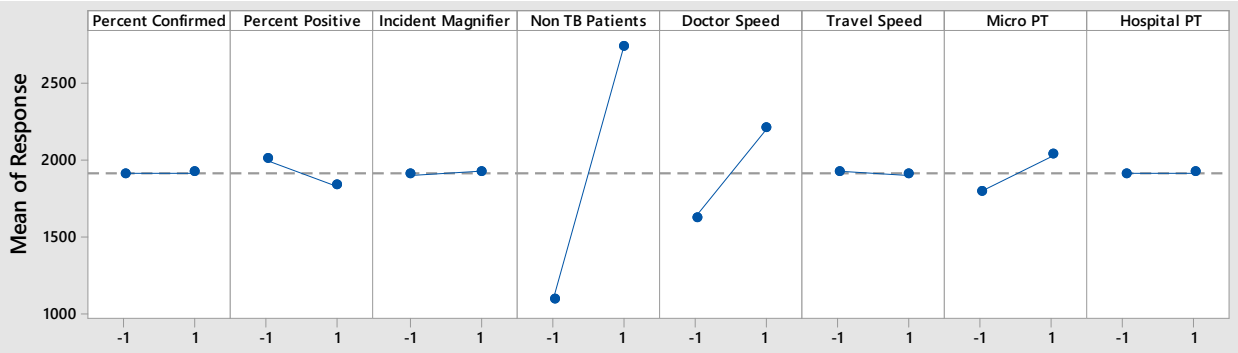


Figure 16 - Sensitivity of Variables on Mean Average Diagnostic Period

The change in the response (average diagnosis period) based on the change of each variable logically makes sense. When the number of patients with confirmed symptoms increases, the ADP increases. When the percentage of samples testing positive at the microscopy center increases, the ADP decreases because further testing is not required. When arrivals in the system increases based on the incident magnifier and non-tuberculosis patient arrival rate increasing, the ADP increases due to more congestion queuing. When the time it takes for a doctor to handle a patient increases, the ADP increases. When the travel speed increases, the ADP decreases because the samples can be transported quicker. Finally, when the processing times at the microscopy centers and hospitals increase, the ADP increases.

The results of the test with a corresponding coefficient and p-value for each variable is shown in Table 6. Any variable with a p-value with less than 0.1 is considered to have statistically significant effect on the average diagnosis period. Additionally, the variables with the higher absolute coefficient have a larger effect on the average diagnostic period.

Table 6 - Results of Partial Factorial Analysis

Term	Coefficient	P-Value
Constant	1908.98	0
Percent Confirmed	3.65	0.456
Percent Positive	-86.34	0
Incident Magnifier	11.69	0.018
Non-TB Patients	829.37	0
Doctor Speed	288.65	0
Travel Speed	-9.1	0.065
Micro PT	120.61	0
Hospital PT	4.15	0.397

It can be observed in Table 6 that the variable for the arrival rate of patients without tuberculosis has the largest effect on the ADP. At first, the arrival rate did not appear to be a sensitive parameter, but once the doctor utilization neared 100%, the ADP rose sharply. Indicating if the doctors are always working, each additional patient in the system has a significant impact on tuberculosis patients. The patient arrivals at clinics and doctor utilization is a component of the system worth further investigation. Additionally, the incident magnifier and doctor diagnosis speed are significant factors indicating the overall congestion in the clinics is a significant factor. The results indicate that significantly more detail should go into modeling the clinics such as bed and room utilization and collecting better data on doctor utilization.

Another significant variable is the percentage of samples testing positive at the microscopy center. The variable only pertains to configuration one. The reason the ADP decreases as the percent positive decreases is because more samples must go to the hospital for further testing. It is interesting that the microscopy processing time is significant, and the hospital processing time is not significant. This may be due to the range of hospital time only being seven days compared to the possible range of microscopy processing time being twenty-five days.

The only notable change in sensitivity between methods is the travel speed. The coefficient on the travel speed for method four was much higher than the other methods. Logically this makes sense because method four is dependent on the machine traveling around by road. Even though some variables have a much larger effect on the ADP than others, it is certain much more data must be collected prior to making decisions on the placement of the new POC machines.

5 CONCLUSION AND FUTURE WORK

The model sets the framework to test the placement of different point-of-care machines effectively. It is clear that implementing POC machines would drastically decrease the average diagnostic period. However, much future work is possible on this model. Possible improvements include developing upon the current processes in the model, optimizing truck routing, and making it an agent-based simulation.

