CONTACT NETWORK BASED FRAMEWORK FOR INFECTIOUS DISEASE INTERVENTIONS

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Abstract

Infectious diseases are life-threatening and often incur the enormous amounts of economic cost and social cost all around the world. As a densely populated hub city, Singapore has suffered from almost every pandemic in the recent decades. Controlling the spread of infectious diseases is challenging to the public health system and there is a need for policy makers to make wise decisions on the choices of intervention measures as well as the implementation in a timely manner. However, there is the lack of sound contact network model for Singapore community and there are few quantitative evaluations to support the decisions on public health interventions as well. In this thesis, we address these problems by introducing contact network based simulation framework for evaluating epidemic interventions in Singapore. The framework consists of a contact network generator “HPCgen” and an intervention-oriented simulator “IntSim”. HPCgen is a fast and scalable contact network generator for urban cities. We demonstrate that HPCgen is able to generate a labelled contact network of 13.4 million population in 7.27 minutes. IntSim is an extremely efficient multi-agent simulator that is able to simulate cyclic interventions, multi-level interventions and combined interventions. Using our framework for a practical study on influenza outbreak, we first create an idealised contact network based on real-life data in Singapore, including demographics, social structure information and contact behaviour surveys. Running IntSim with the idealised contact network for Singapore, we simulate the spread of influenza under multi-level school closure, cyclic workforce shift and their combination, with varying temporal parameters and transmissibilities. Our results show that social distancing is sensitive to temporal factors as well as intervention scale and frequency. The effect of all-school closure and workforce shift is saturated at 8 and 6 weeks respectively. All-school closure of the duration shorter than 6 weeks tends to be more effective if starting later in an epidemic and the closure of the duration longer than 6 weeks is wise to start as early as reasonable. Moreover, individual class closure is observed to excel in reducing the overall attack rate. All-school closure is the most effective to lower the peak incidence. We also discover if duration is longer than 6 weeks or school closure is triggered at prevalence of symptomatic infection equal to 5%, combined interventions outperform each individual intervention working alone. Combined interventions tends to be more effective when
either school closure starts first and lasts for less than 4 weeks or workforce shift starts first and lasts for more than 4 weeks.
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# Contents

Abstract ................................................................................................................................. ii
Acknowledgement ................................................................................................................. iv
Contents ................................................................................................................................. v
List of Figures ....................................................................................................................... viii
List of Tables ......................................................................................................................... x
List of Publications ............................................................................................................... xi

Chapter 1 Introduction ....................................................................................................... 1
  1.1 Motivation ..................................................................................................................... 1
  1.2 Problem Statement ...................................................................................................... 2
  1.3 State of Art .................................................................................................................. 4
    1.3.1 Infectious Disease Modelling for Singapore ....................................................... 4
    1.3.2 Network based Intervention Simulation Model ................................................. 6
    1.3.3 Evaluations of Social Distancing Interventions ................................................. 7
  1.4 Summary of Contributions ....................................................................................... 9
    1.4.1 Idealised Contact Network Model for Singapore ............................................. 10
    1.4.2 Intervention-Oriented Simulator .................................................................... 11
    1.4.3 Evaluation of Social Distancing Interventions ............................................... 12
  1.5 Structure of Thesis .................................................................................................... 13

Chapter 2 Background ....................................................................................................... 15
  2.1 Epidemiology Terms ................................................................................................. 15
  2.2 Mathematical Modelling of Infectious Diseases ....................................................... 17
  2.3 Network Models ....................................................................................................... 22
    2.3.1 Typical Network Models ................................................................................... 23
    2.3.2 Network Measures ......................................................................................... 25
    2.3.3 Network Algorithm ....................................................................................... 27
  2.4 Public Health Intervention ....................................................................................... 29

Chapter 3 Contact Network Generation ......................................................................... 32
  3.1 Introduction ............................................................................................................... 32
  3.2 Model ........................................................................................................................ 33
    3.2.1 Model Design ................................................................................................... 34
    3.2.2 Network Generation ....................................................................................... 36
    3.2.3 Optimization ................................................................................................. 41
List of Figures

Figure 2-1 Influenza disease model ................................................................. 16
Figure 2-2 Transmission dynamics of SIR and SEIR models ......................... 20
Figure 2-3 A partial contact network of a school ............................................. 24
Figure 3-1 Conceptual design of HPCgen ...................................................... 34
Figure 3-2 Flow chart of generation process .................................................. 36
Figure 3-3 Illustration the effect of mapping process ...................................... 40
Figure 3-4 Log reduction scheme ................................................................. 42
Figure 3-5 Comparison between HPCgen network, random network and scale-free network ................................................................. 49
Figure 3-6 Evolution of cumulative degree distribution during contact network generation ................................................................. 50
Figure 3-7 Sensitivity analysis on mean contact degree and structure size ........ 51
Figure 3-8 Efficiency and Scalability of HPCgen ............................................ 53
Figure 4-1 Epidemic intervention simulation framework ................................. 58
Figure 4-2 XML definition for a 4-week class closure ................................. 60
Figure 4-3 Illustration on parameters of cycle .............................................. 61
Figure 4-4 Partial XML definition for workforce shift ................................. 61
Figure 4-5 Disease transmission process ....................................................... 63
Figure 4-6 Sample of PBS script prepared by IntSim ..................................... 67
Figure 4-7 Comparison between 10% and full-scale contact networks ........... 69
Figure 4-8 Daily incidences and average attack rates of the uncontrolled scenario ...... 70
Figure 4-9 Epidemic curves under workforce shift ....................................... 71
Figure 4-10 Attack rates under workforce shift ........................................... 72
Figure 4-11 Peak incidences under workforce shift ....................................... 72
Figure 4-12 Peak days under workforce shift ............................................. 73
Figure 4-13 Daily symptomatic incidences from day 1 to 52 ......................... 73
Figure 4-14 Attack rates under 6-week school closure at different levels ........ 75
Figure 4-15 Peak incidences for 6-week school closure at different levels ........ 75
Figure 4-16 Runtime under multithreading ................................................ 76
Figure 5-1 Epidemic curves under all-school closure ($R_0 = 1.9$) ................. 82
Figure 5-2 Attack rates under all-school closure ($R_0 = 1.9$) ......................... 83
Figure 5-3 Attack rates under 2-week all-school closure ($R_0 = 1.9$) ........................................ 84
Figure 5-4 Peak incidences under all-school closure ($R_0 = 1.9$) ........................................ 85
Figure 5-5 Peak days under all-school closure ($R_0 = 1.9$) ..................................................85
Figure 5-6 Attack rates under all-school closure ($R_0 = 1.5$) ..............................................86
Figure 5-7 Attack rates under all-school closure ($R_0 = 2.3$) ..............................................87
Figure 5-8 Attack rates, peak incidences and peak days under combined intervention .... 88
Figure 5-9 Comparison on daily incidences (A) and attack rates (B) ........................................ 90
Figure 5-10 Attack rates, peak incidences and peak days under combined intervention
($R_0 = 1.5$) ..................................................................................................................93
Figure 5-11 Attack rates, peak incidences and peak days under combined intervention
($R_0 = 2.3$) ..................................................................................................................94
Figure 5-12 Attack rates, peak incidences and peak days under combined intervention
with weekend effect ($R_0 = 1.9$) ..................................................................................96
List of Publications

Journal


Conference Paper


(ii) **Tianyou Zhang**, Soh Soon Hong, Xiuju Fu, Kee Khoon Lee, Limsoon Wong, Stefan Ma, Gaoxi Xiao, Chee Keong Kwoh, "HPCgen – A Fast Generator of Contact Networks of Large Urban Cities for Epidemiological Studies", International Conference on Computer Modelling and Simulation, Brno, Czech Republic, 7 – 9 Sep 2009
Chapter 1
Introduction

1.1 Motivation

Infectious diseases are the leading causes of mortality of human beings. “Black Death” (1347 – 1352) killed 25 million people, “Smallpox” in 18th century killed 60 million, and “Spanish Flu” (1918-1920) killed 25-50 million [1]. According to the WHO (World Health Organization) Report 2002 [2], there are five categories of infectious diseases that kill more than one million people each, and a cumulatively 14.7 million of deaths (25.9% of all deaths) worldwide are attributed to infectious diseases. Apart from the mortality burden, infectious diseases often lead to massive hospitalization and public panic in the community. As the world has become more and more connected, a local outbreak might soon develop to a global pandemic, leading to enormous economic and social cost. Since March 2009, within three months, the H1N1 influenza had spread from its origin in Mexico to 105 countries worldwide [3]. Similarly, the epidemic of SARS (Severe Acute Respiratory Syndrome) started in China in November 2002 and quickly spread all around the world. According to Asian Development Bank, the estimated loss of annual GDP (Gross Domestic Product) in Asia was 28.4 billion US dollars, and the annual GDP growth reduction was up to 4% [4].

The key to combating infectious diseases is public health interventions, which are a set of measures to prevent diseases, contain and mitigate the spread of infection. Implementing intervention measures can disrupt the propagation of contagion in the community so as to reduce the incidences of infection. However, carrying out intervention measures often consumes a significant amount of public health resources (e.g. vaccine, face masks, quarantine stations, hospital beds, etc). Moreover, implementing different interventions, or the same intervention but in different scales or at different points of time could substantially influence the outcome of the interventions. In order to determine the optimal intervention, it is necessary to understand the transmission dynamics of infectious diseases in a population as well as the interactions with the influential factors.

Mathematical models are powerful tools for estimating how an outbreak progresses, providing valuable projections of outbreak size and time evolution of disease propagation.
Conventional mathematical models of infectious diseases are based on differential equations, on the assumption of homogeneous mixing population [5]. It has been increasingly recognized that contact heterogeneity could have considerable influence on the dynamics of the spread of diseases, and furthermore, differential-equation models could rapidly become overwhelmingly complex, intractable and there is the lack of readability when interventions, especially those interactions targeted to some particular subpopulation, are added. In contrast, using a network-based model, which explicitly represents a population in a structure of network, we can easily simulate the spread of infection in a city-scale population, where the arbitrary details of the individuals such as demographic, socio-economic, behavioural characteristics as well as sophisticated intervention strategies could be easily incorporated for differential analysis.

1.2 Problem Statement

Controlling infectious diseases is a major challenge for the public health system, especially for those high-density metropolises. Singapore is a heavily urbanized city-state in Southeast Asia with a total land area of 778 km² and 5.31 million population as of June 2012. As an international hub city in the region, Singapore has become the victim in almost every epidemic and pandemic in the region. Since year 2003, the outbreak of SARS, Dengue, HFMD (hand-foot-mouth disease), Chikungunya, H1N1 Influenza and etc, all had occurred in Singapore. In spite of the severe threat from infectious diseases, to our best knowledge, there has been no contact network model developed for the Singapore community, leading to few network-based simulation studies working on the practical problems helping Singapore against contagious propagation as well as lack of quantitative analysis to evaluate interventions to be implemented.

Part of reason of lacking city-scale network model is due to the availability of data. In order to build up a contact network, we need a variety of data including demographics, social structure data and contact behaviour surveys at the appropriate level of details. Demographic data can be usually extracted from the census but the other two are often scattered or simply not available at all. By far, United State of America (U.S.) has the most comprehensive data available in all three types. Consequently, the majority of city-scale network-based models are developed for U.S. cities, such as [5]–[10]. As social structures and contact heterogeneity are known to play a central role in the spread of infectious disease [10]–[13], and structural characteristics and contact patterns may differ
across cities and countries, creating a contact network model for Singapore community is desirable.

Collecting data is not the only challenge. Generating a contact network for millions of population with real-life data is difficult in the perspectives of genericity, efficiency and scalability. There are many types of social structures that exist in our community. It is impossible to model all of them at once. Therefore we need to have a generic representation of social structures, in order to allow easily adding or removing social structures in the network. A city-scale contact network may comprise millions of nodes and even more edges. We need an efficient algorithm to generate such giant networks at a tolerable cost of computational time. Furthermore, we may generate contact networks for different sizes of cities so that the algorithm also needs to be scalable both in memory footprint and runtime cost when the size of network grows larger.

Another challenge to be faced is how to simulate epidemic spread, and further, with complex interventions in an efficient manner. Simulating the interactions between millions of nodes in the entire period of epidemic is a time-consuming task. Due to stochasticity in our epidemic simulations, a robust result can be only obtained by a number of repeat simulations. Moreover, simulating intervention strategies may be much more time-consuming because there might be many possibilities to configure an intervention strategy, in terms of number of interventions, temporal parameters, intervention scale, efficacy (also called the compliance rate) of each intervention. Different configurations of the intervention strategy may end up with the diverse outcome on effectiveness.

Besides those challenges to computational efficiency, we also aim to answer some unknown epidemiological questions about social distancing interventions. In particular, we are interested in school closure and workforce shift. Workforce shift [14], [15] refers to the intervention that separates the entire workforce in an establishment into two work teams, each team is scheduled to be away from workplace for a certain time span and then return to work by shifting with the other team. A list of questions that we attempt to answer is listed as follows:

- Is workforce shift effective in lowering epidemic severities?
- Is there diverse outcome from school closure at different levels?
- How do temporal factors affect the effectiveness of all-school closure and workforce shift as well as their combination?
- Does a combined intervention always outperform each individual intervention working alone?
• Does the implementation sequence in a combined intervention make a difference in its overall effectiveness?

1.3 State of Art

There are different models that have been applied to simulate the spread of infectious diseases and evaluate the intervention strategies. Those models are differentiated from each other by their assumptions on population mixing, design of compartments, levels of detail and etc. Furthermore, the effect of an intervention can be greatly affected by its temporal settings, target and scale, efficacy, as well as the influence from other interventions which are implemented in a combined manner. Various “what-if” scenarios attributed to different configurations of intervention strategies have also been simulated and evaluated to understand the impact of those factors, ultimately assisting in epidemic preparedness planning.

1.3.1 Infectious Disease Modelling for Singapore

To the best of our knowledge, there are few studies of infectious disease modelling for the Singapore community, and those studies mainly use differential equation models to simulate the transmission dynamic of locally prevalent diseases, such as dengue, SARS and influenza. Burattini et al [16] modelled dengue spread in Singapore by adopting SIR (Susceptible-Infectious-Recovered) models for humans, SEI (Susceptible-Exposed-Infectious) model for mosquitos, and SI (Susceptible-Infectious) model for eggs. They simulated two types of intervention measures, named as “adulticide” and “larvicide”, and then showed the combination of adulticide and larvicide delivered the most effective result. Lipsitch et al [17] modified the standard SEIR model to accommodate quarantine and isolation, and applied this model by stochastic simulation to estimate the basic reproduction number in the 2003 SARS outbreak in Singapore. Drake et al [18] also modified the SEIR model by incorporating a new parameter “societal learning”, which models the acceleration of removal rate due to development of clinical diagnosis and information dissemination to the public. They fit their simulation results to the epidemiological data during the 2003 SARS outbreak in Singapore, and concluded that the rate of societal learning could greatly affect the final size of disease outbreaks. Ong et al [19] built a real-time forecasting model for the 2009 H1N1 influenza outbreak in Singapore by stochastic simulation with SEIR (Susceptible-Exposed-Infectious-
Recovered) model. The model parameters are estimated by “particle filtering”, which iteratively incorporates the incoming data into prior distributions to obtain a time series of posterior distributions of the parameters.

The above models are all differential equation models on the assumption of homogeneous mixing of the population, meaning that all individuals in a population make contacts at the identical rate and transmit diseases at the identical probability. Those models ignore contact heterogeneity of individuals, which determines the influence of intervention to each individual in terms of contact removal or transmissibility reduction. In general, differential equation models can offer reasonable approximation to disease transmission in a large population, but it might become overwhelmingly complex, intractable and there is the lack of readability when complex interventions are incorporated.

To best simulate such interventions, network-based models which represent contact heterogeneity explicitly by network structure are the natural choice. Ong et al [20] adopted agent-based model to simulate the spread of influenza through the close contacts between individuals in a ward of a local hospital in Singapore. Each agent is assigned with activities according to their roles (patients, doctors, nurses, cleaners) and mobilised within a two-dimension schematic map that represents the spatial environment of the ward. The possible transmission of influenza takes place while two agents are at the same Cartesian coordinate at the same time step with a certain possibility. The results of simulations are used to estimate contact frequencies between individuals of different roles, as well as to predict the outbreak size and epidemic duration.

Ong’s model [20] is in fact a time-dependent spatially-explicit bipartite network model. It is able to simulate arbitrary interventions with great details. However, such model might be too complicated if expanding its scale from a ward to a city. Assuming time resolution is one minute and Singapore city is of 4.8 million population, for a single day, it will yield 1440 networks, each with 4.8 million vertices and different formation of edges. Moreover, activity assignment to individuals requires diary-like social behaviour data of individuals. It is manageable if the scale of the model is within a single ward but might be practically difficult if modelling a city of population, especially there is lack of social behaviour data of Singapore in the literature.
1.3.2 Network based Intervention Simulation Model

In the recent decade, many network based simulation models have been developed to facilitate epidemiological studies. Epigrass [21], FluTE [22] and GleamViz [23] are spatially explicit network models at the national or international scale. In their geographic networks, each vertex is either a city or pre-defined square area and each edge represents population flow between vertices due to population mobility. The individuals are distributed to vertices based on demographic distributions such as population density, age distribution and etc. Those macro-scale models are suitable to replicate the diffusion patterns during an outbreak of pandemic in a geographically extensive area, but less useful to simulate the spread of infection within a city due to lack of details on contact behaviour between individuals.

EpisimS [24] is an individual-based bipartite network model at city scale, which comprises both persons and locations vertices as well as edges representing time-dependent activities of people visiting locations. The individuals are created based on the real-life demographic distributions and then assigned with schedules of activities derived from social behaviour surveys. Compared to chain binomial mechanism in macro-scale models, disease transmission in EpisimS only occurs between two individuals who visit the same location at the same time by a certain chance. EpisimS is powerful to simulate the spread of infection with the detail in individuals’ behaviour but at the cost of higher complexity which may impose the limit to its scalability. BioWar [25] is a multi-agent network model for simulating bioterrorism events as well as disease outbreaks. It takes account of many inputs including disease models, social behaviours, geographic topology, wind, climate and communication technology, and is able to simulate in a refined resolution on how individual persons get exposed to infectious disease and transmit diseases from one location to another. Similar to EpisimS, BioWar also suffers from high complexity due to the extensive details captured in the model. EpiSimdemics [26] is the successor of EpisimS. It has the same level of complexity as EpisimS but excel with superior parallel paradigm. EpiSimdemics adopted an efficient algorithm, named as semantics-aware parallel discrete event simulation (PDES), to simulate the interactions between individuals at all locations concurrently with less synchronization. EpiSimdemics scales well when the size of network goes up to 100 million.

Epigraph [27] is a contact network simulation model, inspired by our work in HPCgen [28]. Different from static contacts in HPCgen model, Epigraph allows interconnections between individuals changes with time dependence to reflect the contacts might vary as
time goes by. But Epigraph is relatively slower and can only support simple intervention simulations such as vaccination with different triggers. One interesting feature of Epigraph is using interaction graphs extracted from social networks to infer contact patterns within social groups. It is novel but questionable as there is no solid evidence to support that contact patterns in remote communication via social networks can replicate disease-transmitting contact patterns that potentially transmit diseases. EpiFire [29] is a new open-source library and application for contact network epidemiology. It comprises contact network generator, epidemic simulator, efficient network analyser and visualizer, packaged with a user-friendly interface. Its contact network generator works as similarly as our HPCgen [28]. The epidemic simulator is equipped with three simulation models, chain binomial model, percolation model and mass-action model but there is lack of support for intervention simulation. EpiFast [30] is an extremely fast algorithm for contact network based simulations. Its efficiency comes in three folds: firstly, as what we adopt in IntSim [31], it utilizes the pre-constructed person-to-person contact network for simulation and avoid scanning agent activities at each time step. Secondly, it benefits from a larger time step and in the simulation the discrete time increases by day. Lastly, it is parallelized in the distributed memory system. EpiFast also supports sophisticated representation of interventions and is able to evaluate combined interventions with different triggers and durations. However, it does not support multi-level interventions as well as cyclic interventions. Moreover, EpiFast handles contact removal interventions by modifying network structure, which might be computationally expensive.

