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EFFECTS OF VARIOUS PARAMETERS ON THE CONTAINMENT OF PANDEMICS

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MASTER OF SCIENCE THESIS

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A thesis submitted by Ramin NASHEBI in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE is approved by the committee on 12.01.2022 in Department of Mathematics, Mathematics Program.

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Ramin NASHEBI

Signature

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In the name of Allah, the Most Gracious and the Most Merciful

Peace be upon his Messenger Muhammad

This thesis is dedicated to my parents, brother, and sisters

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Ramin NASHEBI

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LIST OF SYMBOLS

$A(t)$	Asymptomatic
d_4	Average time of going to the hospital
R_0	Basic Reproduction Number
θ	Cutoff for distance
d	Distance
$d_{i,j}$	Distance in meters between individuals i and j
R_e	Effective reproductive number
$E(t)$	Exposed Stage
g	Granularity
$H(t)$	Hospitalization Stage
P	Infection Probability
d_1	Mean number of days in the latency stage
d_2	Mean number of days in pre-symptomatic stage
d_3	Mean number of days in the asymptomatic stage
N	Number to Total Contacts
$PS(t)$	Pre-symptomatic Stage
$Ph_{j,i}(t)$	Probability of infection if the contact occurs in houshold
$Po_{j,i}(t)$	Probability of infection if the contact occurs in workplace or social environment
ε	Random number between 0 and 1
ϵ	Random number between 0 and 1
D	Ratio of the effective-outside transmission probability
$R(t)$	Recovered Stage
α	Scaling parameter of distance
$S(t)$	Symptomatic Stage
s	The ratio of symptomatic cases
β_h	Transmission probability per 5 minutes inside of households
β_o	Transmission probability per 5 minutes outside of households
β	Transmission rate

μ_H	Transmission reduction fator for asymptomatic cases inside household
μ_O	Transmission reduction fator for asymptomatic cases outside household

LIST OF ABBREVIATIONS

ABMS	Agent-based modelling and simulation
AIP	Average infection probability
CA	Cellular automata
DTMC	Discrete time Markov chains
GT	Generation time
GIS	Geographic information system
H	Household
HIV	Human immunodeficiency virus
MERS	Middle east respiratory syndrome
O	Non-household (workplace, social environment)
NPIs	Nonpharmacologic interventions
Q	Quarantine
SAR	Secondary attack rate
SI	Serial interval
SARS	Severe acute respiratory syndrome
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
RL	Stay-at-home restriction Level
SIR	Susceptible-Infected-Recovered
SIRS	Susceptible-Infected-Recovered-Susceptible
TG	Transmission generation
TB	Tuberculosis
V	Vaccinated
WT	Wild Type
WH	Working Hour
WHO	World Health Organization
2019-nCov	2019 novel coronavirus

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ABSTRACT

Effects of Various Parameters on the Containment of Pandemics

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MSc. Thesis

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Human behavior, economic activity, vaccination, and social distancing are inseparably entangled in epidemic management. This study aims to investigate the effects of various parameters such as human behavior, economic activity, vaccination, and social distance on the process of the containment of pandemics such as COVID-19. To achieve this, an agent-based model based on a time-dynamic network with stochastic transmission events has been developed via the computer codes produced here in MATLAB 2019b. The network is constructed from a real-world social network. The social network data has been categorized into three categories: home, workplaces, and social environment. Consequently, it has allowed us to understand household and non-household environments contribution to the overall dissemination of the pandemic. The conditions needed to mitigate the spread of wild-type COVID-19 and the delta variant have been analyzed. Tens of thousands of individual-based simulations have been carefully executed by our purposeful agent-based model. A function that fits the simulations has been used and this attempt has given the opportunity to explore the interaction between pharmaceutical and non-pharmaceutical interventions on containment of COVID-19. It has been found that changing working hours or implementing stay-at-home restrictions, up to 4 days, does not significantly reduce the basic reproduction number R_0. It has also been found that successful vaccination does not bring R_0 below 1 when no other measures are implemented. It has been concluded that although most of the infections occurred in homes when $R_0 < 1$, the household transmission does not significantly alter the spread. Note also that the spread ultimately depends on non-household transmissions.

Keywords: Pandemic, COVID-19, Agent-based model, Household transmission, Social network, Working hours

ÖZET

Çeşitli Parametrelerin Pandemilerin Sınırlandırılmasına Etkileri

Ramin NASHEBI

Matematik Bölümü

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İnsan davranışı, ekonomik aktivite, aşılama ve sosyal mesafe, salgın yönetiminde ayrılmaz bir şekilde iç içe geçmiş durumda. Bu çalışma, COVID-19 gibi pandemilerin kontrol altına alınması sürecinde insan davranışı, ekonomik aktivite, aşılama ve sosyal mesafe gibi çeşitli parametrelerin etkilerini araştırmayı amaçlamaktadır. Bunu gerçekleştirmek için, burada MATLAB 2019b'de üretilen bilgisayar kodları aracılığıyla stokastik geçiş (bulaş) olaylarıyla zaman dinamik bir ağa dayalı faktör-tabanlı bir model geliştirilmiştir. Söz konusu ağ, gerçek dünyadaki bir sosyal ağdan inşa edilmiştir. Sosyal ağ verileri üç kategoriye ayrılmıştır: ev, işyerleri ve sosyal çevre. Sonuç olarak, ev içi ve ev dışı ortamların pandeminin genel yayılmasına katkısını anlamamızı sağlamıştır. Yabani tip COVID-19 ve delta varyantının yayılmasını azaltmak için gereken koşullar analiz edildi. Amaca yönelik ajan-tabanlı modelimiz tarafından on binlerce bireysel tabanlı simülasyon dikkatli bir şekilde gerçekleştirilmiştir. Simülasyonlara uyan bir fonksiyon kullanılmış olup bu girişim, COVID-19'un kontrol altına alınmasına ilişkin farmasötik ve farmasötik olmayan müdahaleler arasındaki etkileşimi keşfetme fırsatı vermiştir. Çalışma saatlerini değiştirmenin veya 4 güne kadar evde kalma kısıtlamalarının uygulanmasının, temel çoğaltma sayısı R_0'ı önemli ölçüde azaltmadığı sonucuna varılmıştır. Ayrıca başka hiçbir önlem uygulanmadığında başarılı aşılamanın R_0 'ı 1'in altına getirmediği görülmüştür. Enfeksiyonların çoğunun, $R_0<1$ olduğunda, evlerde meydana gelmesine rağmen, ev içi bulaşmanın yayılmayı önemli ölçüde değiştirmediği sonucuna varılmıştır. Yayılmanın nihayetinde ev dışı bulaşmalara bağlı olduğu da göz ardı edilmemelidir.

Anahtar Kelimeler: Pandemi, COVID-19, Ajan-tabanlı model, Ev içi bulaşma, Sosyal ağ, Çalışma saatleri.

1

INTRODUCTION

This chapter presents an overview about the influence of the interplay of the non-pharmaceutical policies and vaccination in the context of control and containment of the disease and successful management of the economy and the public's health. Also, the mathematical models that have been offered in literature for simulating dynamic, control, and containment of COVID-19. Additionally, the goal of this study of the thesis are given respectively.

1.1 Literature Review

Human behavior in households, workplaces, social environment during weekends and weekdays have a vital role in the spread of infectious diseases such as middle east respiratory syndrome (MERS) [1], H1N1 influenza [2], severe acute respiratory syndrome (SARS) [3], and the current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Household members have frequent and intimate contacts, making the disease spread rapidly within the households [4-5]. We can observe the risk of infection within the household during seasonal and pandemic influenza [6-7], for pneumococcal carriage [8], and childhood infections [9-10].

The ongoing COVID-19 pandemic, instigated by the novel SARS-CoV-2, has rapidly spread from Wuhan, China, to nearly all countries. The diverse clinical and epidemiological features of COVID-19 have contributed to its disastrous effects worldwide [11,12]. This disease transmission occurred via droplets during close contacts and via contaminated surfaces [13-16]. The critical role of pre-symptomatic and asymptomatic individuals in transmitting infection makes symptom-based isolation less effective [12].

The development of strategies for preventing infectious diseases is a priority of health organizations. There are three general containment strategies for

preventing and mitigating infectious disease: antiviral, vaccine, and non-pharmaceutical measures [17]. The non-pharmaceutical measures include a wide range of policies such as changing the number working hours, limiting transmissibility between individuals by distancing measures, and stay at home restrictions [18, 19, 34]. Stay-at-home policy is frequently used [19-22]. The World Health Organization [23,24] and many local authorities [25,26] supported stay-at-home measures and encouraged them. Governmental policies upon stay-at-home orders are grouped into four categories: no measures implemented concerning staying-at-home, recommended to stay at home, moderate restriction concerning stay-at-home (people can do their daily exercise, grocery shopping, and 'essential' trips), and high restriction regarding stay-at-home (people allowed to leave only once every few days, or only one person can go at a time) [27]. The same countries modified the long lockdown to a short-term stay-at-home order, such as France [28,29], Turkey [30,31], India [32]. These countries recommend stay-at-home orders only during weekends. On the downside, stay-at-home orders, limiting work hours, distancing measures have negative effects on mental health, physical health, and the economy [35]. Understanding the interplay of the mentioned non-pharmaceutical policies and vaccination is essential in the context of control and containment of the disease and successful management of the economy and the public's health. Since the experimental study is not compliant to investigate the social dynamic, control, and management of disease among humans, mathematical models are crucial to quantify and investigate such effects [33,36]. Models are developed in order to understand the effect of external influences on outputs, through representation of the interactions between the components of the system, and to communicate ideas about the behavior of the system. In mathematical modelling, those features of system, that being studied theoretically, translate into the language of science for simplification [37-38].

The role of stay-at-home (short-term) orders, limiting working hours, and distancing measures in spreading COVID-19 requires modelling the interplay between agents and their environment. Moreover, the interaction between agents and agents' interaction with the environment directly affects the incidence and persistence of infection disease. The spatial and social heterogeneity of agents, the

interaction between agents, and the emergent effect are produced from these interactions and persists over time make it a complex phenomenon [39]. The problem can be represented by agent-based models simulated on a time-resolved contact network with stochastic events. We have aimed for a model where the duration of stay-at-home restrictions, number of working hours and distancing measures can be varied independently on an individual level. Many mathematical models have been developed to investigate this complex system [40-42].

Standard compartmental models are used to investigate the dynamic of disease in a population by using a set of ordinary differential equations [43]. These models use mean-field [55, 48] approximation, assuming that every infectious member infects any member of the susceptible class with the same probability. Many SEIR compartmental models [44, 45] were conducted to investigate COVID-19 by using mean-field approaches. Hou et al. [46] used a mean-field SEIR model to analyze the role of self-isolation in the control and containment of COVID-19. Some studies [47,49] modify the SEIR model by adding new states to account for asymptomatic cases and the effect of quarantine and hospitalization. However, due to the usage of mean-field approximation, these models do not capture the stochasticity of phenomena and individual-level behavioral effects [43].

Stochastic models are individual-level models, include discrete and continuous-time Markov chains models [43]. In these models, an infectious person infects a susceptible person with a definite probability if there be present a physical connection between them. The link between individuals makes a contact network, where disease spread. Ando et al. [50] established a stochastic model to investigate the role of human mobility in spreading of COVID-19. Stochastic models relax the mean-field approximation hypothesis in infection disease modelling, but when the interaction between individuals is homogenous, or there is an infinite number of individuals, the stochastic models became the mean-field deterministic model [43]. Heterogeneity of contact network has a significant effect in dynamic of disease [43]. Firth et al. [51] used a real-world social network to model control and containment strategies for COVID-19.

Agent-based modelling is a computational approach to modelling complex systems consist of autonomous agent interactions [52,53]. Agent-based modelling composed of three components: agents with behaviours and attributes, agents' relationships and interactions, and agent's environment where they interact. In epidemiology, to decide to control an infection disease, it is essential to understand the interaction between agent, host, and environment affects the transmission of disease and its development in a population [54]. Consequently, agent-based models are essential tools to understanding the impact of human behavior in the transmission of infectious diseases in different environments such as households, workplaces, and social environments. Moreover, they are deficient in linking basic reproduction numbers to complex phenomena like the spatial and time-wise occurrence of infection events. Among spatial places, we are interested in infections occurring in households, workplaces and social environments. Aleta et al. [40] used an agent-based model with three layers: school, workplace, and household. They used human mobility data and constructed artificial contact networks with different weights, which proxy transmission, for each setting (schools, workplace, and households). They used their model to investigate the influence of the closure of schools and stay-at-home restrictions. Another study by Hoertel et al. [41] developed a stochastic agent-based model and run it over a synthetical social network. They investigated the effectiveness of the national lockdown of francs, post-lockdown, distancing measures, and mask-wearing. Braun et al. [42] developed a network-based, agent-based model. Using this model, they simulated the Watts–Strogatz small-world network to catch the efficiency of social distancing, personal protective equipment, and quarantining. In this study, we have developed a discrete-time stochastic agent-based model to investigate the effect of social distancing, stay-at-home restriction during weekends, and working hours on the containment of COVID-19. Our advancement with the above works is that we use real-world social network data and manually classified contacts into the household, workplace, and social environment

Simulation studies have been done using network models to investigate the dynamic of disease [60]. Volz et al. [61] used this approach to investigate the dynamical pattern of an epidemic in complex heterogeneous networks. Sewell and

Miller et al. [62] used the SEIR model and a contact network to investigate the effect of mask and quarantine in spreading COVID-19. In addition, social networking plays a significant role in assessing the potential effectiveness of stay-at-home restriction [40], social distancing [12], economic policies [56], and vaccination [57]. In 2018, the BBC released a human social interaction dataset to explore the dynamics of a pandemic in the UK [58]. Josh et al. [59] developed a branching process model and simulated the COCVID-19 outbreak throw this social network dataset. They assessed the impact of testing and contact tracing strategies for controlling of COVID-19 outbreak.

Some mathematical models and meta-analyses analyzed the dynamic of COVID-19 inside and outside of households [63, 12, 64, 65, 66,71]. Many studies found that the probability of indoor transmission was very high compared to outdoors [65]. Another study shows that even by implementing strong social distance measures, the epidemic peak can occur weeks to months later, and the decline in cases can be prolonged. The efficacy of household transmission plays a vital role in this result [12]. In a study [67], 1587 close contacts of confirmed cases with COVID-19 were traced. In a case study [66], a report from China, 318 outbreaks with three or more cases were identified. In Wuhan, the basic reproduction number (R_0) dropped from 3.54 to 1.18 after lockdown and cordon sanitaire. Nevertheless, the epidemic was only brought under complete control when Fangcang (field) hospitals were introduced to isolate cases outside the home, dropping to 0.51 after two weeks [68]. However, a recent mathematical model [69] suggested that stay-at-home does not play a dominant role in reducing COVID-19 transmission. Despite this, in the presence of widespread community measures, 70% of SARS-CoV-2 transmission occurred between household contacts [70].