Specific processes are models at aggregate or high-levels. Making these processes more detailed will add a further level of accuracy. For example, the time spent in the hospital is a delay on a uniform distribution. Reasonable inferences can be made about the distribution of the time spent in the hospital because a majority of the time is spent waiting for the sample to mature, but with any simulation model, better inputs will produce better outputs. A constraint on this improvement is the lack of information available on the processes in these medical centers. Furthermore, it is unknown what the amount of variation actually is for the process for each medical center.

In this model, the truck routing for configuration four followed a simple heuristic of going to the clinic with the most samples. There is an excellent opportunity to optimize the route the truck follows. Other factors can be considered such as the time the samples are in a queue and the distance to the other clinics.

Since TB is an infectious disease, an agent-based component would be interesting to add to the model. It can be hypothesized if someone gets infected in one area, people the person interacts with having a higher chance to become infected. The spread of the diseases would increase congestion on the diagnosis procedures serving the area. Additionally, it can be hypothesized a reduction in the ADP would lead to a reduced infection rate due to people being contagious for a reduced period. An agent-based spread of the disease would account for the reduction in the arrival rate; in turn it would make the number of diagnosed patients a much more interesting performance measure because reducing the NDP means less people were infected in the first place. The way to most accurately model the rate of the spread would be through an agent-based simulation.

There is a need for enhanced diagnosis methods. Underdeveloped countries do not have the funding to invest in new technology. Hopefully, research and modeling can verify the potential of the technology. The first objective is to enable the collection of enhanced data to fill in the holes for the models. The ultimate goal is to have an effective enough model to entice the funding of these machines.

6 REFERENCES

Daniel, T. M. (2006, November). The History of Tuberculosis. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/16949809

Ghahari, A. (2017). Essays on Applications of Transportation Network Design and Optimization (Doctoral dissertation, University of Arkansas) [Abstract].

Glaziou, P., Sismanidis, C., Floyd, K., & Raviglione, M. (2015). Global epidemiology of tuberculosis. *Cold Spring Harbor perspectives in medicine*, *5*(2), a017798. doi:10.1101/cshperspect.a017798

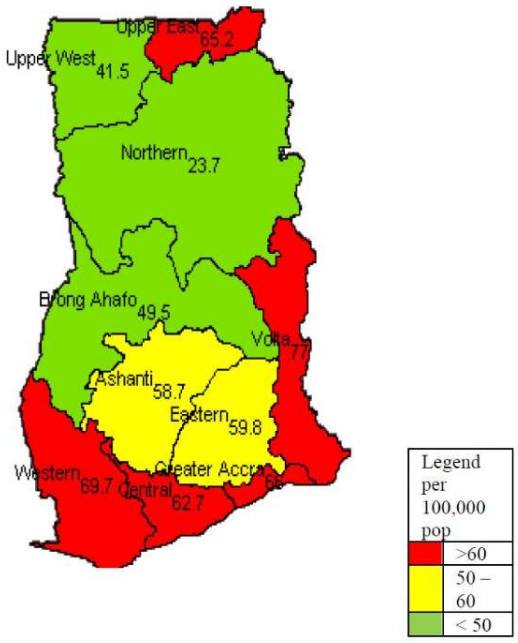
Nitika Pant Pai, Caroline Vadnais, Claudia Denkinger, Nora Engel, and Madhukar Pai. *Point-of-care testing for infectious diseases: diversity, complexity, and barriers in low-and middle-income countries.* PLoS Med, 9(9):e1001306, 2012.

Shama D Ahuja, David Ashkin, Monika Avendano, Rita Banerjee, Melissa Bauer,Jamie N Bayona, Mercedes C Becerra, Andrea Benedetti, Marcos Burgos, Rosella Centis, et al. *Multidrug resistant pulmonary tuberculosis treatment regimens and patient outcomes: an individual patient data meta-analysis of 9,153 patients.* PLoS Med,9(8):e1001300, 2012.

World Health Organization. *Global tuberculosis report 2016*. World Health Organization, 2016.

7 APPENDIX

The following is a user guide for the model developed in this research.



Step 1: Find required information about the country. The information includes the number of clinics in the region, the surface area, population, and diagnosed TB rate. In the case study, parts of Ghana, Africa were used; this information was found in the Global Tuberculosis Report from the World Health Organization.

