

Demand Forecasting for Ebola Responses

by

Robert C. Rains III
B.A. in Business Administration

SUBMITTED TO THE PROGRAM IN SUPPLY CHAIN MANAGEMENT
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF
MASTER OF APPLIED SCIENCE IN SUPPLY CHAIN MANAGEMENT
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

JUNE 2019

© 2019 Robert C. Rains III. All rights reserved.

The authors hereby grant to MIT permission to reproduce and to distribute publicly paper and electronic copies of this capstone document in whole or in part in any medium now known or hereafter created.

Signature of Author: _____
Department of Supply Chain Management
May 10, 2019

Certified by: _____
Dr. Jarrod Goentzel
Executive Director, Supply Chain Management Residential Program
Capstone Advisor

Accepted by: _____
Dr. Yossi Sheffi
Director, Center for Transportation and Logistics
Elisha Gray II Professor of Engineering Systems
Professor, Civil and Environmental Engineering

Demand Forecasting for Ebola Responses

by

Robert C. Rains III

Submitted to the Program in Supply Chain Management
on May 10, 2019 in Partial Fulfillment of the
Requirements for the Degree of Master of Applied Science in Supply Chain Management

ABSTRACT:

The accelerating global trends of urbanization, interconnectivity, and population mobility are creating the conditions to increase the frequency, severity, and velocity of future outbreaks of high threat pathogens. Expeditionary interventional outbreak responses play a critical role in localizing instead of globalizing the devastation from these events. Outbreak responses are resource intense, logistically complicated, multi-disciplinary endeavors that require rapid deployment and implementation of highly specialized staff, structures, and systems. The complexity of an expeditionary interventional outbreak response contains numerous challenges for the supply chain management behind successfully implementing a response. The literature available on outbreak responses are primarily motivated and focused on the dynamics and spread of diseases rather than the operational management of response efforts. This capstone contributes to the field of public health security and humanitarian logistics by presenting a model for forecasting bed-capacity and consumable material requirements essential to response operations. The model in this paper follows the flow of patients from point of origin in the Ebola disease infected (Ebola-positive) and endemic disease infected populations (Ebola-negative) entering the Ebola isolation and treatment (EIT) network through discharge. By mapping patient flow as impacted by several metrics it provides an estimated census in the EIT network under various scenarios. This estimated census is then used as an independent variable to determine the dependent variables of bed-capacity and key material requirements. The analysis of the model's results demonstrates that Ebola-negative, rather than Ebola-positive, patients are the primary driver of capacity and service requirements for the EIT network. Furthermore, capacity and service requirements of isolating Ebola-negative patients can be substantially reduced by improving time between sample collection and testing for Ebola (diagnostic velocity). In conclusion recommendations are made for further research to solidify our knowledge of response dynamics to strengthen a holistic understanding of response operations to focus solutioning on the critical points of failure that can hinder response efforts. Improving operational methods and tools by identifying and quantifying these dynamics will improve future outbreak response and is necessary for humans to adapt faster than the emerging risks of infectious diseases.

Capstone Advisor: Dr. Jarrod Goentzel
Title: Director, MIT Humanitarian Response Lab

ACKNOWLEDGMENTS

I would like to thank Partners in Health (PIH), the Henry Jackson Foundation (HJF), and Pacific Architects and Engineers (PAE) for their past and continued efforts in responding to high-threat outbreaks in austere settings and providing me with the opportunity to support these important endeavors.

I would like to thank my capstone advisor, Dr. Jarrod Goentzel, for making the time amongst all the other important work that he and the MIT Humanitarian Response Lab support to provide guidance and direction a project that is very important to me personally.

TABLE OF CONTENTS

LIST OF FIGURES	5
LIST OF TABLES	5
1. INTRODUCTION	7
2. LITERATURE REVIEW	23
3. DATA AND METHODOLOGY	28
4. RESULTS AND ANALYSIS	44
5. DISCUSSION	51
6. CONCLUSION	53
REFERENCES	56
APPENDIX	59

LIST OF FIGURES

Figure 1: Basic Flow of Patient in an Outbreak Response

Figure 1.4-1: The EIT Network Model – Variables Considered in Results are Indicated in Grey

Figure 2-1: “Impact of Ebola control measures in Sierra Leone” Model Structure for determining impact of bed availability on reduced transmission

Figure 2-2: “Understanding the dynamics of Ebola epidemics” presents a model for how the Ebola virus spreads within the community.

Figure 2-3: “Responding to bioterrorist smallpox in San Antonio” provides a similar model of patient flow through a healthcare network as measured in patient days to determine capacity requirements for the response.

Figure 3.1-1: Overview of Patient Flow between the Endemic disease and Ebola population through the EIT network until discharge – Variables modified highlighted in Grey

Figure 3.1.1-1: Population of Ebola-Positive in Catchment Area by period

Figure 3.1.1-2: Population of Ebola-Negative in Catchment Area

Figure 3.1.2-1: Ebola-Positive and Ebola-Negative Combine to Create Flow Rate of New Suspect Cases Entering the EIT Network for each Time Period

Figure 3.1.3-1: Suspect Case Flow in the EIT for each Time Period

Figure 3.1.3-2: Confirmed Case Flow in the EIT for each Time Period

Figure 3.1.1-3: Suspect and Confirmed Flow of Patients Equals the EIT Patient Census

Figure 3.1.4-1: EIT Capacity Requirement is a Function of the Peak Patient Census Anticipated

Figure 3.1.4-2: Calculating Staff and PPE Requirements for Service Provision to EIT Patient Census

Figure 3.1.4-3: Transfer Teams are a Function of Admit and Discharge instead of Patient Census over Time

Figure 3.1.1-4: Total Number of Service Type Teams Equal the EIT Network Service Requirements

Figure 4-1: Cumulative Patient Days and Peak Census for each of the Scenarios

LIST OF TABLES

Table 3.3.3: Nominal Ebola Outbreak and Capture Rate Flow into EIT

Table 3.3.4: Malaria prevalence and adjustment for frequency of cases meeting case definition

Table 3.3.5: PLOS, CFR, and Diagnostic Velocity

Table 3.3.6: Types of Service Coverage by Frequency for Patient Type and Formulas for Calculating PPE Consumption

Table 4-1: Reduction in Capacity and Patient Days Through Improving Diagnostic Velocity

Table 4-2: Patient Days for Determining Service Requirements

Table 4-2: Ebola Positive Patient Flow and Days

Table 4.2-1: Ebola Negative Results for 100,000 Population

1. Introduction

Outbreaks of high-threat pathogens are human wildfires capable of radiating outward from a single spark in increasing intensity and distance as long as fuel and conditions are accessible. If containment efforts fail and conditions favor the disease, an outbreak of a highly-infectious deadly pathogen will bring a global conflagration as damaging to society as any widescale deployment of weapons of mass destruction. The accelerating global trends of urbanization, interconnectivity, and population mobility are creating the emergent conditions to increase the frequency, severity, and velocity of future outbreaks. Expeditionary interventional outbreak responses to high-threat pathogens are required to localize instead of globalize potential devastation. Outbreak response efforts are resource intense, logistically complicated, multi-disciplinary endeavors that require rapid deployment, mobilization, and implementation of highly specialized staff, structures, and systems. Improving operational methods and tools by identifying and quantifying the dynamics to improve future outbreak response is necessary for humans to adapt faster than the emerging risks of infectious diseases. Improving the capability to mount interventional outbreak response is as essential to the defense of global security as any anti-ballistic missile shield, cybersecurity protection, or chemical countermeasure.

This paper contributes to the field of public health security and humanitarian logistics by presenting a model for patient flow during Ebola responses to forecast capacity and service requirements during an outbreak. It follows the flow of patients from point of origin in the Ebola disease infected (Ebola-positive) and endemic disease infected populations (Ebola-negative) entering the Ebola isolation and treatment (EIT) network through discharge. This model demonstrates that Ebola-negative rather than Ebola-positive patients are the primary driver of capacity and service requirements in the EIT network once a tipping point in the endemic disease population is

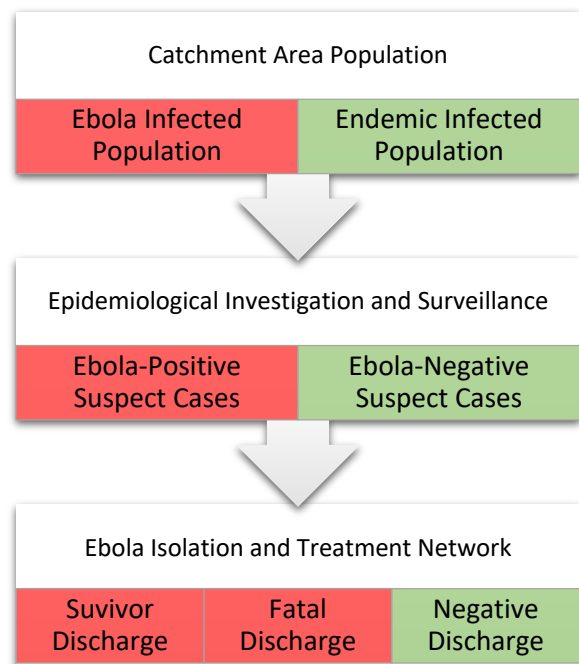


Figure 1: Basic Flow of Patient in an Outbreak Response

reached. Furthermore, capacity and service requirements of isolating Ebola-negative patients can be substantially reduced by improving time between sample collection and testing for Ebola (diagnostic velocity).

In this paper the EIT capacity and service requirements are forecasted using a model that consists of an Ebola and endemic disease afflicted population, epidemiological investigation and surveillance (EIS) efforts that results in capture rate, and the patient-length-of-stay(s) in the EIT network. The external variable is the population size the response has to target, i.e. the catchment area, in order to contain and localize the outbreak. The internal variable is the diagnostic velocity between sample collection and patient results.

This model is then used to vary the external, catchment area, and the internal, diagnostic velocity, to provide comparisons of the expected patient census and the corresponding capacity and service requirements necessary to accommodate in-patient provision of care. Comparing the scenarios where diagnostic velocity and catchment size are varied demonstrates that there is a tipping point where the primary driver of EIT capacity and service requirements switches from Ebola-positive to Ebola-negative patients. The significance of this finding is that the Ebola-negative population drawn from the endemic disease population is likely to be a more dominant factor in response planning the Ebola-positive patients produced from the actual Ebola outbreak.

The variability of the internal variable, diagnostic velocity, demonstrates that Ebola-positive patient EIT absorption is best mitigated by improving diagnostic velocity. These scenario comparisons show that as the catchment area increases, diagnostic velocity becomes an increasingly critical factor in sizing the isolation and treatment network infrastructure and service requirements. This is due to the Ebola-negative population functioning as the prime driver of capacity and service requirements for the EIT network and their PLOS being reduced in-line with increased speed in diagnostic turnaround time. The results in decreasing patient census by increasing diagnostic velocity supports the recommendation that as future outbreaks are likely to contend with increasingly larger catchment areas due to population growth and urbanization, optimization of diagnostic velocity will be key to ensuring successful responses. The following section will provide the motivation for this capstone, the local and general settings of outbreak response operations, and provide the supply-chain problem with a general overview of the model.

1.1 Motivation

The frequency and severity of infectious disease outbreaks from emerging pathogens is growing. The defining characteristics of the 21st century, namely globalization and urbanization, are driving forces behind this growing threat [1]. Globalization is creating a more mobile population, thereby increasing the radius a carrier can cover during a period of infectivity. Urbanization is creating higher-density populations, potentially inflating the rate of infectivity (R_0) for a disease. A disease's infectivity is based on the relation between its innate characteristics and the host environment. Without any change to its innate ability to survive and multiply, changes in the host environment can increase virulence. Tomorrow's global pandemic may not be from a new pathogen by way of mutation or spillover. It may instead be an existing disease held in check for centuries by the environment. Alterations in the human terrain of this environment, such as globalization and urbanization, can be the tipping point needed to provide an outbreak velocity and range to become a pandemic. Defensive measures like disease surveillance, vaccination campaigns, and overall public health initiatives are critically important in increasing containment efforts. However, these defensive measures do not replace the capability to effectively mount expeditionary clinical interventional responses which will continue to be required to localize outbreaks at their source through containment rather to prevent regional or global pandemics. This expeditionary clinical capability will be called into action with increasing frequency, duration, and scope based on our current growth trajectory.

Infectious diseases have likely claimed more lives than all wars, noninfectious diseases, and natural disasters taken together (Inhorn & Brown, 1990). On April 27, 2018 Bill Gates gave a lecture that built upon this theme when calling for better tools, early detection, and a global response system. Pointing to a specific example he highlighted that the 1918 influenza pandemic (a period of 36 months) killed possibly more than 50 million people. Supported by a model built by the Institute for Disease Modeling, he showed an animation demonstrating a similar outbreak today would kill nearly 33 million people in just six months. This lecture concluded with a list of public health efforts and interventions over the 20th and 21st that tackled the challenges of pandemic preparedness and response and emphasized "Somewhere in the history of these collective efforts is a roadmap to create a comprehensive pandemic preparedness and response system. We must

find it and follow it because lives – in numbers too great to comprehend – depend on it (Gates, 2018).”

The same forces of globalization that are bringing us into more frequent and closer contact with one another may also allow humans to adapt faster than emerging infectious diseases. Given the multi-faceted challenges infectious disease outbreaks present there is an increasing need to fuse together multi-disciplinary teams to solve complex problems. Infectious disease outbreak response is and will remain a multi-disciplined endeavor. During the Board on Health Sciences meeting in 2016 to discuss strengthening outbreak management and response systems, one of the key points made by participants was “the importance of the strategic plan being multisectoral, suggesting the integration of clinical care, public health capacity, logistics, information technology (IT), communications, transportation, leadership, traditional healers, NGOs, and civil society. (Board on Health Sciences Policy, 2016)” The same way known, or emerging pathogens, can be introduced from a previously unknown source, appear in a new context, or reach increased levels of virulence, new ideas and methods can come from unsuspecting places or find new applications in novel contexts. In the spirit multisectoral integration to support outbreak management and emergency response, this paper uses a holistic managerial analysis of Ebola response network dynamics that impact isolation and treatment of suspect patients to propose recommendations to improve infectious outbreak responses.