Basic reproduction number (R_0) indicates the transmissibility of infectious diseases [72]. R_0 is an estimate of contagiousness that is a function of human behaviour and biological characteristics of pathogens [72]. Thus, R_0 estimates of COVID-19 are not exclusively determined by the pathogen, and variability in R_0 depends on local socio-behavioral and environmental settings [73]. Anderson and May [74] calculated the basic reproduction number as a function of contacts,

transmission rate, and transmission duration. In this work, we hypothesize that the basic reproduction number (R_0) is the average number of secondary cases [72].

There have been many published works in the efforts to study the role of vaccination [77], social distancing [18], household [18, 71] in understanding the dynamic and control of the SARS-CoV-2 virus. Several authors have been designed and used simple models [76,75,78], complex models [77,79,81], and multi-scale models [80] to simulate the trade-off between pharmaceutical (vaccination) and non-pharmaceutical (social distancing, stay-at-home restriction, decrease in working hours) intervention in the containment of COVID-19 pandemic. This study presents an agent-based model based on a time-dynamic network with stochastic transmission events that allowed us to analyze the interplay between pharmaceutical and non-pharmaceutical interventions. The advancement is by modelling in a way that the following are tunable: stay-at-home restriction, working hours, vaccination, social distancing. Moreover, we represent the trade-offs between complex phenomena in a simple equation. This simple function links the modelled forces with basic reproduction number from the generated data by thousands of carefully executed individual level simulations of multiscale modelling on the real network. Additionally, some of the interesting observations includes that the ratio of household infections increases as effective reproduction number decreases. Moreover, the household infections provide resilience for epidemic eradication but do not contribute significantly to spread.

1.2 Objective of the Thesis

This thesis aims at investigating influence of Human behavior, economic activity, vaccination, and social distancing in context of control and containment of COVID-19. To achieve this major aim, four objectives are outlined:

1. To construct an agent-based model based on a time-dynamic network with stochastic transmission events

2. To construct a network from real-world social network, and categorize edges into household, workplace, and social environment.

3. To accurately modelling stay-at-home restriction, working hours, vaccination, social distancing.

4. To simulate the interplay between pharmaceutical (vaccination) and non-pharmaceutical (social distancing, stay-at-home restriction, decrease in working hours) intervention in the containment of COVID-19 pandemic.

1.3 Original Contribution

Most of the infections occur in homes when $R_0 < 1$. The household infections provide resilience for epidemic eradication but do not contribute significantly to spread. It is also noticeable that the spread ultimately depends on non-household transmissions. Furthermore, changing working hours or implementing stay-at-home restrictions, up to 4 days, does not significantly decrease R_0. Finally, successful vaccination does not bring R_0 below 1, when no other measures are implemented.

1.4 Overview of the Thesis

This thesis consists of five chapters. Chapter 1 presents literature review, objectives, and hypothesis of the thesis. In chapter 2 we will give some preliminaries about graph theory, infection diseases, COVID-19 pandemic, epidemiological modelling, and agent-based modelling and simulation.

In chapter 3 we will describe our methods and material. First, we describe our real-world social network data, and methodology for classification of data into household, workplace, and social environment. Secondly, the development and simulation process of our agent-based model. Finally, the way that we modelled the stay-at-home restrictions, decreasing working hour, social distancing, and vaccination. In chapter 4 we will report the results of our investigation and make discussion about it. Conclusions will be given in chapter 5.

2

PRELIMINARIES

This chapter gives a brief introduction to graph theory to understand the structure and usage of social network data, considering the data that our agent-based model uses to simulate agents (humans) behavior is a real-world social network dataset. Then, we will give information about infectious disease, SARS-CoV-2, and epidemiological modelling. Finally, we will give some preliminaries about the agent-based modelling and simulation. As we will develop an agent-based model based on a time-dynamic network with stochastic transmission events, we will discuss in depth the structure and use of stochastic and agent-based modeling.

2.1 Graph Theory

Many real-world problems can be described through a network consisting of a set of points and lines. The lines show any link and interaction between two points. Networks that are built around people are called social networks. Moreno Jacob was the first person who introduces a sociogram in the 1930s. His sociograms have an essential contribution to social network analysis. A sociogram represents the network, where people are demonstrated by points and their interaction by lines (Fig 2.1). However, to study a network, you need to use accurate terms, such as what it means to talk about the distance between two nodes; similarly, how are we to understand that the network is well connected? These and other statements can be precisely defined by taking the terminology from graph theory [82,83]. Graph theory is a mathematical field that gained popularity in the 19th and 20th centuries, mainly because it allowed the description of phenomena from a wide variety of fields: drawing and coloring maps of communication infrastructures, planning problems and social structures, and many others [82]. The edges in a graph can also have weights, or different numerical values, attached to them. A graph whose edges have weights is called a weighted graph, and one whose edges do not is an unweighted graph. In many situations, weighted graphs are helpful

for capturing additional information about the relationships between vertices. For example, in an epidemiological context, if vertices represent individuals in a population and edges indicate that two individuals are in epidemiological contact, edge weights could give the probability of disease transmission occurring between two individuals per unit time. In a graph, the shortest path between two nodes is called *geodesic distance*, which is a valuable property in characterizing networks.

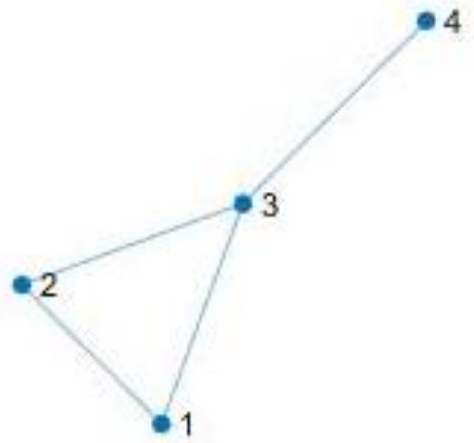

Figure 2.1 Example of sociogram network where nodes (dots) represent individual, and the edges (line segment) represent interaction between these individual

2.2 Infection Diseases

A disease because of pathogen, caused by transmission of pathogen from contaminated person, animal, or inanimate object to a susceptible host is called infection disease [92].

The continuous outbreak of infectious diseases has shaped human history. For centuries, entire countries and civilizations have disappeared from the map. Around 1715 BC, in the middle of the Bronze Age, the bible pharaoh plague ravaged ancient Egypt. From 430 BC to 425 BC, the "λοιμός" in Athens caused about 13 million deaths and destroyed the indigenous population of Central America [93]. In 1348, the Black Death plague broke out in Europe, killing more than 25 million people in just five years. In 1918-1919 the pandemic of influenza virus swept the Asia, Europe, Americas, and Africa and destroyed the world and killed approximately 40 million people. In the following decades, there were two

less severe annual influenza pandemics: the influenza pandemics in 1957 and 1963 killed 2 and 1 million people, respectively [92]. In 2013, infectious diseases caused the loss of more than 45 million people to ailment and more than 9 million mortalities [94]. Tuberculosis (TB), the human immunodeficiency virus (HIV)/AIDS, diarrheal diseases, malaria and inferior respiratory region infections are among the leading reasons of inclusive global death [94]. Epidemic of AIDS caused by the HIV that commence in non-human primates in the Central and West Africa. According to the Joint United Nations Program on the HIV/AIDS, at the end of 2010, an estimated 34 million people worldwide were living with HIV. Of these, 3.4 million are children. The new deaths and related injuries were 1.8 and 2.7 million, respectively [95].

One of emerging infectious diseases, is coronavirus disease in mammals and birds. They can cause mild or fatal respiratory infections in humans and birds. Human mild illnesses include several common colds, and more deadly variants can cause SARS, MERS, and COVID19. The Middle East Respiratory Syndrome (MERS) [96] is caused by the middle east respiratory syndrome coronavirus (MERS-CoV). The first confirmed case occurred in Jeddah, Saudi Arabia in June 2012, and most cases occurred in the Arabian Peninsula [97]. As of January 2021, more than 2,500 cases were reported, including 45 cases in 2020 [98]. Approximately 35% of patients die from it [98]. Severe Acute Respiratory Syndrome (SARS) is a zoonotic respiratory viral disease caused by the severe acute respiratory syndrome coronavirus (SARS-CoV or SARS-CoV-1). The syndrome caused the 2002–2004 SARS outbreak; at the end of the epidemic in June 2003, the incidence was 8,422 cases [99]. As of 2004, there were no reported cases of SARS-CoV-1 worldwide [100]. In December 2019, another strain of the SARS-CoV was identified as SARS-CoV-2. This new strain of coronavirus causes COVID-19, a pandemic that occurred in 2019.

An infectious disease is caused by a combination of a host, agent and environmental factors see Figure 2.2a. Bacteria, non-living viruses, fungi, and living parasites are some of the infection agents. The interaction between host and agent indicates whether exposure has occurred or not see Figure 2.2b. Environmental factors indicate whether a host has been exposed by an agent or

not, and the outcome of exposure is determined by the successive interactions between the agent and the host see Figure 2.2b. The interaction of the host and the agent takes place in a series of stages consisting of infection, illness, and convalescence or death. Following exposure, the pathogen begins colonization, adhesion, and initial proliferation at the entrance gate. Some ailments are always caused by infection, but not always by disease. Illness shows the degree of confusion and damage to the host, resulting in subjective symptoms and objective signs of disease. *Recovery* from infection is either complete (drug removal) or incomplete. When a potential host is exposed to an infectious pathogen, the outcome of that exposure depends on the dynamic relationship between infectious, pathogenic, and pathogen determinants see Figure 2.2b. When the host is exposed to the agent, the potential of the agent to infect the host is called *infectivity*. *Pathogenicity* is the capability of a pathogen (organism) to cause a disease (infectious disease). The result of exposure to infectious pathogens may also depend on various host aspects that determine an individual's susceptibility to infection. Exposed individuals can resist infection or limit disease due to their biological makeup. This ability of individual is called *susceptibility*. There are some factors such as innate factors, genetic factors and acquired factors, such as specific immunity after exposure or vaccination, that affecting susceptibility. There are two basic forms of immunity, active and passive. In active immunity the immune protection produces by host’s own immune response. In contrast, passive immunity is achieved by transferring immune effectors, the most common antibodies (also known as immunoglobulins, antisera) from donor animals or humans. Environmental causes of susceptibility to infectious diseases consist of behavioral, physical, cultural, social, economic, and political factors [111].

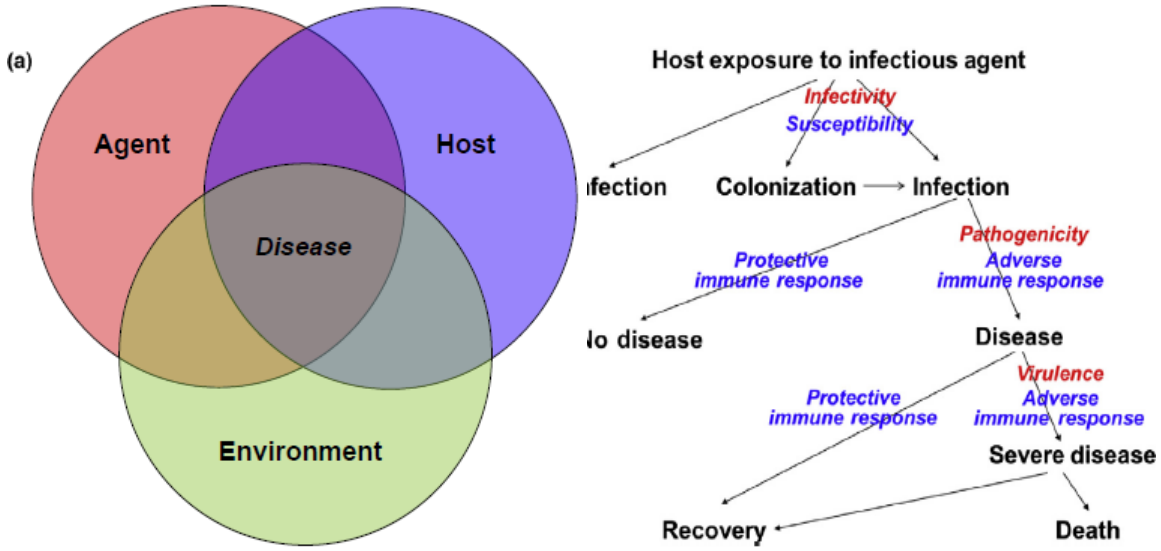

Figure 2.2 Epidemiological triad model of causality of infectious diseases and potential consequences of host exposure to infectious agents [111]

The transmission of pathogens occurs in two ways: directly and indirectly. According to public health, the transmission stages are classified according to the clinical illness and transmission potential. With respect to clinical illness, the first stage is the *incubation period* which host exposed with an infection agent utile the appearances of first signs of symptom. After incubation period the clinical *illness* or *symptomatic period* begin, which is defined as the duration between the first and the last sign of symptom. With respect to the transmission potential, the primary stage is *latent period*, the duration between exposure to an agent and the start of infectiousness. Latent period tracked by the *infectious period*, where infected person can spread an infection agent to others [111]. *Presymptomatic* is the phase when an individual is infected and maybe shedding virus but has not yet developed symptoms [112]. The early or mild stages of this infection, whose symptoms are below the level of clinical evidence, are called asymptomatic infections, and those affected are called asymptomatic carriers. The *serial interval* (SI) refers to the interval between the time points of symptom onset in an infector and his/her infectees. The generation time of an infectious disease (GT) is the time interval between the onset of an individual's infection and the time that person infects another. The period of time during which the first case becomes infected with the virus and then transmits it to the second is called *transmission generation* (TG) [112].

