

Modeling and Simulation of Epidemic Spread: Recent Advances

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Abstract— Epidemics have disturbed human lives for centuries causing massive numbers of deaths and illnesses among people and animals. As the number of urbanized and mobile population has increased, the possibility of a worldwide pandemic has grown too. The latest advances in high-performance computing and computational network science can help computational epidemiologists to develop large-scale high-fidelity models of epidemic spread. These models can help to characterize the large-scale patterns of epidemics and guide public health officials and policy makers in taking appropriate decisions to prevent and control such epidemics. This paper presents an overview of the epidemic spread modeling and simulation, and summarizes the main technical challenges in this field. It further investigates the most relevant recent approaches carried out towards this perspective and provides a comparison and classification of these approaches.

Keywords—*modeling; simulation; epidemic spread; review*

I. INTRODUCTION

Epidemic is an outbreak of a disease that spreads rapidly and widely. Epidemics have played crucial role in human history. Various epidemics have hampered society for centuries such as the Bubonic Plague, Avian flu, H5N1 influenza, H1N1 swine flu, and SARS. Understanding the ways in which diseases propagate has several benefits across societies, such as improving healthcare systems, increasing life spans, and reducing the impact of biological warfare. Thus, it is very important for governmental authorities and healthcare agencies to understand how diseases spread and, therefore, how to limit this spread by selecting the best mitigation and social strategies. Examples of mitigation strategies are vaccination, antiviral treatment, and household prophylaxis. Social distancing strategies include school closure, quarantine, and isolation [1, 2].

Epidemics have been modeled mathematically to understand their dynamics. These models can vary from a few simple equations to complex systems that need to be simulated on supercomputers [3]. Analyzing an epidemic usually requires modeling of biological systems such as viruses, bacteria, parasites, and hosts. Mathematical models of epidemics can be classified into two categories: host and spread. The *host* class models are focused on the effect of disease on the individual person, while the *spread* class models predict how diseases spread among a group of people [2].

To the best of our knowledge, there has been no research recently done on surveying modeling and simulation of epidemic spreads. Authors in [4] surveyed Agent-Based Modeling (ABM) practices from January 1998 to July 2008. Authors in [5] and [6] summarized the recent ABM tools. Both works surveyed ABM in general and not applied to epidemic spread in particular. Further, [7] reviewed several studies on four diseases with different methodologies: measles (patch models), foot-and-mouth disease (distance-transmission models), pandemic influenza (multigroup models), and smallpox (network models). [8] provided an intuitive introduction to the process of disease transmission and how its mathematical representation can be used to analyze the emergent dynamics of observed epidemics. Thus, in this paper we summarize and analyze the recent efforts on modeling and simulation of epidemic spreads to provide an overview of the various models of this paradigm that have lately emerged.

II. MODELING AND SIMULATION OF EPIDEMIC SPREADS

The two main types of models for epidemics at population scale are termed as stochastic and deterministic. Deterministic models describe and explain what happens on the average at the population scale (macroscopic view), whereas stochastic models allow the follow-up of each individual in the population on a chance basis (microscopic view). The latter ones are used when chance fluctuations or heterogeneities are important in populations. Existing deterministic models require less data and are relatively easy to set up. Stochastic models, however, are more complex and need many simulations to achieve useful and accurate predictions [9]. This survey is focused on stochastic modeling. In this section we summarize a number of epidemic spread modeling techniques.

A. Compartment Models

The most typical mathematical model of spread of a disease is a compartment, or state, model where time is divided into periods and each individual is classified to a particular state in each period. The most basic state model is the Susceptible-Infectious-Recovered (SIR) model which was introduced by Kermack and McKendrick [10]. The population is partitioned into three classes: Susceptible (S), Infectious (I), and Recovered (R) as shown in Figure 1. A person who becomes infected moves from class S to class I at a rate which depends on the infectiousness of the virus and the prevalence of infection. Infectious individual recovers and moves to class R when he/she becomes resistant to any future infection [11].