1.2 Local and General Setting

1.2.1 The Ebola Disease

Ebola Virus Disease (EVD), also known simply as Ebola, is a hemorrhagic fever is an infection that causes an acute and serious illness in humans. The case fatality rate (CFR) can range between 25-90%. Although there are five species of the virus, the most common in interventional outbreak response, including the 2014-16 West Africa outbreak and 2018-Ongoing North Kivu, DRC outbreak, is the Zaire Ebola virus species. The Zaire species also has the highest CFR when untreated among the current identified species. There have been 28 outbreaks since Ebola Virus Disease was discovered in 1976, 18 of which the result of the Zaire species (WHO, 2018). While the 2014-16 West Africa outbreak is considered to be the first “urban” outbreak, the 2018 Equateur province Ebola outbreak, and the 2018 Kivu Ebola outbreak have also extended to urban centers. Ebola outbreaks in urban areas are likely to become the new norm as both global and sub-Saharan African experience ever-increasing trends in urbanization, encroachment on natural habitats, and population mobility (Neiderud, 2015).

The virulence of a disease, in this case Ebola, is its R_0 (pronounced r-naught). The R_0 is the reproduction factor for a disease, or rather, how many additional persons are infected by each person carrying the disease. The R_0 factor is a function of both the virus’s potential for spread and the host environment. Population behavior, density, hygiene, sanitation, and external intervention can all amplify or dampen the R_0 factor. These changes in the host environment results in the R_0 changing over time. An $R_0 > 1$ results in an increasing transmission chain while conversely an $R_0 < 1$ results in a decreasing transmission chain of the infected population. The changing R_0 of new cases is what forms the epidemiological curve in most outbreaks. The number of new cases per time period will exponentially as a function of R_0 when the factor is greater than 1, peaks when R_0 equals 1, and trends downward when $R_0 < 1$.

1.2.2 The Ebola Response

An interventional Ebola outbreak response consists of many sets of activities, called pillars or hubs, whose implementation consists of multiple layers involving international agencies, national and local government, and non-governmental organizations (NGOs). It is a complex endeavor as demonstrated by the 2018 Equateur Outbreak Strategic Response Plan that lists 9 technical

commissions: Multi-sectoral coordination; Surveillance, active case finding, contact tracing and investigation of cases (later referred to as Epidemiological Investigation and Surveillance); laboratory diagnostics; case management (later referred to as Isolation and Treatment Network); infection prevention control (IPC); Risk Communication and social mobilization; psychosocial care; immunization and research; and health system support (Reliefweb, 2018) Each of these activities complement each other and enhance the effectiveness of the response. Epidemiological investigation and surveillance (EIS) is the set of activities that are responsible for identifying suspect patients that will enter the EIT network. The removal of suspect cases from the at-risk population is a critical factor in halting transmission in the community and health facilities. The more effective the EIS is at this function the number of possible transmissions from infected persons are reduced. Laboratory diagnostics are important for delivering the results from suspect patients and play a critical role in determining the patient-length-of-stay (PLOS) for Ebola-negative patients. Case management is the in-patient services provided by the Ebola Isolation and Treatment (EIT) network. This is the network that physically absorbs suspect and confirmed patients and provides in-patient services. The quality of care is important in determining the case fatality rate (CFR) and the PLOS for survivor and fatal outcomes of the Ebola-positive population that is isolated and treated within the network. Risk communication and social mobilization, psychosocial care, immunization and research, and health system support can have important impact on the spread of the disease and improving the efficacy of other activities but are not directly included in the model presented in this paper.

Epidemiological Investigation and Surveillance: Surveillance is the monitoring of the catchment area - the entire at-risk population as determined by the response strategy. Screening is conducted at Points of Entry/Exit for the catchment area where all people passing through screening have their temperature checked and may be required to be interviewed verbally or by written form. Any persons who meet case definition are held or identified with an alert being passed to the relevant appointed entities responsible for the alert system for follow-up interviews and potential subsequent follow-on isolation and/or admission to the Ebola treatment network. The same screening will be mobilized at public facilities (schools, government facilities, and healthcare facilities) as well as consenting private facilities (religious institutions, community gathering locations, businesses); although private facilities may be required to comply via fiat from the relevant government authorities. Contact tracing is performed on probable and confirmed

cases in order to identify likely future cases by tracing the contacts that one of these cases may have had during an infectious period (demonstrating symptoms of the disease). Active case-finding can occur in some instances which involves teams canvassing an entire population of a geographic area going door-to-door to interview and identify possible cases both linked and unlinked to known or probable cases. The mobilization of EIS occurs over a significant period of time as training and logistics are considerable and require guidance and monitoring from the relevant response coordinators and leadership.

One of the problems with Ebola, and many other infectious diseases, is that symptoms are similar to many other diseases. This results in both Ebola-positive and Ebola-negative suspects being scooped up by EIS activities. Given the deadly nature of the disease it is critical to identify and isolate suspect and probable cases as early as possible which is why case identification will err on the side of safety to mitigate preventable transmissions from occurring.

The Case Definition: In order to meet suspect case definition the patient will have to fall into one or more of the following category descriptions: 1) Illness with sudden onset of high fever and had contact with a person suspected, probable, or confirmed for EVD or with a dead or sick animal; 2) Sudden onset of high fever and at least 3 of the following symptoms: headache, vomiting, anorexia, diarrhea, lethargy, stomach pain, aching muscles or joints, difficulty swallowing, breathing difficulties, or hiccuping; 3) Have had unexplained bleeding. In order to meet Probable Case definition the patient will have to have been evaluated by a clinician (criteria above) and have an epidemiologic link to a confirmed case (WHO, 2014).

Although there are many diseases that can result in the exhibition of symptoms for Ebola endemic areas the most prominent, and problematic, is malaria. “Diagnosis of hemorrhagic fevers, such as EVD and LF, is challenged by the fact that the presenting syndrome is very nonspecific with a broad differential diagnosis. malaria, typhoid fever, yellow fever, leptospirosis, meningococemia, Rickettsial infections, bacterial sepsis, and many other illnesses can all be confused with VHF in the early stages of disease presentation. Even an experienced clinician may have difficulty distinguishing EVD or LF from each other in the early stages and may misdiagnose the disease on clinical grounds as a common febrile illness (Boisen, Schieffelin, et al., 2015).

Contact Tracing: Surveillance and contact tracing are the monitoring and epidemiological investigation dedicated to identification and mapping the spread of EVD as well as investigating

environmental factors that may increase or decrease the spread of the disease. Although responses vary in their pillar assignment the following generic list of activities will typically fall under this category: Point of Entry Screening; Alert System; Contact Tracing; Case Investigation (Passive and Active). Staff assigned to this function will be highly integrated, if not responsible for, in the collection of samples and receiving of lab results.

The activities under this pillar fuse together to create a shared picture of high-risk contacts and suspect/probable/confirmed cases communicated through the use of database(s). Although there will be a high volume of valuable supporting information, the primary product of these efforts is the development of the “line listing” that follows and attempts to get-ahead of EVD transmission chains. A common metric for success in this effort is the rate of confirmed cases that are previously identified in a line listing. The higher the percentage of confirmed cases coming from this listing is an indicator of accuracy in assessing the current size and trend-lines of the current outbreak.

POE Screening: Point of Entry Screening is the activity that is conducted at points of embarkation/disembarkation for population within the affected or at-risk areas. Staff will be positioned at these points to conduct basic screening through visual examination, temperature checking, and utilization of a questionnaire regarding the traveler’s recent history and health status. These points will likely also be supported with basic IPC activity in the form of hand-washing stations with their use being enforced by staff tasked with conducting screening activities. Screening at points of entry may or may not be mandatory based on the protocol being observed within a particular outbreak.

Management responsible for supporting PoE screening will collect information relating to the number of people screened, number who have refused screening (if applicable), and potentially combining personal information regarding location and duration of stay for possible follow-up (this is much more common and easily accomplished at international PoE as collection of this information is already part of established protocol).

Alert System: An alert system is the method(s) that the response employs for information collection from external parties or the community. The quickest and easiest method is to establish a calling center with staff dedicated to fielding phone calls from the community or external parties. Staff who are assigned to monitor the phone lines should have relevant training to harmonize their

process of collecting information as well as have a working knowledge of what information should be provided to callers. An information capture system should be utilized to make sure that alerts received through the phone line are uniformly documented and able to be fed into the existing information collection systems that have been established to support surveillance activities.

The Ebola Isolation and Treatment (EIT) Network

Diagnostic Testing: The prevailing factor determining the flow between suspect and confirmed is the turn-around time of lab testing. The faster the turn-around time for lab testing the quicker confirmed and negative patients can be separated via transfer or discharge and reduce the chances of nosocomial infections. Both moral and operational imperatives place sample collection and processing as a high priority for activities conducted at the ETC. Lab turn-around time is the principle key performance indicator that determines the patient flow through the suspect ward.

Ebola Treatment Center: Ebola Treatment Centers are the focal point of the Ebola Treatment Network and can range in size from a couple dozen beds to in the hundreds depending on the severity and maturity of the response. The patient area is bifurcated into two sections green and red zones. Red zones are where the patients are treated while green zone is where support functions for ETC activity occur and strict IPC decontamination measures are adhered to. The red zone is further split between suspect and confirmed wards. Each ward has patient beds and bathroom/shower facilities to effectively house the patient population. There may be dedicated or shared discharge points for patients to be discharged from the wards. Patients will enter the facility through triage and most initially flow into the suspect ward to await lab confirmation for Ebola and receive initial care. Some patients may be referred to the unit already as lab-confirmed cases and immediately admitted to the confirmed ward. Staff entering the unit do so by entering a “donning” station where they don PPE and are inspected by support staff before entering. Upon entering the “hot-zone” (area for high risk of infection) they observe a one-way flow to support IPC for personal and patient safety and exit through a “doffing station”. At the doffing station they remove PPE under the supervision of support staff in a carefully choreographed manner to prevent infection and prevent contamination of the “green-zone” where staff work and prepare for ETC activities. The patient flow and the staff activity of ETC’s is the primary focus of this paper and is explored more fully in the following section.

The strategic intent of the ETC is pretty straightforward; provide clinical care to Ebola patients in order to produce as many positive outcomes as possible. Indirectly however, there is a knock-on strategic impact for the entire response. Having the ability to reduce patient mortality rates from Ebola strengthens the entire response. It encourages the affected population to seek treatment and preferably early increasing the ability to remove infectious people from the community. The ability to effectively combat the mortality rate provides confidence in the response and reinforces the belief in the community that responders have the tools, knowledge, and capability to resolve the outbreak. This confidence in the response can reinforce the social mobilization messaging and further enhance behavior modification efforts.

With few exceptions, ETCs are built in response to outbreaks. This means that they are likely to be constructed of temporary or semi-permanent structures that can be rapidly erected and supplied with power and water. Alternatively, sometimes abandoned or unfinished structures within the affected area can be repurposed as functional ETCs. They require significant amounts of barriers both within and around the facility in order to control access and flow of patients and staff in support of IPC protocols. Chokepoints for staff flow will be utilized throughout and coupled with decontamination WASH stations and personnel who enforce and support IPC protocol at all the multiple points throughout the ETC. The entire facility will require a robust chlorinated water mixing station and distribution system or plan in order to keep these decontamination points stocked with the necessary and variable water-chlorine mixtures (.5, .05, and sometimes .01). Power supply is also essential in order to support both the work activity and lightning which becomes a critical safety issue for red-zone staff activity at night. Internet connectivity is often a strong prerequisite to support ETC operations as well. Lastly both the green and red zones need to be relatively self-contained in terms of life support to house the patients and staff (bathrooms, showers, eating, etc.). In some cases, a “blue-zone” may additionally be attached to the ETC to house staff during off-hours if accommodations are not available. There are certain preferences for ETC infrastructure that have been adopted in response to previous experiences. There is a preference for external visibility into the interior of the unit despite the multiple barriers in use in order to combat rumors that can surround Ebola responses in the communities involving nefarious activities taking place in the ETC. Providing visibility into operations for the community can reduce the effects of these rumors. Patient visitors can further erode this and can provide much

needed support to patients and will require some level of safe access for visitors to see and speak with their admitted family and friends.

Case Fatality Rate: This means that the patients are grouped into two categories; survivor and deceased. Patient census metrics based on clinical protocols should be able to provide the mortality rate for determining the proportion of confirmed patients that will fall into either category. The flow for survivors and deceased are therefore based on the mortality rate with the average length of stay for a survivor or deceased minus time spent in the suspect ward calculated separately.

EIT Patient Flow (Negative, Survivor, Fatal)

Collection is the actual drawing of the blood sample from the suspect patient for the purposes of conducting diagnostic testing. This can occur during the patient transfer, upon admission, and during normal clinical rounds after admission. In silo optimization when faced with uncertain demand the collection will occur at lengthy periodic intervals in order to reduce the amount of effort and resources required to accomplish the task. This results in batching. On collection the easiest way to pick up economy of scale is to wait until enough suspects have been aggregated so that one team can collect samples from as many patients as possible. In its most extreme case this would probably result in one blood draw a day from the patient census in the Ebola treatment network. Effectively batching all of these into a single run for the day and using as few resources and staff as possible to accomplish the task. However, there is additional lead-time associated with this process as the patient will have to have already been transported themselves and admitted to the isolation unit.

Admission—Patients will enter the Ebola healthcare network after meeting suspected case definition as determined by an interview or case review by qualified medical personnel at triage stations or on surveillance and case-investigation teams. In most instances samples for diagnostic testing will be collected at this point.