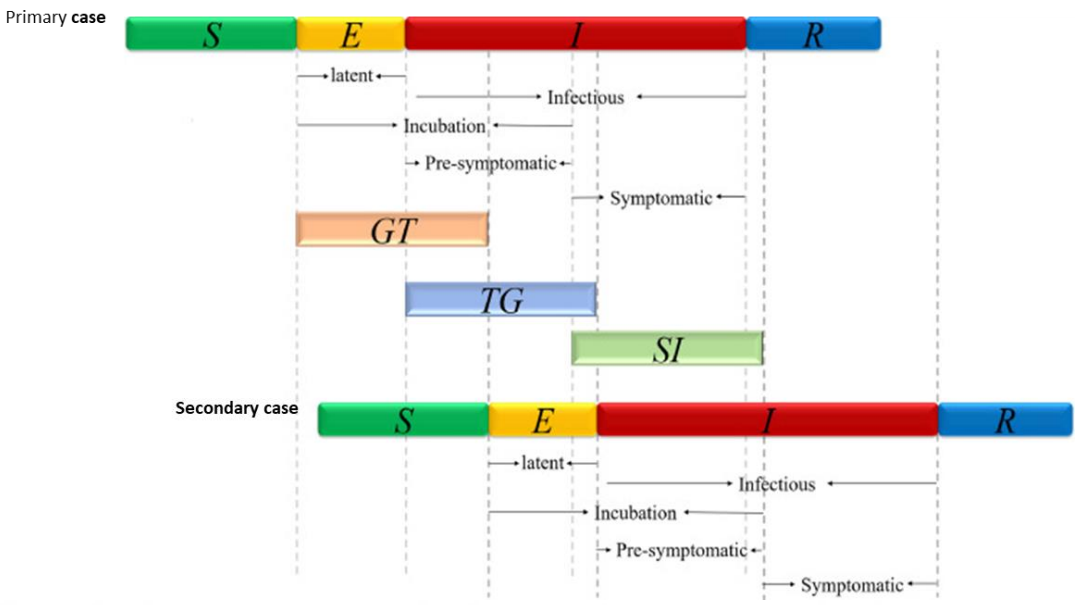

Figure 2.3 Illustrative timelines and various stages during infection and transmission of an infectious disease [112]

In particular region or population numerous expressions are used to describe the outbreak of an infectious disease. Diseases which happen with predictable regularity is characterized as *endemic*, while diseases which occur occasionally and unpredictably is called sporadic. The degree of endemic can be divided into holoendemic, high epidemic, moderate epidemic, or low epidemic, depending on whether the frequency of the disease is extreme, high, medium, or low. The term outbreak is frequently used interchangeably with epidemic, nevertheless it can also state to an epidemic that occurs in a narrower geographic region. In contrast, pandemics are epidemics that spread geographically over large areas, across multiple countries around the world [111].

The measures that characterize frequency of disease are, attack rate, prevalence, incidence, basic reproduction number, effective reproduction number and herb immunity. *Attack rates* is assessed as the proportion of number infected over number of exposed. The *prevalence* estimates the number of existence cases in population. Despite this, *incidence* calculate the rate of new cases that occur in population at a specific time. In certain circumstances, the transmission of disease from an index case to susceptible, exposed individuals in localized population this is called *secondary incidence rate* [111]. The average number of secondary cases generated from a single case in a completely susceptible population is defined as

the basic reproduction number in a completely susceptible population. However, in some population, there already exist some nonsusceptible proportion due to immunization and previous infections; thus, more accurate disease frequency to reflect the potential of population disease spread is needed. The average number of secondary cases generated from a single case in a population which is already infected, is called *effective reproduction number*. The *herb immunity*, which is also defined as *community immunity*, shows the percentage of the population that is resistant to infectious diseases that prevents the infection/transmission chain.

According to a study by Leaver and Clack [113], the prevention of disease is divided into three levels: primary preventions, secondary preventions, and tertiary preventions. *Primary prevention* occurs before the population is triggered by the spread of the disease. *Secondary prevention* is applied in asymptomatic stages [111] to reduce the progression of infection and to prevent transmission of infectious agents [111]. Tertiary prevention is used to reduce the effects of infected individuals, reduce disease progression, enhance function, and maximize quality of life.

The interaction of the agent, host and environmental factors has a linked sequence called the *chain of transmission* or *chain of infection*. This chain starts with an infectious agent, which causes the disease. The infectious agent leaves the reservoir from a *portal of exit.* The portal of exit for infectious agents has several routes with respect to infections; for example, the portal of exit for influenza infectious agents are respiratory sections [111], for rotavirus is gastrointestinal [111]. After exiting from the reservoir, infectious agents reach the portal of entry of the susceptible host by using some mode of transmission. There are two modes of transmission *direct* and *indirect* [111]. In a direct mode of transmission, agents enter directly from reservoir to host by physical contact (skin or mucosa of agent to host), the spread of droplets (sneezing, coughing), direct contact with an agent in environmental reservoirs (inhalation), animal bites, transplacental (pregnancy delivery) and perinatal (breastfeeding) transmission [111]. In indirect mode, transmission agents enter indirectly from a reservoir to a host. Indirect transmission is divided into three categories: biological, mechanical and airborne. *Biological transmission* takes place when the pathogen reproduces

within a biological vector [111] that transmits the pathogen from one host to another. Arthropods are the key vectors responsible for biological transmission [115]. When an infectious agent is transferred physically by using a live entity (mechanical vector) or inanimate object (vehicle) to a susceptible host, this kind of transmission is defined as *mechanical transmission*. *Airborne transmission* is a colloidal suspension of residues or particles containing active substances that can be transported over long distances and over long periods of time and still remain infectious.

Understanding the chain of infection allowed us to prevent and control any infectious disease. One of control and prevention strategies is breaking any link in the chain, which avoid the transmission of the infectious agent. The earlier intervention can implement to eliminate the infectious agent in their reservoirs. The most common intervention is *surveillance activity* [111] which routinely identify infectious agents in the reservoir. When the reservoirs of infectious agents are humans, *case isolation*, *contact tracing* and *quarantine* [111] are intervention activities. When targeting portal of existing for preventing disease, *standard precautions* and *transmission-based precautions* [116] are suggested to reduce transmission level of an infectious agent. Standard precaution consists of hand hygiene, personal protective equipment (gloves, gowns, face protection, masks), and respiratory hygiene/cough etiquette. Targeting the susceptible host to prevent disease immunization (vaccination) are suggested as an intervention activity.

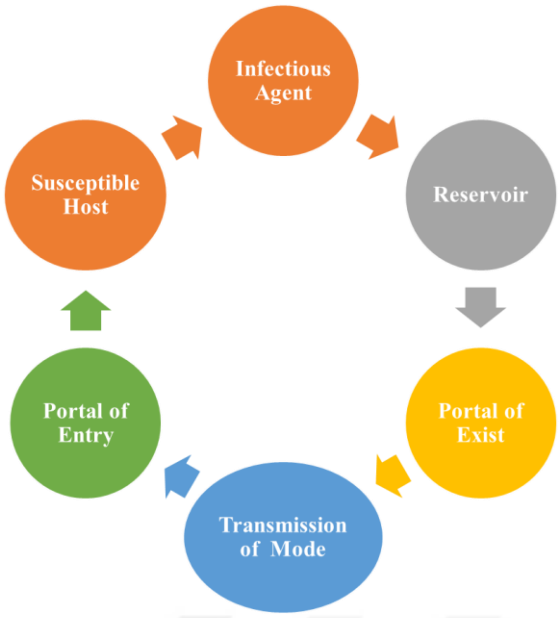

Figure 2.4 Visualization of transmission chain. The spread of agent ensues through six interconnection chain-linked element in a population

2.3 Coronavirus Disease 2019 (COVID-19)

The coronavirus pandemic, also recognized as the COVID-19 pandemic, is the ongoing global pandemic of the 2019 Coronavirus Disease (COVID-19) caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The virus was first detected in Wuhan, China in December 2019. On the 30th of January, the World Health Organization declared an international public health emergency on COVID-19 and declared a pandemic on the 11th of March. As of June 10, 2021, 174 million confirmed cases of COVID-19 had been reported, with more than 3.75 million confirmed deaths to date due to the virus and historically. It has become one of the deadliest pandemics.

COVID-19 is a contagious disease caused by the SARS-CoV-2 virus [101]. Different names were used for the virus during the first outbreak in Wuhan, China. Some names were used by various sources were the "Coronavirus" or the "Wuhan Coronavirus" [108]. The WHO recommended "2019 Novel Coronavirus" (2019-nCov) as the tentative name of the virus in January 2020 [109]. On the 11th of February 2020, the ICTV (International Committee on Taxonomy of Viruses) adopted the official name "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) [110]. Coronaviruses are a family of enveloped RNA viruses that

are distributed widely among mammals and birds, causing principally respiratory or enteric diseases but in some cases neurologic illness or hepatitis [102]. In taxonomy, which is a branch of biology for the scientific study of naming, defining and classifying of a biological organism, Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria* [103]. The viruses are enveloped with a single-stranded RNA genome and a nucleocapsid of helical symmetry [104]. They have club-shaped spikes that protrude from their surface, which in electron micrographs create an image similar to the solar corona, from which their name derives [105]. They are divided into four genera: Alphacoronaviruses, betacoronaviruses, gammacoronaviruses, deltacoronaviruses. Alphacoronaviruses and betacoronaviruses infect mammals, while gammacoronaviruses and deltacoronaviruses primarily infect birds. In 2003 and 2012, the causative agents of SARS and MERS outbreaks were the SARS-CoV and the MERS-related coronavirus, which are a species of betacoronavirus genera [106]. The SARS-CoV-2 is the culprit of the 2019 Coronavirus Disease (COVID-19), a type of coronavirus (SARSr-CoV) associated with severe acute respiratory syndrome Viruses of the genus Betacoronavirus [101]. It is closely related to both SARS-CoV and MERS-CoV. The SARS-CoV-2 is spread more expeditiously, and it is more infectious than the SARS-CoV and MERS-CoV [117]. The SARS-CoV-2 have zoonotic origin, and there are some insinuations that it materializes from bats coronavirus [107], but research is ongoing.

The clinical manifestations of the SAR-CoV-2 infection ranged from asymptomatic lung disease of the upper respiratory tract to severe viral pneumonia with respiratory failure and death [117]. The clinical symptom of the COVID-19 classified into three groups: respiratory symptoms, musculoskeletal symptoms, and digestive symptoms. The respiratory symptoms include cough, shortness of breath, sputum, and fever. The musculoskeletal symptoms include muscle and joint pain, fatigue, and headache. The digestive symptoms include diarrhea, abdominal pain, and vomiting [118]. Besides these symptoms, smell and test loss also added to the chief symptoms [119]

The COVID-19 disease has a direct and indirect mode of transmission. The direct transmission has a respiratory route and occurs via droplets or aerosols released as coughing, sneezing, breathing, and talking. The infectious individual transmits the COVID-19 by making longer and closer, typically within 1 meter [120], contact with susceptible hosts. The virus can also spread in imperfectly ventilated and crowded indoor environments, where people tend to spend more extended periods of time because aerosols remain suspended in the air or travel more than 1 meter. After that, the aerosols or droplets containing the virus are inhaled or come directly into contact with the eyes, nose, or mouth. Some of the aerosols fall to the ground and make surfaces containment with the virus. Whenever people touch the surfaces and touch their eyes, nose or mouth without cleaning their hands, it will infect them. This kind of transmission forms an indirect mode of transmission of the COVID-19.

2.4 Epidemiological Modelling

Epidemiology comes from the Greek words epi, which means upon, demos means people, and logos means study, so we can define epidemiology as the study of how health conditions or events are distributed and defined in a population. Epidemiologists use this information to try to control health problems [131]. Epidemiology relies on research methods, systematic and impartial methods of collecting and analyzing data. Basic epidemiological methods usually depend on careful observation and the use of appropriate comparison groups to assess whether the observed, such as the number of cases of the disease in a given area during a given period of time or the frequency of exposure in sick people, differs from what one might expect.

In epidemiology, to make a decision for control an infectious disease, it is important to understand that how the interaction between agent, host, and environment affect transmission of disease and its development in population. Mathematical models are used to represent and analyze these interactions by combining available knowledge and expert opinion about a disease. In recent years, there have been significant developments in electronic surveillance of infectious diseases, which revised computing, electronic data administration, the

capability to share and deposit data over the internet [132]. These developments have increased the application of mathematical models in epidemiology to study disease processes [133], hypothesized factors involved in endemic persistence in populations [134], give advice on risks associated with emerging and re-emerging disease risks [135], estimate the economic effect of diseases [136], appraise control strategies at different scales [136], calculate the effectiveness of surveillance and control programs [136], and provide inputs and scenarios for training activities [136].

A model is a physical process or system that is designed to imitate relevant features of the system. Models are designed to understand the effect of external influences on outputs by representing the interactions between system components and to convey ideas about the behavior of the system. In mathematical modelling, we translate those features of the system that are being studied theoretically and scientifically into the language of mathematics for simplification [128-129]. Mathematics is an exact, accurate, and concise language, which helps us to formulate and identify underlying assumptions, encourage manipulations. Availability of potentially useful theorems and high-speed computers for calculation make mathematical models more useful. The objectives of mathematical modeling are to develop a scientific understanding of the system, clarification, using our scientific understanding to manage the world, simulated experimentation, testing the effect of changes in a system, the curse of dimensionality and aid decision making [123-126].

A mathematical model is an abstract, simplified mathematical construct related to a part of the system in the real world and created for a particular purpose [121]. Three things are important in modelling a system in the real world. The things the model is designed to study behavior for are called endogenous variables, also called output or dependent variables. The things that affect the model but whose behavior the model is not designed to study is called exogenous variables (also called parameters, inputs, or independent variables), including constants, functions and so on. Things whose effects are neglected exclude from the model and call the neglected part [121-129].

The mathematical modeling process is divided into four parts: building, studying, testing, and use. In general, deficiency found during the investigation and testing phase are fixed by returning to the construction (building) phase. Note that the investigation (studying) and testing phases will need to be repeated if changes are made to the model. This iterative process is a typical feature of a modeling project and one of the most useful aspects of modeling, giving you a better understanding of how the system works [122]. Figure 2.5 illustrates different routes through the modelling process:

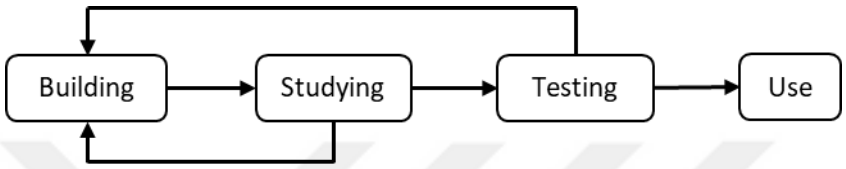

Figure 2.5 Pictorial representation of modelling process

The mathematical model in epidemiology developed by Daniel Bernoulli in 1766 [137]. Bernoulli developed the model to analyze the mortality due to smallpox in England. The purpose of his model was to show that vaccination against the virus would increase the life expectancy at birth by about three years. Lambert [138] extended the Bernoulli's model by including age-dependent parameters. The modern mathematical modelling in epidemiology established by Ross [139-140]. He represented mechanistic form of the earlier modeling approaches by set of equations to estimate the discrete-time dynamics of malaria through the mosquito borne pathogen transmission. Kermack and McKendrick [141-143] found the first deterministic compartmental epidemic model. They introduced the mass-action incident [144] in disease transmission cycle. They suggested that the probability of infection of susceptible is comparable with the number of its contacts with infected individuals. Their model holds strong analogy with the law of mass action [145] which was introduced by Guldberg and Waage and called *SIR model*. MacDonald [146] extended the work of Ross and proposed method of eradication of disease in an operational level. He used his method to explain the transmission of malaria deeply. In general, the mathematical models for explaining the dynamics and control of transmitted pathogens are known as the *Ross-MacDonald models* [146]. Enko [139] used a probabilistic model to analyze the dynamic and

control of measles epidemic. He assesses the number of contacts between infective and susceptible in population. Frost [147], by using the Enko model, developed the famous Reed-Frost chain binomial model. His model assumes that an infection spreads through discrete time Markov chain events from infected individual to susceptible one, which set the basis for stochastic modelling.