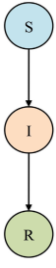


Figure 1: A basic SIR model of disease transmission

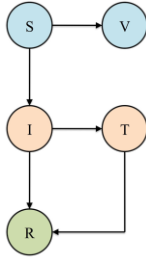


Figure 2: An SIR model of disease transmission including vaccination and treatment

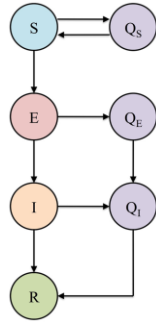


Figure 3: An SEIR model of infection including quarantine and isolation measures treatment

An extension to the SIR model which includes two biomedical interventions is shown in Figure 2. A susceptible individual (S) can be vaccinated (V), and an infected individual (I) can be treated with antiviral drugs (T) and then moved to the recovered state (S). Figure 3 shows the Susceptible-Exposed-Infectious-Recovered (SEIR) model with an extension that includes two behavioral interventions which are quarantine (Q_s) and isolation (Q_i).

B. Equation-Based Modeling

Equation-based Modeling (EBM) is a very common method for modeling spread of infectious diseases. The model of EBM consists of a set of equations that express relationships among observables. The evaluation of these equations produces the change of these observables over time [12]. Thus, the characteristic of the SIR model is represented by the following differential equations [13]:

$$dS/dt = -\beta SI, dI/dt = \beta SI - \gamma I, dR/dt = \gamma I, S + I + R = N \quad (1)$$

where, $S = S(t)$ is the number of susceptible individuals at a time t , $I = I(t)$ is the number of infected individuals at time t , $R = R(t)$ is the number of recovered individuals at time t , N is the total number of the whole population, β is the global transmission rate, and γ is the recovery (or death) rate.

C. Simulating the Spread of a Disease Using Contact Networks

Contact networks are typically used for modeling epidemics. A contact network models chance, or probability, that an individual can infect another individual. Given a set of n people, an $n \times n$ probability matrix P is constructed where p_{ij} is the probability that an infectious person i spreads the disease to an uninfected person j [2]. Social networks represent the interrelationships between individuals of the population. Other aspects of the model, such as the daily activities of each individual, are integrated within social networks to provide specific occurrences of individuals to have contact with an infectious person and, therefore, to be infected by a disease [1].

[14] presented the idea of small-world social networks characterized by highly clustered connections and short paths between nodes. This work was followed by [15] description of

scale-free networks that follow power law connectivity distribution laws. [16] proposed the use of a mean-field rate equation for representing homogeneous complex networks. They used a simplified equation to represent infected node behavior over time in certain disease scenarios. For balancing differences in densities among nodes, they presented an advanced version and applied it to an epidemic spread model according to BA scale-free network [17].

D. Agent-Based Modeling

Agent-based Modeling (ABM) approaches have been recently applied to study epidemic transmission processes where non-agent-based modeling approaches are incapable to be applied [17]. The model of ABM consists of a set of agents that encapsulate the behaviors of the various individuals of the system, and execution consists of emulating these behaviors. ABM is more suitable for areas characterized by a high degree of localization and distribution and governed by discrete decisions. These models are more appropriate to domains where the natural unit of decomposition is the individual rather than the observable or the equation. The internal behaviors of an agent are not required to be visible to the rest of the system. EBM is most naturally applied to systems that can be modeled centrally, and in which the dynamics are controlled by physical laws rather than information processing [12]. Whereas EBM assumes homogeneity and perfect mixing within compartments, ABM can represent heterogeneity across individuals and contact networks. ABM relaxes aggregation assumptions, but requires computational and cognitive costs that may limit sensitivity analysis and model scope [18]. One of the reasons behind the popularity of EBM is the availability of several intuitive drag-and-drop tools for constructing and analyzing system dynamics models. State-of-the-art ABM tools can be found at [5].

Examples of ABM in epidemic spread are [19], and [20] which developed agent-based models for HIV spread in Papua New Guinea, and a South African village, respectively. [21] used an agent-based model to study how dynamic interaction between human activities affects the pandemic of avian influenza in Indonesia.

E. Basic Reproduction Number

To determine whether an epidemic is about to occur or the disease will diminish, the *basic reproduction number*, R_0 , is calculated. R_0 is a threshold quantity which can be defined as the expected number of new infections caused by a single infection in a population where all individuals are susceptible. This infective individual makes βN contacts per unit time producing new infections with a mean infectious period of $1/\gamma$. Therefore, the basic reproduction number is

$$R_0 = (\beta N)/\gamma \quad (2)$$

The value of R_0 measures the transmission potential of a disease as it determines the spread rate and the ratio of the population infected. If $R_0 < 1$, the infected individual may not pass the infection on during the infectious period, and therefore, the infection dies out. If $R_0 > 1$, there will be an epidemic in the population. If $R_0 = 1$, the disease becomes endemic, meaning the disease remains in the population at a consistent rate, as one infected individual transmits the disease to one susceptible [9].