Discharge—All patient admits are classified as suspect cases until lab confirmation is completed. A suspect case receiving a negative laboratory testing will exit the network immediately from a suspect or isolation ward. Expediency of discharge suspects negative for Ebola are critical in preventing nosocomial infections incurred by comingling Ebola-negative patients in holding or isolation centers where they are at increased risk of Ebola infections from Ebola-positive patients.

Suspects positive for Ebola become classified as confirmed. Confirmed cases will be separated from suspects by transfer to a confirmed ward. Discharge of confirmed cases occurs either when a patient has a fatal outcome or becomes asymptomatic and receives two negative tests – classified as a survivor. Once a patient enters the Ebola treatment network there are only three ways to be discharged or exit the network: Ebola-negative discharge, Ebola-positive fatal discharge, and Ebola-positive survivor discharge. An Ebola-negative discharge occurs when a suspect patient is provided with confirmation from diagnostics that they are negative for the disease. Ebola-negative patients are discharged via a decontamination process from the suspect ward and released back to the community or transferred to a medical facility. An Ebola-positive discharge occurs when a patient has tested positive for Ebola but has recovered from the disease and will be discharged as a survivor. The discharge process follows a similar decontamination process as the Ebola-positive survivor discharge in order to prevent contamination from inside the facility exiting during the discharge process. An Ebola-positive fatal discharge occurs when a patient that has been tested positive for Ebola dies inside the isolation and treatment facility. The discharge process for Ebola-positive fatal cases involves moving the body for the morgue where a safe burial team will retrieve the body and bury and dispose of it in accordance with the current protocols in place for the response. Instances where patients voluntarily exit the network, or are ‘liberated’ by community members, have occurred but are infrequent and statistically anomalous; as such they are not included in the model.

1.4 The Supply-Chain Problem

Planning and preparing for expeditionary interventional outbreak responses are a complicated endeavor where success is critical. The provision of care in the EIT network is critically important in supporting a successful intervention. If the EIT network does not possess the absorptive capacity to admit and treat Ebola suspect and confirmed patients, they may be turned-away or receive insufficient care, i.e. service failure. Suspect cases refused admittance may remain in the community continuing the spread of infection. Insufficient care in the EIT can increase the case fatality rate, increase nosocomial infections, and deter future admissions.

In order to prevent the adverse outcomes of admittance refusal and service failures, it is critically important that the EIT network has sufficient bed-capacity, materials, and staff. While the physical and social environmental context of each outbreak will vary there are important dynamics within response operations that can greatly influence implementation and successful outcomes. This paper presents a model as a framework to establish bed-capacity, materials, and staff necessary for supporting an EIT network in order to mitigate the challenges of admittance refusals and service failures. Furthermore, we use the model to demonstrate that diagnostic velocity functions as a force multiplier of the EIT network as catchment area size increases.

The model presented broadly maps the movement of patients from the outbreak at-risk population and their flow through the EIT network through discharge. We establish the patient population as coming from two sources, those infected with Ebola and those suffering endemic diseases that still meet case definition for EIT admission. The rate of flow between these populations and the EIT network is dependent on the efficacy of the Epidemiological Investigation and Surveillance (EIS) team to identify suspect cases from these two populations to EIT facilities. All patients admitted to the EIT network are suspect cases who undergo diagnostic testing. Those who are negative for Ebola are discharged immediately. Those who are positive are discharged as survivors or deceased

based on the case fatality rate (CFR) for the EIT network. The model is completed by analyzing the patient volume in the EIT over time in order to determine what capacity and service requirements are needed to support the EIT. Treatment and EIT support activity are incremental based on standard operating procedures that are directly divisible by the census and rounded up to the nearest increment.

The Input (Suspect Cases):

The size of the at-risk population targeted by the outbreak response is the catchment area. Patients entering the EIT network will originate from one of two populations within the catchment area. First are those who are infected and presenting symptoms of Ebola. The size of this population is based on the rate of infectivity (R_0) over time and after entering the EIT network will form the Ebola-positive patient flow. This population will grow over time unchecked if conditions remain unchanged. The epi-curve of an outbreak is the ability of the response to halt the transmission of the outbreak through a combination of isolation of suspect patients, social mobilization to encourage behavior modification, and improvement in infection prevention control (IPC) at health and public facilities. Second are those suffering from endemic diseases capable of meeting Ebola suspect case definition. Patients from this population will represent the total potential of the Ebola-negative flow in the EIT network.

The patient flowrate into the EIT network is based on the efficacy of the EIS team in identifying suspects meeting Ebola case definition within the catchment area. The EIS team is responsible for contact-tracing, screening, active case-finding, and responding to alerts in a concerted effort to identify suspect patients throughout the catchment area that meet case definition. The combined efficacy of their activities begins in earnest early in a response and grows over time. This is a result of both the mobilization of their activities and community acceptance requiring a period of

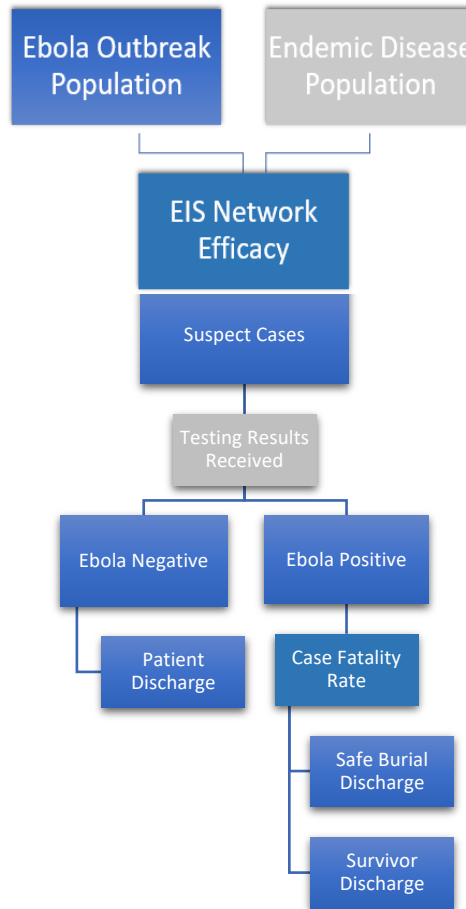


Figure 1.4-1: The EIT Network Model – Variables Considered in Results are Indicated in Grey

time to become fully operational and/or accepted by the communities in the catchment area. Since these activities occur within a constrained population area there is also a diminishing rate of increase in capture rate as the activities saturate the catchment area. This results in the efficacy rate resembling an s-curve where the y-axis represents number of successful outcomes in identification and referral across the x-axis time period.

The relationship between the Ebola and endemic disease population and the EIS team efficacy results in the suspect patient flowrate into the EIT network. In the population of potential Ebola-negatives being directly proportional to the catchment area size; while their flow into the EIT is based on the EIS capture rate. Increasing the size of the catchment area and improving EIS efficacy will create a larger endemic disease afflicted population and larger volume of flow of these patients into the EIT. The volume of Ebola-negative patients flowing into EIT is a function of the catchment area size and the capture rate of the epidemiological investigation and surveillance (EIS) team.

EIT Network Cycle Rate:

Not all patients who enter the Ebola Isolation and Treatment (EIT) network have Ebola. This is the reason the term “suspect” is applied to the admit population until they receive diagnostic confirmation for the presence of Ebola (Brett-Major, et al., 2015). Suspects who are negative for Ebola (Ebola-negative) are present in EIT only for the time between sample collection and testing results i.e. diagnostic velocity. Slowing diagnostic velocity will increase the patient length-of-stay (PLOS) for Ebola-negative patients. While the inverse, increasing diagnostic velocity will decrease PLOS for Ebola-negative patients. Increasing Ebola-negative PLOS increases their saturation of the EIT network, driving up its capacity and service requirements.

Patients who are Ebola-positive will exit the EIT network as either a survivor or a fatal case. The split between these two populations is called the case fatality rate (CFR). This is an important rate in determining the patient census in an EIT network as survivors tend to stay inside the EIT for significantly more time than fatal cases.

Ebola-negative patients can only exit the EIT based on the diagnostic velocity of the response. A mismatch of EIS and diagnostic velocity can quickly create a backlog of Ebola-negative patients in the EIT network that swamps the system. If the EIT network does not have the bed-capacity

and resources to handle this patient census, then isolation and treatment for the Ebola outbreak incurs service failures. Capacity service failure results in refusing admits and turning away patients from the network. Service failures due to a lack of resources results in being unable to provide effective treatment due to lack of supplies, staff, and support activity. Both have serious consequences for the overall response. A capacity service failure results in the inability to bring suspect patients into isolation and they may remain in the community or health facility poses a risk of transmission. A service failure results in a work stoppage at worst and degraded in-patient service at best. Degraded in-patient service will produce worse health outcomes and bad in-patient services. A complete work stoppage results in patients not being able to enter or exit the network or receive basic support as meal delivery and physical assistance. All of these adverse effects have the additional adverse impact of degrading the perceived efficacy and trust within the at-risk population whose cooperation and acceptance are necessary to end the outbreak including the promotion of health seeking behavior to fulfill the objective of halting the risk period for transmission of the disease.

Diagnostic velocity during the 2014 West Africa could be prolonged, several days or more, due to a variety of reasons. Processes and procedures for sample collection, transportation, and lack of sufficient proper materials were contributing factors (Broadhurst, Brooks, & Pollock, 2016).

2. Literature Review

There has been substantial research and writing that has been done on the subject of the Ebola disease. However, the majority of the literature revolves around specific fields relating to pieces of dealing with an Ebola outbreak and the associated response. This presented a significant challenge as the intent of this paper is to present a model that crosses several of these fields to demonstrate the interaction between different elements and their associated impact on the service requirements and bed-capacity that is required for supporting the Ebola Isolation and Treatment (EIT) network. The literature review selections included in this section look at the classical model of Ebola transmission that underpins the intent of the entirety of the response if not holistic in their approach individually.

“Impact of Ebola control measures in Sierra Leone” Adam J. Kucharski, Anton Camacho, Stefan Flasche, Rebecca E. Glover, W. John Edmunds, Sebastian Funk PNAS November 17, 2015 112 (46) 14366-14371

In comparison to other Ebola outbreak responses, the 2014 West Africa outbreak involved a massive international coalition consisting of dozens of agencies and numerous implementing partners establishing Ebola Treatment Centers (ETCs), Community Care Centers (CCCs), and triage and isolation (T&I) centers at health facilities. This was part of a concerted effort to isolate enough of the Ebola infected population

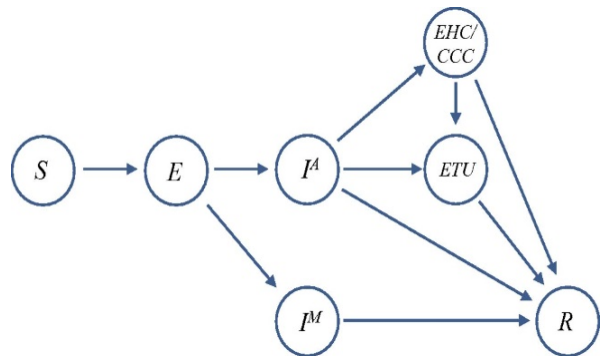


Figure 2-1: “Impact of Ebola control measures in Sierra Leone” Model Structure for determining impact of bed availability on reduced transmission

to lower the transmission reproductive rate below 1 to slow and stop the outbreak. This strategy hinged on creating enough bed-space separate from health facilities in order to provide this isolation function. Given the scale of the outbreak in West Africa the solution was a massive campaign to build the Ebola Isolation and Treatment network (ETCs, CCCs, T&I) from the ground up. The capacity of this EIT network was based on numerous, often conflicting, predictions on the trajectory of the Ebola outbreak.

At the end of the outbreak much of the infrastructure for the West Africa region’s EIT network had been underutilized with many of the isolation and treatment centers never admitting a single

patient. This prompted a frequent criticism regarding the predictions and methodology utilized in determining the capacity of the EIT network. This journal article provides an estimate to how many additional cases of Ebola were likely to have been prevented in Sierra Leone due to the availability of additional bed-capacity during the outbreak response. The specific findings were that an “estimated 56,600 Ebola cases were averted up to February 2, 2015 as a direct result of additional treatment beds being introduced.” This is based on a model of isolation availability and efficacy driving Ebola cases towards the EIT network and reducing the time period of transmission in the community from isolated cases.

This article underscored the importance of bed capacity in the EIT network in Ebola responses which supports the aim of this paper in providing a framework to determine EIT capacity requirements. It also includes the role of Ebola-negative cases in absorbing available capacity in the EIT network. It cites the impact of capacity failure in turning patients away from the EIT network and the associated increase in the risk of infectivity in the community. It effectively looks at the damping of the epi-curve that occurred due to the bed availability and removes that effect to determine what the Ebola positive population would have potentially been had isolation not occurred during the time period evaluated.

The model uses a 50% allocation of bed capacity as being occupied by Ebola-negative cases as derived from Sierra Leone Ministry of Health situation reports. This is effectively a plug number that acknowledges the role of Ebola-negative cases in diminishing the absorptive capacity of the EIT network. However, the level-set nature of this number does not provide an estimated impact of what a variation in the Ebola-negative population in the EIT would incur significant additional challenges to the provision of in-patient services. In comparison, this paper looks to provide an input for Ebola-negative cases into the EIT as a function of the rate of endemic diseases capable of meeting case definition for Ebola multiplied by the catchment area size the EIT is supporting. By varying the impact of this dynamic in determining the capacity and service requirements it demonstrates where the role of the Ebola-negative population in the EIT network can have dramatic effects in the capacity requirements and the service requirements. The model in this paper also goes a step further in providing a formula for extrapolating what the personal-protective-equipment (PPE) necessary would be based on the service requirements.

