Modelling and Simulation of Resource Constrained Enhanced Vaccination Strategies and Optimized Epidemic outbreaks

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***Abstract*—Pandemic occur and lead to extensive morbidity and mortality worldwide. Agent-based models are increasingly being used to model and predict the spread of epidemic. As long as there is life there will be fight for infectious diseases and will never cease. The work is aimed to provide a deep analysis of the way the virus propagates in the population. We have explored the impact of different vaccination strategies and one of the demographic characteristic of agents i.e. agent mobility on the spread of virus in case of epidemic outbreak. It is hypothesized that due to limited resources, vaccination of whole population is not feasible. Therefore effects of vaccination need to be analyzed on a random portion of whole population. In this model, it is assumed that an agent becomes immune if he has received 80% of total recommended vaccine dosages in his lifetime. Virus acquisition probability is modeled as random event that can be changed externally. The effect of vaccination can hence be seen on a fixed and randomized set of population. The effect can be analyzed to see which vaccination strategy could be adopted to minimize the spread of disease and evade the loss. Further at any point in time the model can give information regarding the health status of population. Ultimate objective of this contribution is to assist different stake holders (policy makers, health agencies and executives) to make decisions regarding cost-effective vaccination strategies to mitigate of spread of diseases.**

I. Introduction

According to Bill Gates the deadliest disaster the world is most likely to suffer from in next twenty years is a pandemic disaster and not ready to face it [1]. Gates by looking at the death charts observed a spike after World War 1 (about 25 million deaths) and about as large as World War II (about 65 million) and that was the Spanish flu. Infectious diseases have always threatened human lives. In a study Marcia Inhorn and Peter Brown found that infectious diseases "have likely claimed more lives than all wars, noninfectious diseases, and natural disasters put together" [2]. History has seen many global epidemics that ripped around the world, leaving behind piles of dead bodies. The black plague of 14th century wiped out 70 percent of Europe, the 1918 flu pandemic resulted in about 75 million deaths, and the ongoing HIV pandemic has reached almost every country of the planet and has taken more than 30 million lives since 1980 when the virus was first discovered [3,4]. Human viruses like tuberculosis, smallpox [5,6] and the most recent of these H_1N_1[7], Ebola [8] had devastating effects on populations. In U.S States, 5% to 20% of population are infected every year by seasonal influenza and some of the fatal cases lead to death [9]. Some viruses constantly go through mutations, so individuals that have no or very low immunity get exposed to disease. According to the World Bank a pandemic flu besides millions of deaths would bring down the global wealth by 3 trillion. To prevent such a catastrophe, deserves the worlds time and attention at most [10]. A report produced by the Gates funded foundation concludes that with right investments we can eliminate the health difference between rich and poor countries. Investing in health is an extremely effective way to break the poverty cycle [11].

This paper models a complex emerging phenomenon whereby micro level agents generate macro level behavior following simple rules. The advantage of modeling is that we are able to simulate conditions which are not practicable to visualize in the real world. In addition, one can ascertain parameter values that can lead to a dead end. Models in general have two objectives: understanding and prediction [12]. Mathematical modelling of infectious disease was first contributed by Kermack and McKendrick [13] which has now increased more than fourfold [12]. The complex and stochastic nature of pathogen dynamics makes it impossible to be predicted by use of simple tools as decision trees or step-by-step simple derivations. Particularly in epidemiological studies the agent based models help in assessing various scenarios with the help of parameter sweeps and provide support in making policy decisions regarding eradication of disease [14]. This is especially important when timely decision is required.