III. RECENT APPROACHES TO EPIDEMIC SPREAD MODELING

Research in epidemic spread modeling and simulation varies in a wide range according to the type of modeled disease, modeling technique, compartment model, simulation tool, and the modeled geographical location. This section discusses and evaluates the most recent approaches.

A. Agent-Based Modeling and Simulation of Influenza

In [22] an agent-based epidemics model for a typical Chinese city using a dynamic contact network to simulate the spread and control of epidemics is developed. City locations are divided into four classes: household, school, workplace, and place of entertainment. All locations are further divided into sub-locations called mixing groups. Each person in the city is represented as an agent in the virtual community and has a contact with others who share the same household and mixing group. Contacts were classified as normal contacts that take place in a mixing group, and random contacts that take place across mixing groups.

A simulation package QAST was developed, which utilizes parallel computing technology to simulate the spread of infectious diseases for millions of people and explore whether a particular control strategy will be effective. The model was evaluated by simulating the propagation of influenza in a community of Xi'an city which has the population of 30,000 persons who live in 10,252 households. They concluded that control policies effect individuals' behavior and, in turn, may lead to mitigation of disease. The authors reported that this model is useful in studying the effects of countermeasure for infectious disease, and individual-based models are more accurate than mathematical models in describing the details of large-scale population.

This approach makes the assumption that an individual mainly moves only between his/her house and his/her other assigned location. For example, a school age child mainly stays at home or in the school which he belongs to. Further, it is assumed that each individual is in one of twelve different states, including both disease-related states and intervention-related states with the assumption of an exponentially distributed duration of each state. It is also assumed that with a mass pre-vaccination policy, 80% of the population has taken vaccine.

B. Simulation of Strategies for Containing Pandemic 2009 H1N1 Swine Flu

The work presented in [23] uses a stochastic simulation model of pandemic influenza (2009 H1N1 Swine flu) to investigate realistic intervention strategies that can be applied in response to rising outbreaks. The simulation model represented a typical mid-sized North American city and predicted average illness attack rates and economic costs under various intervention strategies including low-coverage reactive vaccination, limited antiviral use, disruptive social distancing policies, and short-term closure of individual schools. The model was based on the SIR compartment model. It was concluded that certain combinations of these strategies can be significantly more effective than vaccination alone from both epidemiological and economic points of view. It was found that all of the interventions can decrease attack rates. However, all

of these strategies have associated costs of implementation that would affect their adoption.

The simplifying assumptions in this approach are the following: independence among infected household members, latent period same as incubation period, antiviral courses are available for 10% of the population, and that school closure is triggered by five children appearing with symptoms on any given day.

C. Adaptive Markov Chain Monte Carlo Forward Simulation for Epidemic Modeling of Human Papillomavirus

[24] introduces a Bayesian statistical model based on Forward Projection Adaptive Markov Chain Monte Carlo (MCMC) to calibrate a high dimensional non-linear system of ordinary differential equations (ODE) that represent an epidemic model for Human Papillomavirus types 6 and 11 (HPV-6, HPV-11). The model is based on an SIGPN compartmentalization which includes five states; Susceptible, Infected, Genital warts, Seropositive, and Seronegative. The developed Bayesian model estimates HPV-6 and HPV-11 epidemic parameters such as probability of transmission, HPV incubation period, duration of infection, genital warts treatment, and immunity, and probability of seroconversion per gender, age-group and sexual activity-group. This work extended the development of a sexual mixing matrix which was first suggested in [25]. The authors also proposed an extension to the class of adaptive MCMC algorithms to incorporate a forward projection simulation strategy for the ODE state trajectories. They performed posterior predictive inference for the effect of vaccination on the modeled population. Their work was evaluated with simulation on both recent real and synthetic data in Australia.