Understanding the dynamics of Ebola epidemics. *Epidemiology and infection*, Legrand, J., Grais, R. F., Boelle, P. Y., Valleron, A. J., & Flahault, A. (2006). 135(4), 610–621. doi:10.1017/S0950268806007217

This paper pre-dated the 2014 West Africa outbreak and informed most of the decision making behind the design and scale of the response. This article was a commonly cited research paper in

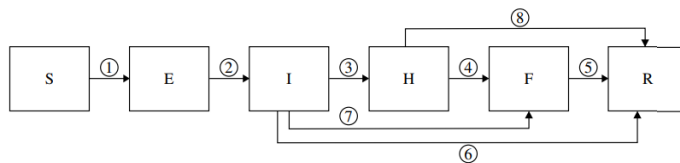


Figure 2-2: “Understanding the dynamics of Ebola epidemics” presents a model for how the Ebola virus spreads within the community.

many of the policy papers at the onset of the outbreak that were making recommendations of the required size and unit capacity for the isolation and treatment network to contain the 2014 West Africa outbreak. The model presented in this paper and the importance of removing suspected cases from the at-risk population is arguably the largest driver in the rationalization of isolating Ebola suspect patients to halt the flow of transmissions occurring in the community. This is what caused the response to focus on isolating patients suspected of Ebola since it quantified the risk of subsequent infections with the time period that they were allowed to remain in the community and the role of burials in spreading the disease. It shows the flow from the susceptible population, through the exposed, to infected, then provides the outcomes – including the bypassing of the treatment unit. By applying differential equations to the arcs and nodes within the compartmental model this model can be used to estimate the potential dynamics of the response when provided accurate and timely data to complete the equations. Specifically, this demonstrates that a tipping point exists between the population outside of treatment (H) that will impact the rate of infectivity to equal greater or less than 1 which indicates whether the exposed and infected populations are growing or decreasing in size.

This paper focuses primarily on modeling the outbreak population growth and decline. However, it does not cover or accommodate for the role in Ebola negative cases and its associated impact on reducing the population that would exist in treatment (H). This model was used to understand the dynamics at play in the spread of the disease. This paper attempts to determine bed-capacity and service requirements by incorporating both populations (Ebola negative and positive) in determining the patient census in the EIT network and the derived capacity and service requirements.

Multiple circulating infections can mimic the early stages of viral hemorrhagic fevers and possible human exposure to filoviruses in Sierra Leone prior to the 2014 outbreak. Boisen, M. L., Schieffelin, et al., Viral Hemorrhagic Fever Consortium (2015). *Viral immunology*, 28(1), 19-31.

This journal article provides documentation relating to the challenge of identifying Ebola from non-Ebola infections during a response. This identification is important because it demonstrates that there is not training that can provide clarity on Ebola diagnosis without lab confirmation. The inability to provide diagnosis short of lab confirmation demonstrates that there will be a continued presence of Ebola-negatives in the EIT network in future responses. Assuming that there is not subsequent breakthroughs on point-of-care diagnostics or similar methodology that will replace the case definition process for identifying and referring suspect patients to isolation.

Responding to bioterrorist smallpox in San Antonio. Miller, G., Randolph, S., Patterson, J., 2006. *Interfaces* 36, 580–590

This journal article provides a model for determining the bed capacity required for treating victims of a nominal smallpox attack in the San Antonio area. The authors use the estimated affected population and patient-length-of-stay to determine what the bed-capacity requirement would be to effectively provide in-patient care. Their model uses a very similar branching mechanism used in this paper’s model in allocating patient flow by type and their associated PLOS while in the healthcare network. The Miller

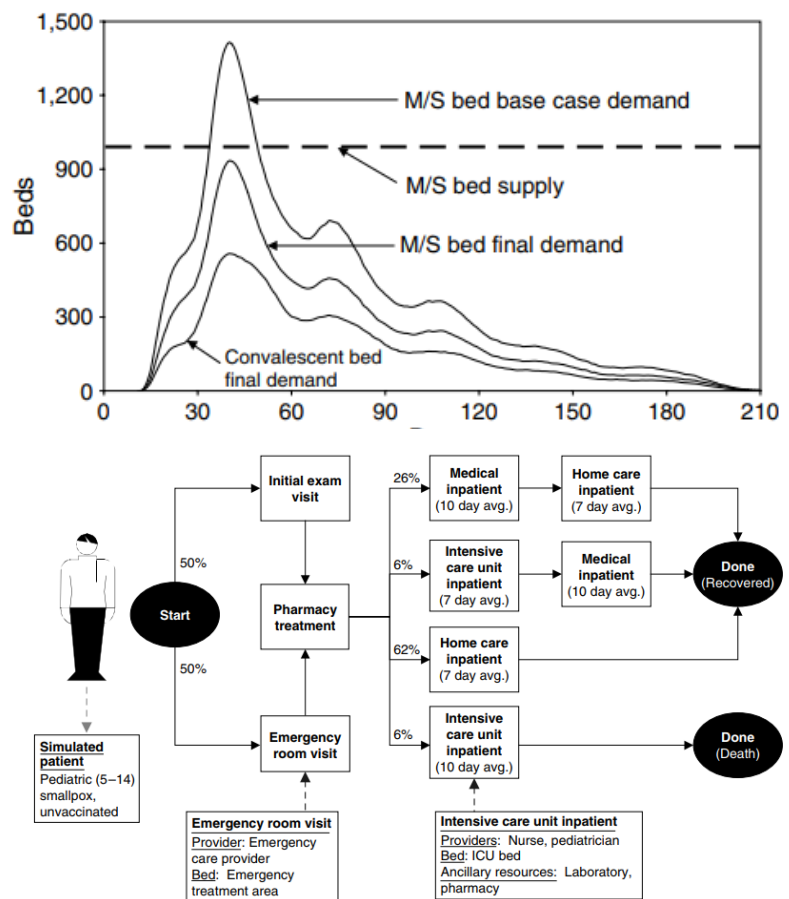


Figure 2-3: “Responding to bioterrorist smallpox in San Antonio” provides a similar model of patient flow through a healthcare network as measured in patient days to determine capacity requirements for the response.

paper looks at the likely point of entry and subsequent steps the patient will take in receiving treatment while providing a time period for each step in the process. This paper uses branching based on the diagnostic outcomes of the endemic disease and Ebola positive population to determine their type. PLOS is based on type of patient they are classified as and assigns a value based on historical data; in this case from Sierra Leone reporting on average length of patient stay.

The aggregate of flow and PLOS is what allows the Miller paper to calculate the bed-space that would be required. This method also provides them with the total patient days that would be required during the response which provides a basis for determining the staff and material requirements that would go into the response. Miller follows the same methodology of calculating patient days in order to determine patient census over time. However, this paper also uses a nominal clinical protocol for the service requirements in order to determine the number of staff and their frequency in entering the red zone to provide services. These figures are then able to be applied to determine the volume of consumable material that is required for each of these trips which provides a forecast for material requirements necessary for the outbreak response scenario.

The last difference between the model presented in the Miller paper and the one presented in Section 2 is inclusion of the intake from non-infected persons that are pulled into in-patient care from the endemic disease population. This Ebola-negative population is due to the limitations of case definition providing a broad capture of both positive and negative Ebola cases. The Miller paper did not have to contend with the isolation and treatment for patients that are not suffering from the nominal smallpox attack in San Antonio under there scenarios. Additionally, the model presented in this paper also has an additional component that provides the epidemiological surveillance and investigation function providing an increasing flowrate of patients over time as this function mobilizes and increases its efficacy. Again, this is due to the circulating nature of a viral outbreak rather than the sudden but singular incidence of a chemical weapons attack as provided in the Miller paper.

3. Methodology

3.1 Overview

The objective of the model is to forecast resource requirements for a nominal Ebola outbreak scenario. The model consists of the flow Ebola-positive and Ebola-negative patients will take through the EIT network, beginning at identification in the catchment area and ending with discharge. The rate of admission and their associated patient-length-of-stay (PLOS) in the EIT network will determine the patient census. The patient census over time is what drives the capacity and service requirements required for isolation and treatment.

All Ebola-positive and Ebola-negative patients pulled from the catchment area will enter the EIT network as suspect cases. The catchment area size is the total population classified as at risk from the Ebola outbreak. The Ebola-positive population in the catchment area increases and decreases as a function of the infection rate of reproduction referred to as the R_0 . The Ebola-negative population is determined by the prevalence of endemic diseases and frequency of their symptoms ability to meet the case definition for Ebola.

The epidemiological investigation and surveillance (EIS) network are responsible for identifying and capturing Ebola suspect cases in the catchment area based on case definition. As EIS efficacy increases over time, an increasing number of Ebola-positive and Ebola-negative suspect cases from both the Ebola and endemic disease populations are pulled into the EIT network.

All suspect cases entering the EIT network will undergo diagnostic testing to confirm or deny Ebola infection. Diagnostic velocity is the time between suspect admit and notification of

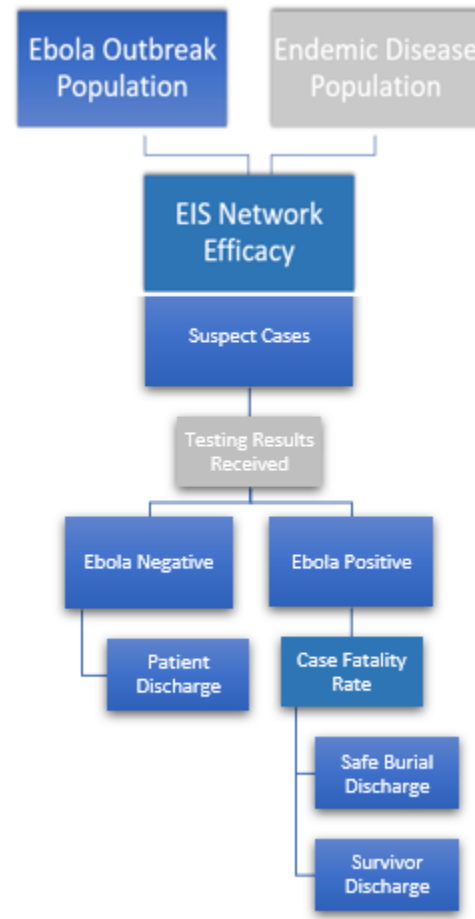


Figure 3.1-1: Overview of Patient Flow between the Endemic disease and Ebola population through the EIT network until discharge – Variables modified highlighted in Grey

diagnostic results for Ebola. Upon receiving diagnostic confirmation, the admitted suspect patients are formally split into groups: Ebola negative or positive. The Ebola-negative group, pulled from the endemic disease population, exits the network immediately with a PLOS equal to diagnostic velocity.

The Ebola-positive group, pulled from the Ebola infected population, is classified as confirmed. The confirmed population receives an additional categorical split based on the case fatality rate (CFR). This percentage determines the survivor and fatal cases in the EIT and assigns a PLOS accordingly. Confirmed cases resulting in fatal outcomes are discharged via safe burial. Confirmed cases resulting in survivor outcomes are discharged back to the community or via another care provider.

The EIT impact is determined by a quantitative measurement of EIT capacity (bed-count) and service requirements (staff and material) when different catchment area sizes and diagnostic velocity are applied. EIT capacity requirements are based on the peak patient census under each scenario, e.g. the total beds needed in the network. EIT service requirements are the staff and material required to provide clinical care and support to the admitted patients. This figure is quantified as the sum of daily staff and material required by the patient census over time in the EIT.

At the end of the scenario, the peak census reached over the forecasted period for the combined groups indicates the capacity requirements of the EIT. The sum of patient days throughout the scenario provides the EIT service requirements after being divided by the formula for determining red-zone activity necessary to provide treatment and care. In Section 4: Results and Findings, the quantitative contrast between scenarios and subsequent analysis of results are provided.

3.1.1 Ebola and Endemic Disease Population

The entire population that is determined to be at-risk or is otherwise determined to be included within the Ebola response efforts is the catchment area. The Ebola response will strive to achieve an increasingly higher capture rate through epidemiological investigation and surveillance efforts. Identification and subsequent admission to an EIT network is based on meeting the suspect case definition for Ebola within the catchment area.

R_0 Suspect cases that enter the EIT network are pulled from two different populations within the catchment area. First are those who are actually infected with Ebola and exhibiting the signs and symptoms of the disease. Second are those who meet case definition due to an unrelated infection or illness capable of presenting signs and symptoms similar to those of an Ebola infection.

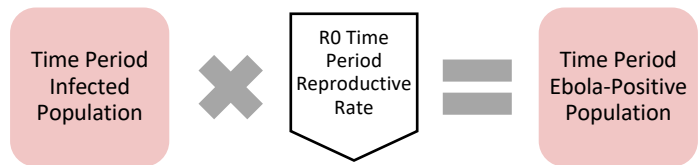


Figure 3.1.1-1: Population of Ebola-Positive in Catchment Area by period

The Ebola-positive population starts as an index case or cluster. The population grows over time based on the rate of infectivity (R_0 pronounced r-naught). The R_0 is variable based on interventional efficacy and/or behavior modification of catchment area population. An $R_0 > 1$ reflects an increasing transmission chain while an $R_0 < 1$ results in a decreasing transmission chain of the Ebola infected population.

The changing R_0 of new cases is what forms the epidemiological curve in most outbreaks. This is the increase in new cases per period observed when $R_0 > 1$, peaks when $R_0 = 1$, and trends downward when $R_0 < 1$.



Figure 3.1.1-2: Population of Ebola-Negative in Catchment Area

In the EIT network suspect cases pulled from this Ebola outbreak population will create the Ebola-positive group in EIT following diagnostic testing.

The second population of suspect cases are pulled from is the catchment area percentage afflicted by endemic diseases whose symptoms meet case definition for Ebola. There are many different diseases and ailments whose symptoms can meet the case definition for Ebola. However, the most common in sub-Saharan Africa that is mistaken for Ebola is malaria.

Malaria is an endemic disease throughout sub-Saharan Africa and is most likely to be present in areas prone to Ebola outbreaks (Khan, Naveed, Dur-E-Ahmed, & Imran, 2015). This model will use malaria as the basis for determining the endemic disease population of the catchment area capable of meeting suspect case definition. Patients identified and isolated from the endemic disease population will become the Ebola-negative group in the EIT after diagnostic results are received.