Most of the infectious epidemic outbreak results in devastating effects on the entire population. About 1415 human viruses are known and of these 53% are micro-parasites [15]. The infection begins when these viruses penetrate the host and reproduce. Immune system attempts to respond to these viruses by producing antibodies and if it fails to resist, infection occurs and the host is able to transmit virus to other hosts. It is not the case with humans only. Animal viruses propagate the same way. As in livestock farming the most notable is foot-and-mouth disease. This epidemic had substantial effects on human, animal and economy in UK in 2001 [16]. It is important to understand the underlying interaction and influence of factors and the appropriate preventive measures that can help in eradication of disease minimizing the loss. Many researcher efforts are being made to contain the spread of epidemics [17,18, 19].

There are various factors which influence the survival of a directly transmitted virus in a population [20]. Some of these factors were illustrated in model by Uri Wilensky in 1998 [21, 22]. The interaction of these factors leads to different outcomes and behaviors depicting how virus will propagate in population. This model basically depicts the persistence and perpetuation of a micro parasitic pathogen in a human population. Persistence means how long virus will survive in populations which can be through generations. Its converse is eradication which looks for ways that can lead to measures to help wipe out the disease. The factors which might affect the survival of a directly transmitted virus in a population are population density, population turnover, immunity, infectiousness and duration. Population density determines the extent to which the agents approach each other. High population density leads to dense populated areas and hence the chances of interaction between infected and susceptible agents increase. Population turnover i.e. the rate by which new agents will be introduced to population is determined by healthy agents as only they are capable to reproduce four times into healthy and susceptible off springs. In this model immunity is assumed as eternal i.e. once acquired lasts forever. In real life, this depends on disease and the infected person life style. Infectiousness refers to the ease with which the virus propagates in population. As some diseases have high probability of spread with minor contact with infected persons e.g. tuberculosis, flu, chicken pox. Whereas some require frequent contact e.g. Aids. Lastly duration determines the time for which the infected agents will survive before recovery from infection or death.

In this paper, an extended version of virus model [20] was used to analyse the impact of vaccination strategy as a preventive measure on epidemic dynamics. Different patterns of emergence were identified from the original model. The effect of restricting the movement of sick was analysed. The agents involved in the system are the people that initially may have either of two states; healthy and infected. Infected are the ones that carry the virus and are capable of transferring it. It can be further extended by using more precise parameters to produce refined output. This model is a general abstraction and can be applied to different scenario of an epidemic outbreak. At any point in time the model can give information regarding the health status of agents.

II. Proposed Model Design

The original virus model simulates the persistence and perpetuation of a micro-parasitic pathogen in a human population. Persistence means how long virus will survive in populations which can be through generations. It does not account for any counter-measures that can lead to eradication of disease. Eradication means to help wipe out the disease from population. Extinction refers to obliteration of population. The world in split into equally sized patches which is a square piece of ground. A turtle can on average produce four offspring's in lifetime and new born are all initially in healthy state. We have set average lifespan of agent to 50 years and each tick corresponds to one week. The agents can freely move inside the world. The model follows the simple SIR model state transition rules with demographics in a bounded population of fixed size. In this model the world is confined to a size to allow for maximum agents but the population size is allowed to vary with time subject to births and deaths. The agents can be in one of three states and undergo state transitions. Initially all agents are in healthy state and a few are in the infected state.

A. Agent

A typical agent-based model can be defined as agents, environment, behavior, rules, and also agents attribute in a typical Netlogo model can be turtle, patches, links, observer. All agents that can move around in the world are termed as turtles and then move over patches. The world in split into equally sized patches which is a square piece of "ground". Links shows the relationship between agents. Observer is the person observing the interaction of other agents and cant observe silently but also gives instructions to other agents. This model comprises of only turtles and observer agents.

B. Rules

Agents act according to some rules. Rules are the source of agent intelligence and observed in the model are

- **Acting Rule:**The acting rule is the random movement of agents in the model.
- **State-Transformation Rule:**The state transformation rule is the SIDR model.
- **The Interact Rule:**Agents interact with their environment.