The afore-described model is based on the following assumptions: population age range is 15-59 with the assumption of absence of sexual activity in people below 15 and above 59, the modeled population of Australia is assumed constant over time, the number of males in the whole population and every sexual activity or age-group is equal to the number of females, and that no transition between genders is allowed, the modeled population is considered heterosexual with all people belonging to one of the sexual activity groups, people seek treatment immediately upon becoming aware that they have genital warts, and immunity is life-long for all individuals in the population.

D. DTMC Approach to Contact-Based Disease Spreading

The authors in [25] introduced a framework for the contact-based spreading of diseases in complex networks based on probabilistic discrete-time Markov chains (DTMC). The framework generalizes the existing Heterogeneous Mean-Field (HMF) approach and applies it to weighted and un-weighted complex networks. Authors considered a discrete two-state, susceptible (S) and infected (I), contact-based process. Each node of the network represents an individual or a place (such as a city or airport) and each edge is a connection along which the infection spreads. At each time step, an infected node makes λ trials to transmit the disease to its neighbors with probability β per time unit. This forms a Markov chain (MC) where the probability of a node being infected depends solely on the last time step. To validate their approach, they performed MC

simulations on different scale-free (SF) networks. Paper reports that numerical solution of analytic equations overcomes the computational cost of MC simulations. In addition, the presented formalism is used to study behavior of critical epidemic threshold for different values of the probability of contacting a fraction of neighbors per time step.

One of the limitations of this approach is that it is based on a simple two-state compartment model. The second limitation is that while all neighbors in the reactive process are contacted, the contact network was designed according to the assumption of one contact per unit time, $\lambda = 1$. In real life, the number of stochastic contacts per unit time is a variable of the problem, and when $\lambda = 1$, the model is not a standard contact process as reinfections are not considered. Furthermore, this model deals with infections only due to direct contacts between nodes.

E. Agent-Based Simulation on Avian Influenza in Vietnam

Based on the daily reported number of dead poultry due to avian influenza in northern Vietnam in November of 2005, [13] used a mathematical model to estimate the basic reproduction number R_0 of the disease. The significant value of the estimated R_0 explained the explosive outbreak in the poultry population. The authors developed an SIR compartment using a combination of EBM and an ABM to recapture the recorded data of the outbreak of avian influenza and to evaluate the efficiency of existing control measures. Their model assumes a totally homogeneous and well-mixed poultry population where the interaction between infected and susceptible individuals is a random process. The work concluded that the infection process of avian influenza in poultry is not significantly affected by external factors. The results inferred that a comprehensive strategy of culling, bio-security control and large-scale vaccination campaign should be taken promptly to keep the disease under control.

Advantages of this approach include evaluation of control and vaccination strategies, as well as combining EBM and ABM. One of the limitations of this approach is the assumption that poultry population is totally homogeneous and well mixed.

F. Multiagent-Based Simulation of the HIV/AIDS Spatial and Temporal Transmission among Injection Drug Users

The work presented in [26] proposes HIV/AIDS spatial and temporal transmission model of injecting drug users (IDUs) based on the multivalent system and geographic information systems (GIS) in an urban environment. They simulated the HIV/AIDS spatial and temporal transmission process among injection drug users during ten years on the Repast (REcursive Porous Agent Simulation Toolkit) Symphony1.2 platform. Individuals were categorized into 5 types: healthy person, HIV person, AIDS person, IDU person and HIV-IDU person. Individuals represented by agents are associated to places where they interact with each other. Each agent has its own features such as age, gender, education, career, and geographic location. Relationships among agents were described using random social network. For every time step, agents' specific behavioral rules are defined. The model was implemented for the propagation of HIV/AIDS among IDUs in Kunming, the capital of Yunnan Province, southwest of China as a case study. Simulation was performed to improve the understanding of HIV transmission dynamics and to provide the basis to

prevent and control the spread of this disease. Simulation results indicated that the number of initial HIV persons in injection drug users, the proportion of needle sharing among them, and individual social impact have a significant effect on the spread of HIV/AIDS.

There are several simplifying assumptions in this approach: random network was used to describe relations among people, population size is 1000, each agent has twenty friends and contacts five to eight of them every day, all healthy people act positively by encouraging their friends to leave drugs, and all drug abusers act negatively by inspiring others to begin or continue taking drugs. A major limitation is that transmission through sex between drug abusers was not taken into account.