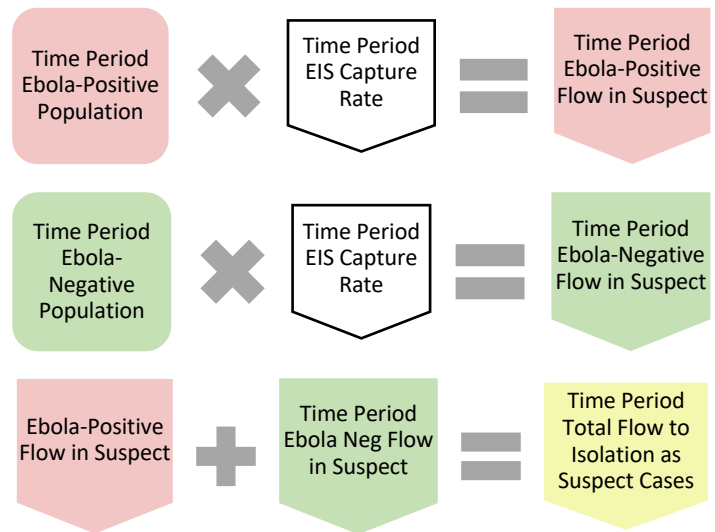


Figure 3.1.2-1: Ebola-Positive and Ebola-Negative Combine to Create Flow Rate of New Suspect Cases Entering the EIT Network for each Time Period

3.1.2 Epidemiological Investigation and Surveillance

The epidemiological investigation and surveillance (EIS) response pillar is responsible for identification of Ebola suspect patients in the catchment area for isolation and testing at the EIT network. The EIS will capture both Ebola negative and positive patients since identification is based on symptoms observed and reported, which can be a result of both Ebola infections and other endemic diseases capable of presenting similarly to Ebola.

The percentage of these two populations identified and isolated by EIS will grow over time as this function grows in efficacy. This growth is contingent on mobilization of efforts and permissibility and visibility increases from sustained operations. The flow-rate of suspect patients into the EIT is based on the epidemiological investigation and surveillance network (EIS) efficacy, or capture rate, of the two populations.

3.1.3 Ebola Isolation and Treatment Patient Flow

The Ebola Isolation and Treatment (EIT) network is the case management function that provides diagnostic testing and supportive care for Ebola suspect and confirmed patients. The total population contained within the EIT is the patient census in the network. This census level is what drives the capacity and service requirements of the EIT provided in the following section.

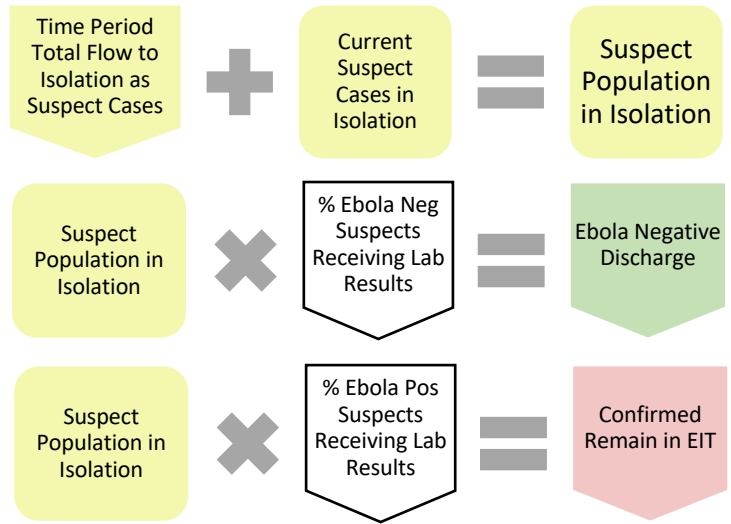


Figure 3.1.3-1: Suspect Case Flow in the EIT for each Time Period

The EIT patient census is comprised of three distinct types: Ebola-negative, Ebola-positive survivors, and Ebola-positive fatalities. All patients enter the network as suspect cases captured by EIS and join the suspect population in EIT. This flow aggregates with the existing population.

Diagnostic testing to confirm or deny the presence of Ebola is performed on the suspect population in EIT. Upon notification of test results, the suspects are split into Ebola-positive and Ebola-negative groups.

The Ebola-negative population is discharged upon receiving results. This fact provides a patient length of stay (PLOS) for the Ebola-negative population equal to the turn-around time required for diagnostic confirmation.

The Ebola-positive population in EIT will become the confirmed population in isolation upon diagnostic confirmation. In order to determine the Ebola-positive flow and PLOS, the population will further split again based on the case fatality rate (CFR) of the EIT.

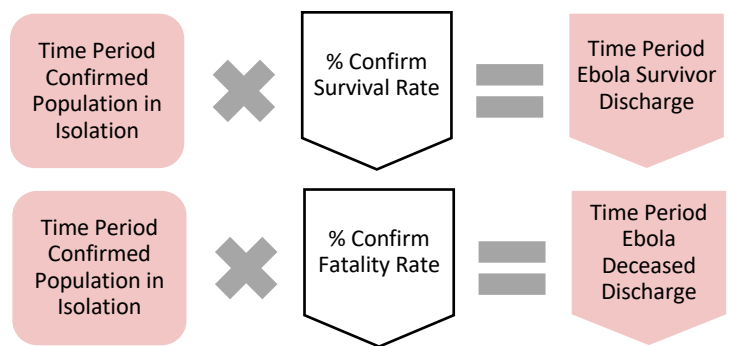


Figure 3.1.3-2: Confirmed Case Flow in the EIT for each Time Period

CFR is the rate at which Ebola-positive patient outcomes result in survival or death. Each of these types has a distinct PLOS spanning the time between admit and discharge. The Ebola-positive PLOS for survivor and fatality categories differ due to the inclusion of survivor recovery period before discharge. This results in survivors spending significantly more time in the EIT network than fatal cases. Ebola-positive fatalities are discharged via transfer to the morgue before receiving a safe burial in accordance with response standard operating procedures.



Figure 3.1.1-3: Suspect and Confirmed Flow of Patients Equals the EIT Patient Census

3.1.4 Capacity and Service Requirements Determination

Capacity and service requirements for the EIT network are a function of the patient census over time. Capacity refers to the actual operational footprint required to house the anticipated patient census over the course of the response.

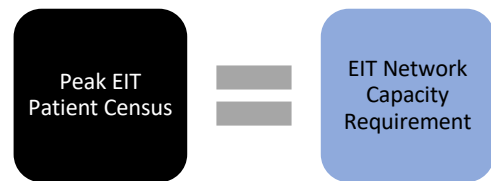


Figure 3.1.4-1: EIT Capacity Requirement is a Function of the Peak Patient Census Anticipated

Capacity is the maximum bed-count required to physically accommodate the patient flow through the EIT network. Capacity is an important objective function to determine because it determines the numerous support requirements associated with an increasing the operational footprint.

Service requirements for the EIT refer to the red-zone activity required to care for the patient census while in the EIT network. The core of patient care is the staff required to enter the unit while wearing personal-protective equipment (PPE) to provide services to the patient census in the form of treatment, sanitation, transfer, and facility maintenance. The frequency and coverage

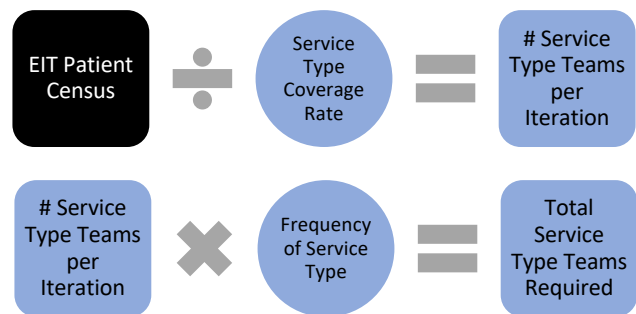


Figure 3.1.4-2: Calculating Staff and PPE Requirements for Service Provision to EIT Patient Census

rate of staff entering the unit is a function of the implementing partner responsible for the unit's standard operating procedures.

Coverage rate is the number of patients inside the unit that the service team can effectively manage. This number is typically lower than in standard healthcare settings since the wearing of PPE greatly reduces the amount of time available to provide services. This time period is typically 45-60 minutes depending on type of PPE and environmental conditions.



Figure 3.1.4-3: Transfer Teams are a Function of Admit and Discharge instead of Patient Census over Time

Frequency is the rate at which services are required to be provided. For instance, provision of meal service will occur three times a day. Implementing partners will retain standard of care requirements that dictate the frequency at which they provide these services. Care requirements can include, but is not limited to, treatment and sanitation service for each patient that is dictated to occur every four and two hours respectively. A breakdown of this activity would result in each patient receiving clinical care service 6x daily and sanitary support service 12x daily.

Service requirements in the patient isolation and treatment wards will require a minimum of a two-person team. The two-person minimum of personnel required is a staff safety precaution. If there is any issue where a staff member requires assistance, e.g. a breach, fall, or other incident, their partner(s) is able to directly assist or at least notify staff outside of the red-zone for help. The impact of this requirement is that teams are always composed of at least two persons, which eliminates single consumption of PPE in calculating service requirements material consumption.

Transfer service is the admission and discharge requirements that occur independent of normal services. Each patient entering and exiting the EIT network will require the support of a transfer team. This function is based on the flow of patients in and out of the network independent of the total patient census.

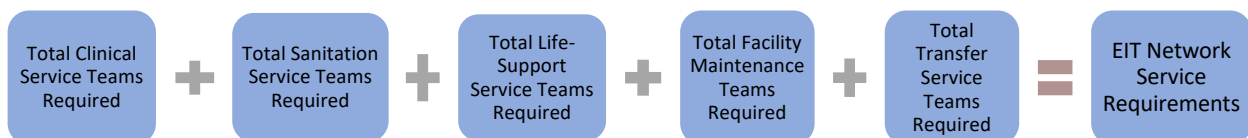


Figure 3.1.1-4: Total Number of Service Type Teams Equal the EIT Network Service Requirements

3.2 Assumptions

The issue of patients exiting the EIT network voluntarily prior to discharge and false positives from diagnostic testing have been excluded from the model. Sufficient data is not available to provide a reliable incidence rate of patients voluntarily exiting the EIT and their impact is minor in response scenario comparison.

Seasonality of endemic diseases has not been included. Despite prevalence waning and increasing during periods of the year and possible asymmetric distribution, the average yearly incidence rate has been held constant through the scenario. This provides a standardized environmental scenario for comparison purposes of the two variables selected: diagnostic velocity and catchment area size.

Efficacy of EIS is equal within the Ebola infected and endemic infected populations in this model based on following *ceteris paribus* for comparison purposes. Higher levels of community permissibility for investigation may increase contact tracing efficacy and favor growth in capture rate of Ebola infected population. Community sensitivity to messaging and social mobilization may increase surveillance alerts and/or self-reporting, which favors growth in the capture rate of the endemic infected population. The inverse of both these factors can also decrease the efficacy of capture rate in these populations. Given that it would be difficult to predict the likelihood of differing efficacy in these populations, the capture rate was level-set to support scenario comparisons.

In determining service requirements, the EIT model consists of a single unconstrained bin that contains all patient flow activity. Often the EIT can consist of more than one isolation or treatment facility. A single unconstrained bin was selected because it allowed for the most effective impact comparison in the scenario as fixed costs of service requirements for each facility would absorb the variability contrasted between scenarios.

3.3 Scenario Breakdown

3.3.1 Scenario Selection (Diagnostic Velocity and Catchment as Variables)

To determine the scenarios only two variables in the model were changed: the catchment area and the diagnostic velocity. The catchment was scaled over 4 values: 100,000, 300,000, 600,000, and 1,200,000. The variation in the population within the catchment area is to demonstrate the trends that will occur between a relatively small catchment area and a large one. The figures chosen to approximate a rural outbreak and then scale towards a major urban outbreak. The 10-fold increase in population size is important in demonstrating what the requirement of the EIT would be as it has to contend with an increasing large population coverage.

The diagnostic velocity was scaled over 4 iterations: 3, 2, 1, and 0.5 days. These time periods for generating results on Ebola sample testing have been observed repeatedly throughout previous Ebola outbreaks. However, in outbreak response this is rarely a static number and velocity changes over time based on the capacity of the diagnostic equipment available and the ability to collect and transport the samples necessary for testing. This variation in diagnostic velocity is why this variable is scaled for each of the scenarios, it provides a bracket for determining where this process will increase the service and capacity requirements despite being fluid in an actual response.

3.3.2 EIS Capture Rate Efficacy

The EIS capture rate efficacy reflects the percentage of Ebola-positive and Ebola-negative patients identified within the catchment area. Penetration of surveillance and investigation is limited in the beginning of a response to the mobilization of activities and required scaling of the operation to fully cover the catchment area. To simulate the effect of the EIS increasing in efficacy over the response period a sigmoid curve was used with an initial x, y intercept of 10% that increases exponentially with tamping occurring after day 50 before reaching 100% at day 110.

To determine the saturation of EIS campaign a logarithmic function for determining growth coverage in a bounded population was used with a y-intercept of 10% which reached full coverage at 120 days. This capture rate is shown in row 3 'Epi-Cover' in Table 3.3.3 below.

3.3.3 The Nominal Ebola Outbreak

The nominal outbreak included in the scenarios consist of a 12-case index cluster (initially infected population), an R_0 of 2, with a variable R_0 over a 150-day period (5 Months). The total afflicted population is 264 with EIS capturing 127 during the course of the response. These figures were developed looking at 9 of the 11 Ebola outbreaks (Zaire strain) that have occurred since 2000. The two excluded were the 2014 West Africa outbreak and the 2018-19 DRC outbreak. The West Africa outbreak was excluded because of the skewing it causes as an outlier compared to other outbreaks. The current DRC outbreak was excluded because it is ongoing and total time period and number of cases are still growing. Looking at the nine outbreaks since 2000 we are able to determine that the average patients captured by the EIT network is 117, while the range of outbreak duration is between 2-11 months. Starting with an initial infected population of 12 a varied R_0 over five months was used to create a plausible nominal outbreak that was then captured by the EIS network as a function of increasing efficacy. The numbers used for the nominal Ebola outbreak and flow into the EIT network through capture rate is provided in Table 3.3.3.