There is no agreed classification system for models [136]. Different researchers have focused on different aspects of models which may distinguish them from each other. According to the work of Siettos et al. [139], there are three general categories: statistical-based methods for epidemic surveillance, State-space models, and machine learning-based models for forecasting the evolution of ongoing epidemic [139]. These categories are also divided into subgroups see Figure 2.6. Since in our thesis, we use a discrete-time stochastic agent-based model, so we will only focus on state-space mathematical models in epidemiology.

State-Space mathematical models are representations of the dynamic order system consisting of input, output and state variables to a first-order differential equation on the vector of state [148]. A state variable is a variable whose value changes over time in a way that depends on the value at any given time and the externally imposed value of the input variable. State-space mathematical models can be divided into the following categories, depending on the level of approximation, and increasing complexity of reality:

I. *Continuum models, deterministic SIR models*
II. *Stochastic models*
III. *Complex network models*
IV. *Agent-based simulations*

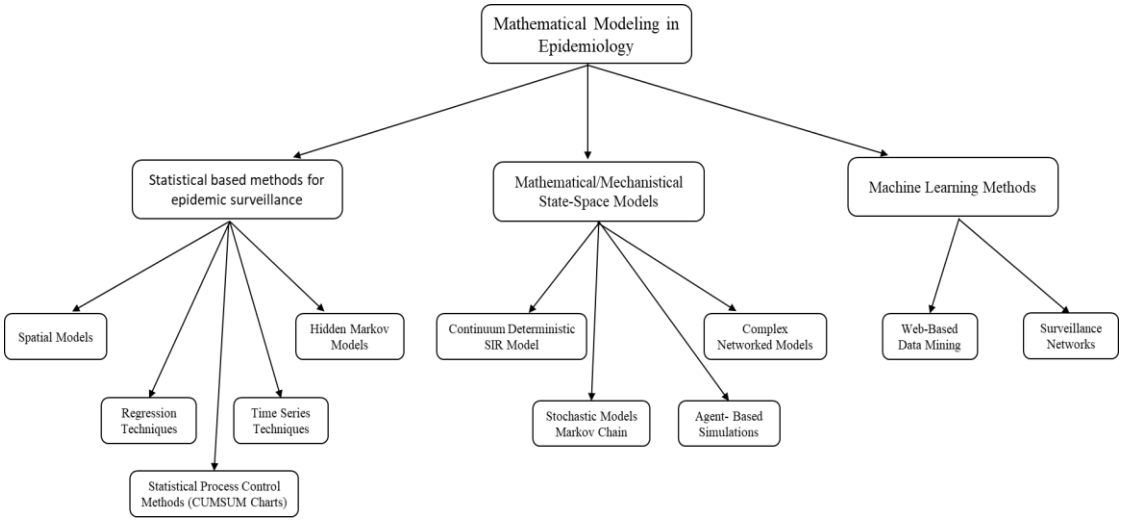

Figure 2.6 Classification tree of Mathematical models for epidemiology.

Continuum models describe the simplified dynamics of the epidemics in the population [139]. Generally, they represent physical systems in the form of differential equations. The Kermack and McKendrick [141-143] SIR compartmental models make up the continuum models of differential equations. In the SIR model, the population is segmented by health state, such as susceptible (S), Infected (I), recovered (R), or quarantined (Q), vaccinated (V) by policy makers. The inputs could be age or time, and output may be the vaccination or efficiency of quarantine or isolation.

Stochastic models are used when the variability or randomness in transmission, recovery, births, deaths, or the environment affects the outcome of an epidemic. These models include discrete and continuous-time individual-based Markov-chain models. Markov chain model is a series of possible events, where the probability of each event only depending on the state approach in the prior event [150]. The key illustration in the Markov chains is the discrete-time Markov chains (DTMC). In the DTMC time and states are described on a discrete set of values. At every discrete time step, individuals make their own decisions based on their own current state and the current state of their links. The decisions are made with respect to the simple rules including their own states and the states of their links satisfying the Markov property. This property defines that the future values of the states at time $t + \Delta t$ related only to the values of the states at the previous time step t. Stochastic models are individual-level models. The advantage is that this

model loosens the mean-field approximation hypothesis of the models for infinite population. Stochastic models use perfect mixing that familiarize the distinctiveness of individual behavior, with multiple heterogeneous features.

The elements and interactions of real-world systems are modelled by complex network models. The complex network models proxy elements with sets of nodes and interactions with sets of edges. The 'complex' term mentions any collection of interlinked things which have meaningful pattern their links [151]. These models relax the hypothesis of the above stochastic model about homogeneity of interaction between individuals, by using an heterogenous contact network [139]. In addition, the topology of contact social networks shapes the epidemic spread in many situations. In the occurrence of various epidemics, changes in the epidemic state of a particular population can lead to major changes in the characteristics of the grid. Understanding this complex behavior is paramount to public health interventions and policies to address the outbreak of illness. Vaccination, quarantine, and/or the use of antivirals in specific population groups must be carefully planned so that they can effectively combat new epidemics. If the dynamics of infectious diseases are poorly understood, they can have serious adverse effects because they are caused by non-uniform contact interactions. Over the past few years, active exertions have been made to study the relationship between the new dynamics of infectious diseases and the fundamental topology of the network [139].

2.5 Agent-based Modelling and Simulation

Agent-based modelling and simulation (ABMS) are used to model complex systems, complex adaptive systems, and artificial life [157]. Complex systems are composed of interacting, autonomous 'agents' [155]. Complex adaptive systems give the capability for agents to adapt at the individual or population levels [156]. Agents have behaviours, often defined by unpretentious rules and interactions with other agents, persuading their behaviours. Occasionally self-organization can be detected in agent-based modelling. Patterns, structures, and behaviors appear that were not explicitly programmed into the models but emerges through the agent interactions. Two significant features that extricate agent-based simulation

from other simulation techniques, such as discrete event and dynamic system simulations, are modelling the heterogeneity of agents across a population and the presences of self-organization. Agent-based modelling can also model social systems composed of agents that interact and stimulate each other, acquire from their experience, and regulate their behavior to make it more appropriate for their environment. Agent-based modelling has a comprehensive range of applications, such as modelling agent behaviour in the stock market [152], forecasting the supper of disease [153], modelling adaptive immune systems [154] and many others.

The agent-based model has three elements: a set of agents, a set of agent relationships and methods of interaction, and the agents' environment. Agents have certain characteristics such as self-contained and identifiable, autonomous and self-directed, state that varies over time, social and having dynamic interactions, adaptive, goal-directed and having goals to achieve, and heterogeneous. Agents usually interact with a subset of other agents called agents' neighbours. How agents relate to each other is commonly referred to as the topology or connectivity of an agent-based model. Typical topologies include a spatial mesh or network of nodes (agents) and links (relationships). The topology describes who communicates information to whom. The most common agent interaction topologies are cellular automata (CA), Euclidean 2D/3D space, and network and so on [155]. The environment helps define the space in which the agent operates and supports interaction with the environment and other agents [158].

To develop an agent-based model, first of all, we should specify the problem that we will solve by model, the answer that we want to answer, and the value that should be added to the problem that other models cannot bring. Then we should describe agents of our model (decision-maker, entity that has behaviors, static attributes, dynamic attributes). After that, we need to mention the agents' environment of our model. Consequently, we must mention agents' behaviours of interest, decisions that they are going to make, and actions that are taken by agents. Introducing the way that agents interact is our next step—finally choosing

accurate data with respect to agents' behaviour for our model and validating the model according to agents' behaviours.

Agent-based modelling can be implemented by exploiting several software or programming languages such as MATLAB, Mathematica, Python, Java, C++, and C. In our thesis investigations we use MATLAB R2019b.

3

METHODS AND MATERIALS

In this section, the multi-scale model developed in this study for the first time will be introduced to explore the balance between pharmaceutical (vaccination) and non-pharmaceutical (social distancing, stay-at-home restriction, and decrease in working hours) intervention in the containment of COVID-19 pandemic. Also, we will describe the classification methods that we have developed for categorizing our social network data edges into household, workplace, and social environment. Finally, we will explain the general methodology of our study and how we took into account stay-at-home restrictions, social distancing, working hours, and vaccination in our model.

3.1 Data

To make our simulation more realistic to human interaction patterns, we use the BBC documentary 'Contagion! The BBC Four Pandemic' demonstrate social network data of 469 volunteers from Haslemere, England. The data is not categorized as where the interactions occur. Our main goal is to order each interaction, whether it occurred in workplaces, social environment or households. By categorizing edges of the graph, we can understand which of the settings and behaviors of staying in that environment would affect the COVID-19 dynamics.

The Haslemere dataset consists of the pairwise distances of up to 50m resolution between 469 volunteers from Haslemere, England, at five-minute intervals over three consecutive days (Thursday 12 Oct – Saturday 14 Oct 2017). Graphical representation of Haslemere dataset is given in Figure 3.1. It gives users' data to 16 daytime hours only, between 07:00:00am and 22:55:00pm, excluding the hours between 11 pm and 7 am. There are 576-time points for each user. According to the 2011 UK census, volunteers of the Haslemere dataset establish a sample of 4.2% of the total population of Haslemere. Participants downloaded the BBC Pandemic mobile phone app and then went about their daily business, with

the app running in the background. The study restricted to volunteers who are at least 16 or 13 years of age with parental consent. The pairwise distances between volunteers were calculated using the Haversine formula for great-circle geographic distance and are based on the most accurate GPS coordinates that the volunteers' mobile phones could provide [159,166].

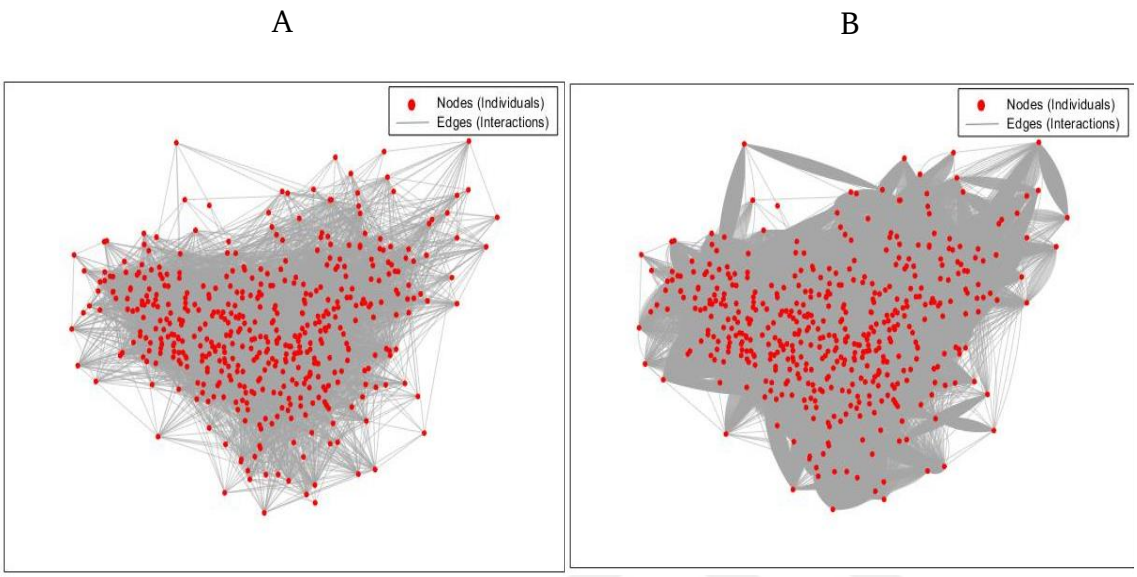

Figure 3.1 Graphical representation of our social network dataset. A) Unique interaction between nodes during three consecutive days. B) 5 minutes time step interactions between nodes during three consecutive days

3.2 Model

We have developed a discrete-time stochastic agent-based model, parameterized to simulate different types of COVID-19 outbreak across the Haslemere data set. An agent in our simulation can be in the following states: $E(t)$ (exposed), $PS(t)$ (pre-symptomatic, documented), $A(t)$ (asymptomatic, undocumented), $S(t)$ (symptomatic, documented), $H(t)$ (hospitalized) and $R(t)$ (recovered) (Figure 3.2).

In our model, symptomatic individuals are symptomatic with respect to medical records, anyone who do not report symptoms are regarded as undocumented (asymptomatic). The agent-based model starts with an exposed individual. Initially, j^{th} individual is exposed to the virus, and he/she cannot infect others during his/her latent period for $d_1 = 2.7$ days (Table 3.1). After the latency period

finishes, the j^{th}individual tends to one of the two branches: pre-symptomatic with a ratio of s or asymptomatic with a ratio of $(1 - s)$. When the period of delay from the onset finishes, we generate a random number ε, there are two probabilities for j^{th} individual to proceed; the first one, if $\varepsilon < 1 - s$ he/she proceeds to the asymptomatic stage. The infectious period of the asymptomatic stage is $d_3 = 5.4$ days (Table 3.1). Through the infectious period of the asymptomatic stage, when the j^{th} individual comes in contact with i^{th} individual, then we infect the i^{th} individual with probability $\mu_H Ph_{j,i}$ if the edge is classified as household and $\mu_o Po_{j,i}$ if non-household. The μ_H and μ_o are the reduction factor for asymptomatic transmission in households and non-household. $Ph_{j,i}$ and $Po_{j,i}$ are the probability that j^{th} individual infects i^{th} individual of his/her contacts in household and non-household. When the infectious period of the asymptomatic stage finishes the j^{th} individual proceed to the recovered stage.

Alternatively, the j^{th} individual can be in pre-symptomatic stage. The infectious period of the pre-symptomatic stage is $d_2 = 2.4$ [160]. The probabilities of infection are $Ph_{j,i}$ and $Po_{j,i}$ in household and non-household. When the pre-symptomatic stage finishes, the j^{th} individual proceed to the symptomatic stage and stays for $d_4 = 3$ days [163]. The infection probabilities are the same as in pre-symptomatic stage. When the delay period from symptomatic finishes, j^{th} individual proceeds to the hospitalization stage where he/she will recover or die. The hospital stage does not necessarily mean that the agent is hospitalized. All reported cases end up in hospital stage, regardless of severity (which is not modelled). The default parameter values for the simulations with their sources were presented in Table 3.1.