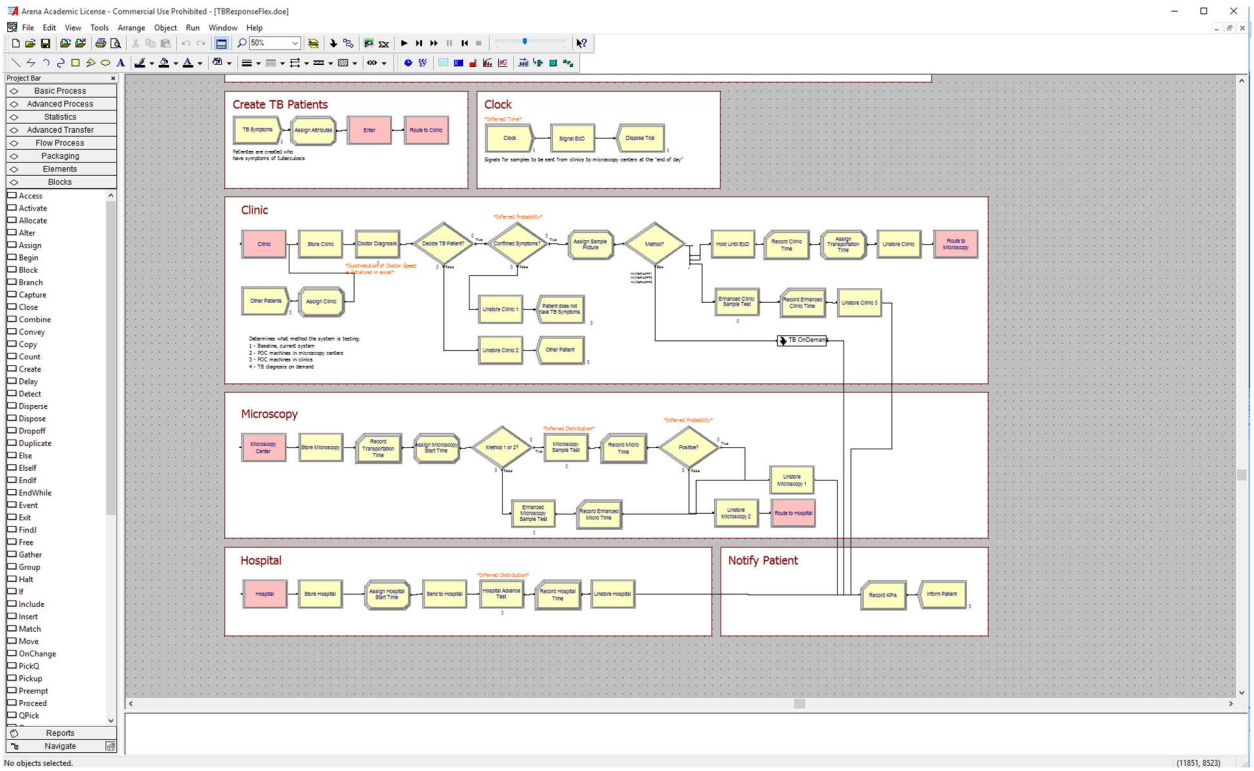
Simulation of Alternative Tuberculosis Diagnosis Methods
Excel Dashboard

Theoretical Country Information				**System Initialization**		
Surface Area	3245			Method	1	
Population	3909764			Incident Magnifier	5	
Theo. # Clinics	123			Doctor Speed	2	
Diagnosed TB Rate	66			Infrastructure	1	
	Boundry	56				
Clinic Information						
	X Location	Y Location	Percent Served	Micro Assignment	# of Doctors	# of POC
1	1	1	0.1	1	1	1
2	4	4	0.1	1	1	1
3	7	7	0.1	2	1	1
4	10	10	0.1	2	1	1
5	13	13	0.1	3	1	1
6	16	16	0.1	3	1	1
7	19	19	0.1	4	1	1
8	22	22	0.1	4	1	1
9	25	25	0.1	5	1	1
10	28	28	0.1	5	1	1
			1	*Must equal 1		
Microscopy Center Information						
	X Location	Y Location	# of POC			
1	1	28	1			
2	28	1	1			
3	16	13	1			
4	10	12	1			
5	3	20	1			