Nominal Ebola Outbreak and Capture Rate Flow into EIT															
Day	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150
Count	24	36	44	40	35	28	20	12	7	3	2	1	0	0	0
Epi-Cover	10%	18%	30%	47%	64%	79%	88%	94%	96%	98%	99%	100%			
Capture	2.4	6.48	13.2	18.8	22.4	22.12	17.6	11.28	6.72	2.94	1.98	1	0	0	0

Table 3.3.3: Nominal Ebola Outbreak and Capture Rate Flow into EIT

3.3.4 The Endemic Disease Population

As the efficacy of EIS increases through mobilization of response activities and community acceptance and permissibility for activities or referrals an increasing number of Ebola-negative suspects will be captured. There are a number of diseases that circulate in Ebola afflicted regions that are capable of meeting case definition for Ebola. However, the most commonly mistaken endemic diseases in Sub-Saharan Africa that creates this problem is malaria. In order to approximate the impact of Ebola-negative patients entering the EIT network malaria was selected

as the leading candidate to form the endemic disease population that would contribute to the suspect patient flow.

To determine the likely prevalence of malaria in an Ebola outbreak afflicted region data was pulled from a World Bank study provided. This data provides the following statistics for incidence for malaria per 1000 over a year in Sub-Saharan countries and 4 countries that experienced Ebola outbreaks. The total malaria cases were then divided by 365 (days in the year) to provide a daily incidence rate for malaria in these at-risk population areas. The malaria prevalence for DRC was selected for use in this model since the DRC has seen more Ebola outbreaks than any other country since 1976 and is the location of the current Ebola outbreak at the time of writing. This data provides that the annual rate of malaria prevalence for each 1000 population is 308 per year which provides a rate of 0.84 instances per day (World Bank, 2018).

Malaria by itself does not always present the necessary symptoms to meet the case definition for Ebola. To determine the frequency with which malaria symptoms mimic the case definition from Ebola, the symptoms prevalence of malaria was pulled from a study in Ethiopia listing the frequency of symptoms (Geleta & Ketema, 2017). The percentages of symptoms exhibited were then calculated on a percentage based on case definition guidelines from the WHO. Symptoms from the Ebola case definition guidelines (WHO, 2014) that presented in those suffering from malaria in the above study are as follows:

Fever = 72.58% Headache = 98.4% Vomiting = 53.22% Diarrhea = 37.1%.

To determine the likelihood that a patient would present with all four of these symptoms the percentages of each symptom were multiplied against each other to determine the percentage of malaria inflicted patients that would present as meeting case definition for Ebola. The total product of this percentage reduction across all four symptoms resulted in a net percentage of 14.1% of symptom prevalence that could result in meeting the case definition for Ebola due to malarial infection.

This percentage was then applied to the per day incidence rate of malaria for 1000 persons in DRC based on the World Bank data which provided an incidence rate of .13 per 1000 persons that would meet case definition for Ebola as a result of a malarial infection. The .13 incidence rate was then extrapolated over the catchment area population for each of the four population scenarios selected

which produced a daily population of endemic disease infections that could meet case definition for Ebola. The breakdown of this is provided in Figure 3.3.4. This daily population can then be multiplied by the days included in each time period for the scenario, in the results section this was done in increments of 10-days, which provides the daily rate at a multiple of 10 to determine the total population of endemic diseases that could be captured by the EIS network each period.

Malaria Prevalence						
	Per 1000 a Year	Per Day	100,000	300,000	600,000	1,200,000
DRC	308	.84	84	253	506	1011
Malaria Cases Adjusted for Frequency of Meeting Ebola Case Definition						
DRC	47	0.13	13	38	77	154

Table 3.3.4: Malaria prevalence and adjustment for frequency of cases meeting case definition

3.3.5 Determining Patient Census in the EIT Network

Ebola-Positive Patient Length-of-Stay (PLOS)—PLOS varies depending on patient outcome and status. The PLOS for suspects that test negative for Ebola is determined by lab diagnostic turn-around and treatment unit discharge protocols. According to Schieffelin, et al. (2014) the mean time between admission to discharge for fatal cases was 4.58 days while nonfatal cases were 15.33. For this analysis a PLOS for Ebola-positive survivors is provided as 15.33 and Ebola-positive fatalities is 4.58.

Case Fatality Rate (CFR)— Northern Clinic of Istanbul (2014) provides that the untreated mortality rate of Ebola virus disease is around 90% it states that due to improved medical facilities CFR has varied between 25-90%. As of December 10, 2018, the North Kivu, DRC outbreak of EVD (Zaire strain) was experiencing an overall CFR of 58% according to the European Center for Disease Prevention and Control Rapid Risk Assessment for the Ebola virus disease outbreak in North Kivu and Ituri Provinces released in December 2018. The CFR is critical to the model as it determines the population percentage split between fatal and survivor Ebola-positive cases which determines the average census over time by weighting PLOS between the two subsets accordingly. In the scenario comparison a case fatality rate of 58% is used to split the Ebola-positive survivors and fatalities into their respective groups and assign PLOS accordingly.

Patient Length of Stay			Case Fatality Rate	Diagnostic Velocity in Days (Varied over Scenarios)			
Positive-Survivor Days	Positive-Fatality Days	Negative Days					
15.33	4.58	Diagnostic Velocity	.58	3	2	1	.5

Table 3.3.5: PLOS, CFR, and Diagnostic Velocity

Diagnostic Velocity—The PLOS for Ebola-negative patients is equal to the turnaround time between admit and diagnostic results since patients have samples collected at admit and are discharged immediately after receiving negative results from testing. The aggregate of the three types of patients (Ebola-negative, Ebola-survivor, and Ebola-fatal) flowing into the EIT and their respective PLOS from admission to discharge creates the census over time of the Ebola treatment

network. This patient census over time determines the capacity and service requirements as described in section 3.3.5

3.3.6 Capacity and Service Requirements

Ebola Treatment Network Requirements—The primary consumable of material required for service requirements in the EIT network is personal-protective equipment (PPE). PPE is single-use disposable jumpsuits, gloves, masks, and aprons that collectively form a PPE set. These PPE sets are donned during an intricate procedure before entering the red-zone and are removed in a doffing process upon decontamination and exit from the red-zone. This material is destroyed upon doffing. Certain other pieces of durable equipment are used which includes goggles or face-shields, thick rubber gloves (maintenance and other support staff), and boots. This part of the uniform is decontaminated and reused throughout the response. Due to the durable nature of these items and a lack of information to provide a reusability rate these items are not included in the material requirements forecast. In order to determine the amount of PPE that will be consumed in providing services in the red-zone the best method for calculating is to determine the number of rounds and number of staff required to provide service. The number of staffs entering the red-zone to provide services to the patient population in isolation and treatment is equal to the amount of consumable PPE sets that will be required. The calculation for determining this under the scenarios included in this paper is provided in Figure 3.3.6.

Additional Considerations—Clinical, Sanitation, and Support Teams will all enter the “red zone” to provide services to the patients in isolation, suspect, or confirmed wards. Red-zone care is a labor and resource intensive effort in which the volume demanded is dependent on the patient census within the Ebola treatment network. There are several factors that constrain the provision of services in the red-zone. These factors include, the time in which staff is able to work inside the isolation and treatment unit, the requirement that no staff works alone, and the restriction on the amount of times per day that the staff member is allowed to enter the unit. This will all work to drive up the number of staff and number of trips inside the unit that will have to be taken. This service is also directly proportional to the number of patients that are in the isolation and treatment at any given time.

Constraints: Personal-protective equipment (PPE) restricts airflow to provide a critical barrier necessary to prevent contamination. Staff entering the red zone could only spend 45-60 minutes “suited-up,” which, after deducting for 15-minute PPE removal procedures, resulted in 30-45 minutes of patient services. The limited time able to provide patient care and services results in a frequency increase of entering the red zone to compensate. Staff are limited to entering the red zone 3 times a day – this constraint increases the number of staff members required to work inside the red zone.

The level of the activity necessary inside the red zone is directly dependent on the patient census. Due to the time constraints of wearing PPE, teams will be able to provide services for only a limited number of patients. As the census increases, the amount of clinical and WASH activity will also have to increase to support the patient census. While different agencies and organizations have variable protocols for the treatment of Ebola within their respective units, the staff and material consumption required will remain correlated with the census level. This model uses a nominal protocol but can be adjusted to protocol specific calculation. This can be accomplished by determining the constraints placed on the staff per safety precautions and evaluating the coverage rate as provided by the time requirements to provide in-patient services per service level dictated. Additionally, the operational footprint, e.g. the physical infrastructure of the treatment network, will have to remain able to house the level of expected and actual patients.

There is also a knock-on effect relating to green and blue zone activity that is required to support all red-zone activity. In short, patient census levels have a dramatic impact directly correlated to the level of labor and resources required to support clinical care inside the Ebola treatment network.

Calculating Staff Entering the Red-Zone—In determining the level of service requirements that would be derived from the scenarios under this model the following breakdown of service to be provided are included in figure 3.3.5. The far-right column of Figure 3.3.5 “PP” is the per patient breakdown of the red-zone trips that will be applied per patient per day while in treatment. Including the transfer service which provides an admit and discharge requirement for each patient by a team of two staff adds a fixed service requirement of four staff trips to facilitate admit and discharge. Adding the fixed service requirements of admit/discharge with each patient’s level of

service requirements per day allows for the total service requirements for each patient to be calculated.

Each of the rounds conducted by a staff member entering the red-zone will consume one set of disposable personal-protective equipment (PPE). By calculating the number of staff that enter the red-zone to provide services it allows the calculation of the consumption of PPE that will occur through the scenario.

Types of Service Coverage and Frequency for In-Patient Service				
PLOS Variable Service	Team Size	Coverage	Freq.	Staff Rounds Per Patient Per Day
Clinical	2	8	6	1.5
Sanitation	2	12	12	2
Life-Support	2	24	3	.25
Facility Maintenance	2	24	2	.17
			Total =	3.92
Fixed Service	Team Size	Coverage	Freq.	Staff Rounds Per Patient Per Day
Transfer	2	1	Admit/Discharge	4 Per Patient Total
Formula				
Patient Service Requirements	$(\text{Patient Type Length of Stay} \times \text{Sum Per Patient Per Day Req}) + \text{Fixed Service}$			
Ebola-Negative Patient	$(\text{Diagnostic Velocity} \times 3.92) + 4$			
Ebola-Positive Survivor	$(15.33 \times 3.92) + 4$			
Ebola-Positive Fatality	$(4.58 \times 3.92) + 4$			

Table 3.3.6: Types of Service Coverage by Frequency for Patient Type and Formulas for Calculating PPE Consumption

4. Findings or Results

Each of the scenarios assumes the same nominal Ebola outbreak since the outbreak spreads as a function of R_0 and not the size of the population. The same nominal outbreak range of total and captured population can be used when contrasting the different scenarios. The nominal outbreak provided in Section 3.3.3 is used with the CFR and PLOS applied from Section 3.3.5 to produce the figures provided in Section 4.1. The patient days in the EIT network are a function of Ebola-positive patient flow and the corresponding PLOS for patient type. The aggregated is then divided by the service requirements as determined by the types of service coverage and the formula from Section 3.3.6. These results remain constant for each of the scenarios. Intuitively as the catchment population increases the demand for service requirements derived from the Ebola-positive population shrinks as a percentage of total demand.

Sections 4.2-4.6 shows the breakdown for each scenario where the catchment area population are varied. Each of these section moves progressively from a population of 100,000 to 300,000, to 600,000, to 1,200,000. In each of the section numbers are provided that demonstrate the effect of

POP: 100,000	Lab Velocity			
	3-Day	2-Day	1-Day	.5 Day
Total Positive Census	127	127	127	127
Total Negative Census	146	146	146	146
Total Survivor Days	818	818	818	818
Total Fatal Days	337	337	337	337
Total Negative Days	438	292	146	73
Cumulative Days	1593	1447	1301	1228
Peak Census	53	43	32	27

POP: 300,000	Lab Velocity			
	3-Day	2-Day	1-Day	.5 Day
Total Positive Census	127	127	127	127
Total Negative Census	432	432	432	432
Total Survivor Days	818	818	818	818
Total Fatal Days	337	337	337	337
Total Negative Days	1296	864	432	216
Cumulative Days	2451	2019	1587	1371
Peak Census	120	85	53	37

POP: 600,000	Lab Velocity			
	3-Day	2-Day	1-Day	.5 Day
Total Positive Census	127	127	127	127
Total Negative Census	865	865	865	865
Total Survivor Days	818	818	818	818
Total Fatal Days	337	337	337	337
Total Negative Days	2595	1730	865	432.5
Cumulative Days	3750	2885	2020	1588
Peak Census	232	156	84	52

POP: 1,200,000	Lab Velocity			
	3-Day	2-Day	1-Day	.5 Day
Total Positive Census	127	127	127	127
Total Negative Census	1729	1729	1729	1729
Total Survivor Days	818	818	818	818
Total Fatal Days	337	337	337	337
Total Negative Days	5187	3458	1729	864.5
Cumulative Days	6342	4613	2884	2020
Peak Census	463	308	155	85

Figure 2-1: Cumulative Patient Days and Peak Census for each of the Scenarios

varying the diagnostic velocity within each of the scenarios as demonstrated by both the per patient days and the derived service requirements. The summary of patient days and the census are included in Figure 4-1.

Using the 3-day lab turnaround time as the upper limit of the scenario and subsequently lowering diagnostic velocity results in a reduction in capacity and service requirements as provided in Table 4-1.