C. Extensions made to the original model

To assess whether fixed population vaccination or random population vaccination proves to be more effective in case of an epidemic outbreak an additional chooser controlling vaccination strategy was added. More option to introduce disease at any point of time in population was added. For vaccination, it was assumed that an agent becomes immune if he has received 80% of vaccine dosages in his lifetime. In the model of the lifespan was set at 100 weeks. However, it

can also be modified to be left over to user. The agent has to complete vaccination in th part of his lifespan. In this regard, the th life of agent is divided into 8 parts to set time for relative vaccine dosages. In original model immunity was assumed to be eternal i.e. once recovered lasts forever. Another extension of the model that immunity was made in last two months. So from recovered state, individuals move back to the susceptible state and the behavior of the system was analyzed in both scenarios.

D. Macro-Level Behaviour

Firstly, the macro-level behaviour of original model was analyzed and emergent patterns were identified using parallel coordinates technique. Then the extended model was analyzed for certain parameter space.

- **Emergence:**Different patterns of emergence can be seen in different parameter settings.
- **Population dynamics:**Behaviour of the system change over time. Changes in the size of populations and the factors affecting those changes were observed.
- **Unpredictability:**Same parameter values may yield different results in multiple runs. An action is never certain but has an intrinsic probability of occurring such as moving randomly or behaving in a probabilistic way.

III. Experiment Results

The macro-level behavior of original model was analyzed for certain parameter space using parameter sweeping. The impact of FP-Vacc and RP-Vacc was also observed for same parameter space and the impact on emergent patterns was analyzed. We have broadly categorized infectious diseases in these experimental settings. The behavior of parameters is analyzed using parallel coordinates technique which is

- Common way of visualizing and analyzing multivariate data.
- Different axis arrangements may lead to different results.
- Some set of combinations will show same result.

Using parallel coordinates technique the first pattern analysed was with low infectiousness value and maximum duration. The chance of recover in this case didnt appear to have any significant impact. These parameter values result in epidemic outbreak that appears slow initially but the disease will survive in population in long time as shown in Fig 1. Here, we can elucidate the spread of infectious disease as Aids caused by the HIV virus. Besides other factors it has extremely low infectious value, spans over long duration and low recovery rates. To explains the persistence of virus in population and disease with long duration appear to survive in population despite of infectiousness rate. Second pattern emerged at high infectiousness and short duration. Highly infectious disease but with very short duration will disappear early. Ebola a deadly disease has very high infectiousness, short duration and extremely low recovery rates. Disease with short duration ultimately eradicates from population after showing its effects in Fig 2 and Fig 3. This depicts the initial break out of viral infection; one that has adverse consequences on humans.

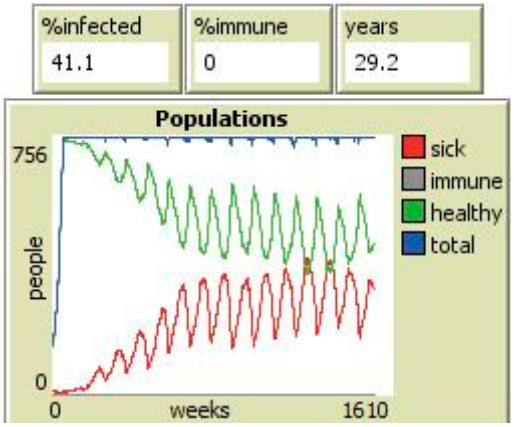

Fig. 1. Emergent pattern 1(Original Model)

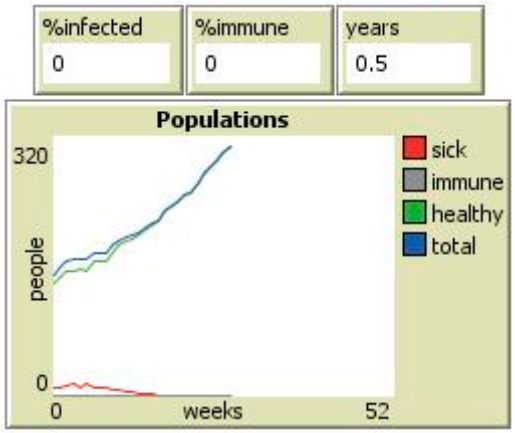

Fig. 2. Emergent pattern 2(Original Model)