1.3.3 Evaluations of Social Distancing Interventions

Schools are the common social structures with an urban city, which are particularly important in epidemic preparedness planning. The pupils are believed to be more vulnerable during an epidemic outbreak because they usually have more frequent close contacts with their peers. Single incidence of a contagious case within a school might quickly transmit from one to another and spread all over the campus. In order to protect the pupils against infection, a temporary closure of school may be implemented in practice. School closure, as a conventional non-pharmaceutical intervention [32], has been extensively evaluated in the literature. However, there is lack of consensus on whether school closure is effective on reducing epidemic severity [7], [33]–[35]. Cowling et al [36] studied the 2-week closure of all primary schools in Hong Kong in March 2008 in order to mitigate a uprising wave of seasonal influenza. Their results showed school
closure has no substantial effects in terms of overall attack rate and peak incidence. On the contrary, Heymann et al [37] observed the significant reduction of respiratory infections due to school closure in Israel from January 16 to January 28 in year 2000. Cauchemez et al [38] reviewed various aspects of school closure and concluded that there exist many uncertainties in the benefits of school closure as a mitigation method. Hence it is wise to evaluate school closure in the local context in terms of demographics, contact behaviour patterns and compliance to closure (the chance that pupils stay at home during the closure). Furthermore, Milne et al [35] suggested the effect of school closure might be sensitive to its temporal settings such as trigger threshold (when to close schools) and intervention duration (how long to keep schools closed). Lastly, Halder et al [34] compared three levels of school closure – case isolation, individual school closure and all-school closure, of 1-week duration and triggered immediately after one diagnosed case is identified within their respective scopes. The results showed all three closures have minimal effect on reducing overall attack rate. It is argued that 1-week closure might be too short to exhibit any noticeable influence.

Workplaces are another type of social structure that commonly exists in an urban city model. High contact rate and prolonged contact duration in workplaces could prompt the rapid spread of contagious diseases. Workplace closure could considerably improve the chance of containment [11] but may result in significant disruption of economic activities and social functioning. Therefore, mass closure of workplaces is seldom implemented in practice and policy makers have to seek alternative interventions. Workforce shift is a newly proposed strategy that has appeared in the influenza contingency plans of the United Kingdom and Singapore [14], [15]. To the best of our knowledge, there are no studies on workforce shift intervention in the literature, therefore its effectiveness is yet to discover.

In the real-life practice, multiple interventions might be implemented together so as to achieve the greater effect. In the literature, there are several attempts to evaluate combined interventions for mitigating an influenza epidemic. Germann et al [39] combined vaccination, school closure and travel restriction. Carret et al [40] combined antiviral treatment, household prophylaxis, school/workplace closure and home confinement. Milne et al [35] combined school closure, workplace nonattendance and community contact reduction. In the above three studies, all interventions last from the start of an epidemic until the end. Halder et al. [34] evaluated the combinations of antiviral drug treatment, household/extended prophylaxis and individual school closure with different durations. Longini et al [41] and Ferguson et al [33] studied how
effectiveness and coverage of combined vaccination and quarantine could affect the cumulative attack rates and peak incidences. Halloran et al [42] and Rizzo et al [43] discussed how trigger thresholds of combined vaccination and social distancing can render different outcomes at the end of an epidemic. Duerr et al [44] tested the combination of antiviral treatment and contact reduction where antiviral treatment starts at the beginning of an epidemic for different durations, followed by contact reduction lasting until the end of the epidemic.

1.4 Summary of Contributions

In this thesis, we aim to create a contact-network-based simulation framework for helping on planning the optimal intervention strategy to mitigate the spread of infectious disease, in particular, influenza, and protect the health of the public in Singapore. In order to achieve this goal, firstly, we create two efficient tools: contact network generator “HPCgen” and intervention-oriented simulator “IntSim”, which are featured with genericity & scalability and sophisticated support for intervention simulation respectively. By using HPCgen, we generate the first idealised contact network model for the Singapore community. Running IntSim with the generated contact network, we make insightful discoveries on the effectiveness of cyclic workforce shift, multi-level school closure and combined intervention, as well as the impact of temporal factors. Both tools are helpful in carrying on the epidemiological studies, demonstrated but not limited by social distancing evaluation presented in the thesis.

Secondly, we produce the valuable results produced by HPCgen and IntSim. Using HPCgen, we create the first person-to-person contact network to approximate the social grouping and contact behaviour in Singapore community. This network lays the foundation for the following intervention evaluation studies presented in this thesis as well as the epidemiological work of other local researchers [45]. Furthermore, by simulating influenza outbreaks under various “what-if” intervention scenarios in the Singapore contact network, we make the insightful discoveries on the effectiveness of school closure, workforce shift and their combination under different settings of temporal factors. We also identify the optimal temporal conditions that allow combined intervention outperform each individual measure and the sequence order of individual measures in a combination that render the greatest effectiveness.
1.4.1 Idealised Contact Network Model for Singapore

A time-dependent spatially-explicit network in city-scale often suffers from high complexity because of the level of details incorporated into the model. It would be much easier and more feasible if working on a projected static person-to-person network model, which is adopted in our study. A static person-to-person network is equivalent to a network aggregated from a set of time-dependent networks by including every edge which represents two individuals make contacts in any of the time-dependent networks. Correspondingly, we also call the time-dependent network models as dynamic models. In the literature, there are both static ([28], [46]–[48]) and dynamic ([5], [10], [35], [42], [49]–[51]) network models. Dynamic models incorporate the reality that a person’s contacts might change as time goes by, through creating dynamic transitory contacts between persons during simulation. Static models form contacts between persons before simulation and assume those contacts remain constant unless they are affected by control measures. Compared to dynamic network, simulating an epidemic in static network is easier and faster as person-to-person contact creation is moved away from simulation. Building a static network requires only the aggregated contact behaviour data, less demanding on data collection. The trade-off of those advantages is that static networks neglect the time dependence of contacting events so that it is not suitable for contact tracing. Volz et al [52] argued that when contact changing rate is slower than rate of contagious propagation (commonly true for airborne diseases such as influenza and SARS), static network approximation may be appropriate.

In order to generate a static contact network for Singapore, we develop the HPCgen, a fast and scalable to generate person-to-person contact network for urban cites, which has inspired the successors such as Epigraph [27] and EpiFire [29]. HPCgen excels in three perspectives: 1) genericity of representation of social structures allows easily incorporating new social structures into the model; 2) efficiency and scalability that is demonstrated by generating a contact network of population size up to 13.4 million within 7.27 minutes; 3) intervention-readiness by the labelled nodes and edges sufficient for sophisticated intervention simulation.

In HPCgen, we model six types of social structures that are known to be notably influential on the spread of contact transmissible diseases [47]: households, hospitals, schools, workplaces, shopping malls and public transport. Then we approximate the contact behaviours taking place in those social structures based on a first-hand survey conducted in Singapore in year 2009.
As a result, we create the first static person-to-person contact network model that embrace both the characteristics of social grouping and contact behaviour in Singapore community. By applying network analysis to our generated network, we discover that the Singapore population is closely connected with average degree of contacts of 33.87 and average clustering coefficient of 0.6021. Its mean path length is 4.4450, exhibiting a strong small-world effect as expected. It may explain why Singapore is so vulnerable to outbreaks. The network is also positive assortative of 0.2555, meaning people tend to connect to those with the similar degree of contacts. The validity of our network has been assessed through alignment with the network models [6], [33], [39] in the literature.

### 1.4.2 Intervention-Oriented Simulator

Simulating disease interventions is far more complicated than simulating epidemic spread alone in terms of complexity and variety of intervention scenarios. We develop an intervention-oriented simulator, IntSim, to address the complexity from two perspectives: multiple measures and multiple hierarchical levels. In the real-life practice, more than one intervention may be implemented together to better mitigate the spread of infectious diseases, either simultaneously or one followed by another with or without overlap. Moreover, there are multiple hierarchical levels in social structures, e.g. schools (all schools > individual school > individual class) and hospitals (all hospitals > individual hospital > individual ward). Intervening at different hierarchical levels in a social structure may lead to diverse intervention scales in terms of number of people being affected. IntSim can incorporate multiple intervention measures into epidemic simulation, and each intervention measure can be parameterized by trigger, duration, target, efficacy and cycle. It offers genericity for accommodating most types of interventions and flexibility in specifying when an intervention starts, how long it lasts for, which persons or contacts it intervenes, how much chance it can achieve the desirable result, and how it intervenes cyclically.

Functionality always comes at the price of computational cost. By taking account of those intervention parameters, together with different epidemic parameters to be simulated, such as transmissibility, a large variety of possible combinations can be expected for a comprehensive study for an intervention strategy. IntSim is developed to be as efficient as EpiFast [30] by: 1) use pre-constructed person-to-person contact network to avoid contact creation during simulation; 2) use larger time step of 1 day in the simulation; 3) “agentize” contact edges with transmission blocking to simulate...
contact removal instead of modifying network structure; 4) adopt hybrid parallelization that leverages on both multi-threading and distributed memory parallelism; 5) use active node switching to reduce number of infection events and use fixed fan-out [53] to minimize number of random number generation.

1.4.3 Evaluation of Social Distancing Interventions

Social distancing interventions disrupt the transmission of infectious diseases by reducing frequency and duration of person-to-person contacts. Typical social distancing measures include school closure, hospital lockdown, cancellation of public events etc. In this thesis, we focus on two types of social distancing measures – school closure and workforce shift. School closure is a conventional social distancing measure that implements a temporary closure of schools or classes. School closure can be classified into all-school closure, individual school closure and individual class closure based on different intervention scales in terms of the population being affected. The smaller the intervention scale is, the more times such intervention may be triggered during the epidemic period.

Workforce shift is an alternative to closure of the entire workplace, which separates the workforce in an establishment into two work teams. For individuals in each team, their contacts with colleagues are cyclically removed and then restored during rotational shifting with other teams. We design a modular arithmetic based mechanism to accommodate such cyclic intervention, which allows intervention to function cyclically within its duration. The same mechanism can also facilitate weekend effect simulation, which can be decomposed into three cyclic interventions influencing schools, workplaces and shopping malls.

In this thesis, we explore the impact of temporal factors, specifically intervention triggers and durations, as well as intervention scale and frequency. We discover that the effect of school closure and workforce shift is saturated at 8 and 6 weeks respectively. No additional benefit can be observed for prolonged intervention beyond the saturation point. We also find that all-school closure of shorter duration (< 6 weeks) is overall more effective if it starts with larger intervention trigger (meaning higher prevalence in the overall population). For all-school closure of longer duration (> 6 weeks), on the contrary, it is better to start as early as reasonable. Our results show that the effect of school closure and workforce shift is sensitive to the choice of timing so that planning intervention timing wisely might notably improve the overall effectiveness at lesser cost. Furthermore, we evaluate multi-level school closure for 6 weeks at prevalence equal to 5%. Our results
show individual class closure is the most effective to reduce the overall attack rate and all-school closure is the most effective to suppress the peak incidence.

As school closure and workforce shift target different types of social structures, it is believed that the combination of the two interventions may be more effective than each individual intervention working alone. However, due to the complexity in evaluating combined interventions, those prior studies on temporal factors [34], [42]–[44] were often simplified by allowing one variable to vary and fixing the other. We conduct a more comprehensive study on all-school closure combined with workforce shift with varying intervention triggers and durations. Our results show when the duration is longer than 6 weeks or school closure is triggered at prevalence equal to 5%, combined interventions outperform each individual intervention. Combined intervention tends to be more effective when school closure starts first and lasts for less than 4 weeks or workforce shift starts first and lasts for more than 4 weeks.

1.5 Structure of Thesis

The thesis is structured as below. In Chapter 2, we introduce epidemiological terms and measures and give an overview on mathematical modelling of infectious diseases, differential equation models, network models, network measures and public health interventions.

In Chapter 3, we introduce our novel network generator HPCgen followed by the first contact network model for Singapore. We discuss the design of HPCgen, with a detailed explanation on how a contact network is generated, and then articulate the parallelization paradigm adopted in the HPCgen. Finally we move on to Singapore contact network model by explaining our data collection and utilization, characteristics of the generated contact network, sensitivity analysis and validation, and time efficiency of network generation.

In Chapter 4, we propose an intervention-oriented simulator, namely IntSim, in order to simulate epidemic outbreaks under intervention in the Singapore contact network in an efficient manner. We explain the workflow in the IntSim with its three components: Intervention Measure Builder, Epidemic Simulator and Intervention Evaluator. Lastly, we address the parallelization and optimization adopted in the IntSim for speeding up the simulations.
In Chapter 5, we leverage on our contact network based simulation framework to evaluate social distancing interventions under various “what-if” scenarios during an influenza outbreak in Singapore contact network. We focus on two social distancing measures in this thesis – school closure and workforce shift. Comprehensive simulations are conducted to evaluate the effectiveness when those two interventions work individually as well as in a combinatorial manner. The impact of temporal factors is also investigated intensively for both individual interventions and combined interventions, followed by sensitivity analysis on influenza’s transmissibility.

Finally, Chapter 6 concludes the thesis with a summary of work and addresses our plan for future work in the contact network based simulation for epidemic interventions.
Chapter 2
Background

In this chapter, we first introduce the epidemiological terms and measures used in the thesis and then review the mathematical modelling of infectious diseases, including differential equations models and network models. Furthermore, we define the network measures to be used in analysing Singapore contact network, and also review two types of network algorithms, as well as public health interventions.

2.1 Epidemiology Terms

This section introduces the epidemiological terms for disease statuses, time spans associated with disease statuses and other related epidemic parameters. It also defines the epidemiological measures that are used in epidemiological analysis.

**Susceptible** $(S)$ refers to the persons that have not been infected yet but may acquire the infection later.

**Exposed** $(E)$ refers to the persons that are infected but have not been infectious yet.

**Infectious** $(I)$ denotes the persons that are infected and have turned infectious.

**Symptomatic** $(I_S)$ denotes the persons that are infectious with onset of symptoms.

**Asymptomatic** $(I_A)$ denotes the persons that are infectious but without any symptoms.

**Removed** $(R)$ denotes the persons that are either dead or recovered from the infection.

**Symptomatic Rate** $(r_S)$ refers to the fraction of symptomatic incidences in the total infected cases.

**Latent Period** $(t_L)$ is the time between exposure to infection and subsequent infectiousness.

**Incubation Period** $(t_c)$ is the time elapsed from exposure to infection to clinical onset of the disease.
**Infectious Period** \((t_I)\) is the duration of being infectious.

**Disease model** (also called disease progression model) defines the mutually exclusive disease statuses of a particular disease as well as the time spans in or between the disease statuses. Figure 2-1 illustrates the disease model of influenza to be used in this thesis, which is similar to the model of Colizza et al [54].

![Influenza disease model](image)

**Figure 2-1 Influenza disease model**

**Basic Reproduction Number** \((R_0)\) [55]. \(R_0\) is the average number of the secondary infections in a wholly susceptible population. If \(R_0 > 1\), each infected will infect more than one susceptible generally so that the infection will probably spread to the large portion of the population. The higher the \(R_0\) is, the higher chance that a full-blown epidemic may arise. If \(R_0 < 1\), the number of infectious persons will decrease eventually and the infection is likely to fade out from the population in a long run.

**Transmissibility** \((T)\) [47] is the average likelihood that the disease can transmit through an arbitrary contact in the contact network. **Critical transmissibility** \((T_C)\) [47] is the phase-transition threshold of transmissibility between small outbreak and full-blown epidemic. If \(T < T_C\), the disease will spread to a limited fraction of the population and only lead to small outbreaks. If \(T > T_C\), the disease will spread to the majority of the population and cause full-blown epidemics. \(T\) and \(R_0\) are both epidemic parameters that determine the size of outbreak. The difference between the two is that \(T\) indicates the intrinsic infectivity of pathogens, but \(R_0\) is the statistics of observations to the spread of diseases in a particular population. Hence \(T\) is generally considered as a constant value for a pathogen (for the same strain, assuming no effect of interventions) and \(R_0\) varies with different populations as it is influenced by their topological properties. \(T\) and \(R_0\) can be further related by the value \(T_C\) that represents the topological property of a particular population.
\[ T_c = \frac{\langle k \rangle}{\langle k^2 \rangle - \langle k \rangle} \]

\[ R_0 = \frac{T}{T_c} \]  

(2.1)

**Attack Rate (AR)** is the cumulative symptomatic incidence rate of infections in the overall population observed within a period of time during an epidemic [33].

**Peak Incidence (PI)** is the highest number of the daily symptomatic incidences in the overall population observed within a period of time during an epidemic [33].

**Peak Day (PD)** refers to the day when the peak incidence occurs [33].

### 2.2 Mathematical Modelling of Infectious Diseases

Mathematical modelling of infectious diseases is the use of mathematical language to describe the progress of transmission dynamics of the diseases. Mathematical modelling is the important tool to explore the mathematical traceability of the transmission of infectious diseases, and further the understanding of the spreading dynamics in an epidemic. It is particularly useful in epidemic preparedness planning by producing the predictions and insights about the spreading of infectious diseases [56], [57].

In general, mathematical modelling can offer two perspectives: understanding and prediction. A good model can produce accurate and robust predictions about the epidemic propagation, such as how much of the population will get infected, when the peak of outbreak will come and how many daily incidences will occur, etc. This information is critical in policy making to decide which control measure should be implemented and how the public health resources should be allocated. Therefore, mathematical modelling is valuable in intervention planning whenever an outbreak takes place. Moreover, a comprehensive model can provide the ideal platform to study how infectious diseases spread in the population as well as how an intervention affects the spread of an infectious disease, e.g. how school closure protect pupils from infections, how much herd immunity is required to prevent the epidemic, etc. Those insights to the epidemic dynamics can then feedback to our modelling process to develop more accurate and sophisticated models.

The primary assumption in the models of infectious diseases is the classification of mutually exclusive disease statuses. In the simplest, SI model, each individual is either **susceptible (S)** or **infectious (I)**. An individual’s disease status could transit from one to
another through disease progression within person (e.g. an infected patient gets recovered after a while) or disease transmission between persons (e.g. a susceptible person is infected by someone else and then become infectious).

According to their assumptions on the population, models of infectious diseases can be classified as differential equation models and network models [58]. Differential equation models assume homogeneous mixing (also referred as fully-mixed) population, which means that everyone has the equal chance to contact with anyone else in the population. As individuals are homogeneous except for their disease status, people with the same disease status can be grouped together as “compartments”. Differential equation models describe the population flow between compartments as the collective result of change of disease status of every individual.

Network models do away from fully-mixed population and allow heterogeneity on an individual basis. Each individual in a population is represented as a vertex in the network and its contacts with other are represented as the edges emanating from the vertex. Different from compartmental models, disease transmission in network model is allowed only through interconnecting edges, meaning a susceptible individual can be only infected by an infective person who he or she contact with.

In the following paragraphs, we will introduce differential equation models of infectious diseases in detail and network models will be discussed in the next section (Section 2.3).

A **differential equation** (DE) model of infectious diseases is a Markov chain model with the finite distinct states. It follows mean-field theory to employ by a system of ordinary differential equations to depict the average behaviour of the system:

\[
\frac{dx}{dt} = f(x,a)
\]

(2.2)

where \(x\) is a compartment (subdivision of the population) and \(a\) is the state-transition rates. The common differential equation models include SIR (Susceptible → Infectious → Removed), SEIR (Susceptible → Exposed → Infectious → Removed), seasonally-forced SEIR (include seasonality in transmission function of SEIR) and age-structured SEIR (divide compartments of SEIR to sub-compartments based on age structure).

SIR model [59] divides the population into three distinct compartments – “susceptible”, “infected” and “removed”, written as \(S\), \(I\) and \(R\) respectively. In SIR model, a susceptible individual may acquire infection from the infected and subsequently removed because of death or recovery. Therefore, at the population level, the individuals flow from \(S\) to \(I\) and then from \(I\) to \(R\) with certain state-transition rates. Given that the
total population remains constant \( S(t) + I(t) + R(t) = S(0) + I(0) + R(0) = N \) in the basic form of SIR models and the transmission dynamics can be described as below:

\[
\begin{align*}
\frac{dS}{dt} &= -\frac{\beta IS}{N} \\
\frac{dI}{dt} &= \frac{\beta IS}{N} - \lambda I \\
\frac{dR}{dt} &= \lambda I
\end{align*}
\]  

(2.3)

where \( \beta \) and \( \lambda \) are the infection rate and recovery rate respectively.