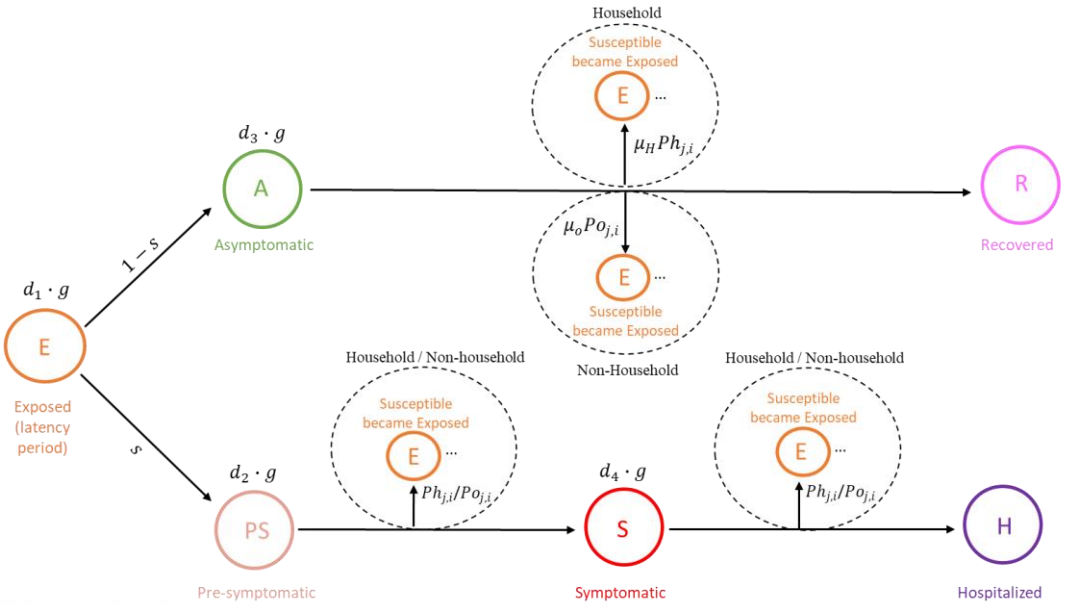

Figure 3.2 Graphical representation of our discrete time, stochastic agent-based model

Table 3.1 Agent based model parameters and their values

Parameter	Definition	Value	Source
d_1	Mean number of days in the latency stage	2.7 day	Derived by finding the difference between incubation period and pre-symptomatic period. We take incubation period 5.1 day [165]
d_2	Mean number of days in pre-symptomatic stage	2.4 day	[160]
d_3	Mean number of days in the asymptomatic stage	5.4 day	Assumed to be the same duration as the total infectious period for symptomatic cases, including pre-symptomatic transmission [161]
s	The ratio of symptomatic cases	0.83	[162]
d_4	Average time of going to the hospital	3 days	[163]

Table 3.1 Agent based model parameters and their values (continued)

α	Infection Probability constant	0.9841	Derived (Fitted to COVID-19 R_0 and SAR of household by sampling see Fig. 3.5
β	Infection Probability constant	0.1672	Derived (Fitted to COVID-19 R_0 and SAR of household by sampling see Fig. 3.5
μ_H	Transmission reduction fator for asymptomatic cases inside household	0.696	[164]
μ_O	Transmission reduction fator for asymptomatic cases outside household	0.42	[164]
g	Granularity	192	Derived by converting 1 day to 5 minutes intervals (16×12)

3.3 Methods

3.3.1 Social Network Data Classification

We want to categorize this network into three categories, including household, workplaces, and social environment. For doing this, we use a visualization method that demonstrates the behaviour and contact member of every individual during these three consecutive days, and a classification algorithm. We choose those contacts with an average pairwise distance 20m or less. In our primary analysis, we identify those contacts whose average pairwise distances are 5m or less because we have aimed to capture household encounters and understand their daily routine and behaviour. After investigating the behaviour of each individual during these three days, we have come up with some procedures. Table 3.2 describes the procedures for households, workplaces, and social environment for example: Individuals who contact for three consecutive nights after 19:00 and have distance of less than 2 are classified as household encounter. Consequently, we have developed a classification algorithm to classify the remaining encounters

between 6m and 20m distances. The pseudo code for the algorithm produced here is given below. To test the performance of the algorithm, we create a confusion matrix of the algorithm by choosing the classified data points (by using the visualization method) as actual data and the algorithm classified data points as predicted data.

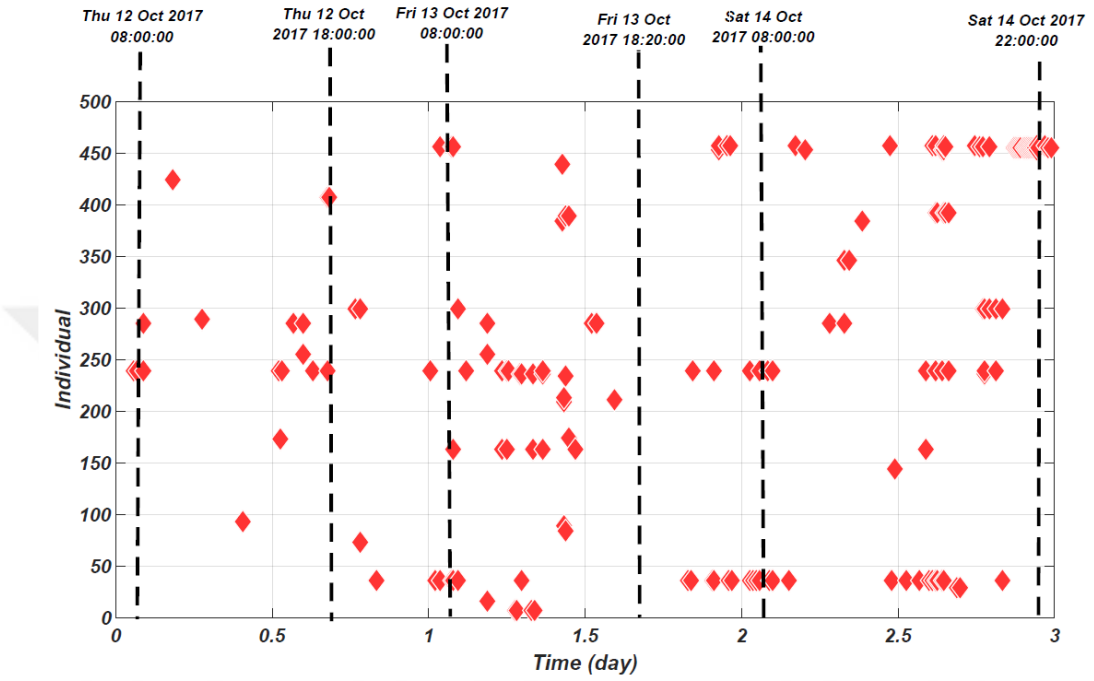

Figure 3.3 Visualization method, which demonstrates the behavior and contact member of every single individual Haslemere data set during these three consecutive days. This figure illustrates the behavior of 21st individual during three consecutive days. The red diamond shapes represent every single individual. The black dash line illustrates specific hours during these three days

Table 3.2 List of procedures that are obtained by using visualization method which demonstrates the behavior and contact member of every single individual of Haslemere data set during these three consecutive days

Categories	Procedures
Household	1) Individuals with at least 10 logged data points between 22:00 and 07:55 AM on any of the dates [159] 2) Individuals who contact for three consecutive nights after 19:00 and have distance of less than 2 3) Individuals who have more than 80 logged data point during three consecutive days

Table 3.3 List of procedures that are obtained by using visualization method which demonstrates the behavior and contact member of every single individual of Haslemere data set during these three consecutive days (continued)

Workplace	1) Encounters which occurred on Thursday and Friday between 8:30 AM and 18:00
Social Environment	1) Individuals with a lease than ten logged data points between 22:00 and 07:55 AM on any of the dates 2) The encounters which are occurred after 19:00 clock for one-night lease than five logged data point 3) Encounters which occurred on Saturday from 8:00 AM and 18:00 less 15 logged data points

3.3.2 Classification Algorithm Pseudocode

Let Y represent encounters which occurred between 6m and 20m distance in Haslemere data point set, and X represent total number of logged data points of each Y during three consecutive days. The duration between 07:00 AM up to 08:30 AM and 18:00 PM up to 23:00 PM on Thursday and Friday represent by t_1. The duration between 07:00 AM up to 23:00 PM on Saturday represent by t_2. The duration between 08:30 AM up to 18:00 PM on Thursday and Friday represent by t_3. Let $Z(t_1 + t_2)$ give the total number Y which occurred in t_1 and t_2 duration, and $Z(t_3)$ give the total number Y which occurred in t_3

```
if X ≤ 80
    if X > 15
        if Z(t1 + t2) > Z(t3)
            Y classified as household contact
        else
            Y classified as workplace contact
        endif
    else
        if Z(t1 + t2) > Z(t3)
            Y classified as social environment contact
        else
            Y classified as workplace contact
        endif
    endif
endif
```

Figure 3.4 Classification algorithm pseudocode

3.3.3 Constructing Contact Matrices and Simulation with Real-world Social Network Data

We construct classification matrices for households, $H_{i,j}$, workplaces, $W_{i,j}$, and social environment, $S_{i,j}$, which we have classified from Haslemere data. $H_{i,j} = 1$ if the contact of j^{th} and i^{th} agent occurs in a household environment, and $H_{i,j} = 0$ otherwise. The simulations are made for 5 minutes time step. At each time step, each contact is checked if one of the agents is infectious, also if the other one is susceptible, then it is infected by the precomputed probability. There are three days in the Haslemere data: Thursday, Friday and Saturday. Our simulations take 14 days, so we construct the longer contact network by using the real data. The weekday contacts are taken from Thursday and Friday. We repeat each day sequentially and in whole. We do not mix the data in a day. The weekend contacts are replicated from Saturday contacts of the Haslemere data. We start the simulation with two exposed individuals. The first 14 days is designed as a

warmup run. After 14 days, we randomly choose 2 individuals whose state are exposed, presymptomatic, asymptomatic, or symptomatic, convert all others back to susceptible. By this method we start with a more realistic initial sample of states. Then, we restart the simulation for another 14. We calculate effective reproduction number (R_e), infection occurence ratio, and secondary attack rate (SAR) of household from the second set of 14-day simulations. We run 500 trial simulations for each scenario. The default parameter values for the simulations were present in Table 3.1. By starting with only 2 infected individuals, we have aimed those total cases at the end of 14 days do not exceed 10% of the total population. Otherwise, the small population and repetitive use of data would have more effect on the estimates. In line with our decision, even after 2 years, COVID-19 cases of countries did not reach substantial percentage [167].

3.3.4 Calculating Infection Probability (P) and Basic Reproduction Number (R_0)

We specify the probability that a susceptible agent i^{th} becomes infected by an infectious j^{th} agent in a 5-minute interval is given as a function of distance in equation (3.1) for household and in equation (3.2) for non-household (workplace, social environment).

$$Ph_{j,i}(t) = \begin{cases} \beta_h e^{-(\alpha d_{j,i})} & d_{i,j} \leq \theta \\ 0 & d_{i,j} > \theta \end{cases} \tag{3.1}$$

$$Po_{j,i}(t) = \begin{cases} \beta_o e^{-(\alpha d_{j,i})} & d_{i,j} \leq \theta \\ 0 & d_{i,j} > \theta \end{cases} \tag{3.2}$$

$Ph_{j,i}(t)$ is the probability of infection if the contact occurs in a houshold. $Po_{j,i}(t)$ is the probability of infection if the contact occurs in workplace or social environment. Also, $d_{j,i}$ is the distance in meters between individuals i and j at time t; α, β_h, β_o are distance scaling parameter, transmission probability per 5 minutes in and out of households, respectively. θ defines the cutoff distance, after which the infection probability is assumed to be zero. Our social network consists of a pairwise distance of up to 50m. Since we choose only those interaction which occurred less than or equal to 20m, so θ=20. Infection probability ranges between 0 and 1. Our network consists of 102831 interactions in 5 minutes time intervals

for three consecutive days (Tuesday, Friday, Saturday). We calculate infection probability for each interaction separately. Effective reproduction number (R_e) is estimated directly by counting the descendants of a discovered agent after simulation finished, then averaged for 14 days. Percentage reduction of transmission probability is computed as a ratio of the effective-outside transmission probability with respect to WT (default, estimated) transmission rate. Thus

$$D = \frac{\beta_o}{\beta_{WT}} 100 \tag{3.3}$$

3.3.5 Estimating Infection Occurrence Ratio

Throughout the simulations we track down ancestors and descendants of infected agents. Each infection pair is an edge of the classification matrices, $H_{i,j}, W_{i,j}, S_{i,j}$. Then each classified edge is calculated.

3.3.6 Calculating Household Secondary Attack Rate (SAR)

The household secondary attack rate is defined as the probability of transmission per susceptible household member when there is a single infected individual in the house [12, 168]. The SAR of households calculates the number of cases among contacts of primary cases divided by the total number of primary cases. Our model starts the simulations with ten exposed individuals executed with a daily life contact matrix to calculate the SAR of households. After that, we tract the infection occurrence environments (household, workplace, social environment). We identify those who are members of different households. We accept those initially exposed individuals who are members of different households as our primary case in each household. At the end of the simulation, we calculate the SAR of each household by the following formula:

$$\frac{\boldsymbol{Number\ of\ cases\ among\ contacts\ of\ primary\ cases}}{Total\ number\ of\ contacts\ of\ primary\ cases} \times \mathbf{100} \tag{3.4}$$

3.3.7 Calculating Scaling Parameters of Distance (α), and Transmission Rate (β) of COVID-19

We estimate scaling parameters of distance and transmission rate by sampling to obtain a baseline $R_0 = 2.87$ [169] and $0.46 \leq SAR \leq 0.72$ [170], which are basic reproduction number and secondary attack rate of households of COVID-19, respectively. Figure 3.4 shows the sampling results for calculating α and β constants for COVID-19. To do this, we calculate the absolute error between the estimated model R_0 and the exact COVID-19. We also compute the absolute error between the estimated and the exact household SAR model for COVID-19. Finally, we add these two errors and choose α and β values that give the required smallest error.