Viruses too successful initially may not persist in the long run. The same pattern can be observed under same parameter setting extending duration to 20 weeks. The duration parameter set at value above 45 produces the same effect for this model. The default parameter setting of the model the chance-recover parameter adds its effect. As the people after recovery become immune they act as barrier between healthy and infected people. As despite of high infectiousness and long duration some healthy people are seen in the world. The duration parameter set at value above 45 produces the same effect. This effect is also termed as herd immunity as shown in Fig 4.

TABLE I
Emergent Patterns

Sr.No	Emergent Behavior	I	C-R	D
E-1	Persistence	5	0	99
E-2	Eradication	99	0	2
E-3	Extinction	99	0	99

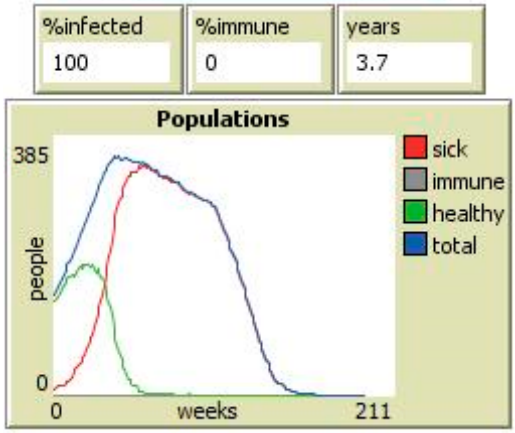

Fig. 3. Emergent pattern 3(Original Model)

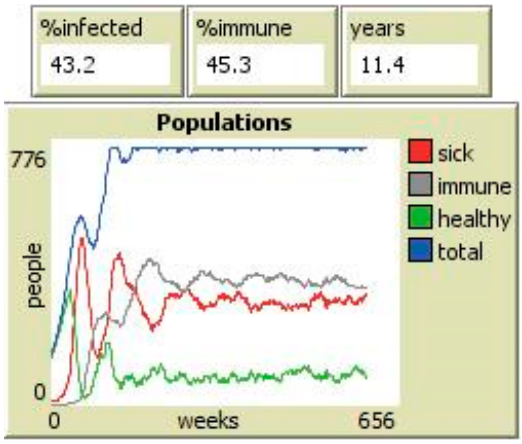

Fig. 4. Herd Immunity

In above table, I denotes Infectiousness, C-R stands for chance-recover and D refers to time duration. These patterns are represented graphically with respect to time-series representation as shown in Fig 5. Then random and fixed population strategy was applied to the above identified emergence patterns. All the scenarios were executed for a period of 30 years. Disease was introduced in population after every 10 years in all cases.