Reduction in Patient Days Through Reducing Diagnostic Velocity (Percentage Reduction from 3-Day Highlighted in Green)							
Catchment Area Size	3-Day	2-Day	%	1-Day	%	.5-Day	%
100,000	1593	1447	90.8	1301	81.7	1228	77.1
300,000	2451	2019	82.4	1587	64.8	1371	55.9
600,000	3750	2885	76.9	2020	53.9	1588	42.3
1,200,000	6342	4613	72.7	2884	45.5	2020	31.9
Reduction in Bed Capacity Through Reducing Diagnostic Velocity (Percentage Reduction from 3-Day Highlighted in Green)							
Catchment Area Size	3-Day	2-Day	%	1-Day	%	.5-Day	%
100,000	53	43	81.1	32	60.4	27	51.0
300,000	120	85	70.8	53	44.2	37	30.8
600,000	232	156	67.2	84	36.1	52	22.4
1,200,000	463	308	66.5	155	33.5	85	18.4

Table 4-1: Reduction in Capacity and Patient Days Through Improving Diagnostic Velocity

Using the patient days and the admits from each of the scenarios the formula for calculating service requirements and consumable PPE sets can be calculated. In Figure 4-3 the fixed and total service requirement by diagnostic velocity are broken down. The two columns of data under the “Fixed Service Req.” are the number of patient admits for each scenario in the left-hand column and PPE consumption requirements in the right-hand column. PPE consumed from the transfer of patients from admit and discharge is “fixed” in that regardless of patient type or PLOS that they will all enter and exit the facility via a transfer team. Unlike other services that have a variable coverage rate, each patient will require this activity at a steady rate that will remain constant and is calculated differently than the other service types for in-patient care.

The subsequent columns provide the fixed cost added to the variable consumption that is added throughout the scenario. The contribution to service requirements from the Ebola positive population is provided in the first row of data labeled “Ebola Outbreak”. Note that this contribution is stable throughout the variation in diagnostic velocity since the PLOS for Ebola-

positive population is unaffected by the time it takes to receive results resulting in a constant level of requirements. In each of the rows the admits from each scenario and the patient days incurred include both the Ebola-negative and the Ebola-positive population in the calculation. These numbers are then divided by the percentage of service requirement for only the Ebola-positive population to demonstrate the amount of consumption that the Ebola-positive population is responsible for throughout the scenarios.

Patient Days for Determining Service Requirements										
(Percentage of Ebola-Positive Consumption is Included in N/P Ratio Rows)										
	Fixed Service Req.		Total Service Requirements (Includes Fixed) by Diagnostic Requirements							
	Admits	Req	3-Day	Req	2-Day	Req	1-Day	Req	.5 Day	Req
Ebola Outbreak	127	508	1155	4528	1155	4528	1155	4528	1155	4528
100K	273	1092	1593	7337	1447	6764	1301	6192	1228	5906
N/P Ratio	47%	47%	73%	62%	80%	67%	89%	73%	94%	77%
300K	559	2236	2451	11844	2019	10150	1587	8457	1371	7610
N/P Ratio	23%	23%	47%	38%	57%	45%	73%	54%	84%	59%
600K	992	3968	3750	18668	2885	15277	2020	11886	1588	10193
N/P Ratio	13%	13%	31%	24%	40%	30%	57%	38%	73%	44%
1200K	1856	7424	6342	32285	4613	25507	2884	18729	2020	15342
N/P Ratio	7%	7%	18%	14%	25%	18%	40%	24%	57%	30%

Table 4-2: Patient Days for Determining Service Requirements

4.1 Nominal Ebola outbreak

The nominal outbreak remains constant regardless of variation of the catchment area since the transmission rate is an independent function. This constant state is important because as the catchment area varies it demonstrates how the endemic disease population, and derived Ebola-negative flow into the EIT, impacts the material requirements and bed-capacity required for the response. The Ebola Positive Patient Flow and days findings from the nominal outbreak are presented in Figure 4.1-1. This breakdown stays consistent for each of the catchment area size and diagnostic velocity variations in the scenarios that are run. This holds the level of service

requirements and bed capacity as being equal for the Ebola-positive patients regardless of each scenario. The first row titled “day” provides the time period in which the following rows contain values. The Ebola population is the amount of total Ebola-positive persons that are available to be captured by the EIS activity in the catchment area. The Epi-Cover is the rate at which the Ebola-positive population is drawn into the EIT network during the time period. The combination of Ebola-positive population amount by the capture rate is provided in the Ebola intake row and indicates the volume of flow from this population that is entering the EIT network. The Survivor row is the result of applying the CFR rate for survivors to the intake to determine the percentage of Ebola-positive patient flow that will result in survivor outcomes. The following row is the PLOS for survivors applied to the number of survivors in the intake to determine the amount of patient days that Ebola-positive survivors will contribute to the scenario. The Fatal row is the CFR rate applied to the intake to determine fatal outcomes with the subsequent row below the result of applying the PLOS for fatal cases to their intake during the time period. The results of both the fatal and survivor contributions to the patient days during the time period is summed in the total patients’ days row. Each of the rows, with the exception of the Epi-Cover, is summed in the far-right column to give the total contribution of each of these rows in the scenario.

The contribution to the total admits and patient days for the Ebola-positive flow into the EIT will remain constant for all of the scenarios in which the catchment population and diagnostic velocity is varied. The percentage at which the Ebola-positive population in the EIT network contributes to the consumption of materials through service requirements is then provided in Figure 4-3)

Ebola Positive Patient Flow and Days								
Day	10	20	30	40	50	60	70	80
Ebola Pop.	24	36	44	40	35	28	20	12
Epi-Cover	10%	18%	30%	47%	64%	79%	88%	94%
Ebola Intake	2.40	6.48	13.20	18.80	22.40	22.12	17.60	11.28
Survivor	1.01	2.72	5.54	7.90	9.41	9.29	7.39	4.74
Patient Days	15.45	41.7	84.99	121.0	144.2	142.42	113.32	72.63

Fatal	1.39	3.76	7.66	10.90	12.99	12.83	10.21	6.54
Patient Days	6.38	17.21	35.06	49.94	59.50	58.76	46.75	29.96
Total Patient Days	21.83	58.9	120.0	170.9	203.73	201.18	160.07	102.59
Day	90	100	110	120	130	140	150	Sum
Ebola Pop.	7	3	2	1	0	0	0	252
Epi-Cover	96%	98%	99%	100%	100%	100%	100%	Null
Ebola Intake	6.72	2.94	1.98	1.00	0.00	0.00	0.00	127
Survivor	2.82	1.23	0.83	0.42	0.00	0.00	0.00	53
Patient Days	43.27	18.93	12.75	6.44	0.00	0.00	0.00	817
Fatal	3.90	1.71	1.15	0.58	0.00	0.00	0.00	74
Patient Days	17.85	7.81	5.26	2.66	0.00	0.00	0.00	337
Total Patient Days	61.12	26.74	18.01	9.10	0.00	0.00	0.00	1154

Table 4-2: Ebola Positive Patient Flow and Days

4.2 Scenario Results Population 100,000

The scenarios read-out for the 100K population are provided below in Figure 4.2-1. The subsequent results for population scenarios ranging from 300K, 600K, and 1200K are provided in the appendix.

The read-out follows the same time breakdown as provided in Section 4.1 with the time period designation running across the top row. The endemic population in the second row is the total population available to be screened and isolated. This population are not infected with Ebola but meet case definition due to an endemic disease (malaria in this model) whose symptoms will meet case definition for isolation referral. The frequency rate is based on the calculations provided in the methodology section. The epi-cover row follows the same capture rate as provided in Figure 4.2-1 and provides the rate at which Ebola-negative patients will be pulled from the available

population in the row above. The sum of the Ebola-negative population as captured by the epi-coverage is provided in the row titled “negative” and is the number of Ebola-negative patients that will flow into the EIT network.

The subsequent three sections titled by diagnostic velocity show the contribution of patient days as contributed by varying the time it takes for the Ebola-negative patients to receive their test results. In each of these sections the Negative Patient days row is the number of patients entering the EIT network as multiplied by the time it takes to receive results which is provided as the diagnostic velocity. $\text{Negative Cases} \times \text{Diagnostic Velocity} = \text{Negative Patient Days}$

This amount is then added to the number of days contributed from the Ebola-positive population provided in Figure 4.2-1 for the total patient days the network will incur from the time period. $\text{Negative Patient Days} + \text{Positive Patient Days} = \text{Total Patient Days}$

The patient days for the time period is then multiplied by the service requirements calculation from Section 3.3.6 to determine how many staff rounds and corresponding consumable PPE sets will be required to provide service during the time period. $\text{Total Patient Days} \times \text{Sum Staff Round Per Patient Per Day (3.92)} = \text{Service Requirements}$

The far-right column then provides the sum for contributions to the network to determine the total input and requirements for each of the scenarios.

Ebola Negative Catchment Population 100,000																
Day	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	SUM
Endemic Pop.	128	128	128	128	128	128	128	128	128	128	128	128	128	128	128	252
Epi-Cover	10%	18%	30%	47%	64%	79%	88%	94%	96%	98%	99%	100%	100%	100%	100%	Null
Negative Cases	13	23	38	60	82	101	113	120	123	125	127	128	128	128	128	1437
3-Day Lab																
Negative Patient Days	38	69	115	180	246	303	338	361	369	376	380	384	384	384	384	4312
Total Patient Days	60	128	235	351	449	505	498	464	430	403	398	393	384	384	384	5467
Service Req	266	561	1025	1534	1969	2223	2211	2079	1942	1835	1817	1798	1760	1760	1760	24540
2-Day Lab																
Negative Patient Days	26	46	77	120	164	202	225	241	246	251	253	256	256	256	256	2875
Total Patient Days	47	105	197	291	368	403	385	343	307	278	271	265	256	256	256	4029
Service Req	216	470	874	1299	1648	1827	1770	1608	1461	1344	1321	1296	1259	1259	1259	18910
1-Day Lab																

Negative Patient Days	13	23	38	60	82	101	113	120	123	125	127	128	128	128	128	1437
Total Patient Days	35	82	158	231	286	302	273	223	184	152	145	137	128	128	128	2592
Service Req	166	380	724	1063	1327	1430	1329	1136	980	853	824	795	757	757	757	13280
.5-Day Lab																
Negative Patient Days	6	12	19	30	41	51	56	60	61	63	63	64	64	64	64	719
Total Patient Days	28	70	139	201	245	252	216	163	123	89	81	73	64	64	64	1873
Service Req	141	335	649	945	1167	1232	1108	901	739	607	576	544	507	507	507	10465

Table 4.2-1: Ebola Negative Results for 100,000 Population

5. Discussion

The analysis demonstrates that the larger the catchment area the more the challenge of coping with Ebola-negative patients in the suspect population of the EIT network will become. Diagnostic velocity is in a critical enabler in determining the absorptive capacity of the network. Increasing the speed for diagnostic results will greatly reduce the operational capacity and service requirements to support the outbreak response in the case management pillar.

The impact of the Ebola negative population and the role of diagnostic velocity in reducing the bed-capacity, service, and material requirements is the most salient contribution from this analysis. The impact of these two variables, Ebola-negative patients and diagnostic velocity, is an important consideration in response planning and the supply-chain management necessary to support expeditionary outbreak responses. Due to the limitations on the scope of this paper the majority of variables that could impact response planning were level-set or nominal in order to isolate the key drivers of demand forecast variability in response planning. Additional probabilistic aspects to the variables should be added to support simulation of different scenarios with more variables in order to better support optimization of processes and planning for outbreak responses. Incorporating these variables, providing probabilistic outcomes, and running numerous scenarios to determine sensitivity and policy suitability would greatly improve forecasting robustness.

This paper is a very broad and shallow approach to tackling the intricacies of the Ebola Isolation and Treatment (EIT) network as impacted by a number of different factors both inside and outside of the response. It provides an underlying logic to how the two types of patients, Ebola-negative and Ebola-positive, flow through the EIT network. However, it relies on largely nominal processes and deterministic calculations to demonstrate the interdependency between different elements within the response and the EIT network.

In the endemic population there are other considerations than just the static level of the malarial infections throughout the year. Within malaria itself the prevalence peaks and recedes throughout the year rather than remains constant and can cause variability in the Ebola-negative flow. Additionally, in many response planning scenarios some form of anti-malarial health campaigns are being included which could further impact this effect on an actual response. This is not to mention the challenge of calculating other endemic diseases that can crop and present similarly within different regions that may be faced with an Ebola outbreak.

In the epidemiological investigation and surveillance metric where the capture rate of Ebola-negative and Ebola-positive patients are pulled into the EIT network these two rates are level-set, effectively being equal to one another. The EIS in itself is an aggregate of five to six different activities that can have varying rates of success. Contact tracing, for instance, is likely to actually capture much more of the Ebola-positive population than the Ebola-negative population since it's following the specific transmission strain. Conversely, point of entry/exit screening and triage at public health facilities is much more likely to capture the Ebola-negative population. Depending on where the response places it's priorities in this area and how the receptive the community is to comply with requests for access and volunteering information these rates and efficacy can vary dramatically. Without further research on efficacy over time or a method to quantify the efficacy of different approaches in capturing either or both Ebola-negative and Ebola-positive populations this function will remain nominal despite high variability affecting ability to forecast the efficacy of these functions.

Diagnostic velocity is not static throughout the response, while this is addressed in the paper, it's important to emphasize that locking a time window for turn-around negates the very real effects of increasing flow rates of Ebola-positive and Ebola-negative patients into the EIT network actually being the cause for slower turn-around times. When the flow-rate increases concurrently with the diagnostic velocity decreasing this can cause a significant exogenous shock to the system that would create operational capacity and service requirements to peak well above what is forecasted in this paper. More research should be done on how to best build resilience and efficiency into the collection, transport, and processing of specimen samples during a response to eliminate these risks.