SIR model has a threshold behaviour so that the infected population grows monotonically if \( R_0 > 1 \) and it decreases monotonically if \( R_0 < 1 \) [60]. This threshold behaviour is applicable to all differential equation models, and critical to answer the essential epidemiological question about whether the infectious diseases will persist in the population or fade out in the long run. The determinant \( R_0 \) can be defined as the expected secondary infections from a single infection within the average infectious period:

\[
R_0 = \frac{\beta SI}{N} \times \frac{1}{\lambda I}
\]  

(2.4)

Based on Equation(2.4), \( R_0 = 1 \) is the threshold value. If \( R_0 > 1 \), \( \frac{\beta SI}{N} > \lambda I \) and \( \frac{dI}{dt} > 0 \), so the disease can spread widely. If \( R_0 < 1 \), \( \frac{dI}{dt} < 0 \) and the disease will become extinct in the long run. At the beginning of an outbreak, it is assumed that \( S \approx N \) and Equation(2.4) is simplified to:

\[
R_0 = \frac{\beta}{\lambda}
\]  

(2.5)

Although SIR is a simple model, it demonstrates the fundamental merit of all compartmental models – using ordinary differential equations to describe the time-evolution of the spread and mathematical traceability in transmission dynamics. However, mathematical models are only as good as the assumptions that they are subjected to. The simplicity of SIR model is built on three assumptions: (1) infinite (abundantly large) size of population; (2) homogeneity on both population mixing and contact patterns; (3) constant infection rate and recovery rate. The first assumption is usually acceptable because a large population is frequently encountered in the epidemic modelling. But the rest two assumptions are hardly true in the reality and leave rooms for further improvement.
SIR model only considers three compartments: “susceptible”, “infected” and “removed”, lack of representation of the persons being infected but not infectious yet. So SEIR model [61], [62] is introduced. The “infected” compartment is divided to form two new compartments: “exposed” (E) and “infectious” (I). The system of a SEIR model can be described by:

\[
\begin{align*}
\frac{dS}{dt} &= -\beta IS \\
\frac{dE}{dt} &= \beta IS - \nu E \\
\frac{dI}{dt} &= \nu E - \lambda I \\
\frac{dR}{dt} &= \lambda I
\end{align*}
\]  

Figure 2-2 shows the difference after introducing “exposed” compartment in a simulation of 10,000 population with single-seed infection. Both SIR and SEIR models exhibit the typical bell-shape curves. However, in SEIR model, the spread of infections is delayed, the duration of the epidemic is extended and the peak size of the infectious population is reduced.

![Figure 2-2 Transmission dynamics of SIR and SEIR models](image.png)

Figure 2-2 Transmission dynamics of SIR and SEIR models
(10,000 population, 1 infectious seed; \(R_0 = 2.0\), 5-day latent period, 7-day infectious period)

SEIR model can be further extended to more complex epidemic models by dividing the existing compartments. For example, incorporating the incubation period to
differentiate the symptomatic and asymptomatic infectious within the “infectious” compartment [63].

Seasonally-forced SEIR models [64], [65] are used to address the influence of seasonality in the spreading dynamics of infectious diseases. It is observed that the SIR assumption of “constant infection rate” does not hold all the time in the reality and the infection rate may change over time. Seasonal flu is a great example since its outbreaks replicate the seasonal patterns, perhaps by influence of climatic factors or holidays. The introduction of seasonality leads to seasonally-forced SEIR models. For mathematical convenience, the seasonal variation is often represented by a sinusoidal function of time:

\[ \beta(t) = \beta(1 + \sigma \cos(2\pi t)) \]  

(2.7)

where \( \sigma \) measures the strength of seasonal influence on the infection rate. Holiday-related seasonality can also be represented by “term” function, which is commonly found in studies of childhood diseases [65]:

\[ \beta = \beta_0 (1 + \beta_T \text{Term}(t)) \]  

(2.8)

where \( \text{Term}(t) \) is a periodic function that is \( 1 \) if in school term and \( -1 \) if in holiday.

Besides the seasonality, age property of both contacting parties is another factor that influences the variation of infection rates. Age-dependence of the force of infection has been documented in the literature from serological data to records of case notifications, as a result of age-related immunity, resistance and etc [56], [66], [67]. In the recent outbreak of H1N1 2009, the age group “5-29” accounts for 70.72% and 59.11% of the confirmed cases in the US and Mexico respectively, demonstrating strong age dependence of infection rate [68]. To complement SEIR models with age dependence, age-structured SEIR models [66], [69] were introduced by dividing the population to a number of cohorts with the distinctive age groups (e.g. age 1-5, 6-10, 11-15 etc) and then building a SEIR model for each individual cohort. To address the heterogeneity between cohorts, the infection rate \( \beta \) is re-formulated in the form of WAIFW (Who Acquires Infection From Whom) matrix [70]:

\[
\begin{bmatrix}
\beta_{11} & \beta_{12} & \cdots & \beta_{1n} \\
\beta_{21} & \beta_{22} & \cdots & \beta_{2n} \\
\vdots & \vdots & \ddots & \vdots \\
\beta_{n1} & \beta_{n2} & \cdots & \beta_{nn}
\end{bmatrix}
\]  

(2.9)

where \( n \) is the number of cohorts, \( i \) and \( j \) are both cohort indices and \( \beta_{ij} \) is the infection rate from cohort \( i \) to cohort \( j \).
The above differential equation models are for deterministic versions that describe the average behaviour of an epidemic dynamics system at the population scale. They generally work well for large populations. However, in situations where fluctuations or individual heterogeneity could impact the spreading dynamics substantially, stochastic versions of the models are more suitable especially for small populations. In the stochastic version of differential equation models [71]–[75], the continuous variables of population of the individual compartments \((S, I, R, \text{etc})\) are replaced by the discrete numbers, and the state-transition rates (e.g. infection rate \(\beta\), recovery rate \(\lambda\), etc) are replaced by the probabilities. In Equation (2.10), \(P[\cdots]\) are the probability functions and \(\Delta t\) is a small time interval so that \(\forall P[\cdots] < 1\).

\[
P[S(t) = S(t - \Delta t) - 1] = \beta I(t) S(t) \Delta t \\
P[I(t) = I(t - \Delta t) + 1] = (\beta I(t) S(t) - \lambda I(t)) \Delta t \\
P[R(t) = R(t - \Delta t) + 1] = \lambda I(t) \Delta t
\] (2.10)

In the deterministic models, \(R_0\) determines the persistence or fade-out of the infectious diseases in the population. In the stochastic models, if \(R_0 < 1\), the outbreak of infectious diseases will be confined to a limited size of the infected. If \(R_0 > 1\), the disease will spread to the majority of the population with a certain probability \(p\) where \(p \in [0,1]\) and \(p \propto R_0\).

### 2.3 Network Models

Network models address the heterogeneity in population mixing and contact pattern. For an individual, his or her contacts are preferentially selected from the population by either relationship-based (e.g. classmates) or distance-based (e.g. neighbours) closeness. Compared to a stranger, it is reasonable to assume a person has a higher chance to contact his/her family members, classmates, colleagues and friends through the social activities, as well as to be in contact with the neighbours while shopping nearby or commuting via public transport. Such contact heterogeneity has been documented many times in the literature to claim its significant impact on the spreading dynamics of infectious diseases [5], [46], [56], [76], [77]. A case study on the 2003 SARS also demonstrates that \(R_0 = 2\) for the entire infected population, but for those super-spreaders, \(R_0\) could increase up to several tens [78], [79].
2.3.1 Typical Network Models

To take account of contact heterogeneity into mathematical epidemic models, the common approach is to adopt the network representation by a graph structure where the persons are represented as vertices and the contacts as edges. In the network representation, every vertex in the network complies with the disease progression model, and transmission of infection is subject to the structure of the network, i.e. an infected node can only infect the susceptible nodes that are directly connected to itself in the network. Based on their topological property, there are different types of networks used in epidemic modelling. Examples are regular network [80], [81], random network [82], [83], scale-free network [84]–[86] and realistic network [5], [47].

Regular networks, also known as lattices, are the simplest network structure that defines a regular contact pattern applicable for every vertex in the network and degree of vertex is constant throughout the network. The Watts-Strogatz [84] networks are modified from lattices by rewiring each edge with probability $p$ to create the shortcuts between vertices. The addition of shortcuts introduces the small-world property into the network, meaning most vertices can be reached from any other vertices by a small number of hops.

Random networks adopt the topology of random graph which can be obtained by randomly adding edges between a set of vertices in an independent manner. In such random graph, denoted as $G(n, p)$, each of the possible $n(n-1)$ edges occurs independently with a probability $p$.

In a scale-free network, degree distribution decays as a power law. Let $P(k)$ be the fraction of nodes with degree $k$, $P(k) \propto k^{-\gamma}$, where $\gamma$ is a constant and within the typical range of $[2,3]$. The topological properties of scale-free networks have critical implications about infection dynamics. As power law distribution implies, a small group of nodes has exceptionally higher degrees than the rest of the nodes and would be the super-spreaders in an outbreak. The clustering coefficient of a scale-free network also follows the power law distribution, suggesting the low-degree nodes are clustered by connecting to the high-degree nodes. It makes those super-spreaders critical in spreading an infectious disease.

Different from the above theoretical network prototypes, a realistic person-to-person contact network is constructed based on real-life data. A contact network can be formally defined as follows:
Definition 2.1 Contact Network

A contact network \( G(V, E) \) is a simple undirected network with a set \( V \) (vertices/nodes) of people and a set \( E \) (edges) of person-to-person contacts. An edge \( e_{ij} \) is present if the person \( i \) might contact person \( j \) or vice versa.

Every node in a contact network represents an individual person, which is characterized by demographic properties and social activities. The individuals are connected by edges if they appear in close proximity at the same point of time. The probabilities of connecting persons are related to their activities taking place in the respective social structures. For example, the persons have a higher chance to be connected if they are family members, classmates, colleagues and etc. Therefore the constructed networks can represent the social organization of the real world, embodying personal characteristics of individuals as well as their interactions. Figure 2-3 illustrates a partial contact network of a school.

![Figure 2-3 A partial contact network of a school](image)

Generating a realistic contact network often adopts a divide-and-conquer approach. Meyers [47] elaborates that the generation starts from creating the individual social structures and allocating people to those structures based on their social activities such as students should go to school, patients should stay in hospital, and then in each social structure, the allocated individuals are connected randomly by a predefined contact rate. Other than uniform randomness in contact creation, in the literature, there are generally two types of models for connecting individuals in a network representation of social structure: (1) Incremental generation models [87]–[90] start from an initial node, gradually add new nodes and connect them to the existing nodes by preferential attachment. (2) Configuration models [91]–[94] compute the degrees of every nodes by the given degree distribution and connect those nodes based on excess degrees. A new edge is always connected from the node of the highest excess degree to another node which is selected by the probability proportional to its excess degree.

Meyers’ contact network model [47] creates an unweighted and undirected person-to-person network. This approach has the advantage that it does not requires priori assumptions of the global contact network and is able to facilitate both network based
simulation and mathematical analysis such as bond percolation [46]. However, it does not contain any information to differentiate the contact edges from the perspective where the contacts take place. It is therefore not suitable for simulating epidemic interventions, which may require re-generating the contact network in order to reflect the structural changes due to intervention. A further extension of Meyers’s model is to take account of asymmetric contacts between patients and caregivers to create a semi-directed person-to-person contact network [48].

Other than person-to-person contact networks, bipartite network model [49] comprises two types of vertices: persons and places. An edge only exists between person and place vertices, representing an individual visit to a particular place. The disease can be transmitted between two individuals while both are visiting the same place at the same time. Bipartite networks are typically used in discrete-event simulations which are able to adopt any arbitrary details about demographic, socio-economic, behavioural characteristics as well as sophisticated intervention strategies, in a refined time step but at the price of enormous computation cost.

2.3.2 Network Measures

In order to understand the topological properties of contact networks, the following measures are commonly used to characterize those networks.

**Definition 2.2 Degree, Degree Distribution, Mean Degree**

*Given a contact network $G(V,E)$, the degree of a vertex $v \in V$ is the number of edges emanating from $v$ in $G$, written as $k_v$. The degree distribution is the probability distribution of degrees of nodes in $G$, written as $P(k)$. The mean degree of $G$ is the average of degrees for all $p$ in $P$, written as $\langle k \rangle$.*

$$P(k) = \{Pr(k_v) : \forall v \in V\}$$

$$\langle k \rangle = \frac{\sum k_v}{|V|}$$ (2.11)

**Definition 2.3 Clustering Coefficient, Average Clustering Coefficient**

Cluster coefficient is one of the key network characteristics that measure the connectivity among the neighbouring nodes. *In a network $G(V,E)$, $i,j,v \in V$, $e_{ij}$ denotes an edge*
connecting node \(i\) to node \(j\), then cluster coefficient \(C_v\) and average clustering coefficient \(C\):

\[
C_v = \frac{|\{e_{ij}\}|}{k(v)(k(v)-1)}; e_{ij}, e_{jk} \in E
\]

\[
C = \frac{1}{N} \sum_{v=1}^{N} C_v
\]  

(2.12)

**Definition 2.4 Degree Assortativity Coefficient**

Degree assortativity coefficient is the Pearson correlation coefficient of the degrees at either ends of an edge [95]. In a network \(G(V,E)\), \(k_1, k_2 \in \{k_v\}, \forall v \in V\), \(P(k_1, k_2)\) is the fraction of edges connecting a node of degree \(k_1\) to a node of degree \(k_2\), then degree assortativity coefficient \(r\):

\[
r = \frac{\sum_{k_1k_2} k_1 k_2 [P(k_1, k_2) - P(k_1)P(k_2)]}{\delta^2}
\]

\[
\delta = \sum_k k^2 P(k) - \left(\sum_k k P(k)\right)^2
\]  

(2.13)

Positive value of \(r\) means a node tends to connect to other nodes which share the similar degree. The value of \(r \in [-1, 1]\). When \(r = 1\), the network has perfect assortative mixing. When \(r = -1\), the network is completely disassortative.

**Definition 2.5 Mean Path Length**

In a network \(G(V,E)\), let \(D(v_1, v_2)\) denotes the shortest path between vertex \(v_1\) and \(v_2\), \(v_1, v_2 \in V\), then mean path length \(L\):

\[
L = \frac{1}{n(n-1)} \sum_{v_1, v_2} D(v_1, v_2)
\]

(2.13)

The mean path length is an important network measure to infer the small-world effect. A small-world network exhibits a relatively short mean path length, meaning most pairs of nodes can be connected by a limited number of intermediate nodes.
2.3.3 Network Algorithm

2.3.3.1 Percolation

Percolation theory [96] originally describes the fluid dynamics in a random media. If the medium holds a lattice structure, bond percolation formulates the process of fluid flowing through the medium via random open or closed edges. Let $Z^2$ be the square lattice and $p_c$ is the probability that an arbitrary edge is open. There is a percolation threshold $p_c$ that exhibits the phase-transition phenomenon: If $p_c > p_c$, the fluid will flow through the giant portion of the lattice and if $p_c < p_c$, the fluid will pass the small portion of the lattice. It is an interesting property of critical values that remind us about $R_0$ in the epidemiology. In fact, bond percolation is applicable to transmission dynamics in epidemiology. In a contact network model, human contacts are the edges and individual transmissibility ($r_{ij}$: $i$ and $j$ are the contacting parties) can be treated as open probability of the edges. In such formulation, the study of outbreak size is equivalent to find the portion of medium being flowed through.

However, there is a tricky problem that open probabilities of edges are identical to all the edges but $r_{ij}$ varies depending on attack rate of infection, contact duration, susceptibility of both $i$ and $j$, and other factors. Newman [46] proved that if $r_{ij}$ and $\tau_i$ (contact duration) are independent and identically distributed (i.i.d.) random variables, the variation of $r_{ij}$ makes no difference whatsoever; in the population as a whole the disease will propagate as if all $r_{ij}$ are equal to average transmissibility $T$. Therefore, $T$ can be used as the open probability of all edges in the contact network.

Based on percolation theory, Newman [46] and Meyers et al [47] proposed the analytical model of contact network epidemiology. Critical transmissibility $T_c$ is defined as

$$T_c = \frac{\langle k \rangle}{\langle k^2 \rangle - \langle k \rangle}$$

(2.14)

where $\langle k \rangle$ and $\langle k^2 \rangle$ are the average degree and average square of degree respectively. If $T < T_c$, the infectious disease will spread in the limited size of the population. The average size of small outbreaks $\langle S \rangle$ could be computed by

$$\langle S \rangle = 1 + \frac{T \langle k \rangle}{1 - T \langle k_c \rangle}$$

(2.15)
where average excess degree $\langle k_e \rangle = \left\langle k^2 \right\rangle - 1$. If $T > T_c$, an outbreak will develop to a full-blown epidemic with the probability $S$:

$$S = 1 - \sum_{k=1}^{\infty} p_k (1 + (u - 1)T)^k$$

$$u = \frac{\sum_{k=1}^{\infty} kp_k (1 + (u - 1)T)^{k-1}}{\sum_{k=1}^{\infty} kp_k}$$

(2.16)

2.3.3.2 Simulation

Over the past decade, computational epidemiology has moved into a new direction: large-scale, individual-based, disaggregated models [5], [7], [26], [30], [42], [97] for realistic epidemic simulation. Network based simulations refer to the agent-based simulations running in a network structure to study the time evolution of the spread of infectious diseases. In general, epidemic simulation replicates two processes at each time step: disease transmission between persons and disease progression within person.

Disease Transmission between Persons

For a bipartite network, each person in the network is assigned with a schedule of activities. Then let every person visit different locations at the pre-specified time frame according to their schedule. An infection event may occur at a certain chance between the two persons who visit the same location at the same time. At the end of each time step of simulation, disease status of each individual is updated. For a person-to-person contact network, simulation is simplified as there is pre-constructed contact between individuals. At each time step, each infectious person will infect his or her susceptible contacts one by one at a certain infection rate. Alternatively, let every susceptible person acquire infection from his or her infectious contacts by the chance of infection rate.

Disease Progression within Person

Same to bipartite network and person-to-person network, each person will progress in his or her disease status according to the disease progression model at each step. The status transition could be deterministic or stochastic. In a deterministic status transition, for example, after latent period $t_L$, an “exposed” person turns to “infectious” and latent period $t_L$ is derived from $\mu t_L$ by a certain distribution. On the contrary, in a stochastic status transition, an “exposed” person will have a chance $p$ to become “infectious” at each
time step, where $p$ is also derived from $h_{t_{L_i}}$ so that $h_{t_{L_i}^0} = h_{t_{L_i}}$, where $h_{t_{L_i}^0}$ is computed based on simulation results.

The network simulation is often time-consuming because of 1) size of network up to tens of millions; 2) details of social behaviours; 3) stochasticity of simulation require repeat simulations. Therefore, network simulation is usually parallelized. Disease progression within person is independent of all other persons and so very parallelizable. But disease transmission between persons carries the natural dependence between the statuses of two persons, posing a challenge to parallelism. It suggests the speedup attributed to parallelization may be significantly affected by size of time step of simulation. EpiFast [30] shows that substantial speedup can be achieved by increasing time step to one day.

Compared to percolation approach, simulation approach is highly flexible and configurable, supporting more complicated interventions (such as combined intervention) and disease models (such as SEIAISR) as well as refined time scale (such as hourly). Moreover, temporal and spatial evolution of epidemic dynamics is traceable and readable in simulation, particularly suitable for contact tracing and visualization purposes. However, percolation approach is much faster and is able to produce statistically significant results by a single execution. In all, percolation approach is good at producing quantitative insights about the final state of epidemic with varying transmissibility at the minimal cost of computation and time. But it loses out on evaluating sophisticated time-dependent interactions targeted to some particular subpopulation.

### 2.4 Public Health Intervention

Public health intervention is a series of programs to protect public health by containing and mitigating the spread of infectious diseases. In general, there are pharmaceutical interventions (such as antiviral treatment and vaccination) and non-pharmaceutical interventions (such as school closure, workforce shift). During the outbreak of a certain infectious disease, medical resources such as antiviral drugs and vaccines might not be ready at the time when an outbreak of epidemic occurs or are not adequate for accommodating all the treatment requirement when number of patients surge. Non-pharmaceutical interventions are useful in isolating the infection source, and mitigating the transmission of pathogens so as to lessen community-acquired infections. However
those interventions often incur enormous cost both economically and socially because of their massive disruption to normal socio-economic activities.