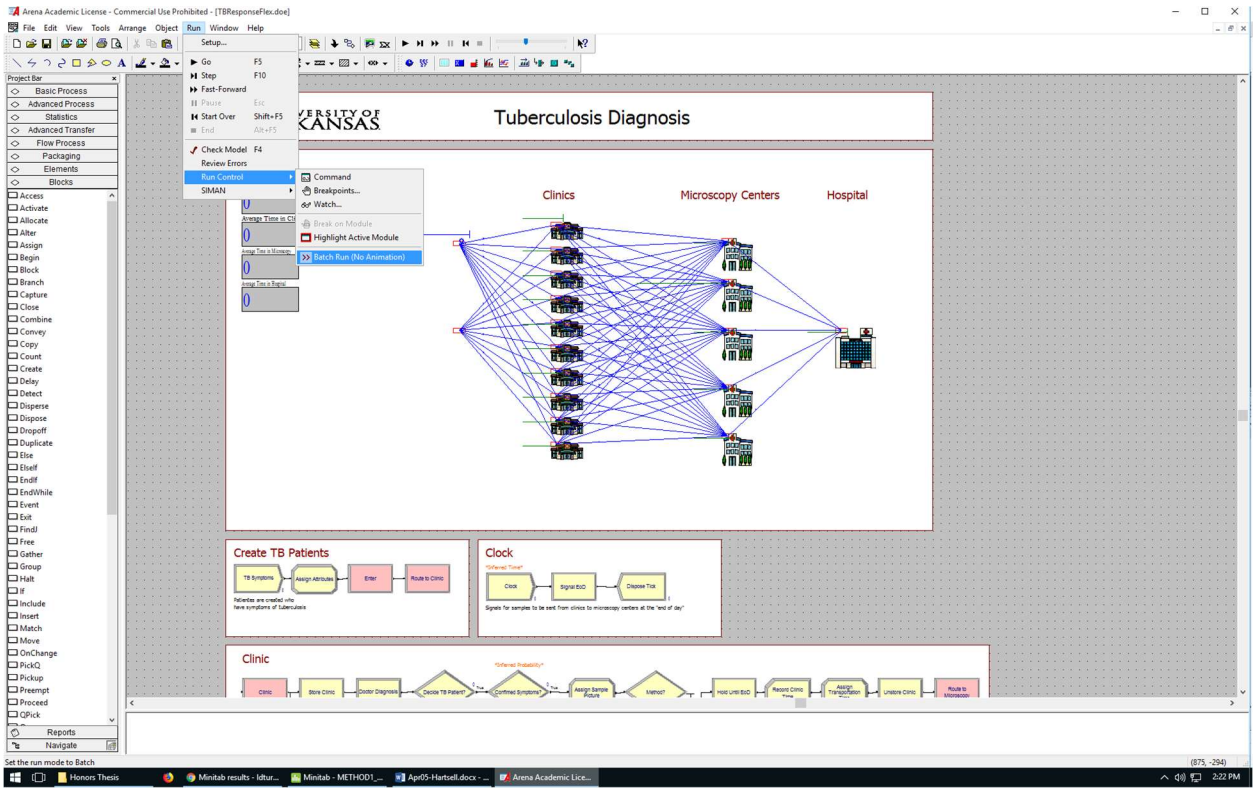
Step 2: Enter the found information into the Excel dashboard titled “TBResponse.xlsx”.

Step 3: Enter values for the system parameters being tested in the configuration. The information includes the method, incident magnifier, doctor speed, and travel speed. The doctor and travel speed are indexes (1 through 3) for slow, medium, and fast. The distributions are in expressions in the model.

Step 4: Enter the required information for each clinic and microscopy center. Each clinic needs and x and y coordinate (must be within the boundary), the percentage of the population the clinic serves (there will be an error if the total of the clinics do not serve 100% of the population), the microscopy center the clinic is assigned, the number of doctors at the clinic, and the number of POC machines at the clinic. Each microscopy center needs and x and y coordinate (also must be within the boundary), and the number of POC machines at the center.



Step 5: Open the file “TBResponseFlex.doe” to open the model in Arena. Press play and examine the results. The key performance indicators will be in the “User Specified” tab.



Step 6: To observe the model with animation, click Run -> Run Control -> Batch Run, then hit the same play button. The animation pane is above the modules.