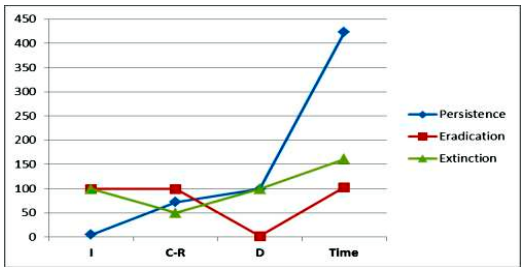

Fig. 5. Time-Series representation

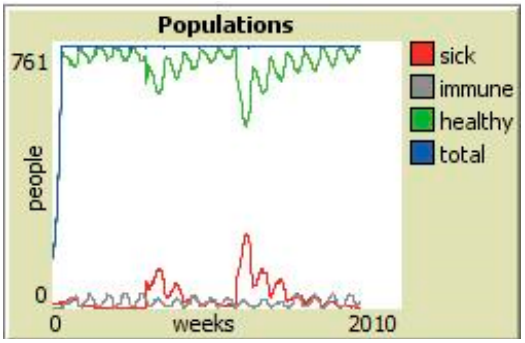

Fig. 6. E-1:Random population vaccination

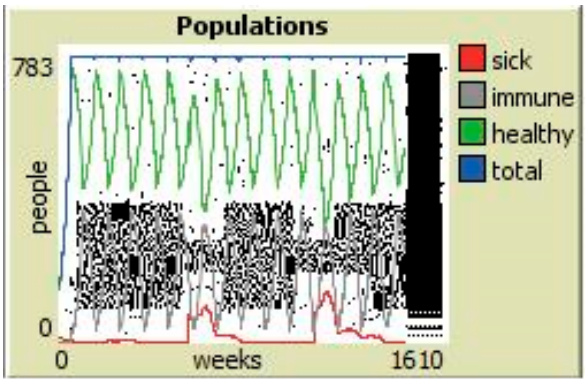

Fig. 7. E-1:Fixed population vaccination

A. *Emergent Pattern E-1*

Random Population Vaccination: The pattern changed to E-2 in each case, from persistence to eradication even though the disease was introduced in population at regular intervals. Thus it can be concluded that if individuals are selected randomly from population for vaccination it would lead to eradication of disease as shown in Fig 6. Fixed Population Vaccination: Here again in case of fixed-population vaccination the disease eradicated from population, somewhat early as was observed in case of random-population vaccination. The vaccination changed the persistence pattern of epidemic to eradication as shown in Fig 7.

B. *Emergent Pattern E-2*

Random Population Vaccination: In first run the emergent pattern sustained. Disease was introduced in population after every 10 years and the pattern changed to E-1 in Fig 8. Fixed Population Vaccination: In case of fixed population vaccination the pattern E-2 sustained. The disease eradicated from population. Hence we can conclude that in case of fixed-population vaccination the immune serve as barrier in between infected and healthy and lead to eradication of epidemic from population in Fig 9.

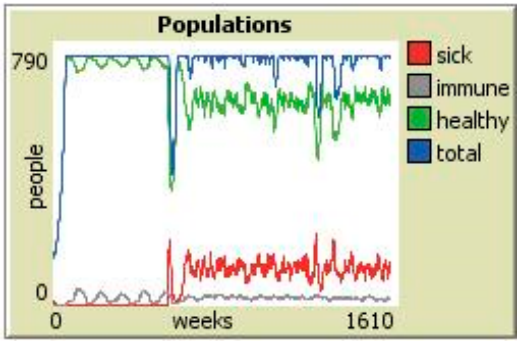

Fig. 8. E-2:Random population vaccination

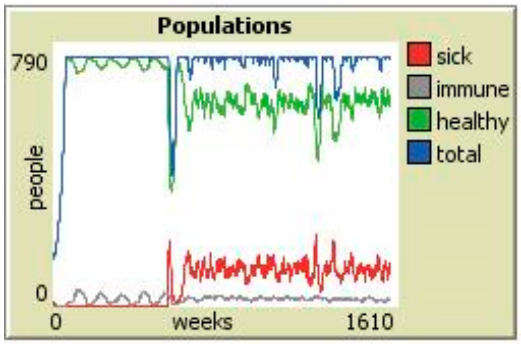

Fig. 9. E-2:Fixed population vaccination

C. Emergent Pattern E-3

Random Population Vaccination: In case with Random-vaccination the pattern of extinction sustained in Fig 10. Fixed Population Vaccination: In these parameter settings it was observed that the disease sustained in the population in long run as shown in Fig 11.