Based on the effect of interventions, we can also classify them to two categories — transmission interventions and contact interventions. Transmission interventions refer to the set of control measures that reduce the likelihood by which pathogens can transmit through the contacts. For example, hand washing and wearing face mask are both transmission interventions, which do not remove or reduce person-to-person contacts, but impose the extra barrier for pathogens transmission or reduce the colony size of pathogens that can be communicated via the contacts. Contact interventions refer to the set of control measures that eliminate or reduce the contacts between the susceptible and the infected persons (or carriers). Individual isolation is the typical contact intervention to isolate the infected persons from the susceptible population. Social distancing is a major group of measures in contact interventions, including school closure, workforce shift and etc, for disrupting the regular contacting activities in the respective social structures where the disease transmission is likely to take place. Lastly, vaccination is also a contact intervention which equivalently eliminates all disease-transmitting contacts connecting to the vaccinated persons.

The decision on whether to implement epidemic interventions may affect thousands of lives under the threat of infectious diseases and cost millions of dollars. To make wise decisions, there are three key questions to be considered:

**“How to control”** — refers to the choice of controls (or combination of controls) that could minimize the probability of full-blown epidemic, reducing the total incidences and the peak size of infected cases as well as postponing the peak as far as possible. From the perspective of the final-state, an effective control measure should be able to restrain the spread of diseases and reduce the individual risk of infection. On the other hand, from the perspectives of time evolution, an effective intervention should slow down the spread of the epidemic to allow more time to respond, and also decrease the peak size of daily incidences to relieve the pressure on healthcare facilities.

**“When to control”** — refers to the timing and duration of the implementation of a certain control measure. There is no doubt that the earlier and the longer the control measures are implemented, the smaller the size of the epidemic would be. However, many control measures are associated with substantial economic and social costs. So there is clearly a trade-off between epidemic severity and cost when varying triggers and duration of interventions.
“What to control” — refers to the selection of intervention targets. The individual risk of infection in the population is heterogeneous. The ones with more disease-transmitting contacts or the more vulnerable individuals bear the higher risk of infection than the average person. That is why hospital lockdown and school closure are commonly considered. By knowing “who”, instead of massive or system-wide intervention, precise targeting controls not only reduce the cost but are also more effective. Practically, mass-scale intervention is a demanding task that requires considerable effort in administrative coordination and resource arrangement. Targeting control would be advantageous because of its smaller scale, leading to much more responsive actions.
Chapter 3
Contact Network Generation

In this chapter, we propose the HPCgen, a fast and scalable contact network generator for urban cities. We elaborate on the design of the generator, step-by-step network generation and the adopted optimization techniques. As the data is important to contact network generation, we also go to the details on the sources and content of the data that are utilized in the contact network generation. Lastly, we carry out the experiments by generating contact networks for Singapore city of 4.8 million population, followed by network analysis, sensitivity analysis, network validation as well as quantitative comparison for efficiency and scalability. The content in this chapter mainly comes from the publications\textsuperscript{1,2}.

3.1 Introduction

Contact network generation lays the foundation for our contact network based framework for intervention evaluation. The generation of contact networks could be challenging on account of the large population size and hierarchical social structures. There are three major issues to address in the contact network generation:

Genericity

As known, there are many types of social structures and modelling all of them is practically infeasible. So it is preferable if we could build the contact network with a set of chosen social structures and then later add more social structures incrementally, provided that the network generation model is generic so that incorporating a new social structure needs no more than providing structure-specific parameters.

Scalability and Efficiency

The network generation model is designed for contact networks of urban cities so the scale of networks will depend on the population size of the city proper (an urban locality.

\textsuperscript{1} Tianyou Zhang, Soh Soon Hong, Xiuju Fu, Kee Khoon Lee, Limsoon Wong, Stefan Ma, Gaoxi Xiao, Chee Keong Kwoh, “HPCgen – A Fast Generator of Contact Networks of Large Urban Cities for Epidemiological Studies”, International Conference on Computer Modelling and Simulation, Brno, Czech Republic, 7 – 9 Sep 2009

without its suburbs [98]). Singapore has 4.8 million population and the largest city on the earth is Mumbai, ~13.4 million population as of 2008. So the generation model should be capable of handling the network size of millions.

**Intervention Readiness**

In order to simulate epidemic interventions, the contact network must contain information such as demographic properties of individual persons and whereabouts of each contact edge taking place, so that interventions can be simulated to affect some particular type of persons or contacts. For example, school closure is simulated to remove a fraction of school contacts of students where “school contacts” refers to those contacts taking place in school, with classmates or schoolmates.

### 3.2 Model

We propose HPCgen, a fast generator of the labelled person-to-person contact networks for urban cities. HPCgen is developed based on Meyers’ model [47] to first initialize the population by demographics, then construct individual social structures based on size distributions to accommodate those individuals, and create contacts between individuals in a social structure by average contact rate, and finally aggregate contacts from all social structures to form a global contact network. In spite of the types of social structures, HPCgen adopts a generic and modularized model to represent a social structure and generates its subnetwork with the connected vertices so that every social structure can be generated, by using the same “engine” with some structure-specific parameters. Therefore, incorporating new social structures in HPCgen is undemanding and does not require any modification to the underlying codes.

The output of HPCgen is a labelled undirected person-to-person contact network in a matrix form. There are two types of labels: edge labels indicate where those contacts take place and node labels indicate the ages of nodes. Both labels are designed to facilitate intervention simulation which may target to a specific age group in a population or the contacts which take place in some particular social structure.

The scalability and efficiency of HPCgen are achieved by memory-efficient matrix representation, operation optimization as well as MPI (Message Passing Interface) parallelization. HPCgen is able to generate a Singapore contact network of 4.8 million population in 1.55 minutes and generate a contact network of 13.4 million nodes (the
population size of the largest city, Mumbai, as of 2008) in 7.27 minutes. It approximates a near linear relationship between the size of network and the runtime cost.

### 3.2.1 Model Design

Among many types of social structures, HPCgen chooses six types in the urban setting as suggested in [47]: 1) households; 2) hospitals; 3) schools; 4) workplaces; 5) shopping malls; and 6) public transport. The potential disease-transmitting contacts taking place within those social structures are mainly on a regular basis, meaning daily or at least once within the infectious period. There is also the non-regular type of contacts, like standing in proximity to some strangers in a shopping mall or on a bus. We argue that there is a significantly higher chance (due to frequency and contact duration) for transmitting the disease to a regular contact compared to an occasional transient contact and we therefore neglect them in HPCgen.

![Figure 3-1 Conceptual design of HPCgen (six types of social structures with hierarchical groupings) [28]](image)

Figure 3-1 gives a graphical illustration to the social structures modelled in HPCgen. Note that each green box in the figure represents a collection of social structures of the same type. For example, grey boxes at the outer circle are the individual households, in which the dwellers are represented by the black dots. Solid lines connecting between
dwellers and social structures denote the persons visit the social structures regularly. A school is a 2-level structure, which contains several classes and each class contains a number of students (denoted by the black dots as well). Similarly, a hospital is also a 2-level structure which contains sub-level structure “wards”. Note that HPCgen generates idealised contact network models for urban cities based on simplification assumptions. HPCgen creates social structures by daily population size and then assigns people to those social structures and let them make contact with each other. Other researchers [35], [47] adopted the similar modelling approach as HPCgen and Milne et al [35] claimed their idealised network models could yield the comparable attack rates with other models in the literature. The list of assumptions used in HPCgen is elaborated as follows:

1) Schools include three types: primary, secondary schools and junior colleges. Every school is modelled identically in regardless to its type. Size of a school/class refers to the number of students in the school/class.

2) Public transport refers to railway stations and bus stops. Size of a subway station or bus stops refers to the average number of visitors in a day.

3) A workplace represents a company or institution. Size of a workplace refers to the number of employees in the workplace.

4) Any inner structures like individual shops in a shopping mall are not modelled. Size of a shopping mall refers to the average number of visitors in a day.

5) Hospitals only model the inpatients who stay in the wards. Inpatients are assumed to stay in hospital all the time so that they have no external contacts except with household members. Size of a hospital/ward is the number of beds in the hospital/ward.

6) People are classified to 4 groups: infants (0 – 6 years old), students (6 – 18 years old), adults (19 – 65 years old) and the elderly (65+ years old). A household can be formed by at least one adult or elderly. Genders of dwells are neglected. Within each household, persons are assumed to be fully connected.

7) For households, schools, railways stations and bus stops, proximity preference is enforced. For example, students living in the neighbour residence have a higher chance to go to the same school or class.

Note that for simplicity, all the persons in any single social structure are of the same role. For example, school structure contains only students, hospital structure contains only inpatients, teachers and caregivers are not modelled.
3.2.2 Network Generation

Figure 3-2 shows the flow chart of the contact network generation process. It starts with initializing the age attribute and index for each individual in the population. The ages of individuals are calculated from the population age distribution and all individuals are indexed sequentially from 1 to \( N \), where \( N \) is size of the population.

![Flow chart of generation process](image)

After the initialization, a list of social structures is then created with the specific sizes that are computed from the respective size distributions of social structures. Once the structures are generated, contacts are then created within or across structures. Assume a structure is of size \( n \) and has the mean contact degree of \( \langle k \rangle \), a subnetwork \( G_s(V_s,E_s) \) of \( n \) nodes is created and the degrees of every nodes can be determined by a Poisson random number generator \( \text{randp} \),

\[
k_i = \text{randp}(n,\langle k \rangle), i \in V_s
\]  

(3.1)

As known, a degree sequence \( \{k_1,k_2,\ldots,k_n\} \) in which \( k_1 \geq k_2 \geq \cdots \geq k_n \), is realizable if and only if it satisfies Erdős–Gallai theorem [99], which states:

\[
\sum_{i=1}^m k_i \quad \text{is even}
\]

\[
\sum_{i=1}^m k_i \leq m(m-1) + \sum_{i \neq j} \min(k_i, m) \quad \text{for} \quad m \in \{1\ldots n\}
\]  

(3.2)

In HPCgen, we skip the Erdős–Gallai test and realize a degree sequence as follows:
Algorithm 3-1 Contact creation algorithm for a given degree sequence

1: function createContact(deg_seq, tag)
   Ensure: deg_seq is sorted descendingly by degrees; deg_seq[1] < number of nodes
2:   max_deg := deg_seq[1]          . highest degree
3:   n := length(deg_seq)          . number of nodes
4:   network := sparseMatrix()
5:   for i := 1; i < n do         . index of 1st node in a contact
6:      for j := i + 1; j < n do   . index of 2nd node in a contact
7:         if deg_seq[i] >= 1 then
8:            if deg_seq[j] >= 1 then
9:               deg_seq[i] := deg_seq[i] - 1
11:              network.add(makeContact(i, j, tag))
12:            else
13:               break
14:         end if
15:      else
16:         break
17:   end for
18:   residue := sum(deg_seq)      . sum of unused degrees
19:   if residue > 1 then           . create extra contacts by unused degrees
20:      for m := 1; m < max_deg - 1 do
21:         for j := max_deg + m; j < n do  . index of 2nd node in a contact
22:             network.add(makeContact(1, j, tag))
23:             residue := residue - 2
24:             if residue < 2 then
25:                break
26:         end for
27:      end if
28:   end if
29:   network.shuffle()
30: return network
31: end function

As shown in Algorithm 3-1, the first stage in our method is similar to the configuration model [91]. We sort the degree sequence in a descending order and connect the nodes based on excess degrees of all nodes. For the sake of computation cost, we assume the selection of connecting nodes is deterministic so as to avoid massive need for random number generation. In the second stage of contact creation, any unutilized degrees ("residue") in the degree sequence, are used to create the extra edges emanating from the highest-degree node, for achieving the expected mean degree as well as strengthening
the strong-spreaders in the structure. Each contact is created by the indices of two nodes as well as “tag” which denotes the type of the social structure where this contact takes place. At the final step, the indices of vertices are shuffled randomly to get rid of correlation between indices and degrees.

When creating contacts across the structures, for example, creating inter-class contacts between students who belong to the different classes in a school, we use the same mechanism to create the contacts but with different parameters – school size instead of class size; inter-class mean contact degree (average number of contacts between students from different classes) instead of intra-class mean contact degree (average number of contacts between students from the same class). For example, if there are 5 classes in a school and class sizes are \{30, 20, 40, 30, 30\}, then the students in class 1 are indexed from 1 to 3, the students in class 2 are indexed from 31 to 50, and those in classes 3, 4 and 5 are indexed similarly. So we can test the validity of inter-class contacts based on its pair of indices, such as a contact between indices 10 and 50 is valid. A contact between indices 10 and 20 is an intra-class contact and is invalid. All intra-class contacts are then mapped to randomly chosen indices and re-tested for validity. This procedure is repeated until all contacts are inter-class contacts.

For schools and hospitals, as they are both 2-level structures, the generation of subnetworks is carried out in a recursive fashion. As shown in Algorithm 3-2, function “generateNetwork” is called recursively in order to generate contact networks at the different hierarchical levels of a social structure. For example, assuming “generateNetwork” function is called to generate an all-school network, the first step of network generation is to compute the sizes of individual structures. At this stage, each structure denotes a school and “structure_size” are sizes of individual schools. If “mean_degree” (mean contact degrees) of all-school level is specified, the contacts are created followed by a fixing procedure to ensure all connected nodes are from the distinct schools. After cross-school contact generation, an iterative process starts to generate the subnetworks in each individual school.

In each school, as it is not at the bottom level in the hierarchy of school model, “generateNetwork” function is called again to generate a sub-level network that is comprised of all classes in this school, where “level” is incremented and “total_pop” is the size of this school. In the generation of sub-level network, similarly as before, if “mean_degree” of school level is specified, the contacts between students who belong to distinct classes, namely cross-class contacts, are created. Then all the subsidiary classes are looped over. As class is at the bottom level, a class network is generated with in-class
contacts (contact between students who belong to the same class). All class networks are integrated to form a school network by correcting the indices of vertices based on the sizes of classes. The obtained school network is then returned to the upper level routine.

At the upper level (all-school) routine, the school networks returned from the sub-level routine are integrated by correcting the indices of vertices based on the sizes of schools. The final network after integration is the all-school network for school model in HPCgen.

**Algorithm 3-2 Contact network generation algorithm**

```python
1: function GENERATE_NETWORK(level, total_pop, size_dist[], mean_degree[])
2: struct_size[] ← computeStructSize(total_pop; size_dist[level])
3: network ← sparseMatrix()
4: if mean_degree[level] > 0 then
5:   deg_seq ← computeDegSeq(struct_size[]; mean_degree[level])
6:   subnetwor k ← createContact(deg_seq)
7:   subnetwor k ← fixNonCrossStructContact(subnetwor k; struct_size[])
8:   network ← subnetwor k
9: end if
10: level ← level + 1
11: for i ← 1; length(struct_size[]) do
12:   s ← struct_size[i]
13:   if isBottom(level) then
14:     deg_seq ← computeDegSeq(s; mean_degree[level])
15:     subnetwor k ← createContact(deg_seq)
16:   else
17:     subnetwor k ← generateNetwork(level; s; size_dist[]; mean_degree[])
18:   end if
19:   network: integrate(i; struct_size[]; subnetwor k)
20: end for
21: return network
22: end function
```

After the network of a particular type of social structure is generated, the next step is to map the vertices in the network to the people. HPCgen selects candidates from the population based on age requirement and exemption. To be specific, schools network requires students, workplaces network requires adults and households network requires at least one adult or elderly in each household. Exemption requirement refers to the people mapped to the hospitals network is forbidden to map to any other network except for households.

Once the candidates are selected, a mapping procedure is then carried out and eventually the indices of vertices are replaced with the population indices. Figure 3-3 demonstrates the mapping process. In the array of population candidates, the number in each box denotes the age group of the person (1 – infants; 2 – students; 3 – adults; 4 – elderly), and the numbers on the right side of the boxes are the population indices; in the
network, the numbers in the circles are the indices of vertices. After mapping, the original indices of vertices are replaced with the population indices so that the networks generated from all different types of social structures can be integrated together based on the uniformed population indices.

![Diagram showing before and after mapping of population indices](image)

**Figure 3-3 Illustration the effect of mapping process**

There are three extra remarks in the mapping process: 1) in those models with proximity preference, the indices of selected population will be not shuffled before mapping to preserve proximity tendency in the population indices. But in the rest of models, population indices are shuffled randomly. 2) A single person might visit more than one shopping mall regularly. So a single candidate might be mapped to multiple vertices from the distinct shopping-malls. 3) Multiple edges between the same pair of vertices are not supported in our contact network. So we implement a procedure to locate the duplicate edges. Once a duplicate edge $e_{ij}$ ($i; j$ are the connected nodes) is located, $e_{ij}$ is rewired to another pair of nodes $(u; v)$ where $k_i = k_u + 1$ and $k_j = k_v + 1$ before rewiring. It ensures the degree distribution will remain intact after rewiring.

The entire generation process is modularized and generic for all types of social structures. So adding a new type of social structures into our contact network is undemanding, simply calling “*generateNetwork*” function with the structure-specific parameters such as size distribution and mean contact degrees.
3.2.3 Optimization

In HPCgen, a labelled adjacency matrix is used to represent a contact network. Different from the common adjacency matrices in which edges are denoted as “1” in the matrix, we represent an edge by an integer “tag” (label) of social structure in the adjacency matrix, indicating where this contact takes place. The advantage of using matrix representation is its capability of encapsulating millions of pair-wise operations during contact generation into a single matrix operation and such operations have been highly optimized in the existing toolkits such as MATLAB/Octave. As the nature of the network is far from being fully connected, there would be numerous “0”s (no edge) filled up in the adjacency matrix of a contact network. In order to reduce memory footprint and improve scalability, we adopt sparse matrix representation in the compressed column format [100] to only store those non-zero matrix elements. Furthermore, as HPCgen generates the undirected network, its adjacency matrix is symmetric along the diagonal. That inspires us to represent only the upper triangular matrix and set the rest to be “0”s. It would reduce the memory footprint to nearly half.

We also employ MPI parallelization to speed up the network generation. Each type of social structures in HPCgen is comprised of a number of individual structures. These structures could be distributed to multiple parallel processors and carry out the network generation concurrently.

In HPCgen, as the nature of incursive operations, contact generation in any particular structure is “peer-independent” and “parent-dependent”. For example, in the school model, all-school is at level-0, individual school is at level-1 and individual class is at level-2. Contact generation within a class is independent from its peer classes, but dependent on its parent level-1 school to determine the size of the class. Therefore, we only distribute the level-1 schools to parallel processor nodes to run concurrently. At the end of contact generation of each type of social structures, all the generated contact networks are collected back to the master node to perform the global network integration.

The speedup gained from MPI parallelization comes at the price of the extra overhead for the coordination and communication among parallel processor nodes, which may offset some fraction of the speedup. In the master-slave paradigm, after the completion of the job at the slave nodes, a MPI reduction will be performed in either linear or log fashion. In linear reduction, the master node calls each slave node to send the result back one by one. In log reduction, as shown in Figure 3-4, half of the slave nodes will send their results to neighbouring nodes simultaneously in each run. In terms of efficiency, log
reduction is obviously superior as its time complexity is $O(\log N)$ compared to $O(N)$ for linear reduction. Therefore we chose the log reduction scheme for collecting the generated networks back to the master node and implemented it with MPI_send() and MPI_recv() from MPITB library as MPI_reduce() in MPITB [101] does not support sparse matrix data type that we use for representing the networks.

![Log reduction scheme (solid stars denote active nodes; hollow starts denote inactive nodes; arrows indicate matrix passing)](image)

### 3.3 Data

HPCgen takes account of three types of data: population demographics, social structure information and contact behaviour surveys. Demographic data including population size and age distribution facilitate the initialization of population, people selection and allocation to the respective social structures. Social structure information refers to age requirement, levels of hierarchy, number of structures and size distribution at each level. Here “size” refers to number of persons in a structure. Contact behaviour surveys are the statistics of contact degrees derived from the survey records related to the respective social structures, including both within-structure and cross-structure contacts. For simplicity, we mainly use mean contact degrees to create contact connections between individuals.
Demographics

As of 2008, the total population of Singapore is 4,839,400, including both Singapore residents and non-residents [102]. Non-residents include foreign workers, students or others who stay in Singapore for at least one year. The age distribution within the Singapore population is as shown in Table 3-1.

<table>
<thead>
<tr>
<th>Type</th>
<th>Age</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant</td>
<td>0–5</td>
<td>4.93%</td>
</tr>
<tr>
<td>Student</td>
<td>6–18</td>
<td>17.24%</td>
</tr>
<tr>
<td>Adult</td>
<td>19–64</td>
<td>71.30%</td>
</tr>
<tr>
<td>The Elderly</td>
<td>65–100</td>
<td>6.53%</td>
</tr>
</tbody>
</table>

In HPCgen, we select six types of social structures to build the Singapore contact network. The list of the applied data and their sources are tabulated in Table 3-2.