G. Comparing Large-Scale Computational Approaches to Epidemic Modeling

Authors in [27] compared an agent-based model with a structured meta-population stochastic model for the propagation of a baseline pandemic event in Italy, as an example of a large and heterogeneous European country. The agent-based model is based on the explicit representation of the Italian population through highly detailed data on the socio-demographic structure. The meta-population simulation uses a Global Epidemic and Mobility modeler (GLEaM) and the integration of an airline travel flow data with short-range human mobility patterns at the global scale. The model also considers age structure data for Italy. This work suggested the development of hybrid models which combines agent-based and meta-population approaches.

Comparing agent-based and meta-population stochastic models is one of the advantages of this work. Although this approach assumes distance-dependent random contacts in the general population, it assumes homogeneous mixing in households, schools and workplaces. While the agent-based model is highly structured and considers households, schools and workplaces, GLEaM model just considers both the spatial and age structure. Furthermore, the distance kernel for random contacts in the population considered in the agent-based model might be unable to reproduce some of the complex properties that are found in the air travel flows with North-South heterogeneities. One limitation of this approach is that it did not implement intervention strategies.

H. Modeling the 2010-2011 Cholera Epidemic in Haiti

[28] built a compartmental transmission model for the Vibrio Cholera Epidemic in Haiti in 2010 and 2011 and explored potential effects of disease-control strategies. They developed an SIR model with the addition of a water compartment. The water compartment could be contaminated by infected or infectious persons and could in turn infect susceptible persons. The models represented the population of each of Haiti's ten administrative regions. These populations were combined to form a meta-population model, in which disease could spread both within a given region and between regions reflecting the movement of people between different regions. It was found that Cholera spread between two regions is proportional to the population size of both regions and inversely proportional to the square-distance between regional centroids. Analysis of changes in disease dynamics over time suggests that public health interventions have substantially

affected this epidemic. A limited vaccine supply provided late in the epidemic was projected to have a modest effect.

One major assumption is that cholera could be transmitted through either close contacts or contaminated water. However, waterborne transmission and consumption of food items contaminated with infective water are important ways of cholera transmission that were not considered in this work.

IV. SUMMARY OF THE PRESENTED APPROACHES

Research in epidemic spread modeling and simulation is a wide domain with respect to several aspects such as the type of modeled disease, modeling technique, compartment model, performance metrics, simulation tool, and modeled city or country that is object of the study. A number of research approaches are ABM, while others are EBM. Some of them model specific human diseases, whereas others model poultry and other animal epidemics. There are also those that study epidemics in general. Some approaches investigated different intervention and health care strategies. The previous section presents some of the state-of-the-art approaches in this field. Table 1 summarizes these approaches and compares them. We believe that the table can be beneficial to practitioners in healthcare that plan on applying some of these approaches for their goals. It presents, in particular, the assumptions that each of these approaches makes, as well as the performance metrics that are calculated.

Table 1 shows that the studied approaches vary from equation-based such as [24] and [25], to agent-based such as [22] and [26]. Some of these approaches combine equation and agent-based modeling, such as [13] and [27]. A number of modeling approaches develop their own tool such as [22] who developed QAST while others rely on existing modeling tools. Some of the research approaches examined control policies and intervention scenarios, such as [23] and [13].

It is noticeable that there is more research done in the modeling of influenza than other diseases. This is due to the wide spread of this disease in different parts of the world. All approaches agree that ABM is more precise in describing details of large-scale population than EBM. The most commonly calculated performance metric is the infection rate.

V. CONCLUSIONS

This survey is focused on modeling and simulation of epidemic transmission with a focus on the most recent advances in the field. Apparently, it is a problematic of high importance for all regions of the World, as the collection of the most recent approaches to solve this paradigm stems from all around the World. We have presented the main challenges that this field faces. First, we presented the most common types of models that exist for this problem. Further, we investigated most of the relevant recent approaches carried out towards this perspective and provided a comparison and classification of these approaches. Modeling and simulation of disease spreading approaches are mainly classified into two categories: differential equation-based, and agent-based. The combination of both approaches in a hybrid model has only been recently investigated. In addition to this, ABM allows for a lower number of simplifying assumptions as they model individuals with a high level of detail. In addition to this, the presented

models are also dependent on the goals of the simulation, i.e. the relevant performance metrics, and thus they all differ in the approach that they use.