Where R-P denotes Random Population vaccination and F-P denotes Fixed Population vaccination. When infected agents were made to move slowly an interesting pattern of disease emergence was observed. Figure 12 shows the time comparison in case of rapid and slow movement of infected. A minor difference was observed in case of pattern E1. Patterns E2 and

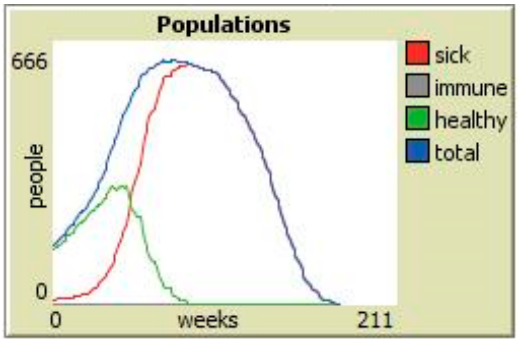

Fig. 10. E-3:Random population vaccination

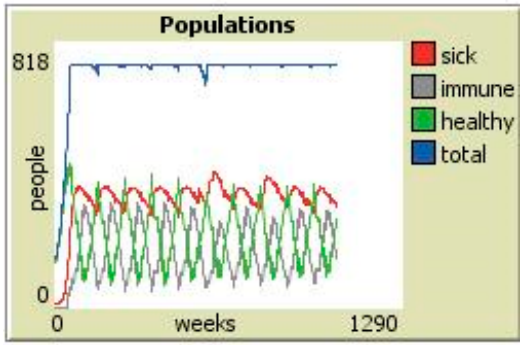

Fig. 11. E-3:Fixed population vaccination

TABLE II
RANDOM VS FIXED POPULATION VACCINATION

Sr.No	Emergent Behavior	I	C-R	D	R-P Vacc	F-P Vacc
E-1	Persistence	5	0	99	E-2	E-2
E-2	Eradication	99	0	2	E-1	E-2
E-3	Extinction	99	0	99	E-3	E-1

E3 showed a significant difference in time. In the former case the disease took long to eradicate from the population. With slow-infected the disease eradicated early from population. Whereas in case of extinction with slow-infected it took long and the disease spread in form of clusters.

IV. CONCLUSION

The experiments revealed that if the movement of infected agents was restricted that the disease spread was in the form of clusters. This phenomenon can help to explicate the regional disease spread. In case of diseases with low infectiousness random and fixed population vaccination strategies worked equally well. Highly infectious diseases with a longtime span resulted in pandemics. With fixed population vaccination it was observed that some individuals have a chance to survive, which can then reproduce into healthy offspring. In case no healthy individual survives both strategies have parallel results. Whereas, for diseases with high infectiousness and short duration fixed population vaccination must be applied to obtain the optimal results. Though agents represent human

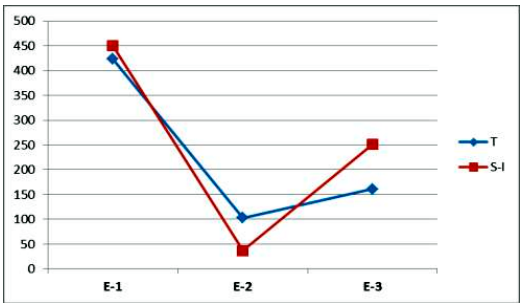

Fig. 12. rapid movement and slow infected

population in the model, but it can be adapted to the livestock animals or marine life as well. Overall evaluation was that fixed population vaccination is more favorable to attain herd immunity. Based on this study we suggest that if some individuals in population take responsibility and complete their dosage courses they serve as barriers between infected and susceptible and can help avoid worst case scenarios.

Hence, It can be concluded that agent-based models can effectively be used in policy making, regarding mitigation of disease. Moreover, agents in this model move freely and interact with others. Other demography characteristics, transmissibility, and social networks can be introduced in the model to present a real-world scenario. It can be further extended to simulate emergency management and assess what preventive measures can be taken to avoid the worst-case scenario. We plan to extend this model further by applying it to infectious disease scenarios using more precise parameters and applying it to different case studies.

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