<table>
<thead>
<tr>
<th>Social Structures</th>
<th>Data</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Households</td>
<td>number of households; household size distribution; mean contact degree;</td>
<td>1) Census of Population 2000 [103] 2) survey</td>
</tr>
<tr>
<td>Hospitals</td>
<td>number of hospitals; hospital/ward size distribution; mean contact rate;</td>
<td>1) Tan Tock Seng Hospital 2) survey</td>
</tr>
<tr>
<td>Schools</td>
<td>number of schools; school/class size distribution; mean contact rate;</td>
<td>1) Ministry of Education 2) survey</td>
</tr>
<tr>
<td>Workplaces</td>
<td>total workforce population; company size distribution, mean contact rate;</td>
<td>1) Ministry of Manpower 2) survey</td>
</tr>
<tr>
<td>Shopping Malls</td>
<td>number of shopping malls; visitor traffic size; mean contact rate;</td>
<td>1) IMM Shopping mall 2) survey</td>
</tr>
<tr>
<td>Public Transport</td>
<td>number of rail stations / bus stops; commuter traffic size; mean contact rate;</td>
<td>1) Land Transport Authority 2) survey</td>
</tr>
</tbody>
</table>

Households

Household size is extracted from Census 2000 [103]. Note that we worked on the contact network generation for Singapore in year 2009, and Singapore conducts the census every ten years, so Census 2000 was the latest as of that time. We assume the household size distribution keeps unchanged from year 2000 to 2018, and the number of households is proportionally increased from 906,022 (2000) to 1,112,587 (estimated for 2008). The
population $N$ of Singapore as of 2008 is 4.3894 million [102]. Our household size
distribution is shown in Table 3-3. For “8+” households, we first create those households
in their lower bound size (size = 8). It will work out a new total population $N'$. The
difference $N - N'$ is then randomly distributed into those “8+” households.

**Table 3-3 Household size distribution [103]**

<table>
<thead>
<tr>
<th>Household Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8.16%</td>
</tr>
<tr>
<td>2</td>
<td>17.08%</td>
</tr>
<tr>
<td>3</td>
<td>19.08%</td>
</tr>
<tr>
<td>4</td>
<td>25.79%</td>
</tr>
<tr>
<td>5</td>
<td>17.89%</td>
</tr>
<tr>
<td>6</td>
<td>8.00%</td>
</tr>
<tr>
<td>7</td>
<td>2.72%</td>
</tr>
<tr>
<td>8+</td>
<td>1.47%</td>
</tr>
</tbody>
</table>

**Hospitals**

As of 2008, total number of hospitals including specialty centres in Singapore was 25
with a total number of beds = 10,756 [104]. Our hospital and ward sizes (number of beds)
were obtained from Tan Tock Seng Hospital in Singapore. The acquired data were the
numbers of beds per ward. To compute the size distribution, we discretize those ward
sizes as shown in Table 3-4. As we have no data from other hospitals, we have to assume
all the hospitals share the same structure.

**Table 3-4 Ward size distribution**

<table>
<thead>
<tr>
<th>Ward Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 – 17</td>
<td>29.17%</td>
</tr>
<tr>
<td>18 – 31</td>
<td>14.58%</td>
</tr>
<tr>
<td>32 – 45</td>
<td>56.25%</td>
</tr>
</tbody>
</table>

**Schools**

As of 2008, total number of schools, including primary, secondary schools and junior
colleges, in Singapore was 353 with the total number of students in the age of $[6, 18] = 529,893$. Based on our data from Ministry of Education, Singapore, the sizes of schools
and classes can be discretised as shown in Table 3-5 and Table 3-6 respectively.
Table 3-5 School size distribution

<table>
<thead>
<tr>
<th>School Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>350 – 949</td>
<td>11.05%</td>
</tr>
<tr>
<td>950 – 1549</td>
<td>54.96%</td>
</tr>
<tr>
<td>1550 – 2149</td>
<td>22.66%</td>
</tr>
<tr>
<td>2150 – 2749</td>
<td>9.92%</td>
</tr>
<tr>
<td>2750 – 3349</td>
<td>0.85%</td>
</tr>
<tr>
<td>3350 – 3949</td>
<td>0.57%</td>
</tr>
</tbody>
</table>

Table 3-6 Class size distribution

<table>
<thead>
<tr>
<th>Class Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 – 10</td>
<td>0.20%</td>
</tr>
<tr>
<td>11 – 15</td>
<td>0.70%</td>
</tr>
<tr>
<td>16 – 20</td>
<td>3.03%</td>
</tr>
<tr>
<td>21 – 25</td>
<td>7.21%</td>
</tr>
<tr>
<td>26 – 30</td>
<td>24.73%</td>
</tr>
<tr>
<td>31 – 35</td>
<td>12.33%</td>
</tr>
<tr>
<td>36 – 40</td>
<td>38.60%</td>
</tr>
<tr>
<td>41 – 45</td>
<td>12.94%</td>
</tr>
<tr>
<td>46 – 50</td>
<td>0.26%</td>
</tr>
</tbody>
</table>

Workplace

The statistics from the Ministry of Manpower, Singapore show the total employment was 2,952,400 as of year 2008, including both residents and foreign workers [105]. Company size distribution was obtained as in range of {[25, 99], [100, 249], 250+}. The portion “250+” is handled as similarly as “8+” portion in household data. Therefore, the workplace size distribution is as shown in Table 3-7.

Table 3-7 Workplace size distribution

<table>
<thead>
<tr>
<th>Workplace Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 – 99</td>
<td>75.59%</td>
</tr>
<tr>
<td>100 – 249</td>
<td>15.97%</td>
</tr>
<tr>
<td>250+</td>
<td>8.44%</td>
</tr>
</tbody>
</table>
Shopping malls

As of 2008, total number of shopping malls in Singapore was 141. We were only able to acquire data from IMM Shopping Mall that its average visitor traffic per day = 45,000 and 25% of visitors spend ≥ 60 minutes in the mall. By discarding the transient visitors (< 60 minutes), we calculate the effective size of a shopping mall is 11,250. So we create 141 shopping malls of each size = 11,250, and total size is \( V = 11,250 \times 141 = 1,586,250 \).

On the other hand, from our survey results, we found 22.38% of interviewees are regular shoppers (a regular shopper refers to an individual who visits the shopping mall at least once a week and spends ≥ 60 minutes). Then we calculate the total number of population in the shopping-mall network \( N = 4839400 \times 22.38\% = 1,083,058 \). We argue that the difference between \( |V| \) and \( N = 1,586,250 - 1,083,058 = 503,192 \) is attributed to those individuals who visit multiple shopping malls regularly, and therefore, a fraction of candidate individuals may be mapped to multiple vertices originating from the distinct shopping malls.

Public transport

As of 2008, total number of railway stations was 93 and total number of bus stops was 4142. We extract the size distributions of railway stations and bus stops from our study of the public transport system in Singapore [106] and tabulate the data into Table 3-8 and Table 3-9. We assume that every commuter will travel back and forth on the same route on a daily basis. For example, if a passenger travels from station \( A \) to station \( B \), we assume he/she will travel from station \( B \) back to station \( A \) later in the day. According to our survey and census, there are 47.91% of working adults and 42.38% of students taking public transport, so it works out a total population for public transport model is 1,768,077, assuming few of infants and the elderly travel by public transport on a daily basis.

<table>
<thead>
<tr>
<th>Rail Station Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 20000</td>
<td>63.44%</td>
</tr>
<tr>
<td>20001 – 40000</td>
<td>25.81%</td>
</tr>
<tr>
<td>40001 – 60000</td>
<td>10.75%</td>
</tr>
<tr>
<td>60001 – 80000</td>
<td>10.75%</td>
</tr>
</tbody>
</table>
Table 3-9 Bus stop distribution [106]

<table>
<thead>
<tr>
<th>Bus Stop Size</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 500</td>
<td>58.07%</td>
</tr>
<tr>
<td>501 – 1000</td>
<td>23.55%</td>
</tr>
<tr>
<td>1001 – 1500</td>
<td>9.58%</td>
</tr>
<tr>
<td>1501 – 2000</td>
<td>3.28%</td>
</tr>
<tr>
<td>2001 – 2500</td>
<td>1.85%</td>
</tr>
<tr>
<td>2501 – 3000</td>
<td>0.94%</td>
</tr>
<tr>
<td>3001 – 3500</td>
<td>0.71%</td>
</tr>
<tr>
<td>3501 – 4000</td>
<td>2.02%</td>
</tr>
</tbody>
</table>

Mean Contact Degree

Obtaining real-life contact rates is a challenging task that involves a huge amount of work on surveying and data processing. To the best of our knowledge, there is no contact behaviour data publicly available in Singapore at the time of our study that can be used to derive potential disease-transmitting contacts between individuals. Therefore we decided to obtain first-hand data through conducting a survey in Singapore in year 2009. The key question of interest is how many persons an interviewee contacts with at our modelled social structures on a regular basis. At the end of surveys, a total of 1040 survey records were collected. The derived mean contact degrees are summarized in Table 3-10. Our questionnaire is available at Appendix A.

Table 3-10 Mean contact degrees of different types of social structures

<table>
<thead>
<tr>
<th>Social Structure</th>
<th>Mean Contact Degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>5.83</td>
</tr>
<tr>
<td>Ward</td>
<td>9.12</td>
</tr>
<tr>
<td>School</td>
<td>18.02</td>
</tr>
<tr>
<td>Class</td>
<td>29.65</td>
</tr>
<tr>
<td>Workplace</td>
<td>20.55</td>
</tr>
<tr>
<td>Shopping Mall</td>
<td>21.21</td>
</tr>
<tr>
<td>Public Transport</td>
<td>18.48</td>
</tr>
</tbody>
</table>
3.4 Results

HPCgen is implemented in Octave [107] with the MPITB [101] library. For efficiency purpose, some of non-matrix-related operations were implemented in C++ and dynamically linked to Octave. The hardware platform is an Intel 3GHz 2x quad-core (2 nodes with 4 cores per node) machine with total 32 GB memory.

3.4.1 Network Characteristics

By applying all the obtained data into HPCgen, we generate the contact network for Singapore. The network has 4,839,410 vertices and 81,936,456 edges. As shown in Table 3-11, the contact network exhibits the small-world property, with high average clustering coefficient and short mean path length. Moreover, the network is positive assortative, tending to connect the nodes with the similar degrees.

<table>
<thead>
<tr>
<th>Network Measures</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of nodes</td>
<td>4,839,410</td>
</tr>
<tr>
<td>number of edges</td>
<td>81,936,456</td>
</tr>
<tr>
<td>mean degree</td>
<td>33.64</td>
</tr>
<tr>
<td>average clustering coefficient</td>
<td>0.6013</td>
</tr>
<tr>
<td>mean path length</td>
<td>4.4452</td>
</tr>
<tr>
<td>degree assortativity coefficient</td>
<td>0.2554</td>
</tr>
</tbody>
</table>

Figure 3-5 plots the cumulative degree distribution of our generated contact network, in comparison with an Erdos-Renyi (random) network as well as a scale-free network. As consistent with Meyers’ finding [47], the cumulative degree distribution of our contact network also approximates more towards power-law distribution exhibited in the scale-free network – they both have the fat tails at the higher-degree region, representing those super-spreaders in the network. Note that our contact network has a substantial amount of “socially-inactive” nodes: 16.01% of nodes are of degree ≤ 10. This is expected because we heavily model the social activities for the working adults and the students who attend the public schools in Singapore. For those infants, students who attend to private schools (such as foreign students), college students, unemployed adults and the elderly, they may exhibit lower connectivity in our contact network due to the social structures they belong to.
Figure 3-5 Comparison between HPCgen network, random network and scale-free network (4,839,410 vertices; 81,936,456 edges; $\gamma = 2.9$)

Figure 3-6 shows how the cumulative degree distribution evolves step-by-step in the network generation process. It is observed that school model and workplace model introduced the two dominant groups with high connectivity. As the network is positive assortative, it is expected that the subsequent addition of contacts are attached more to the high-degree nodes, exhibiting the non-trivial portion of low-degree nodes.
3.4.2 Sensitivity Analysis

As shown in Section 3.2, the generation of contact network in HPCgen mainly depends on two types of parameters: structure sizes and mean contact degrees in the individual structures.

Figure 3-7 illustrates the variation of cumulative degree distribution of the entire network when mean degrees vary. When the mean degree in each structure changes by [+5%, +10%, -5%, -10%], the mean degree of the entire network becomes [35.38, 36.81, 32.41, 30.84] respectively, which are [+4.46%, +8.68%, -4.31%, -8.95%] compared to the baseline – average degree of 33.87 in the original setting.
Figure 3-7 Sensitivity analysis on mean contact degree and structure size

A similar test is also conducted for structure sizes. It is shown that the fluctuation of structure size induces negligible alteration on the cumulative degree distribution of the entire network. When each structure size changes by [+5%, +10%, -5%, -10%], the mean degree of the entire network become [33.97, 34.03, 33.76, 33.74] respectively, which are [+0.30%, +0.47%, --0.33%, -0.38%] compared to the baseline – average degree of 33.87 in the original setting.

Therefore, we conclude that the generated contact network is much more sensitive to the mean contact degrees in individual structures compared to the sizes of the structures. It suggests that extra attention should be paid to acquire the mean contact degrees within the respective social structures as accurately as possible. On the other hand, approximate values for structure sizes would be sufficient.

3.4.3 Network Validation

Network validation has been a challenging problem in network-based epidemic modelling studies. Due to the complicated nature of social contact network and its scale, the scientific community has not yet acquired the full extent of knowledge about the characteristics of the contact network. A lack of reliable field data makes the validation extremely difficult [108]. Location-based contact network generation is therefore adopted commonly, in which sub contact networks at locations (social structures) are constructed first and then joined together to form the full network. This is because the social contacts within a social structure can be more easily obtained through survey, device-based
tracing, and also approximation from known distributions such as power law and Poisson. However, it is still difficult to validate the full contact network after joining all sub contact networks.

Although direct validation of the contact network is generally not feasible, indirect validation is possible through model alignment – by comparing the output of epidemic simulation running in the contact network with either the historical incidence records or the commonly accepted models of comparable settings in the literature. EpisimS [5] is one of the most renowned models for stimulating disease outbreaks in a social contact network. There has been no direct validation to the network structure generated by EpiSimS in the literature, but it has been well accepted by the scientific community and policy makers because of its years of approved alignment with historical data and congruence with other well-built network models [5], [50], [109]–[112].

Similar to EpisimS, it is very challenging to validate the contact networks produced by HPCgen. However, as inspired by Milne et al [35] on how they validate their model, we compare our simulation results (presented in Section 4.4.2) with the models in the literature too. Our simulations of an influenza outbreak in the HPCgen contact network produce the average attack rate of 44.47%. It coincides with 44% attack rate from Ferguson’s model [33] and 43.5% attack rate from German’s model [39] at a comparable $R_0$ without any interventions. Moreover, a recent study [6] in the UK found that school closure had no impact if it started after 27% of students already had symptoms. That echoes with our finding that a school closure after 20% of the population are infected has a trivial effect (a school closure at {20%, 25%, 30%} thresholds in an influenza outbreak will ends with {44.05%, 44.23%, 44.34%} attack rates respectively while baseline attack rate is 44.47% (baseline refers to a simulation scenario with no intervention).

### 3.4.4 Efficiency and Scalability

With the same inputs to HPCgen, the runtime costs of network generation are measured for parallelization over 1 – 8 processor nodes and at each setting, 20 generations were repeated to obtain the average runtimes. As shown in Figure 3-8, it is observed the average runtime of HPCgen falls from 758.52 seconds to 92.96 seconds (~8.16 time of speedup) when the number of processor nodes increases from 1 to 8. The speedup factors are {2.16, 3.30, 4.43, 5.50, 6.47, 7.31, 8.16} for 2 – 8 parallel nodes respectively. The effect of speedup is because of the concurrent execution of the network generation routine for different social structures of the same type. Furthermore, the speedup might be also
attributed to the reduced memory footprint. Executing contact network generation in HPCgen requires frequent matrix operations which are often memory intensive tasks. When the physical memory is heavily utilized, swapping in a Linux system might be triggered too frequently to cause considerable overhead. By parallelizing the network generation tasks in a distributed memory system, the memory consumption at each processor node is reduced significantly. As a result, less swapping might be triggered so that the execution would suffer from smaller overhead correspondingly.

![Figure 3-8 Efficiency and Scalability of HPCgen](image)

We also investigate the scalability of HPCgen by generating larger networks of size from 4.8 million up to 13.4 million (size of the largest city proper in the world as of 2008). The population allocated to distinct types of social structures as well as the number of level-1 structures are scaled-up proportionally. It is observed that the runtime increases approximately linearly when the size of network increases. At the largest scale, a contact network of 13.4 million vertices requires a generation time of 7.27 minutes.

### 3.5 Discussion

Modelling and simulation allow quantitative understanding about the transmission dynamics in an epidemic. The recent emerging contact network based modelling addresses the lack of heterogeneity in the traditional mathematical modelling of infectious diseases, leading to higher realism in representing contagious propagation within a real-life community. Moreover, the inclusion of social structures in contact network modelling approximates the hierarchical social groupings in the real world and can be
used to annotate the connections in a contact network so as to facilitate epidemic intervention simulation, which is practically valuable for epidemic preparedness planning.

Our proposed HPCgen is a fast and scalable contact network generator for urban cities. We model different social structures in a uniform representation and modularize the network generation routine to make the generator flexible to incorporate new social structures provided with the structure-specific data. In a generated contact network, its vertices and edges are labelled with demographic properties of individual persons and whereabouts of each contact edge taking place. It is particularly favourable for intervention simulations which might make use of those labels to target a specific type of contacts (such as school contacts) or a specific scale (such as a school or class). Furthermore, we also address the efficiency and scalability of HPCgen by applying the efficient matrix representation and contact creation algorithm, together with MPI parallelization, to reduce both runtime and memory footprint at each processor node. We show that the network generation can be speeded up by 8.16 times by parallelizing on 8 processor nodes and can be scaled up to 13.4 million of population.
Chapter 4

Intervention-Oriented Simulation

In the chapter, we propose IntSim, an intervention-oriented simulation model for evaluating complex interventions. We elaborate three components in the model – intervention measure builder, epidemic simulator and intervention evaluator, and also address the parallelization and optimization adopted in the model for efficiency. In the experiment section, we demonstrate our model with two types of complex interventions – cyclic intervention and multi-level intervention, followed by quantitative comparison to show the speedup contributed by multithreading. Finally we compare with EpiFast from the efficiency perspective. The content of this chapter mainly comes from the publications\(^3,4\).

4.1 Introduction

In many situations, simulating the epidemic dynamic in an outbreak of an infectious disease is not the only objective of a computational epidemiologist. In any real outbreak in a community, the spread of infectious disease may be contained or mitigated by various intervention measures implemented by the individuals voluntarily due to epidemic-awareness (e.g. washing hands more frequently and thoroughly, wearing face masks), and most importantly, by the public health agencies (e.g. closing schools, vaccinating the core population). Public health interventions can be crucial in controlling the spread of infectious diseases. For example, mass vaccination and closing down social structures with high population density could significantly impact the epidemic dynamic by reducing the susceptible population and diminishing the disease-transmitting contacts. Therefore, it is necessary to incorporate those interventions into the epidemic simulations so as to yield meaningful and practical results.

Simulating the spread of infectious diseases in a large community is computationally intensive, and may involve millions of population interconnected by tens of millions of

\(^{3}\) Tianyou Zhang, Xiuju Fu, Michael Lees, Chee Keong Kwoh, Gary Kee Khoon Lee, Rick Siow Mong Goh, “A Contact-Network-Based Simulation Model for Evaluating Interventions under “What-If” Scenarios in Epidemic”, Winter Simulation Conference, Berlin, Germany, 9-12 Dec 2012

the potential disease-transmitting contacts. Adding public health interventions will further complicate the scenario. There is a large variety of possible combinations in configuring intervention strategies – “which” (intervention measure to choose), “when” (to intervene), “how long” (to intervene) and “who / where” (to intervene), are the four critical questions to be answered whenever making a decision on public health intervention. It is because those decisions not only involve a huge amount of economic and social costs, but most importantly, thousands of human lives may be at stake.