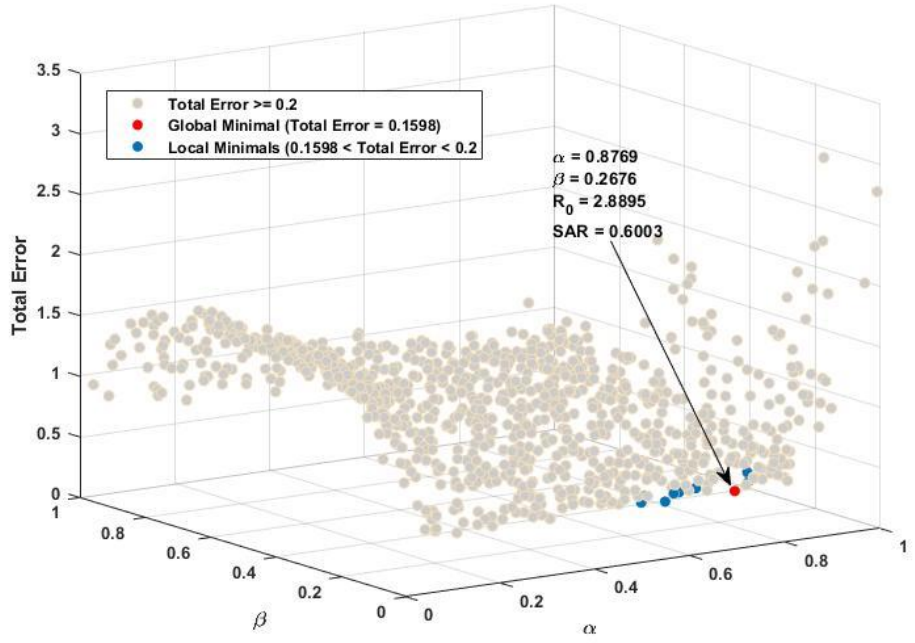

Figure 3.5 Illustration of sampling result for calculating scaling parameters of distance (α), and transmission rate (β) .

3.3.8 Changing Number of Work Hours During Weekdays

We alter working hours during weekdays by changing the work edges of the network. According to our classification methodology of the network, individuals work for 9 hours from 09:00 AM up to 06:00 PM during weekdays. To decrease working hour from 9 hours to $9 - i$ $(1 \leq i \leq 9)$ hours during weekdays, firstly, we

identify home, work, and social environment edges between 06:00 PM and $9 - i$ hours before 06:00 PM of each weekday. Secondly, we randomly change only work edges with work, home, and social environment edges from edges between 06:00 PM and 11:00 PM of each weekday. For example, if we want to decrease working hours from 9 hours to 8 hours ($i = 1$) during weekdays. Firstly, we identify every workplace, social environment, and household contacts that occurred between 06:00 PM and 05:00 AM. Then we have changed only every workplace contact with the workplace, social environment and household contacts which occurred between 06:00 PM and 11:00 PM.

3.3.9 Simulating Stay-at-home Restrictions

We have four stay-at-home restrictions scenarios: restrictions on Sunday, restrictions on Sunday and Saturday, restrictions on Sunday, Saturday and Friday and restrictions on Sunday, Saturday, Friday and Thursday. After we form the 14 days of contact network, we replace all non-household (workplace and social environment) contacts that occurred in a 5-minute time step with a household contact that also occurred in that 5-minute interval.

3.3.10 Lowering Transmission Probability, Increasing Social Distancing

The infection probability is parameterized by two parameters, β and α. The α indicates the decay of probability with the distance of contacts, whereas β is the maximum transmission probability (at distance 0). We have obtained these parameters by sampling many simulations that fit the COVID-19's R_0 and secondary attack rate. We use two β parameters, β_h, β_o, to distinguish between the infectiousness in households and outside. In our simulations, we reduce infectious probability to simulate a population where people reduce probability of infection by personal social distancing measures. The parameter β could be thought as the total virus that is present at immediate vicinity of an infectious agent, whereas α is the "loss parameter" (due to diffusion and other effects) with respect to distance. Thus, we have chosen to alter the parameter β on the basis that total number of virus changes when a person engages in protective measures such as wearing masks. The parameter α is left untouched, since the events that leads to the loss due to distance does not change. Alternative explanations can be

made; however, this is the way that our simulation have been conducted. Whenever we mention a reduction in infectiousness, we reduce the parameter β. So, in some simulations we alter both β_h and β_o when agents at home are also engaging in personal protection; in other simulations, we change β_o when agents do not engage in personal social distancing at households.

3.3.12 Vaccination and The Delta Variant.

The simulations with delta variant use different values for β and α parameters. Again, we have left α untouched. We have changed β according to literature [171]. It is assumed that the infectious probability of the delta variant is double of the wild type of virus. We have simply used β for the delta variant as 0.33, whereas the wild type was 0.167.

The agents that are vaccinated are chosen randomly. The vaccinated agents have reduced β value. We have assumed 93% and 88% reduction infectiousness for the wild type and delta variant, respectively [172]. So, β for the vaccinated, wild type and delta variant are 0.012, 0.067, respectively, whilst α is unchanged.

4

RESULTS AND DISCUSSION

In this chapter, we have investigated the contribution of household and non-household environments to overall spread of the epidemic. Also, we have some observation about the impact of stay-at-home restriction, and social distancing in dynamic of COVID-19. Furthermore, we analyze the trade-off between pharmaceutical (vaccination) and non-pharmaceutical (social distancing, stay-at-home restriction, decrease in working hours) intervention in the containment of COVID-19 pandemic.

4.1 Classification of Social Network Data

We have categorized the real-world social network data into household, workplace, and social environment. Firstly, by using the visualization method we have classified 1350 unique contacts, which occurred, between 1m and 5m. From these 1350 unique contacts 123, 514, 713 of them occurred in the household, workplaces, and social environment, respectively. We have categorized 1895 unique contacts, which occurred, between 6m and 20m by using the currently developed algorithm. From these 1895 unique contacts 52, 790, 1003 of them have occurred in the household, workplaces, and social environments, respectively.

Figure 4.1 illustrates the confusion matrix of the algorithm by choosing the classified data points (by using the visualization method) as actual data and the algorithm classified data points as predicted data to test the performance of the algorithm. The first two diagonal cells show the number and percentage of the correct classifications by the algorithm. For example, 110 contacts are correctly classified as household. This corresponds to 8.15% of all 1895 contacts. Similarly, 492 contacts are correctly classified as workplace. This corresponds to 36.44% of all contacts. In the same way, 642 contacts are correctly classified as the social environment. This corresponds to 47.56% of all contacts. 1 of the household

contacts is incorrectly classified as workplace contact and this corresponds to 0.07% of all 1895 contacts. Also, 12 of the household contacts is incorrectly classified as social environment contact and this corresponds to 0.89% of all 1895 contacts. Similarly, 4 of the workplace contacts are incorrectly classified as households and this corresponds to 0.3% of all data. Similarly, 18 of the workplace contacts are incorrectly classified as social environment and this corresponds to 1.33% of all data. 26 of the social environment contacts are incorrectly classified as households and this corresponds to 1.93% of all data. In a similar manner, 45 of the social environment contacts are incorrectly classified as workplace and this corresponds to 3.33% of all data. Out of 123 household predictions, 78.57% are correct and 21.43% are wrong. Out of 514 workplace predictions, 91.45% are correct and 8.55% are wrong. Out of 713 social environment predictions, 95.54% are correct and 4.46% are wrong. Out of 52 household contacts, 89.43% are correctly classified as household and 10.57% are classified as workplace and social environment. Out of 590 workplace contacts, 95.72% are correctly classified as household and 4.28% are classified as household and social environment. Out of 1003 social environment contacts, 90.04% are correctly classified as household and 9.96% are classified as workplace and households. Overall, 91.73% of the predictions are correct and 8.27% are wrong. Figure 4.2 shows the distribution of household, workplace, and social environment interactions through 3 days (Tuesday, Friday, and Saturday) in 5-minute time steps after classification of data.

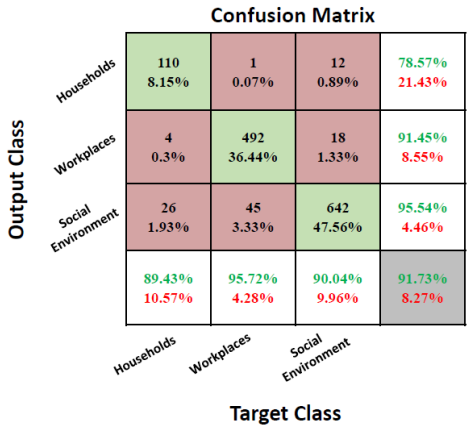

Figure 4.1 Confusion matrix of classification algorithm for clustering Haslemere data set into households, workplaces, and social environment with respect to visualization method classified data

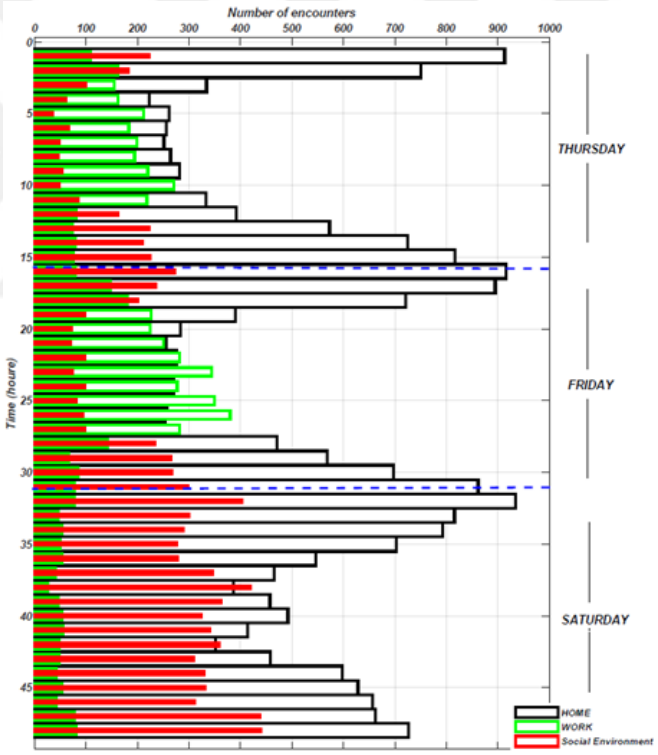

Figure 4.2 Number of encounters that occurred for three days (Thursday, Friday, Saturday) after classification of data

4.2 Estimating Infection Occurrence Ratio in the Household, Workplace and Social Environment Under Two Social Distance Policies

It is vital to know the environment where the infections occur depending on the basic reproduction number (R_0). Here, we estimate the infection occurrence in three environments: households, work, and social environment.

Our agent-based model enables us to simulate R_0 by varying household and/or non-household transmission rates β_h, β_o, respectively. In general, people do not carry out social distancing in their homes [12]. To simulate this phenomenon, we reduce the total transmission rate by decreasing the non-household transmission (β_o) while fixing the household transmission rate (β_h). Squares with a line in Figure 4.3a shows the dependence of R_0 on varying β_o when β_h is constant. Additionally, triangles with a line shows the dependence of R_0 on varying β_o when β_h is also changing, $\beta_o = \beta_h$. The latter simulations are made to assess the effect of making the distinction between β_o and β_h.

Interestingly, until $R_0 < 1$, R_0 does not depend on the decrease of β_h. Only after $R_0 < 1$, further decreasing in β_h decreases R_0 more than when β_h is kept at its maximum.

Additional simulations have been made with random networks. The pairs of contacts are changed randomly without altering the time and probability of infections. Two separate results are plotted: 1) the range of β_o and β_h are the same with the real-network, line with circles in Figure 4.3a; 2) the highest R_0 is fixed to the same value as in real-world network, line with diamonds in Figure 4.3a.

When the ranges of β_o and β_h are kept the same, the random networks show much higher R_0. Except, when the transmission rate is reduced significantly, then R_0 is lower than of the simulations with the real network (β_h fixed), Figure 4.3a. Indicating that, the real networks keep infections more local comparison to the random networks. As expected, the frequency interactions among the selected agents are significantly higher.

When the starting R_0's are aligned with the random networks, the decreasing in R_0's are much faster comparison to the real networks (Figure 4.3a). Indicating that decreasing R_0 in real networks is harder, retains infection chains.

The infection occurrence ratio of household, workplace, and social environment have been counted for R_0 (for real networks). Overall, the household infections are dominant when $R_0 < 1$ and most of the infections occur at social environment when $R_0 > 1.5$.

We capture the only difference between Figure 4.3b (β_h kept constant) and Figure 4.3c (β_h decreases) is in the household infection occurrence ratio when $R_0 < 1$. At $R_0 > 1$, the environments that the infections occur do not change significantly. These results are further supporting the results in Figure 4.3a.

Overall, we speculate that the household transmission reaches its capacity at low β_h due to abundant link frequency. The large size β_h cannot lead to an increase in R_0 value among the infections in the household. It has been concluded that the household transmission contributes to resilience of the eradication but does not contribute significantly to overall spread.

The way we investigate the impact of human behaviour on the household, workplace, and social environment can be generalized to other infectious disease epidemics. The MERS [1] is an infectious disease that first appeared in Saudi Arabia in September 2012. Basic reproduction number (R_0) for the MERS has ranged from 0.42 to 0.92 [173,174,175,176]. In 2017, a cluster of the MERS was reported from Al-Jawf Region, Saudi Arabia, including 7 cases, 6 of which were household contacts [176]. According to our results (Figure 4.3), since $R_0 < 1$ for the MERS, most infections has occurred in households, which is in line with earlier work. It may also be noted that the household infections can increase the resilience of eradication but do not significantly contribute to the spread.