Finally, we believe that our work would present a useful starting point to epidemiologists when considering various modeling approaches to solve a particular problem.

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Table 1: A comparison between approaches of epidemic spread modeling and simulation

Approach	Modeling Technique	Comparison Model	Tools/Programming Lang.	Modeled Disease	Geographical Area	Notes and Performance Metrics (PM)	Model Assumptions
Fa et al., 2011	<ul style="list-style-type: none"> ABM Dynamic contact network 	12-states	QAST C++	Influenza	Chinese city	<ul style="list-style-type: none"> Indicated that ABM is more accurate than EBM in describing details of large-scale population. PM: Infection rate. 	<ul style="list-style-type: none"> Individual moves only between two locations. Exponential duration in each state. 80% of the population has taken vaccine.
Andradóttir et al., 2010	<ul style="list-style-type: none"> Stochastic model 	SIR	C++	H1N1 Swine flu	Mid-sized North-American city	<ul style="list-style-type: none"> Evaluated vaccination and different intervention scenarios. PM: Illness attack rates and cost. 	<ul style="list-style-type: none"> Independency among infected household members. Lengths of the latent and infectious periods follow empirical probability distributions. Antiviral courses are available for 10% of the population.
Korostil et al., 2011	<ul style="list-style-type: none"> Bayesian statistical model Adaptive MCMC Forward Simulation Non-linear ODE Sexual mixing matrix 	SIGPN		HPV-6 HPV-11	Australia	<ul style="list-style-type: none"> Extended the development of a sexual mixing matrix Perform posterior predictive inference for the impact of vaccination on the modeled population. PM: Calibration to seropositivity and genital warts incidence data. 	<ul style="list-style-type: none"> Population age range is 15-59. Population is constant over time. Number of males is equal to the number of females. People seek treatment immediately upon becoming aware that they have genital warts. Immunity is life-long.
Gómez et al., 2010	<ul style="list-style-type: none"> DTMC EBM Air transportation network 	SIS		General disease		<ul style="list-style-type: none"> Indicated that numerical solution of the analytic equations overcomes the computational cost of MC simulations. Examined the behavior of critical epidemic threshold for different values of the probability of contacting a fraction of neighbors per time step. 	<ul style="list-style-type: none"> One contact per unit time. No reinfections.
Nguyen et al., 2010	<ul style="list-style-type: none"> ABM ODE 	SIR	SOARS	Avian influenza of poultry	Northern Vietnam	<ul style="list-style-type: none"> Estimated R_0 of the disease. Evaluated existing control policies. Simulation results fitted recorded data. PM: Characteristics of epidemic SIR model. 	<ul style="list-style-type: none"> Poultry population is totally homogeneous and well mixed.
Xiong et al., 2010	<ul style="list-style-type: none"> ABM Random social network 	Healthy, HIV, AIDS, IDU, and HIV/IDU	Repast-Simphony Java	HIV/ AIDS	Chinese city	<ul style="list-style-type: none"> Understanding HIV transmission dynamics. Providing the basis to prevent and control the transmission of HIV/AIDS. PM: Transmission rates and sensitivity to factor changes. 	<ul style="list-style-type: none"> Total population is 1000. Each agent has twenty friends and contacts five to eight of them every day. Agent can move freely. Healthy people act positively. Drug abusers act negatively. No epidemic transmission through sex.
Ajelli et al., 2010	<ul style="list-style-type: none"> ABM Meta-population stochastic model 	ILI	GLEaM	Influenza	Italy	<ul style="list-style-type: none"> Compared ABM with meta-population stochastic models and assess epidemic predictions that they can achieve. PM: Timeline of incidence profiles and epidemic size. 	<ul style="list-style-type: none"> Homogeneous mixing. Homogeneous transmission rates. GLEaM model considers only spatial and age structure.
Tuite et al., 2011	<ul style="list-style-type: none"> Meta-population stochastic model 	SIR + Water	Berkeley Madonna software	Cholera	Haiti	<ul style="list-style-type: none"> Estimated R_0 of the disease. Cholera spread between two regions is proportional to the population size of both regions and inversely proportional to the square-distance between them. PM: Relative reduction in total cases and reduction in effective reproductive number 	<ul style="list-style-type: none"> No transmission through waterborne and consumption of food. Projections were based on the initial dynamics of the epidemic and not changing.