In order to determine the most appropriate intervention strategy, quantitative evaluation on effectiveness of interventions under different “what-if” scenarios is always desirable. Network-based simulation models have been increasingly applied in epidemiological studies to gain insights into disease spread and to develop the robust estimation on the outcome of the outbreaks in a refined resolution, both temporally and spatially. Among many simulation models, those incorporating intervention strategies are particularly helpful in assisting policy makers to make wise decisions for containing or mitigating the spread of infectious diseases. For example, school closure is a typical social-distancing measure for influenza intervention. Its primary objective is to reduce infection attack to school children but with high costs in both economic and social aspects [38], [113] and there is still open discussion on the effectiveness of school closure in the scientific community [36]. A search on Google Scholar as of 1 April 2012 shows 248 publications using a simulation approach to examine the effectiveness of school closure for the 2009 H1N1 Influenza pandemic alone, covering different factors and different communities around the world. For instance, Lee et al [7] discuss the influence of the scale and duration of school closure on the delay of epidemic peak in Allegheny County, US. Zhang et al [114] systematically describe how the starting threshold and duration of school closure affect the outcome of school closure in Singapore. Miller et al [8] and Halder et al [115] elaborate the impact of compliance rate and disease severity to school closure in Boston U.S. and in Albany Australia respectively.

Simulating public health interventions is more complicated than a typical simulation of disease spread. In addition to simulating stochastic propagation within a huge population, interventions introduce more volatility into the system by altering the contacts between persons in runtime. It often requires a large number of iterations while examining the different settings for the relevant factors of interest. It would become even more complex when simulating combined interventions, as the number of possible combinations of parameter settings is the multiplication among all interventions. Furthermore, many social structures like schools, hospitals and etc have their inherent hierarchical structure, e.g.
classes in a school, wards/clinics in a hospital. This might lead to different outcomes as the interventions could target different levels of social structures.

In the literature, epidemic simulators such as [24], [26], [30] mostly address the efficiency aspect of discrete event simulation as well as parallel paradigms in the distributed architecture. Few focus on the aspect of functionalities, particularly, how to simulate cyclic interventions and multi-level interventions in a sizable contact network.

Therefore, we propose IntSim, an efficient intervention-oriented simulator for evaluating public health interventions to mitigate disease spread in contact networks. IntSim parameterizes the intervention measures to a generic representation which offers the flexibility in creating and investigating arbitrary intervention scenarios. Such scenarios could include cyclic interventions (interventions function in a cyclic manner, such as workforce shift), multi-level interventions (interventions target the specific level of a social structure, such as individual-class closure), and combined interventions (multiple interventions being implemented either simultaneously or one after another with/without overlap, such as the combination of school closure and workforce shift).

Other than functionalities, we also address the efficiency aspect. IntSim is extremely fast because: 1) uses a pre-constructed person-to-person contact network to avoid contact creation during simulation; 2) uses larger time step of 1 day in the simulation; 3) “agentizes” contact edges with transmission blocking to simulate contact removal instead of modifying network structure; 4) adopts hybrid parallelization that leverages on both multi-threading and distributed memory parallelism; 5) uses active node switching to reduce number of infection events and uses fixed fan-out [53] to minimize the number of random number generation.

4.2 Method

Four components constitute the complete framework for epidemic intervention simulation: Contact Network Generator (CAG), Intervention Measure Builder (IMB), Epidemic Simulator (ES) and Intervention Evaluator (IE) as shown in Figure 4-1. CAG produces a contact network that represents persons (nodes) and potential disease-transmitting contacts between persons (edges) in a community. IMB creates an intervention scenario that consists of one or more intervention measures, each with the specifications on intervention trigger, duration, target, efficacy and cycle. ES simulates two dynamic processes within the generated contact network: disease progression within
person (i.e. susceptible $\rightarrow$ exposed $\rightarrow$ infectious $\rightarrow$ ...), and disease transmission between persons (infection), under the effect of interventions. Finally, IE is the “brain” in the framework that drives the entire workflow: it sends the outputs from CAG and IMB to ES and starts the simulation; captures the statistics of simulation and feeds these back to ES, such as the prevalence rate to determine trigger status of interventions; and at the end of the simulation, it prepares the report for post-simulation analysis.

Figure 4-1 Epidemic intervention simulation framework

In Figure 4-1, contact network generator has been described as HPCgen in Chapter 3. The rest of three components: intervention measure builder, epidemic simulator and intervention evaluator constitute IntSim, which will be introduced in this chapter.

4.2.1 Intervention Measure Builder

Public health interventions comprise pharmaceutical and non-pharmaceutical interventions. Pharmaceutical interventions mostly refer to antiviral treatment and vaccination. Non-pharmaceutical interventions refer to social distancing as well as measures such as hand washing, wearing face masks, etc that may reduce the transmissibility of the disease. I proposed five parameters: *trigger*, *duration*, *target*, *efficacy* and *cycle* to define both types of interventions.

- Trigger threshold: defines when an intervention starts, either time-based or case-based. For example, 10 days from the date of patient-zero, 1% of the entire population is infected, 5% of population in a class/school/office/etc shows symptoms.
• Duration: defines how long an intervention lasts, usually in unit of days or weeks. For example, school closure for 2 weeks, wearing face mask until epidemic ends.
• Target: defines who an intervention affects. For example, 80% of the entire population are vaccinated, 100% of symptomatic patients are treated with antiviral drugs, and schools/classes with more than 5 incidences are closed.
• Efficacy: also known as compliance rate, it defines the possibility that an intervention can produce the desired results. For instance, the vaccine has 80% efficacy, 10% of student contacts remain after school closure.
• Cycle: additional parameter for cyclic interventions that defines the time spans of the intervention being active or inactive in a cycle respectively. It can be used to model interventions, for example, all workers are divided into two teams and each team attends work in alternate weeks, 30% less of shoppers during the weekdays compared to weekends.

The user can easily define the desired interventions using the above parameters and write them into a XML format with our defined syntax. Figure 4-2 shows an example for defining a 4-week class closure as follows:

**Trigger**

It says when 5% of population in a class is infected with onset of symptoms, this particular class is closed immediately with 0-day delay. If value \( \geq 1 \), it is parsed as the number of incidences; otherwise, it is parsed as symptomatic prevalence rate of either the global population or local subpopulation in the social structure defined in target ! structure . delay defines the number of days elapsed since the trigger condition is satisfied until the intervention starts.

**Duration**

It says the intervention will last for 4 weeks. If value = 0, this means the intervention will last until the end of epidemic.
It says a level-2 class is to be closed and this intervention is applied to 100% of student contacts in this class. In the school model, level-0 refers to all schools; level-1 refers to a particular school; level-2 refers to a particular class. There are two types of intervention mechanisms: edge or node. Edge intervention will intervene on a fraction (scale) of student contacts. Node intervention will intervene on all the school contacts connecting to a fraction (scale) of student nodes.

**Efficacy**

It says 100% of the contacts affected by the intervention are blocked. In IntSim, if a contact is blocked, we do not remove the contact from the network but modify the status of the contact. If the contact is blocked, it does not allow disease transmit through. “Rotational” is a Boolean parameter indicating if the intervention works in a rotation-like manner. If “rotational” is true, the targeted population will be divided into two teams based on the fraction specified by “efficacy”. Two teams will take turn to be affected by the intervention. For example, there are teams A and B. Team A is affected by the intervention during the “period” in every cycle. Team B is affected by the intervention during the “interval” in every cycle.
Cycle

It says class closure is not cyclic. As illustrated in Figure 4-3, period refers to the time span when the intervention is active within a cycle and interval refers to the time span when the intervention is inactive within a cycle.

![Figure 4-3 Illustration on parameters of cycle (in a cycle, the shaded regions indicate the time span when intervention is active; and the rest is the time span when intervention is inactive)](image)

Figure 4-4 shows a partial definition for a workforce shift. It stipulates a workforce shift blocks all the workplace contacts of 50% of the total workers (referred as Team A) in any establishment in alternative weeks. As “rotational” is true, the rest of the workers (referred as Team B) will be affected by the intervention when Team A is unaffected.

```xml
<intervention>
  
  <target>
    <structure>workplace</structure>
    <level>0</level> <!-- {0|1|2|3|...} -->
    <scale>1.0</scale> <!-- percentage -->
    <type>node</type> <!-- {node|edge} -->
  </target>

  <efficacy>
    <value>0.5</value> <!-- percentage -->
    <rotational>true</rotational>
  </efficacy>

  <cycle>
    <interval>7</interval> <!-- # of days -->
    <period>7</period> <!-- # of days -->
  </cycle>

</intervention>
```

![Figure 4-4 Partial XML definition for workforce shift](image)

4.2.2 Epidemic Simulator

Our epidemic simulator is a multi-agent simulation model that comprises “person” objects and “contact” object which represent every node and edge in the contact network respectively. Each “person” has its own properties such as disease status, timer and
contacts, as well as the methods such as “attack”, “acquire” and “evolve” functions. “Attack” function models the process that an infectious person infects one of its susceptible contacts. “Acquire” function models the process that a susceptible person acquires the infection from one of its infectious contacts. “Evolve” function models the disease progression within person.

The simulation is carried out in a discrete-event manner by time step of one day. At each time step, two types of processes are simulated: disease progression and disease transmission.

**Disease Progression within Person**

Disease Progression refers to the development of disease statuses within the individuals, complying with the disease model. An arbitrary “susceptible” person (denoted as $p$) has a chance (transmissibility) to acquire infections from its contacts that are infectious. If $p$ is infected, $p$ becomes “exposed” but has no infectivity or any symptoms yet. After latent period $t_{L}^{p}$, $p$ becomes “infectious”. As we assume that influenza has an identical incubation period and latent period, upon $p$ becoming “infectious”, $p$ may show the onset of symptoms at a certain chance (symptomatic rate) and turns “symptomatic infectious”; or turns “asymptomatic infectious” otherwise. After the infectious period $t_{I}^{p}$, $p$ is finally “removed”, i.e. recovered or dead. In IntSim, given mean latent period $ht_{L}$ and mean infectious period $ht_{I}$ and Poisson random number generator randp, when $p$ first turns to “exposed” and “infectious”, $t_{L}^{p} = \text{randp}(ht_{L})$ and $t_{I}^{p} = \text{randp}(ht_{I})$.

After obtaining $t_{L}^{p}$ and $t_{I}^{p}$, the following transition of status is deterministic. It is modelled by two disease-status variables and a timer per person. The two variables are the current_status and future_status. The timer keeps track of the time elapsed since current_status is the last status updated. For example, if a person’s current_status is “exposed”, at the end of every time step afterwards, the timer is checked against $t_{L}^{p}$. If timer $> t_{L}$, future_status is set to be “asymptomatic infectious”. Then at the beginning of the next time step, current_status is updated by the value of future_status and future_status is set back to null. The reason for using two status variables is because current_status of the person might be still needed in the disease transmission with other persons after the checking of timer.
Disease Transmission between Persons

Figure 4-5 illustrates the process an infectious node infects a susceptible node through an edge. Each edge in the contact network is represented by “contact” object that has the properties, such as $tag$, $timer$ and blocking rate ($br$) as well as methods such as “transmit” and “set” functions. “Transmit” function models the process that an infection transmits through the contact by generating a random number $x$ and comparing $x$ against the effective transmissibility $T_e = T \times (1 - br)$. If $x \geq T_e$, the transmission is successful and the susceptible agent at the other end of the edge will get infected; otherwise, the transmission stops. When $br = 1.0$, the transmission will be completely blocked so that probability checking can then be skipped for speed.

“Set” function models the intervention process. Interventions are meant to either remove the potential disease-transmitting contacts (contact interventions) or reduce the transmissibility through the contact (transmission interventions). They can be both modelled by the blocking rate per edge. For example, if a school closure is triggered, “set” function is called at every edge. If an edge’s $tag = school$, its blocking rate is then changed from the default value “0.0” to $br = 1 - efficacy$ for the duration $timer$. The timer will count down since the next time step. When $timer = 0$, blocking rate is then restored $br = 0.0$. For a cyclic intervention, $br = 0.0$ if $[timer \mod cycle] > period$, where “mod” is the modular arithmetic operator to compute the residue of a modulo $cycle$. More
than one set of \{blocking rate, timer\} are also possible when multiple interventions influence the same edge. Then $br' = \prod_i br_i$ and the respective timers will act independently.

**Self-Quarantine and Self-Protection**

Self-quarantine or self-protection is another phenomenon that should not be neglected in the epidemic simulations. When a person turns symptomatic, he or she might stay home voluntarily to avoid unnecessary contacts with others because of social responsibility or too sick to go to work. We call this “self-quarantine”. Or many people intend to avoid the contacts with a sick person who exhibits a clear onset of symptoms, such as coughing and running nose, which we call “self-protection”. In IntSim, we implement self-quarantine and self-protection by randomly increasing blocking rates of those “edges” connecting to any symptomatic persons.

### 4.2.3 Intervention Evaluator

Intervention Evaluator (IE) is the “driver” in IntSim, which creates the intervention scenarios to be evaluated by coordinating other components in the framework. An intervention scenario is comprised of an XML representation of intervention measures and a set of epidemic parameters associated with the disease model. The created intervention scenario is then fed into ES to start the simulation in a contact network. During the progress of simulation, IE monitors the statistics such as symptomatic prevalence within the global population. If there is any intervention with local triggers, symptomatic prevalence in the corresponding social structure may be monitored as well. We do not monitor the statistics unless they are necessary in order to minimize the computational overheads.

IE also computes the performance measurement of the interventions. We apply three metrics to evaluate the effectiveness on reducing epidemic severities: attack rate, peak incidence and peak day. As introduced in Section 2.1, AR indicates the total number of diagnosed cases at the end of an epidemic, implying the overall burden on the public health system due to the epidemic. PI exhibits the severity of the peak in an epidemic which can stress the maximum capacity that public health system can handle such as hospitalizations. PD tells how fast the peak of epidemic comes, placing a challenge of a timely response to patient surges in hospitals as well as allocation of other public health resources.
4.3 Practical Design for Computation Efficiency

As mentioned in the introduction, intervention simulations are more computationally intensive than the typical epidemic simulations as there are a number of intervention scenarios to be simulated in order to evaluate a single intervention strategy and the computation cost is multiplied among the individual runtime cost of each intervention scenario. Therefore intervention simulation usually has great demand for efficiency.

IntSim is a fast intervention-oriented simulator because of its practical design for computation efficiency: 1) Contact network instead of bi-partite network is used to run simulations. Compared to EpiSims [24] and EpiSimdemics [26] that run with bipartite networks, IntSim does not need to perform sophisticated discrete event simulation to create infective contacts between persons at each place node at each time step. Instead, possible disease-transmitting contacts are pre-constructed in a contact network. It would significantly reduce computation cost in the simulations. The similar design was used in EpiFast [30] which claimed to run several orders of magnitude fast than other comparable simulation tools while delivering similar results. As EpiFast shares the similar contact network formation and simulation mechanism with IntSim, it would be interesting to compare their efficiencies. However, since EpiFast’s executable and source codes are not accessible, it is impossible to make any accurate comparison and we could only make some rough estimation based on its published results – an average simulation run of 2.09 million population with no intervention on 2.3 GHz PowerPC 970FX 32x dual-core machines is around 84.6 seconds [30]. By proportionally scaling down the Singapore contact network to 2.09 million nodes (through reducing the total population size and number of level-1 structures), our average simulation with no intervention is 90.36 seconds on a 2.93 GHz Intel Xeon 5570 octa-core machine. It would be sensible to estimate that IntSim is at a similar level of efficiency as EpiFast.

2) Larger time step of 24 hours is applied in the simulations. At the end of each time step, simulator needs to update disease status of every node and synchronize different processes or threads, which result in the overheads for update and synchronization. The larger time step is, the lesser number of updates and synchronizations would be, as long as the length of time step is smaller than any state-transition periods such as latent period, infectious period and etc. EpiSimdemics [26] claimed 24-hour is a suitable length for time step in simulation for many diseases.

3) Infection blocking on network edges is used to simulate contact removal of interventions as shown in Figure 4-5. Some interventions such as school closure may
require removing the affected contact edges during the intervention period. In order to simulate such effect, we set blocking rate of an edge to 1 instead of modifying network structure with greater overheads.

Other than the above three merits in design, we also adopt two-level hybrid parallelization. The first level is multi-threading within a single simulation in a shared memory system. Multiple threads are to be created to exploit the advantage of modern multi-core architecture by running the simulations concurrently. The underlying population is partitioned by their interconnections and allocated to the respective threads to reduce cross-thread synchronization. Each thread is responsible for simulating the disease transmission and progression within the assigned subpopulation. A system-wide synchronization happens at the end of each time step. The theoretical upper bound of multi-threading speedup factor is $n$, where $n$ is the number of simulation threads. The value of $n$ is usually limited by the number of CPU cores available. Moreover, there is the overhead for cross-thread synchronization. For example, thread $A$ requests to access person $p$ while thread $B$ is working on $p$ as well, $A$ will have to wait until $B$ finishes. Such wait time constitutes the major portion of the overhead in cross-thread synchronization. In the latter Section 4.4.5, we demonstrate the efficiency of our multi-threading through the experiment results.

In addition to multi-threading, an application-level parallelism is implemented in a distributed memory system as well. As there are multiple intervention scenarios to be simulated, which are completely independent of each other, it is intuitive to run those simulations concurrently. We leverage on scheduling and resource management in the modern workstation clusters, by automatically submitting the simulation job per scenario to the scheduler of the cluster. Launching jobs in a cluster is controlled by PBS software (Portable Batch System). Users can use PBS script to request resources from the cluster, including processor nodes, memory and runtime. Figure 4-6 shows a sample of PBS scripts prepared by IntSim automatically. “nodes=1;ppn=8” says we request a single node with 8 CPU cores, “mem=4000mb” says we request 4000MB memory for a simulation job, “walltime” says our estimate to runtime is no longer than 1 hour, and the last line “java simulator.Main …” is the command-line execution of our simulator.
Benchmarking the wall clock time for application-level parallelism is difficult because the cluster is constantly shared by a number of users and our submitted jobs have to queue for resource allocation. But as different simulation jobs will run on the distinct processor nodes, a linear speedup shall be expected given that sufficient resources are available.

Apart from parallelization, we applied two more practical techniques to further speed up the simulations. The first technique is active node switching modified from Jin’s algorithm [45]. As mentioned in 4.2.2, there are two methods of a “node” object to simulate the infection process: “attack” and “acquire”. Choosing different infection methods might influence the overall runtime. Assume \( n \) infectious nodes with average degree \( k_n \) and \( m \) susceptible nodes with average degree \( k_m \) in a contact network, and constant cost \( c \) of visiting a contact, the cost of simulating disease propagation is either \( n \times k_n \times c \) (for “attack”) or \( m \times k_m \times c \) (for “acquire”). So when \( n \times k_n > m \times k_m \), it is wise to make susceptible nodes as the active nodes and use “acquire” method; and vice versa. IntSim is able to keep track of \( n, m, k_n \) and \( k_m \) and switch the active nodes dynamically to lower the computation cost.

Fixed fan-out [53] is another technique to reduce the computation cost of random number generation. Random numbers are essential to simulate a stochastic process in disease transmission. During every visit to a contact, a random number has to be generated in order to make comparison with the effective transmissibility. Take an example to illustrate how fixed fan-out works. Assume the cost of generating a random number is \( c \), an infectious agent is active and has \( n \) susceptible agents in its contacts. Then \( n \times c \) is the total cost of random number generation. For fixed fan-out, first compute the number of successful infections (fan-out) by \( n \times T_e \), and then iteratively extract one from the list of susceptible agents without replacement until the fan-out is reached. The total cost of fixed fan-out is \( (n \times T_e + 1) \times c \). So its speedup is \( \frac{n}{n \times T_e + 1} \) compared to the traditional approach. As \( T_e \) is a small value, typically less than 0.1, the overall speedup could be considerable.
4.4 Results

In this section, we demonstrate the capabilities of IntSim from two aspects: functionality and efficiency. As an intervention-oriented simulator, IntSim are featured to support cyclic interventions, multi-level interventions and combined interventions. As Chapter 5 will discuss combined interventions intensively, here we focus on the first two types of interventions, in particular, demonstrating the application of IntSim on evaluating workforce shift intervention and multi-level school closure intervention.