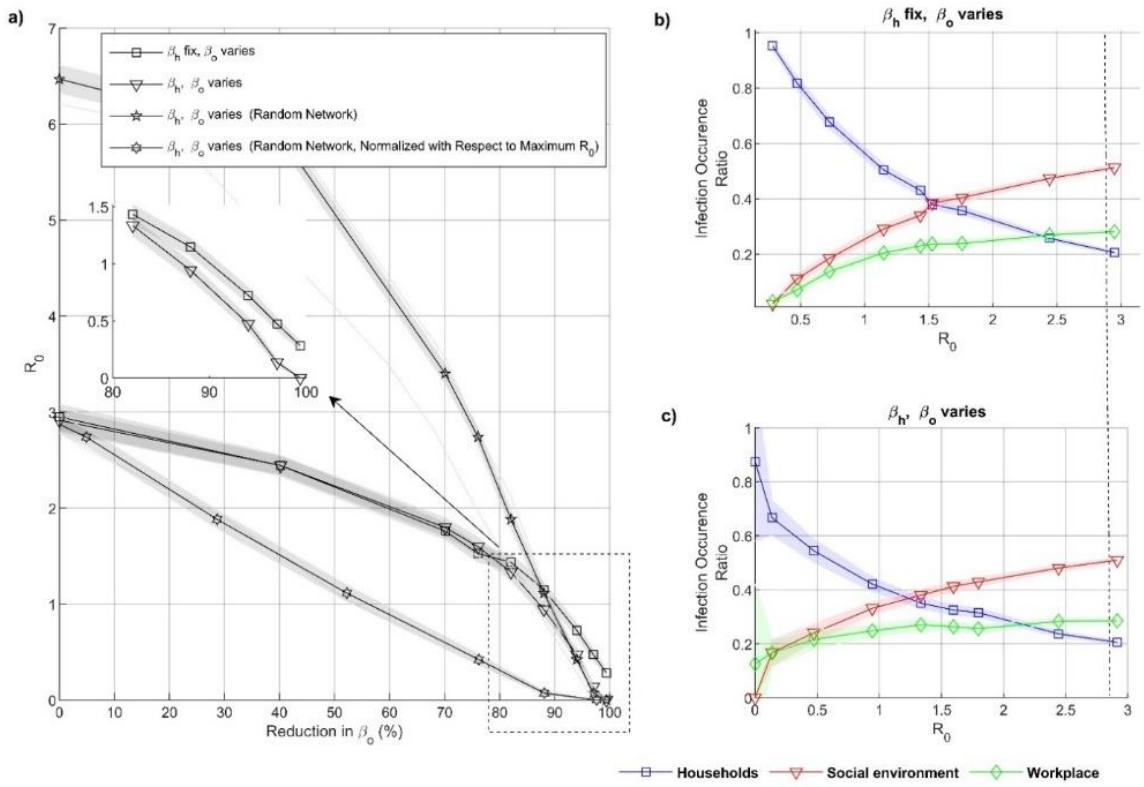

Figure 4.3 Representation of effect of social distancing on localization of infection events. (a) show the R_0 correspond for different reduction level in transmission probability. When agents applied social distance measure only in non-household (graph with square marks) and agents applied social distance measure in household and non-household (graph with triangular marks). The x-axis shows, the percentage of reduction of the transmission probability (see method). (b)-(c) shows the infection occurrence ratio for R_0 in the household (blue graph), workplaces (green graph), and social environment (red graph), (b) when β_h fix and β_o varies, (c) when β_h and β_o varies. The dashed line demonstrates the COVID-19 R_0, the shaded areas in (a)-(c) give 95th confidence intervals. In here, $d_1 = 2.7\ days$, $d_2 = 2.4\ days$, $d_3 = 5.4\ days$, $s = 0.83$, $p = 3\ days$, $\alpha = 0.9841$, $\mu_H = 0.696$, $\mu_H = 0.42$, $g = 192$. For the first scenario, $\beta_h = 0.1672$, $0.001 \leq \beta_o \leq 0.1672$. For the second scenario, $0.001 \leq \beta_h \leq 0.1672$, $0.001 \leq \beta_o \leq 0.1672$

4.3 Estimating Contribution of Household and Non-household in Stabilizing of COVID-19

To better understand the effect of household and non-household transmission on the spread of disease, we study the transmission chain of infections. In the earlier results, Figure 4.3, we counted the place of infections in the transmission chain; namely, the household (H), social environment (S), workplace (W). This can be

regarded as the 0^{th} order knowledge on the transmission chain. To get further information, we first group S and W to non-household transmission (O). We then study the third order knowledge by counting three consecutive places of infections, e.g. HOH (first infection is in Household, the infected person infected another person in O, and that person infected another person in H).

There are total of eight combinations of H and O: HHH, HHO, HOH, HOO, OHH, OHO, OOH, OOO. The combination OOO is the dominant for R_0 at 2.87, the default case. Besides the real-world network, a random network was also simulated for R_0 at 2.87. For the correct comparison, the number of H edges and O edges are kept the same in random and real network.

At R_0 =2.87, the frequencies of the combinations are almost the opposite for the random networks and the real-network, Figure 4.4. The combination OOO dominates the real network, while the HHH is the highest in the random networks. The simulations for R_0 at 1 (real networks) differ greatly compared to R_0 =2.87 (real network). The combination OOO is significantly lower for R_0 =1. Additionally, the combinations that have more than two Hs (HHH, HHO, HOH, OHH) are significantly higher. At high β_h and β_o both H and O infections are very high; as β_h and β_o decrease, the infections at O diminishes faster than H. After a 90% reduction in β, the infection rate of H decreased see Figure 4.3.

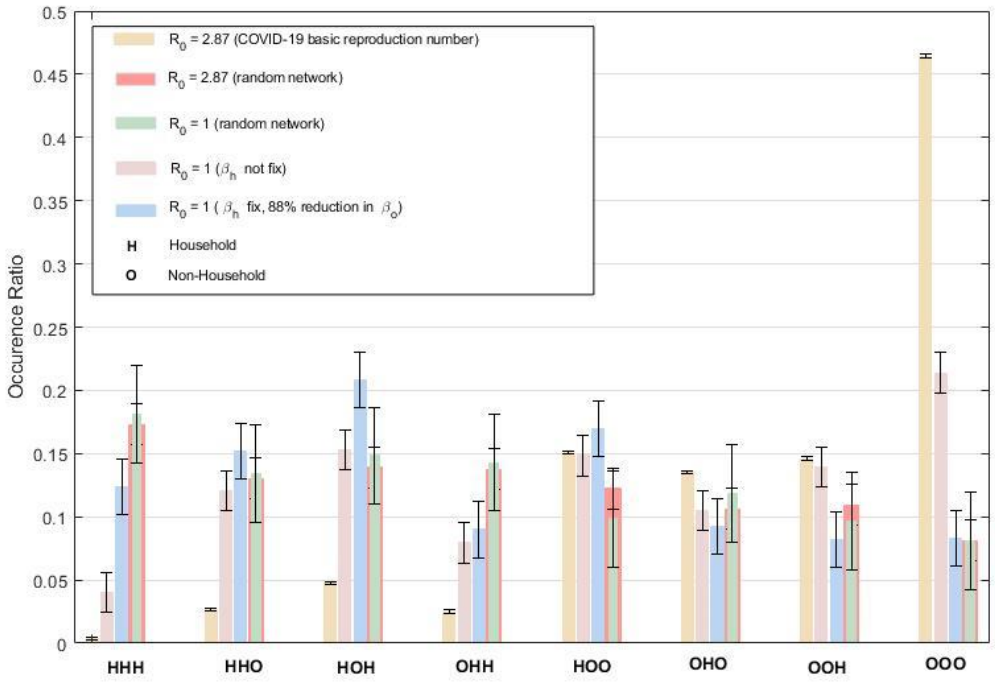

Figure 4.4 Third order transmission chain analysis. Five cases were simulated. The simulations with random networks ($R_0 = 2.87$, $R_0 = 1$) are plotted overlappingly. For $R_0 = 2.87$ the infections occurred the most as OOO combination for real network. Followed by combinations with two "O"s. Then tracked by single "O"s and lastly by HHH. There is a significant decrease in OOO combination for $R_0 = 1$, while others are of comparable frequency. The random simulations are quite the opposite; the HHH combination has the most occurred ratio since total "H" edges are more than "O" edges. In here, $d_1 = 2.7\ days$, $d_2 = 2.4\ days$, $d_3 = 5.4\ days$, $s = 0.83$, $p = 3\ days$, $\alpha = 0.9841$, $\mu_H = 0.696$, $\mu_H = 0.42$, $g = 192$. $\beta_h = \beta_o = 0.1672$ for $R_0 = 2.87$, $\beta_h = \beta_o = 0.0214$ for $R_0 = 1$, $\beta_h = 0.1672$, $\beta_o = 0.0165$ for $R_0 = 1$, 88% reduction applied to β_o. Same parameters are used for random networks simulations.

4.4 Calculating the Influence of Stay-at-home Restriction During Weekends in the Spread of COVID-19

After investigating the effects of contagion probability, we have investigated the effect of stay-at-home restrictions on weekends. To understand the impact of stay-at-home restriction versus transmission probability, we have simulated 3 cases: free weekend without restrictions, restriction on Sunday, and restriction on Saturday and Sunday. We have simulated each restriction scenario when social distancing applied in workplace and social environment (β_h fixed). The edge

frequencies of the altered networks are given in Figures 4.5a-4.5c. To implement the weekend restrictions, the social environment edges are replaced by the household edges, as detailed previously.

We have found that stay-at-home restrictions during the weekends cause a decrease in R_0. Figure 4.6a shows that R_0 drops from 2.95 to 2.71 for restrictions on Saturdays and to 2.56 when restrictions are on Saturdays and Sundays. Figure 4.6b-4.6d shows the ratio of infection occurrence ratio for increasing R_0 when implementing stay-at-home restrictions during weekends. When stay-at-home restrictions increases, the infection at social environment decreases and work infections increase.

Expectedly, decreasing the social environment edges decreases infections at the social environment, however the increase in household edges does not increase the household infections. However, it leads to decrease in R_0 [177-178]

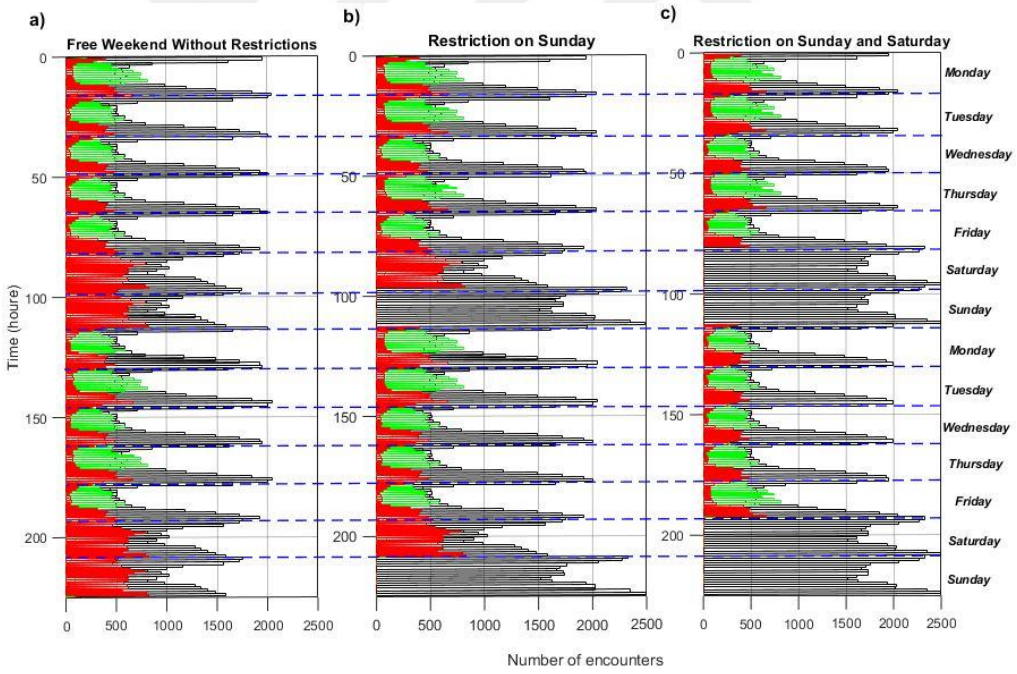

Figure 4.5 The edge frequencies of the altered networks for (a) free weekend without restriction scenario, (b) restriction on Sunday, (c) restriction on Sunday and Saturday

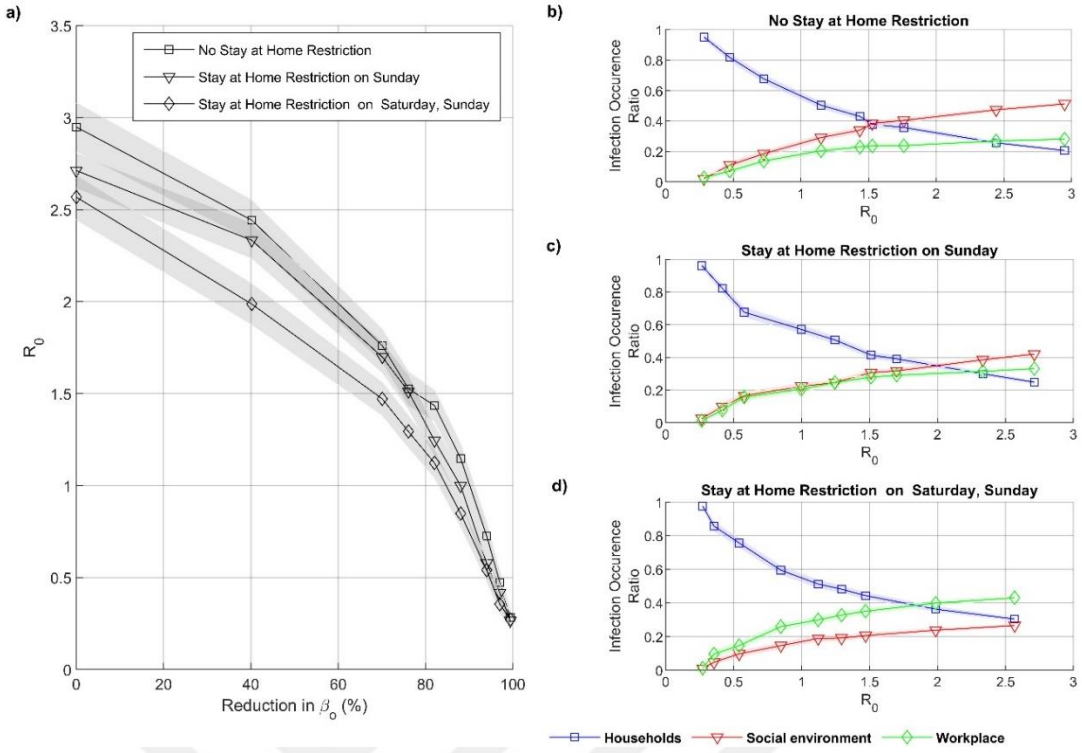

Figure 4.6 Representing the influence of stay-at-home restriction during the weekends, under social distance policy, in the spread of COVID-19. (a) shows the basic reproduction number in three stay-at-home restriction scenarios: free weekend without restrictions (graph with square marks) restriction on Sunday (graph with triangular marks), restriction on Sunday and Saturday (graph with diamond marks). x-axis demonstrate the percentage of reduction in transmission probability (see method for more information). Here agents are only applied social distance measure in the non-household. (b)-(d) show the infection occurrence ratio with respect to R_0 in the household (blue graph), workplaces (green graph), and social environment (red graph), for (b) 1st, (c) 2nd, and (d) 3rd stay-at-home restriction scenarios, respectively. The shaded areas in (a)-(d) give 95th confidence intervals. Here $d_1 = 2.7\ days,\ d_2 = 2.4\ days,\ d_3 = 5.4\ days,\ s = 0.83,\ p = 3\ days,\ \alpha = 0.9841,\ \mu_H = 0.696,\ \mu_H = 0.42,\ g = 192.\ \beta_h = 0.1672,\ 0.001 \leq \beta_o \leq 0.1672$

4.5 Estimating Impact of Daily Working Hour, Stay-at-home Restriction and Transmission Reduction Level, During Weekends and Weekdays, to Stabilize COVID-19

The next alteration to the network is on working hours. We alter working hours by changing working edges. For example, if the working hours decreased from nine to eight hours, the work edges between 5 pm to 6 pm are converted to a

sample from the edges between 6 pm to 11 pm, as detailed previously. The edge frequencies of the altered networks are given in Figures 4.8a-4.8e.