6. Conclusion

The Ebola disease is not the only viral outbreak that would require an expeditionary clinical interventional response to prevent the emergence of a pandemic. The issue of having to contend with endemic diseases that present similarly to the disease targeted by an outbreak response is likely to follow a similar trajectory as the current response plan for Ebola. Outbreak responses of all types will need to make planning around endemic disease afflicted population a major hallmark of outbreak response planning moving forward. This is especially more pertinent provided the fact that in Ebola the role of endemic diseases provided Ebola-negative patients plays an outsized role in determining the capacity and service requirements necessary for the response.

The trend over the last decade in outbreak response in sub-Saharan Africa demonstrates that increasing outbreak responses will have to respond to urban or larger population catchment areas. While there has been discussion and research on demonstrating the increase in rate of infectivity that occurs in urban areas that has become ingrained in response planning the role of the endemic disease population has not. Even with significantly higher R_0 from crowded and cramped conditions of urban outbreaks, from the perspective of operational capacity and service requirements, bigger outbreaks will not produce as much of a demand for bed-space and patient care as the population at large.

Urban outbreak planning is a requirement for preparedness and planning for future responses. These scenarios will have to incorporate larger catchment areas into their planning which means the problem of managing the Ebola-negative population in the EIT network will be an increasingly larger factor in future responses. Even in instances where the R_0 is increased due to the mobility and density of the population the larger problem that will be presented is providing in-patient services to the population at large instead of just the Ebola infected population.

As provided in Section 5 this is a very broad and shallow dive into mapping the dynamics of patient flow from two populations in which contribute to the EIT network in two different methods. Their rate of flow into the network is the result of an aggregate of multiple activities that cumulatively form the capture rate of the response. The process for determining diagnostic velocity which determines the PLOS for Ebola-negative patients varies over the course of the response. The PLOS for Ebola-positive patients is also a moving target based on the afflicted populations pre-existing health conditions and the availability of treatment options within each response. The scenarios in

this paper also assumes a single point-of-care for isolation and treatment which is likely to be varied for each response and tailored towards providing access to populations which may be spread over a large geographical area. Lastly, the consumption of materials as a result of providing service in the EIT network can vary based on the standard operating procedures of the organization that is responsible for providing services. These standard operating procedures can also vary based on the individual organizations of which there will likely be more than one in any given response and provide variability even within the same area of operations. However, a basic outline of these different protocols that include their frequency and coverage rates can be calculated to provide a simple metric that could be inputted into the service requirements formula. The difference in service requirements rate per patient can then be used to extrapolate for the numerous protocols that might exist within any given outbreak as well as keep pace if protocols change during the response.

The total of these efforts means that in order to solidify and development better preparedness strategies for responding to future outbreaks additional research can and should be conducted in the following areas as provided in this paper.

- The variability in R_0 for Ebola as a function of population potential and density
- The prevalence of endemic circulating diseases ability to meet case definition for Ebola as a function of population
- Seasonality and anti-malarial campaigns ability to decrease or increase the Ebola-negative population
- Success rates of epidemiological investigation and surveillance over time based on population receptivity
- The proportion of Ebola-negative and Ebola-positive cases that are referred based on type of EIS activity
- Process mapping to determine optimization for diagnostic velocity as a function of throughput
- Determining staff requirements for EIT networks as a function of patient census over time
- Treatment options and consumables for providing care to patients in the EIT network
- Demand inelasticity in Ebola response to confirm/deny rate of consumption as a function of patient census over time

- Vaccination campaigns ability to reduce spread of transmission
- The frequency and severity of future outbreaks as urbanization increases in Sub-Saharan Africa
- Scenario modeling for the pre-positioning of supplies and the efficacy of early interventions versus later-stage interventions

References

Inhorn, M. (1990). The Anthropology Of Infectious Disease. *Annual Review of Anthropology*, 19(1), 89-117. doi:10.1146/annurev.anthro.19.1.89

Shattuck Lecture Innovation for Pandemics. (n.d.). Retrieved from <https://www.gatesfoundation.org/Media-Center/Speeches/2018/04/Shattuck-Lecture-Innovation-for-Pandemics>

Board on Health Sciences Policy; Institute of Medicine; National Academies of Sciences, Engineering, and Medicine. Washington (DC): National Academies Press (US); 2016 May 6.

Neiderud, C. (2015). How urbanization affects the epidemiology of emerging infectious diseases. *Infection Ecology & Epidemiology*, 5(1), 27060. doi:10.3402/iee.v5.27060

MINISTERE DE LA - who.int. (n.d.). Retrieved from <https://www.who.int/emergencies/crises/cod/DRC-ebola-disease-outbreak-response-plan-28May2018-ENfinal.pdf?ua=1&ua=1>

Case definition recommendations for Ebola or Marburg Virus ... (n.d.). Retrieved from <https://www.who.int/csr/resources/publications/ebola/ebola-case-definition-contact-en.pdf>

Boisen, M. L., Schieffelin, J. S., Goba, A., Oottamasathien, D., Jones, A. B., Shaffer, J. G., . . . Khan, S. H. (2015). Multiple Circulating Infections Can Mimic the Early Stages of Viral Hemorrhagic Fevers and Possible Human Exposure to Filoviruses in Sierra Leone Prior to the 2014 Outbreak. *Viral Immunology*, 28(1), 19-31. doi:10.1089/vim.2014.0108

Brett-Major, D. M., Jacob, S. T., Jacquerioz, F. A., Risi, G. F., Fischer, W. A., Kato, Y., Houlihan, C. F., Crozier, I., Bosa, H. K., Lawler, J. V., Adachi, T., Hurley, S. K., Berry, L. E., Carlson, J. C., Button, T. C., McLellan, S. L., Shea, B. J., Kuniyoshi, G. G., Ferri, M., Murthy, S. G., Petrosillo, N., Lamontagne, F., Porembka, D. T., Schieffelin, J. S., Rubinson, L., O'Dempsey, T., Donovan, S. M., Bausch, D. G., Fowler, R. A., ... Fletcher, T. E. (2015). Being ready to treat Ebola virus disease patients. *The American journal of tropical medicine and hygiene*, 92(2), 233-237.

Broadhurst, M. J., Brooks, T. J., & Pollock, N. R. (2016). Diagnosis of Ebola Virus Disease: Past, Present, and Future. *Clinical microbiology reviews*, 29(4), 773-93.

Adam J. Kucharski, Anton Camacho, Stefan Flasche, Rebecca E. Glover, W. John Edmunds, Sebastian Funk 2015. Impact of Ebola control measures in Sierra Leone. *PNAS* 112 (46) 14366-14371

Boisen, M. L., Schieffelin, J. S., Goba, A., Oottamasathien, D., Jones, A. B., Shaffer, J. G., . . . Khan, S. H. (2015). Multiple Circulating Infections Can Mimic the Early Stages of Viral Hemorrhagic Fevers and Possible Human Exposure to Filoviruses in Sierra Leone Prior to the 2014 Outbreak. *Viral Immunology*, 28(1), 19-31. doi:10.1089/vim.2014.0108

Miller, G., Randolph, S., & Patterson, J. E. (2006). Responding to Bioterrorist Smallpox in San Antonio. *Interfaces*, 36(6), 580-590. doi:10.1287/inte.1060.0228

Khan, A., Naveed, M., Dur-E-Ahmad, M., & Imran, M. (2015). Estimating the basic reproductive ratio for the Ebola outbreak in Liberia and Sierra Leone. *Infectious Diseases of Poverty*, 4(1), 13. doi:10.1186/s40249-015-0043-3

Incidence of malaria (per 1,000 population at risk). (n.d.). Retrieved from <https://data.worldbank.org/indicator/SH.MLR.INCD.P3>

Geleta, Getachew & Ketema, Tsige. (2017). Prevalence of Malaria and Frequency of Severe Symptoms among Pregnant Women in Pawe Hospital, North Western Ethiopia. *Annals of clinical pathology*. 5. 1109.

Sierra Leone - Ebola Virus Disease (MDRSL005). (n.d.). Human Rights Documents Online. doi:10.1163/2210-7975_hrd-9813-2014083

Schieffelin and Shaffer JG (2014) Goba A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. *N Engl J Med* 2014; 371:2092-100

An overview of Ebola virus disease. *Northern clinics of Istanbul*, 2(1), 81-86. doi:10.14744/nci.2015.97269

European Center for Disease Prevention and Control Rapid Risk Assessment for the Ebola virus disease outbreak in North Kivu and Ituri Provinces released on 21DEC18

Appendix

Ebola Negative Catchment Population 300,000																
Day	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	SUM
Endemic Pop.	380	380	380	380	380	380	380	380	380	380	380	380	380	380	380	5700
Epi-Cover	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	Null
Negative	38	68	114	179	243	300	334	357	365	372	376	380	380	380	380	4267
3-Day Lab																
N. Patient Days	114	205	342	536	730	901	1003	1072	1094	1117	1129	1140	1140	1140	1140	12802
Total P. Days	136	264	462	707	933	1102	1163	1174	1156	1144	1147	1149	1140	1140	1140	13957
Service Requirements	613	1184	2064	3163	4187	4960	5260	5336	5269	5231	5247	5263	5225	5225	5225	63452
2-Day Lab																
2 Day Lab P. Days	76	137	228	357	486	600	669	714	730	745	752	760	760	760	760	8535
Total P. Days	98	196	348	528	690	802	829	817	791	772	770	769	760	760	760	9689
Service Requirements	464	916	1618	2464	3234	3784	3950	3937	3840	3773	3774	3774	3737	3737	3737	46738
1-Day Lab																
1 Day Lab P. Days	38	68	114	179	243	300	334	357	365	372	376	380	380	380	380	4267
Total P. Days	60	127	234	350	447	501	494	460	426	399	394	389	380	380	380	5422
Service Requirements	315	648	1171	1764	2282	2608	2641	2538	2411	2314	2300	2286	2248	2248	2248	30024
.5-Day Lab																
.5 Day Lab P. Days	19	34	57	89	122	150	167	179	182	186	188	190	190	190	190	2134
Total P. Days	41	93	177	260	325	351	327	281	244	213	206	199	190	190	190	3288
Service Requirements	241	515	948	1414	1805	2020	1986	1838	1697	1585	1564	1542	1504	1504	1504	21667

Population 600,000

Ebola Negative Catchment Population 600,000																
Day	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	SUM
Endemic Pop.	770	770	770	770	770	770	770	770	770	770	770	770	770	770	770	11550
Epi-Cover	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	Null
Negative	77	139	231	362	493	608	678	724	739	755	762	770	770	770	770	8647
3-Day Lab																
N. Patient Days	231	416	693	1086	1478	1825	2033	2171	2218	2264	2287	2310	2310	2310	2310	25941
Total P. Days	253	475	813	1257	1682	2026	2193	2274	2279	2291	2305	2319	2310	2310	2310	27096
Service Requirements	1149	2150	3673	5683	7619	9196	9979	10377	10417	10486	10556	10625	10588	10588	10588	123673
2-Day Lab																
2 Day Lab P. Days	154	277	462	724	986	1217	1355	1448	1478	1509	1525	1540	1540	1540	1540	17294
Total P. Days	176	336	582	895	1189	1418	1515	1550	1540	1536	1543	1549	1540	1540	1540	18449
Service Requirements	847	1607	2768	4266	5689	6814	7325	7542	7522	7531	7570	7609	7572	7572	7572	89805
1-Day Lab																
1 Day Lab P. Days	77	139	231	362	493	608	678	724	739	755	762	770	770	770	770	8647
Total P. Days	99	198	351	533	697	809	838	826	800	781	780	779	770	770	770	9801
Service Requirements	546	1064	1863	2849	3758	4431	4671	4707	4626	4575	4585	4593	4556	4556	4556	55937
.5-Day Lab																
.5 Day Lab P. Days	39	69	116	181	246	304	339	362	370	377	381	385	385	385	385	4324
Total P. Days	60	128	236	352	450	505	499	464	431	404	399	394	385	385	385	5478
Service Requirements	395	792	1411	2140	2793	3240	3344	3289	3179	3098	3092	3086	3048	3048	3048	39003

Population 1,200,000

Ebola Negative Catchment Population 1,200,000																
Day	10	20	30	40	50	60	70	80	90	100	110	120	130	140	150	SUM
Endemic Pop.	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	1440	10110
Epi-Cover	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1	Null
Negative	144	259	432	677	922	1138	1267	1354	1382	1411	1426	1440	1440	1440	1440	16171
3-Day Lab																
N. Patient Days	432	778	1296	2030	2765	3413	3802	4061	4147	4234	4277	4320	4320	4320	4320	48514
Total P. Days	454	837	1416	2201	2969	3614	3962	4163	4208	4260	4295	4329	4320	4320	4320	49668
Service Requirements	2070	3808	6437	10013	13515	16474	18086	19036	19261	19515	19676	19838	19800	19800	19800	227129
2-Day Lab																
2 Day Lab P. Days	288	518	864	1354	1843	2275	2534	2707	2765	2822	2851	2880	2880	2880	2880	32342
Total P. Days	310	577	984	1525	2047	2476	2694	2810	2826	2849	2869	2889	2880	2880	2880	33497
Service Requirements	1506	2793	4745	7362	9905	12019	13123	13735	13846	13987	14093	14198	14160	14160	14160	163792
1-Day Lab																
1 Day Lab P. Days	144	259	432	677	922	1138	1267	1354	1382	1411	1426	1440	1440	1440	1440	16171
Total P. Days	166	318	552	848	1125	1339	1427	1456	1444	1438	1444	1449	1440	1440	1440	17326
Service Requirements	942	1777	3053	4712	6296	7563	8160	8433	8432	8460	8509	8558	8520	8520	8520	100455
.5-Day Lab																
.5 Day Lab P. Days	72	130	216	338	461	569	634	677	691	706	713	720	720	720	720	8086
Total P. Days	94	189	336	509	665	770	794	779	752	732	731	729	720	720	720	9240
Service Requirements	660	1270	2207	3386	4491	5335	5678	5782	5725	5697	5717	5738	5700	5700	5700	68786