4.4.1 Experiment Settings

Previous estimates of $R_0$ in the past pandemic influenza were in the range of 1.5-2.3 [33], [116]–[119]. Unless otherwise specified, $R_0 =1.9$ is assumed in the following simulations. By using Longini’s approach [41], the base transmissibility is tuned to approximate $R_0 =1.9$. Specifically, it is assumed that only a single individual is randomly infected where everyone else is susceptible yet not able to further transmit the disease, and count the number of secondary infections. The process is repeated for 10,000 times and $R_0 \approx 1.9$ is then obtained as the average number of secondary infections. It is found when the base transmissibility is 0.04, the empirical tests give the best approximation to $R_0 \approx 1.9$ (95% CI, 1.871 – 1.924). During the tuning process, we had incorporated the assumption that symptomatic patients has the higher effective transmissibility, by doubling base transmissibility to be 0.08 because of higher viral shedding and the higher infectivity enhanced by coughing and sneezing etc. Furthermore, we use 66.7% symptomatic rate [120], 1-day mean latent period and 1.5-day mean infectious period [116] in the simulations, assuming symptoms are developed immediately after turning infectious.

Every simulation starts on day 0 with 10 infectious persons seeded into a susceptible population with no prior immunity to the influenza virus. Furthermore, each of the intervention scenarios is simulated for 200 days and iterated for 100 times. All the results described in the following section are the average values of 100 simulation runs.

In the above settings, we found that 100 runs of eight-thread epidemic simulations in the full-scale contact network of Singapore consume 5.76 hours averagely, which is for a single simulation scenario. Taking account of different combinations of triggers and durations, multiple interventions, multiple-level interventions as well as three different values of $R_0$, we will have hundreds of scenarios to be simulated in the entire study of this thesis. In order to make the simulation studies more manageable, we utilize a scaled-
down network for faster simulations. It is done by proportionally reducing the population size and number of all level-1 structures to one tenth so that the mean contact degrees remain unchanged. Figure 4-7 shows that the scaled-down 10% network has nearly identical cumulative degree distribution compared to the full-scale network. In the new one-tenth network, the simulation time per scenario is reduced to 9.36 minutes by eight-thread, 3% of the original cost of time in the full-scale network.

![Figure 4-7 Comparison between 10% and full-scale contact networks](image)

4.4.2 Dynamics of Influenza Spread without Intervention

Figure 4-8 shows the results of the baseline scenario with no intervention. The epidemic reaches its peak on day 26 and ends on day 73. The total attack rate is 44.47% (95% confidence interval (CI), 44.45% - 44.48%); peak incidence is 42.45 per 1000 people (95% CI, 41.72 – 43.17); and the peak day is day 26. This result is comparable with the 43.5% attack rate found by Germann et al [39]. It is noted that the trigger thresholds {0.02%, 0.25%, 1.5%, 5%, 10%, 15%} are reached on day 7, day 13, day 17, day 20, day 22, day 24, respectively.
4.4.3 Workforce Shift

We simulate workforce shift interventions with 7-day interval and 7-day period. It means the workers are divided into two work teams and each team attends work in alternate weeks. Table 4-1 lists the parameters of workforce shift to be simulated. The listed triggers refer to the symptomatic prevalence in the whole population. Taking account of 4 trigger values and 5 duration values, it yields total 20 intervention scenarios.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Workforce Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger</td>
<td>0.02%, 0.25%, 1.5%, 5%</td>
</tr>
<tr>
<td>Duration</td>
<td>2,4,6,8,10 weeks</td>
</tr>
<tr>
<td>Target</td>
<td>all workplace contacts</td>
</tr>
<tr>
<td>Efficacy</td>
<td>50%; rotational</td>
</tr>
<tr>
<td>Cycle</td>
<td>7-day interval/period</td>
</tr>
</tbody>
</table>

Figure 4-9 shows the epidemic curves under workforce shift with different combinations of triggers and duration. We observe that workforce shift suppresses the peak incidences in most of the scenarios but does not postpone the peak days much. The epidemic curves with different triggers apparently have the similar shape but with varying delays in time. The exception occurs when workforce shift lasts for only 2 weeks, showing sudden growth of incidences due to surge of transmissible contacts at the end of workforce shift. To examine the differences between scenarios closely, we look at attack rates, peak incidences and peak days.
Figure 4-9 Epidemic curves under workforce shift  
(symptomatic incidences are per 1000 people)

Figure 4-10 shows the attack rates under workforce shift are in the range from 36.51% to 44.21%, a 0.59% to 17.90% reduction compared to the baseline (simulation with no interventions). The lowest attack rate occurs when the 10-week workforce shift is triggered at 0.02%. The maximal difference of attack rates at different thresholds but same duration declines when the duration increases. For example, an extra 5.72% of the overall population can be saved from infections by choosing the appropriate trigger threshold for 2-week workforce shift.
Figure 4-10 Attack rates under workforce shift [121]

Figure 4-11 shows that workforce shift has a remarkable impact on suppressing the peak incidence of influenza epidemic. Peak incidences under workforce shift ranged from 29.87 to 42.27 per 1000 people, a 0.04% to 29.63% reduction compared to the baseline. The lowest peak incidence occurs when the 2-week workforce shift is triggered at 1.5%. It is noted that 4 weeks are sufficiently long for reducing the peak incidence and no additional reduction is gained by extending the intervention.

Figure 4-11 Peak incidences under workforce shift [121]

Figure 4-12 shows that workforce shift has a mixed impact on the peak day. It appears that varying duration makes no effect on peak day; and trigger threshold is the dominant factor deciding the peak day. When trigger threshold rises from 0.02% to 5%, a consistent decline of peak days is observed.
It could be explained that when workforce shift is implemented at a higher threshold, a larger number of the population has been infected and more potential transmissions will be blocked. Therefore, it reaches the cut-off point sooner and the disease is unable to sustain the growth of incident infections. Hence the peak would occur earlier. On the other hand, when workforce shift is implemented at a lower threshold, there are fewer infectious cases within the population and the amount of susceptible contacts left is still able to maintain the chain of infection. Therefore, the daily incidence could still grow but at a slower pace, consequently leading to a later PD.

Figure 4-13 shows divergent impact of workforce shift on peak day. 6-week workforce shift triggered at 5% advances the peak incidence by 1 day compared to the baseline; on
the other hand, 6-week workforce shift triggered at 0.02% reaches the peak incidence 1 day later than the baseline.

### 4.4.4 Multi-Level School Closure

As introduced, a school has two-level hierarchies in our model. If counting the collection of all schools as level 0, correspondingly, there are three levels of school closure: 1) class closure, i.e., a class is closed if a threshold number of students within the class are infected; 2) school closure, i.e., a school is closed if the threshold of the infected within the school is met, and 3) all-school closure, i.e., all schools are closed simultaneously if the prevalence of infection within the whole population reaches the threshold. It would be interesting to know how these three types of closure perform under the same settings. In order to compare school closure at multiple levels, we use IntSim to investigate the scenario defined in Table 4-2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>School Closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger</td>
<td>5%</td>
</tr>
<tr>
<td>Duration</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Target</td>
<td>all school, a school, a class</td>
</tr>
<tr>
<td>Efficacy</td>
<td>100%; non-rotational</td>
</tr>
<tr>
<td>Cycle</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

In Figure 4-14 and Figure 4-15, class closure is the most effective measure for reducing the attack rate (8.24% of reduction), whereas all-schools closure is the most effective on reducing peak incidence (19.71% of reduction). It is worth noting the trade-off between the scale and frequency of the intervention. In the model, there are a total 33 schools and 1531 classes. For all-schools closure, it closes all 33 schools at once for 6 weeks, which significantly cut down the peak incidence by massive removal of contacts but there would be no intervention impact after 6 weeks. For school closure, it removes a smaller number of contacts but it may be triggered up to 33 times. Although some schools may trigger the closure on the same day, the aggregated length (from the start of first closure to the end of last closure) is more than 6 weeks. Apparently, the extended period of closure cannot compensate for the loss of intervention scale compared to all-school closure. But it works for class closure which may be triggered up to 1531 times. Such higher frequency of closure on a very limited scale results in a lower final attack rate and
less economic and social impact; however, class closure tends to prolong the epidemic period with lower prevalence, i.e. the epidemic period lasted over 150 days under class closure compared to 73 days in the baseline without any intervention.

4.4.5 Multi-threading Efficiency

We develop the IntSim in JAVA for its native support for multi-threading and platform independence. The hardware platform is a workstation cluster of 2.93 GHz Intel Xeon
5570 72x octa-core machines with the installed Platform LSF (Load Sharing Facility) scheduler.

Figure 4-16 Runtime under multithreading
(1/10th network; repeat by 100 times; 4-week workforce shift triggered at 1.5%)

Figure 4-16 shows the speedup attributed to multithreading. The speedup factors are \{1.66, 1.89, 2.00, 2.07, 2.14, 2.21, 2.24\} for 2 – 8 threads respectively. It is observed the speedup effect has gradually diminished along with the increasing number of threads. From 7 threads to 8 threads, the runtime reduction is only 8.27 sec, ~0.66% with respect to single-thread runtime. However, later in Chapter 5, we will investigate a total 360 scenarios of combined interventions for three different $R_0$. If counting collectively, assuming the runtime for different scenarios are constant, 8-thread execution could save up ~3 days compared to single-thread execution.

4.5 Discussion

Public health intervention plays a critical role in combating some epidemics of infectious diseases. Making wise decisions in selecting and implementing those interventions are the areas that we want to address. Our approach is to develop a contact network based simulation framework for evaluating the effectiveness of interventions.
IntSim is capable of simulating epidemic dynamics under various “what-if” intervention scenarios. It has a generic definition to accommodate most types of interventions, through parameterizing them by *trigger*, *duration*, *target* and *efficacy*, together with the additional *cycle*. Specific XML representation of those definitions offers readability and extendibility for both users and the internal parser. IntSim models the epidemic process by the interactions between “person” and “contact” objects, through three types of mechanisms, “attack”, “acquire” and “evolve”. The first two are responsible for disease transmission; and the last one is for disease progression. The influence of interventions is modelled as the “blocking” mechanism at the edges, instead of modifying the network structure. As disease transmission is under the influence of “blocking”, the effective transmissibility is therefore introduced to determine the chance of successful infections passing through the edges.

IntSim is specialized to support evaluating complex interventions, including cyclic interventions, multi-level interventions as well as combined interventions. We demonstrate such functionalities by presenting real-life epidemiological experiments conducted with IntSim. We also address the efficiency aspect of IntSim, highlighting two-layer hybrid parallelism as well as optimization techniques such as active node switching and fixed fan-out. Lastly, we show the speedup benefit from multithreading paradigm. Although the runtime reduction diminishes gradually with more than seven threads, the collective gain in time-savings could be substantial.
Chapter 5
Evaluating Combined Interventions

In epidemiological studies, understanding the transmission dynamics of an infection within the population is a fundamental problem. A comprehensive insight towards such dynamics can lead to a sensible understanding of on-going or potential outbreaks. However, it is not the end of the story. In addition to being aware of the forthcoming risks, knowing how to contain and mitigate an epidemic by effective intervention strategies is far more important. In the previous chapters, contact network generator (HPCgen) and epidemic intervention simulator (IntSim) are introduced as well as the Singapore contact network. This chapter serves to demonstrate their real-life applications in epidemiological studies. Influenza, one of the most important infectious diseases confronting the world today, is chosen for the studies on its transmission dynamics under two types of social distancing interventions in Singapore community. We aim to understand how temporal factors affect the effectiveness of interventions as well as what are the characteristics of combined interventions compared to single interventions. The content of this chapter mainly comes from the publications5,6.

Two types of social distancing interventions are investigated in this chapter: school closure and workforce shift. We are not only interested in how they individually perform under the varying temporal settings, but more importantly, how they perform in combination, whether they outperform each individually and whether the sequential order in the combination makes a difference. The answers to those questions would shed light on the unknown patterns inherent in the influence of combinatorial interventions and ultimately help in designing optimal intervention strategies.

5.2 Method

Considering the importance of social structure in the spread of infectious diseases, a contact network model is used for exploring the effectiveness of interventions in a heterogeneous-structured population to understand transmission dynamics under interventions. Using HPCgen, we create the contact network with real-life data to represent the Singapore community for epidemic simulations. The network comprises six common types of social structures in an urban city setting and exhibits high connectivity and small-world properties. Its feature on edge and node labelling also makes it the perfect choice for intervention studies. We use IntSim to carry out the simulations under a series of intervention scenarios within the person-to-person contact network. In those scenarios, all-school closure, workforce shift or their combinations are applied to mitigate the spread of Influenza, with the varied settings of transmissibility, trigger thresholds and intervention durations. The outcomes of those intervention scenarios are evaluated by three measurements – attack rate, peak incidence and peak day.

Moreover, in this study, we also address the weekend effect and the influence of human response to disease epidemics – self-quarantine and self-protection.

Weekend Effect

It is known that the structure of the contact network might change significantly during the weekends. According to our survey conducted in Singapore in 2009, during weekends, there are 69.9% reduction in workplace contacts and 49.6% reduction in school contacts; during the weekdays, there is 20.89% reduction in shopping-mall contacts. The weekend effect can be modelled by adding 3 additional cyclic intervention measures to school contacts, workplace contacts and shopping-mall contacts respectively to simulate its impact on the epidemic dynamics. Those interventions are all triggered at the beginning of simulation, and operate in a weekly cycle, assuming the simulations always start on
Monday. Table 5-1 tabulates the definitions of three cyclic interventions to replicate the weekend effect.

### Table 5-1 Intervention definitions for weekend effects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>School Contacts</th>
<th>Workforce Contacts</th>
<th>Shopping-Mall Contacts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>reference</td>
<td>global</td>
<td>global</td>
<td>global</td>
</tr>
<tr>
<td>value</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>delay</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Duration</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>value</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Target</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>structure</td>
<td>school</td>
<td>workplace</td>
<td>shopping-mall</td>
</tr>
<tr>
<td>level</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
<td>scale</td>
<td>49.6</td>
<td>69.9</td>
<td>20.89</td>
</tr>
<tr>
<td>type</td>
<td>edge</td>
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<td>edge</td>
</tr>
<tr>
<td>Efficacy</td>
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<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Cycle</td>
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<td></td>
</tr>
<tr>
<td>interval</td>
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<td>5</td>
<td>2</td>
</tr>
<tr>
<td>period</td>
<td>2</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

### 5.3 Results

The uncontrolled scenario on the constructed contact network is firstly simulated to form the baseline results. Note that these baseline results have been presented in Section 4.4.2 with the epidemic curve and attack rate curve. Then all-school closure is simulated with different trigger thresholds, durations and transmissibility, followed by its combination with workforce shift, and further combined with weekend effect. Self-quarantine and self-protection are applied in all scenarios.

#### 5.3.1 Experiment Settings

As the same settings specified in Section 4.4.1, 1) $R_0 = 1.9$, which could be translated to $T = 0.04$ by Longini’s approach [41]; 2) 66.7% symptomatic rate [120]; 3) 1-day mean
latent period and 1.5-day mean infectious period [116], assuming symptoms are developed immediately after turning infectious.

In this study, the impacts of trigger threshold and duration of interventions are examined in terms of effectiveness of mitigating the influenza epidemic. The test scenarios are tabulated in Table 5-2. Each of those scenarios, including the baseline scenario, is simulated for 200 days and iterated for 100 times. All the results described in the following section are the average values of 100 simulation runs.

Every simulation starts on day 0 with 10 infectious persons seeded into a fully susceptible population with no prior immunity to the influenza virus. In our experiments, there are four different trigger thresholds and five different intervention durations to be chosen to form an intervention scenario. Hence there are a total of 120 scenarios per $R_0$ value: 20 scenarios for all-school closure and workforce shift respectively, and 80 scenarios for combined all-school closure and workforce shift (for simplicity, it is assumed that individual interventions in each combination scenario share the same length of intervention duration). As workforce shift scenarios have been discussed in Chapter 4.4.3, we shall focus on all-school closure and combined interventions.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All-School Closure</th>
<th>Workforce Shift</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trigger</td>
<td>0.02%, 0.25%, 1.5%, 5%</td>
<td>0.02%, 0.25%, 1.5%, 5%</td>
</tr>
<tr>
<td>Duration</td>
<td>2, 4, 6, 8, 10 weeks</td>
<td>2, 4, 6, 8, 10 weeks</td>
</tr>
<tr>
<td>Target</td>
<td>all school contacts</td>
<td>all workplace contacts</td>
</tr>
<tr>
<td>Efficacy</td>
<td>100%; non-rotational</td>
<td>50%; rotational</td>
</tr>
<tr>
<td>Cycle</td>
<td>N.A.</td>
<td>7-day interval/period</td>
</tr>
</tbody>
</table>

**5.3.2 Impact of Temporal Factors on All-School Closure**

Figure 5-1 shows the epidemic curves under all-school closure with different combinations of triggers and duration. We observe that all-school closure suppress the peak symptomatic incidences in most of the scenarios as well as postpone the peak days. Compared to Figure 4-9, the epidemic curves with different triggers but the same duration changes more substantially, suggesting for more densely connected school contacts are more sensitive to the choice of triggers. To examine different scenarios of all-school closure closely, we look at attack rates, peak incidences and peak days.
Figure 5-2 shows the effects of trigger thresholds and durations on the attack rate in all-school closure. Attack rates after implementing school closure are in the range of 40.42% to 44.45%, with a 0.05% to 9.10% reduction compared to that of the baseline scenario. The lowest attack rate occurs when 10-week school closure is triggered at prevalence equal to 0.02%.
It is reasonable that the longer intervention duration leads to a lower attack rate. It is noted that the effect of all-school closure is saturated at the duration of 8 weeks in our settings and prolonging the closure further would offer the trivial benefit. In addition, the influences of trigger threshold show an interesting pattern: if the duration < 4 weeks, having a higher threshold leads to a lower attack rate; if duration > 6 weeks, a rising threshold results in a slightly higher attack rate; if the duration of 4 to 6 weeks, a convex shape appears as shown in Figure 5-2.

It can be understood that a short period of closure may be more effective if it is implemented at reasonably higher thresholds but before the epidemic peak. It is because (1) higher threshold means higher prevalence of infectious persons at the point of time when the closure starts. Naturally the closure would be more productive and the number of potential transmissions that are blocked by the closure is expected to be much higher than in a low-prevalence circumstance. (2) In the growth stage of an epidemic, as there are plenty of the susceptible in the community, the epidemic often exhibits an exponential growth of prevalence. The closure that starts when gradient of growth is higher is more effective to suppress the propagation of infections. Our results show that the 2-week closure is the least effective one due to short duration, and its impacts are only noticeable when it is triggered at prevalence equal to 1.5% and above. A 4-week closure is able to influence the attack rate when it is triggered as early as at 0.02%, and a steady decline in attack rate is observed when its threshold rises. When the closure is sufficiently long (> 6 weeks), the duration of the closure can cover the growth stage even if it starts very early. So it is advisable to start the long-duration closure as early as reasonable. At the cut-off
point, the attack rates for 6-week closures have a shape of a convex curve, showing the existence of both trends.

![Figure 5-3 Attack rates under 2-week all-school closure in a shape of a convex curve [114]](image)

Earlier a trend was shown that having a higher threshold will cause a lower attack rate if the closure duration < 6 weeks. It is interesting to determine the upper bound of the threshold at which the trend is still valid. Two extra scenarios are added – 2-week school closure is triggered at the thresholds of 10% and 15%, respectively. In Figure 5-3, 2-week closure at 15% threshold leads to a higher attack rate than those at lower thresholds (5% and 10%), which does not follow the trend anymore. Instead, a convex function is again observed, only that the minimum attack rate is achieved at a rather high trigger threshold of about 10%, probably too high to be acceptable for real-life implementations.

The simulation results could help provide the suggestions for different needs. For cost-cautious or political consideration, policy makers may prefer shorter intervention. For such case, it is recommended to start school closure with a relatively longer delay since outbreak; if policy makers aim for minimizing the size of the epidemic, they should implement school closure as early as reasonable and last for more than 6 weeks. It is also noted that, for interventions with a shorter duration, it is more important to make a wise choice of trigger threshold. For example, for 2-week school closure, it could save extra 6.05% of the overall population from infection at no additional cost by properly choosing the trigger threshold.

Figure 5-4 shows that all-school closure significantly reduces peak incidence of the epidemic. The lowest peak incidence under school closure is 30.75 per 1000 people, 27.55% reduction compared to that of the baseline case. It is achieved when a 6-week closure is triggered at 0.25%. Note that 4-week closure is sufficient for reducing the peak incidence as the extended closure does not bring in any significant benefit on easing the worst-case stress on public health systems. The influence of trigger thresholds on peak
incidence exhibits similar trends as discussed earlier: if duration > 2 weeks, a rising threshold results in a slightly higher attack rate; if duration = 2 weeks, the peak incidences have a shape of a convex curve.