The last alteration is the vaccination. Different vaccination levels have been simulated. At the beginning of the simulations, a certain percentage of randomly selected individuals are vaccinated.

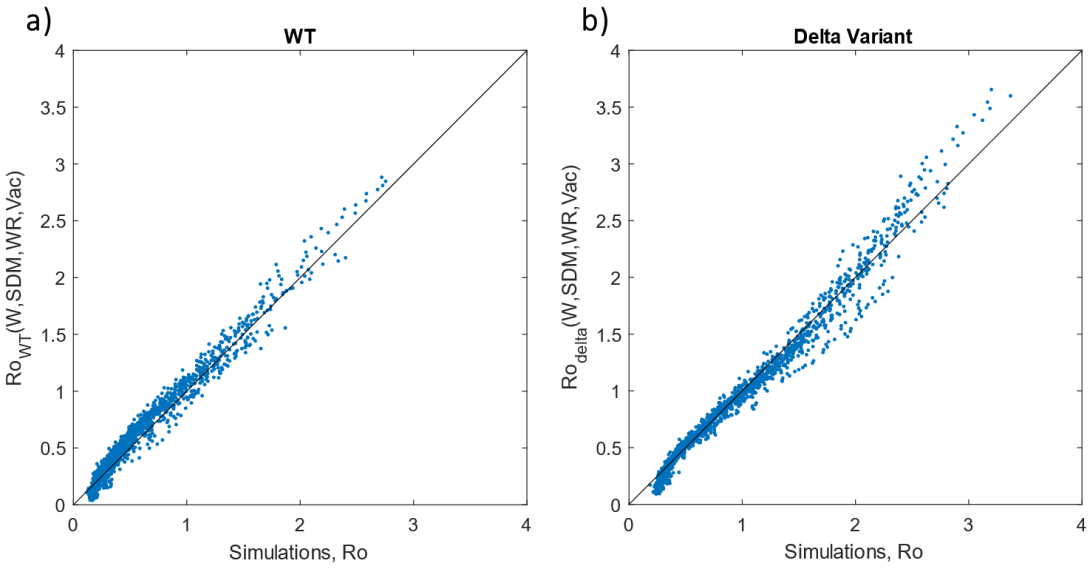

Figure 4.7 Errors of the interpolants. The estimations from the interpolant function and the simulations were plotted. **(a)** for the Wild Type, **(b)** delta variant. In here, $d_1 = 2.7\ days$, $d_2 = 2.4\ days$, $d_3 = 5.4\ days$, $s = 0.83$, $p = 3\ days$, $\alpha = 0.9841$, $\mu_H = 0.696$, $\mu_H = 0.42$, $g = 192$. $\beta_h = 0.1672$, $0.001 \leq \beta_o \leq 0.1672$.

We simulate combinations of different vaccination levels, working hours, social distancing measures (transmission probability), weekend restrictions: total of 30000 simulations were made. The number of parameters hinders us to understand the trade-offs. Instead of plotting $Ro_{WT}(DW, SDM, SH, Vac), Ro_{delta}(DW, SDM, SH, Vac)$, where DW is the decrease in working hours, the SDM is the social distancing measure, the SH is the stay-at-home restriction (in weekends and also in weekdays), Vac is the vaccinated ratio. The functions are chosen for their simplicity. The interpolations are valid in the range of simulations, 0 to 4 hours for the DW, 0 to 1 for the SDM, 0 to 3 for the SH, 0 to 0.9 for the Vac (90 percent vaccination). The scatter plots for the simulated and estimated values are given in Figures 4.7a-4.7b. The coefficients of

determination are 0.9697, 0.9756 for WT and delta variant, respectively. The expressional relations are as follows

$$Ro_{WT} = 2.73 \cdot (1 - 0.0125 \cdot DW - 0.072 \cdot SH - 0.54 \cdot Vac) \cdot \sqrt{1 - SDM} \quad (4.1)$$

$$Ro_{delta} = 3.66 \cdot (1 - 0.015 \cdot DW - 0.074 \cdot SH - 0.35 \cdot Vac) \cdot \sqrt{1 - SDM} \quad (4.2)$$

According to our estimated interpolants, the trade-offs are easily measured. For both the WT and delta variant, changing working hours has the least effect, while vaccination has the most effect. More specifically, for the WT, one day of the weekend restriction is equal to more than 4 hours of work per weekday. While, one day of restriction is equal to 13.3% vaccination. For the delta variant, the effect of decrease in working hours and weekend restrictions act the same, while one day of restriction is equal to 20% percent of vaccination. However, relative effect of vaccination is 20% less effective compared to the WT.

The validity of functions is limited to the simulated ranges of parameters. Full vaccination is expected to lower R_0 below 1, however this is not the case for functions in equations (4.1) and (4.2). This is expected because the simulated range, 0 to 90 percent, has linear effect. Most likely, after 90% vaccination R_0 depends non-linearly on Vac until reaching $R_0 = 0$. The same discussion can be done for other parameters as well.

Unlike other parameters, the SDM (transmission probability) varies from 0 to 100 percent. As seen in Figure 4.3a, the reduction in transmission probability reduces R_0 significantly after 80% reduction. The non-linearity is approximated by the square root function. However, at the limit of SDM near 0, Vac is 0, DW is 0, and the SH is 0. The effect of SDM at the mentioned limit is close to that of the vaccination.

Among the parameters that we have simulated, DW and SH, the parameters vary marginally. For example, DW only changes from 0 to 4 hours. In terms of working hours, the DW varies from 9 hours of work to 5 hours of work. In the simulated range, R_0 is not significantly affected. Perhaps simulating for the remaining hours, from 9 hours of work to 0 hours of work would show the non-linearity that we have suspected. However, the point we want to make is that a marginal decrease

of working hours (several hours) leads to minimal decrease in R_0. To get a significant decrease in R_0, the working hours must be decreased substantially. But its burden on economic activity would be profound.

The range for SH has been simulated from 0 to 4 days. Meaningful range is 0 to 2 days, the weekend. 2 days of restrictions are equal to 26 % vaccination for the WT, 42% for the delta type. However, it should be noted that the simulations on the delta variant with 90 % vaccination and weekend restrictions have about $R_0 = 2$ as the delta variant starts with a substantially higher R_0. The weekend restriction on the wild type is somewhat more meaningful. The simulations with 90 % vaccination with weekend restrictions have $R_0 = 0.98$.

In our simulations, even for the wild type, 90% vaccination has not brought R_0 below 1 (when no other measure was implemented). Many countries such as Singapore and United Arab Emirates have more than 80% [179] vaccination ratios, but they still have cases [180,181]. It should be noted that in those countries, they perform some form of social distancing as well. As mentioned earlier, the weekend restriction can bring R_0 below 1, only for the wild type. Interestingly, the working hour reduction does not show much effect.

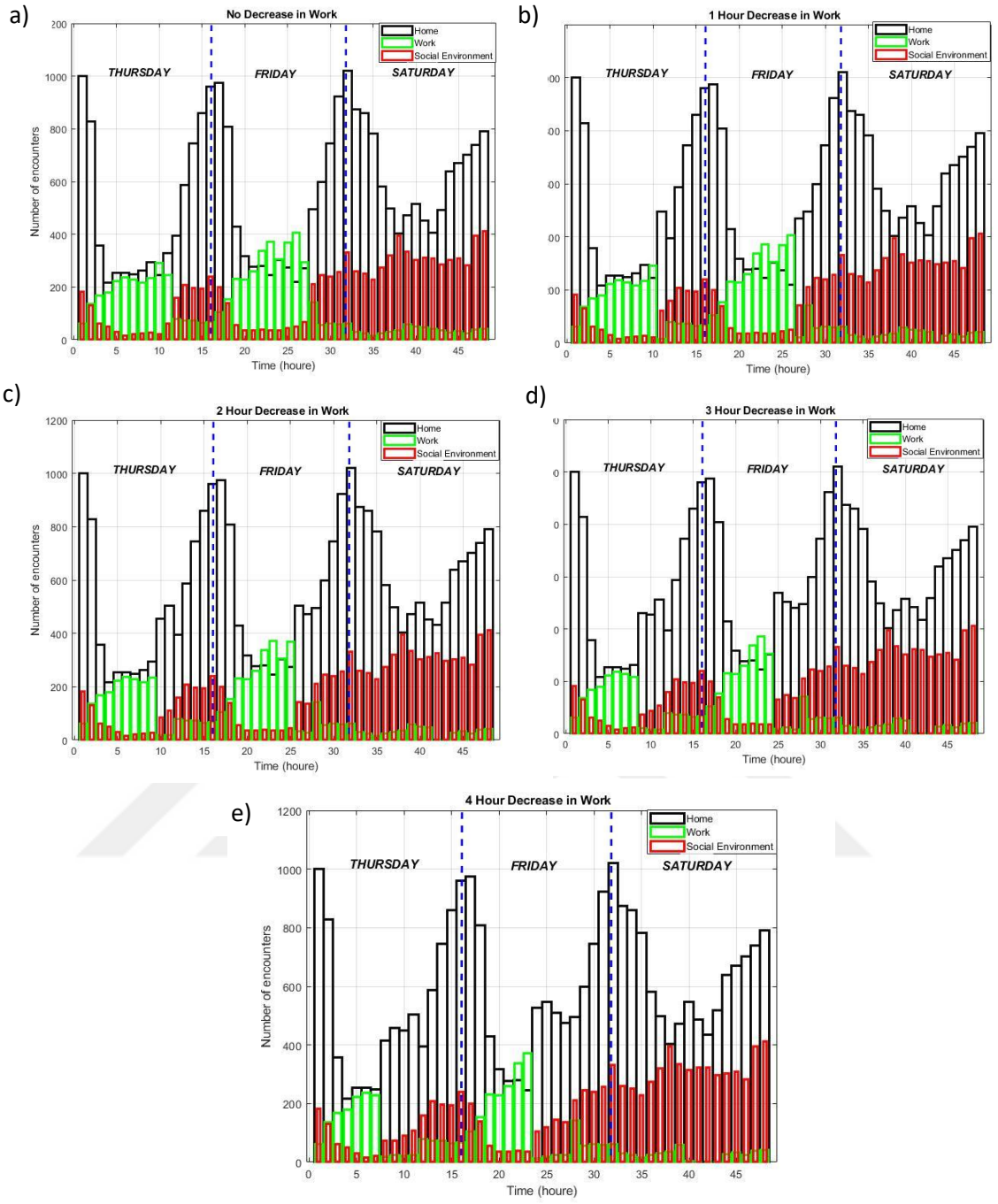

Figure 4. 8 The edge frequencies of the altered work hour for (a) No decrease, (b) 1 hour decrease in work, (c) 2 hours decrease in work, (d) 3 hours decrease in work, (e) 4 hours decrease in work

Numerous valuable theoretical deductions are made on simpler models [182-185]. Also, valuable numerical deductions are made on complex models [186,187]. Here, we have performed complicated simulations on real network. This network is also inherently heterogeneous. Understanding the numerical solutions is troublesome when there are many parameters. To circumvent that problem we have guessed a simple interpolant for the whole simulations. Indeed,

the results can be interpolated with a simple form. The simple interpolant allowed us to compare the decrease in working hours, weekend restrictions, vaccination percentage, and the decrease in transmission probability (social distancing measures).

First of all, the restrictions can be added to each other. All measures are worth considering. However, any measure that is not taken to almost completion does not significantly affect the outbreak. This means that at least one measure must be performed to its maximum level. Mixing marginal effects would not be strong enough so that $R_0 = 1$. For example, the required reduction in transmission probability for $R_0 = 1$ is 86%. With weekend restriction it only decreases to 82%. Worse off, with 3 hours the working hour reduction, the required reduction is 85.5%. Obviously, vaccination and transmission reduction are almost interchangeable. Thus, our simulations show that without vaccination or teaching people how to lower their transmission probability significantly, changing the working hours or weekend restrictions will only make people more frustrated.

There are some areas of improvement in our work. The children under 13 were not included in this data [188]. Children play a crucial role in bringing infection into the household [189]. Since there are only three days of data, we reuse the data 5 times. We tried to decrease the effect of this by only performing brief simulations. Simulations last for 14 days, and we only allow for a maximum of around 20 infections per simulation. We recommend for social network data miners increase their sample size during data collecting from a population.

4.6 Conclusions and Recommendation

In this study, the effects of various parameters such as human behavior, economic activity, vaccination, and social distancing have been investigated in the containment of pandemics such as COVID-19. In this context, a new agent-based model based on a time-dynamic real network with stochastic transmission events has been developed, which is also reinforced by the results of computer codes generated in MATLAB 2019b. The network has been successfully categorized into the household, workplace, and social environment. The contributions of household and non-household environments to the overall spread of the pandemic

have been clarified. The conditions needed to mitigate the spread of wild-type COVID-19 and the delta variant have been analyzed. Complicated simulations have been performed by our agent-based model on the real network. Consequently, the interplay between pharmaceutical and non-pharmaceutical intervention on the containment of COVID-19 have been investigated.

Our simulations have shown that without vaccination or teaching people how to lower their transmission probability significantly, changing working hours or weekend restrictions will only make people more frustrated.

This study could be carried out by incorporating a more realistic network and considering children under 13 years of age in investigating the effect of the corresponding parameters.

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PUBLICATIONS FROM THE THESIS

Conference Papers

1. Nashebi R., Sari M. and Kotil S.E., (2021). “Household Lockdowns on Weekends can Marginally Reduce the Need for Contact Isolation and Social Distancing to Protect Economic Activity”, International Conference on Applied Mathematics in Engineering (ICAME), Balikesir, Turkey, pp.97.

Papers

1. Nashebi R., Sari M. and Kotil S.E., (2022). “Effects of Various Parameters on the Containment of Pandemics”, Mathematical Modelling of Natural Phenomena, (in process)