Figure 5-4 Peak incidences under all-school closure; peak incidences under 2-week closure has a shape of a convex curve (dot line) [114]

Figure 5-5 reveals that all-school closure steadily delays the peak day. Specifically, it can be observed that the peak day is significantly affected by trigger threshold, but not by duration. When the threshold rises from 0.02% to 5%, peak day steadily moves earlier. The longest delay obtained is 5 days compared to the baseline. It is achieved when any closure longer than 2 weeks is triggered at 0.02%.

Figure 5-5 Peak days under all-school closure [114]
5.3.3 Sensitivity Test of $R_0$ for All-School Closure

We observed interesting patterns of how epidemic measures are influenced by temporal factors when $R_0 = 1.9$. To evaluate whether the observations remain valid in social systems exposed to different virus strains, different values of $R_0$ at 1.5 and 2.3 respectively are simulated. The new simulation results demonstrate consistent patterns as observed in earlier sections.

Figure 5-6 shows the attack rates under all-school closure when $R_0 = 1.5$. Similar as that when $R_0 = 1.9$, the attack rate drops when the trigger threshold rises from 0.02% to 5% if the duration is less than 6 weeks. If duration is longer than 6 weeks, the attack rate may increase rather than decrease once the trigger threshold is higher than a certain value. Attack rates show as convex functions of trigger threshold in different cases where school closures last for 6, 8 and 10 weeks, respectively.

![Figure 5-6: Attack rates under all-school closure ($R_0 = 1.5$); attack rates under 6, 8 and 10-week closure all appear to be convex functions of trigger threshold. The dotted line highlights the results for 6-week closure [114]](image)

Figure 5-7 follows the findings in Figure 5-6. It is clearly shown that, when trigger threshold rises, the attack rates decrease for 2-week closure and increase for 6-, 8- and 10-week closures. At the cut-off value of 4-week closure, attack rates clearly form into a convex function of trigger threshold.
5.3.4 Impact of Combined School Closure and Workforce Shift

The results of individual interventions have been discussed; next we examine combined intervention. It is interesting to know the impact of the combination of all-school closure and workforce shift as well as the influence of the temporal sequence order in the combination.

Figure 5-8 A-E show that the lowest attack rate ($AR$) under combined intervention is 31.17%, achieved when workforce shift and school closure are both triggered at 0.25% and lasted for 10 weeks. In the single interventions, the lowest $AR$ is 40.42% for all-school closure and 36.51% for workforce shift. Both happen at the 10-week duration and 0.02% trigger threshold. 8.01% of the population can be further saved from the infection by applying combined intervention compared to the single interventions.

Figure 5-8 F-J show that the lowest peak incidence ($PI$) occurs when 10-week workforce shift and school closure are triggered at 5% and 0.02% respectively. Compared with the lowest $PI$ under single interventions (30.75 under school closure and 29.87 under workforce shift), combined intervention is able to further reduce $PI$ to 14.27.

Figure 5-8 K-O show that combined intervention can delay the peak day ($PD$) by 14 days compared to the baseline. It is much longer than $PD$ delay in individual interventions, i.e. 5-day delay by school closure and 2-day delay by workforce shift.
Figure 5-8 Attack rates, peak incidences and peak days under combined intervention ($R_0 = 1.9$; x-axis shows school closure’s triggers, coloured bar indicates workforce shift’s triggers; in each row, duration = 2/4/6/8/10 weeks from left to right) [121]
a) Do combined interventions always outperform each individual intervention?

It is commonly believed that combined interventions will outperform each individual intervention. But it is noticed that there are some cases in which combined interventions lead to higher attack rates than single interventions at the same trigger threshold and duration. The worst case is observed when the 4-week workforce shift and school closure are both triggered at 0.02%. If applying only workforce shift at 0.02% threshold with a 4-week duration (named as Scenario A), the AR is 38.25%; on the other hand, AR from combined intervention (named as Scenario B) is 43.12%, which is 4.87% higher.

Figure 5-9 further describes what happens in Scenarios A and B. On day 7, the trigger threshold \( t = 0.02\% \) is reached and the epidemic curve of combined intervention grows much slower than the single intervention because more contacts have been removed and chance of infection is lower. On day 35, the interventions in both scenarios end and the removed contacts are restored. Because the growth of infected cases is much slower in Scenario B, there are more susceptible ones left in the population. Specifically, on day 35, 49.65% and 85.88% of the population are susceptible in Scenarios A and B respectively. This nearly doubled size of susceptible population allows more disease-transmitting contacts and higher chance of infection in Scenario B compared to those in Scenario A, leading to the divergent developments of the epidemic after day 35 – the incidence continues to decline and gradually fades out in Scenario A; and oppositely in Scenario B, the incidence number grows exponentially until day 40 and a large number of infections take place after the intervention.

It is observed that 11 out of 16 combined scenarios of 2-week intervention underperform 2-week single interventions; 7 of 16 scenarios of 4-week interventions and 1 out of 16 scenarios in 6-week interventions lead to a similar observation. Apparently combined interventions with a longer duration \((>=6\text{ weeks})\) are less prone to underperform, meaning that combined interventions have to be maintained long enough to prevent the rapid spread of influenza after the intervention period.
**b) How do trigger and duration affect the effectiveness of combined interventions?**

The performance of combined interventions can be affected by both trigger and duration. When the duration increases, $AR$ and $PI$ decline consistently. When trigger threshold rises, $AR$ and $PI$ drop if the duration is shorter than $d$ weeks ($d = 8$ for $AR$; $d = 4$ for $PI$). If the duration is longer than $d$ weeks, $AR$ and $PI$ increase instead. In Figure 5-8 E and G, convex curves clearly show the existence of the above trends. For the peak incidence time, the $PD$ drops when the triggers rises with $d >= 4$ weeks. It also shows that a longer duration of intervention (> 4 weeks) does not bring in any further delay of the peak incidence time.
c) Does the implementation sequence in a combined intervention matter?

The temporal implementation sequence of individual interventions within combined strategy may also affect the outcome of intervention. The maximal differences of the attack rates among 16 threshold combinations are \{6.13\%, 8.24\%, 3.47\%, 3.21\%, 2.59\%\} with \{2, 4, 6, 8, 10\}-week durations respectively. When the duration is less than or equal to 6 weeks, the performance of synchronous interventions (two individual interventions start from the same threshold) improves when the trigger rises. With longer control durations, the trend is not retained anymore. Comparing to the asynchronous combinations (individual interventions start at different thresholds) with the same duration, the relative performance of synchronous interventions turns from “underperformance” to “outperformance” when their triggers rise from 0.025\% to 5\% subject to the condition that the duration is within 8 weeks. When the duration is longer than 8 weeks, synchronous interventions underperform in most of the scenarios and hence it is wise to start them at different thresholds in the implementation.

For asynchronous combinations, the sequential order of implementing single interventions can affect the AR as well. The two combined strategies with the swapped trigger thresholds of their individual interventions are referred as a pair of symmetric strategies. The maximal differences in attack rates between a pair of symmetric strategies are \{2.13\%, 1.31\%, 1.55\%, 2.73\%, 1.66\%\} for \{2, 4, 6, 8, 10\}-week durations respectively. It is observed that school closure should be implemented first when the duration is less than 4 weeks and workforce shift should start first when the duration is longer than 4 weeks.

### 5.3.5 Sensitivity Analysis of $R_0$

The results of temporal effects in combined interventions of school closure and workforce shift are based on $R_0 = 1.9$. To examine if the conclusions hold for other $R_0$ values, $R_0 = 1.5$ and 2.3 are tested. Figures 10 and 11 show the effectiveness of combined interventions of different pairs of thresholds and durations for $R_0 = 1.5$ and 2.3 respectively.

The results are consistent with the findings based on $R_0 = 1.9$. Specifically, the worst combination happens when both school closure and workforce shift are implemented at 0.02\% for 2 weeks. It yields 36.61\% attack rate, 25.71 peak incidence (per 1000 people) on day 28 for $R_0 = 1.5$; 48.52\% attack rate, 53.88 peak incidence (per 1000 people) on day 28 for $R_0 = 2.3$. The majority of single interventions, either school closure or
workforce shift, show a significant impact, except for 2-week school closure or workforce shift at 0.02% threshold.

In Figure 5-10 & Figure 5-11, the significant impact of adjusting temporal settings of combined interventions is observed. When $R_0 = 1.5$, attach rate ranges from 36.90% down to 22.97% (37.8% reduction); peak incidence (per 1000 people) ranges from 27.20 to 6.12 (77.5% reduction); and peak day varies from 28 days to 76 days (171.4% increase). When $R_0 = 2.3$, attach rate is in range from 48.67% down to 37.21% (23.5% reduction), peak incidence from 55.43 down to 27.73 (50.0% reduction), and peak day from 22 days to 31 days (40.9% increase). The observations suggest a stronger impact of temporal factors for a lower value of $R_0$.

For asynchronous combinations, the maximal differences in attack rates between a pair of symmetric strategies are {2.88%, 2.26%, 4.03%, 4.68%, 4.86%} for {2, 4, 6, 8, 10}-week durations where $R_0 = 1.5$, and {3.49%, 1.69%, 2.14%, 0.85%, 0.9%} where $R_0 = 2.3$. Again the observation is that when $R_0$ is lower, switching the order in a combined intervention could make a more significant difference. It is also interesting that the difference is particularly significant when the duration is short (2 weeks) for all the three values of $R_0$. 
Figure 5.10: Attack rates, peak incidences and peak days under combined intervention ($R_0 = 1.5$). X-axis shows school closure's triggers. Coloured bar indicates workforce shift's triggers. Duration = 2/4/6/8/10 weeks from left to right in each row [121]
Figure 5.11 Attack rates, peak incidences and peak days under combined intervention ($R_0 = 2.3$). X-axis shows school closure's triggers. Coloured bar indicates workforce shift's triggers. Duration = 2/4/6/8/10 weeks from left to right in each row. [121]
5.3.6 Study on Weekend Effect

The above simulations run with the contact patterns during the weekdays. In urban life, however, social contact patterns may be significantly different during the weekends. For example, contacts in shopping malls may increase while contacts within workplace/schools may decrease. Such changes are terms as the weekend effect in the context, which recurs for 2 days (Saturday and Sunday) in every week.

It is meaningful to conduct the extra simulations to evaluate the impact of the weekend effect. Specifically, it is assumed that school contacts are reduced by 50% and workplace contacts by 70% during the weekends compared to those during weekdays, and meanwhile shopping mall contacts are increased by 35.79% according to the survey data. Numerical experiments are then repeated at $R_0 = 1.9$ with the same configurations as listed in Table 5-2 for evaluating combined workforce shift and school closure. The simulations are assumed to start on Monday and when workforce shift intervention or school closure intervention is exercised, the population involved in the intervention will follow intervention arrangement regardless of weekday or weekend.

Figure 5-12 shows the spread dynamic after introducing weekend effect. Compared to the experiments shown in Figure 5-8 without considering weekend effect, there exist similar patterns while varying thresholds and durations of combined interventions. Meanwhile, however, we observe that the impact of weekend effect: the baseline attack rate under the weekend effect falls by 3.21% compared to the original one. Peak incidence is only of a 0.18% difference and peak day is postponed by 1 day. Such results may be interpreted: the total removal of contacts from schools and workplaces is more than the increased contacts in shopping malls in the weekends.

When comparing the individual scenarios of combined interventions, it is found that the impact of the weekend effect diminishes gradually with the increase in duration of interventions. This may be due to the enforcement on the control effect by the interventions from weekdays to weekends, i.e., weekend effect may be overridden by the control. For example, part of weekend effect – 50% removal of school contacts in weekends may be overridden by school closure intervention and the 100% removal would happen during the whole period of school control. Therefore, the shorter the inventions are, the more notable the weekend effect is. The most notable decline in attack rate under the weekend effect is spotted in the 2-week intervention scenarios of the average reduction of 3.44% compared to the baseline of the weekend effect.
Figure 5-12 Attack rates, peak incidences and peak days under combined intervention with weekend effect ($R_0 = 1.9$. X-axis shows school closure’s triggers. Coloured bar indicates workforce shift’s triggers. Duration = 2/4/6/8/10 weeks from left to right in each row) [121]
5.4 Discussion

The simulation results show that both the school closure and workforce shift are able to lower attack rate and daily incidence as well as delaying the epidemic in most intervention scenarios. Such social distancing through enforcement from administration is necessary to mitigate the diffusion of influenza virus among the communities, especially when a large number of asymptomatic cases exist.

The experiments provide guidance on choices of trigger threshold and length of duration for implementing school closure, workforce shift and their combination intervention measures. These results will be relevant to future contingency plan for an influenza pandemic, which is estimated to be more pathogenic and might have higher case fatality rates than that shown in 2009 H1N1 pandemic flu [34]. Combining the results with those in Section 4.4.3, it is found that durations of 8 weeks and 6 weeks are sufficiently long for workforce shift and school closure respectively. Short interventions should be implemented after a longer delay since outbreak. In contrast, long interventions should start as early as reasonable. The cut-off values between long and short duration are 6-week for school closure and 4-week for workforce shift, if lowering the attack rate is the priority.

Comparing the effect of workforce shift with school closure, it is observed that workforce shift is generally more impactful. One of the main reasons is because of the difference in the number of people that can be affected by school and workplace interventions. In the constructed Singapore contact network, school closure removes school contacts from ~53,000 people and workforce shift affects ~148,000 people at any time during the intervention. So there are around 2.8 times more population controlled in the workforce shift.

Furthermore, combined interventions as temporal combinations of single policies are examined. For simplicity, durations of single policies in a combination share the same value but different trigger thresholds could vary so that the two policies may be implemented either one after another or concurrently. The results show that combined interventions do not always outperform each individual intervention while varying trigger threshold and duration. It is shown that short closures (less than 6 weeks) are more prone to underperformance compared to that of the workforce shift only. Secondly, it is observed that switching the order of single policies in combination can make a difference in the effect of intervention. Planning multiple interventions in the appropriate order is
able to strengthen the mitigation to the spread of infection without significant additional cost but may be politically difficult to explain.

Among all choices of combined interventions examined, the near-optimal policy happens when all workforce shift and school closure are both implemented at the 0.25% trigger threshold and lasted for 10 weeks (31.17% attack rate; peak incidence of 17.42 per 1,000 people on day 33).

Enforcing social distancing policy is associated with considerable cost, in both economic and social aspects. For example, the major cost of school closure comes from absenteeism of working parents who have to stay home to take care of their children. A UK study [113] estimated 16% of the UK workforce as the main carers of dependent children and likely to be absent due to school closure. This percentage could further climb to 30% if counting healthcare workers only, meaning more absenteeism could happen in the public healthcare system which is already stressed during an epidemic. Besides, there are also problems about social justice, ethical issues etc due to the social consequences of school closure [6]. On the other hand, workplace distancing measures like workforce closure might lead to an abrupt shortage of manpower, lower productivity and inevitable economic losses. As an alternative to workplace closure and uncontrolled absenteeism, workforce shift might be an option for disease containment. Nowadays, accessible infrastructure for telecommunication is widely available at many workplaces and homes. Tele-working has become feasible and can be equipped in advance along with the planned workforce shift. It makes workforce shift of longer duration more acceptable. The planned workforce shift would help companies and other institutions to reduce the impact of mass absenteeism and sustain everyday business and production as much as possible.

Due to lack of information about the compliance rate to school closures, a 100% efficacy is assumed in all the intervention scenarios of this study. However, in real-world school closure, the student compliance rate for social distancing may be lower. The compliance rate of students for social distancing would be increased when implementing workforce shift together with school closure. The variation of compliance rate was ignored to avoid further complicating the analysis on combined interventions. A higher compliance rate is definitely preferred in real-world interventions and needs coordination among education agencies, health agencies and communities to achieve.

Considering the network dynamics in weekends, the influenza spread under the weekend effect is examined. As schools and many workplaces are closed during the weekends, the contacts between schoolmates or between colleagues may be partially
removed (Schoolmates or colleagues may hang out together during the off days) [126] but the shopping mall contacts may increase. In experiments of the weekend dynamics, it is found that the weekend effect does not bring a significant variation to the baseline epidemic curve compared to that of the original setting which does not consider the weekend effect. It is worth noting however that due to the lack of real-world data, assumptions are made about degree reduction of school/workplace contacts during weekends. The actual effect may vary in the real life scenarios.

The evaluation of intervention scenarios in this study is based on Singapore’s social structure. The results presented here should be interpreted with the following caveats in mind. First, the Singapore community is not a closed system. There are millions of visitors arriving in Singapore (e.g., a peak of 10 million visitors in 2007). Singapore has a population size of around 4.8 million as of 2008. The large volume of visitors flowing into the country implicitly indicates that the influence of imported cases should be considered when planning intervention strategies. However, the influence of visitors is not considered in the above studies due to lack of data and concerns for complexity. It would be desirable to further analyse the influence of visitors on the disease spread in the community for combating future pandemics. Further, Singapore is a highly urbanized city and its population density is among the highest in the world, which will definitely lead to high contact numbers in different community structures. The best intervention scenario in terms of control timing may vary when the social structure is drastically different from the one studied here, as the heterogeneity of the social structure is a significant factor affecting disease spread and consequently affecting mitigation planning strategies as well.
Chapter 6

Conclusion & Future Work

In this chapter, we first summarize the work that has been done and conclude the thesis, and then elaborate the plan for future work to address some areas in the current studies that can be further improved.

6.1 Conclusion

Infectious diseases are potentially dangerous from the perspectives of mortality, hospitalization, disease burden as well as the fear of infection that may lead to public panic. Effectively controlling the spread of infectious diseases through interventions is always desirable. However, it is known that there are different types of intervention measures, and each measure could be specified differently in terms of “when”, “how long”, “who”, “how much” to intervene. Among all those options, determining the optimal measure with the right parameters is challenging. We believe such decision should be supported by comprehensive quantitative evaluation. Mathematical modelling and simulation of infectious diseases is able to provide useful insights about the transmission dynamics of the diseases under the interventions, and offer robust estimation to the time-evolution of the effectiveness of interventions.

As a densely populated hub city in the region, Singapore has been a victim in every pandemic in the recent decades. However, there is a lack of contact network model to represent the Singapore community; absence of intervention-oriented simulation tool for contact network; and lastly, lack of quantitative evaluations to support the decisions of intervention to be implemented. In order to address the above problems, we introduce our contact network based simulation framework for evaluating complex interventions to the disease outbreaks in Singapore. There are two components in the framework: HPCgen (a fast generic contact network generator for urban cities) and IntSim (an efficient intervention-oriented epidemic simulation model).

In Chapter 3, we elaborate the design of HPCgen followed by illustration on step-by-step network generation. HPCgen adopts a divide-and-conquer approach by dividing a community into distinct social structures, then connecting the people who regularly visit those structures by chance, and finally integrating connections occurring in every social
structure to form the global contact network. Every connection (contact) is annotated with social structure information, suitable for the purpose of intervention studies. Six types of social structures have been modelled in HPCgen: households, hospitals, schools, workplaces, shopping malls and public transport stations. Each of those social structures is modelled by its size, hierarchical levels and mean contact degrees. As its generic representation of social structure, incorporating new types of social structures would be effortless, simply by providing the structure-specific parameters. HPCgen is also optimized for speed by MPI parallelism and has achieved the remarkable speedup of $8.16\times$ by 8 parallel processor nodes.

Using HPCgen, we apply the real-life data collected from various sources within Singapore to generate a contact network of 4.8 million nodes. Those data include population demographics, the statistics about social structures and the human contact behaviour profiles obtained through a public survey. The generated network exhibits high connectivity, positive assortativity and small-world properties.

After generating contact networks, we develop IntSim to utilize such a network for intervention simulations. Chapter 4 highlights that IntSim is designed for both functionality and efficiency. In term of functionality, IntSim supports simulating complex interventions, including cyclic intervention, multi-level intervention and combined intervention. It is also equipped with capability of simulating weekend effects and self-protection mechanism. IntSim’s versatility is attributed to its generic representation to an arbitrary intervention by parameterizing it with trigger, duration, target, efficacy and cycle. Such definitions of interventions are maintained in XML format for readability and extendibility. Regarding efficiency, IntSim is parallelized at two layers: multithreading within a simulation and application-level parallelism leveraging on the scheduler in the cluster. IntSim is also optimized by active node switching and fixed fan-out to further reduce the computation cost. We demonstrate the collective time-saving by IntSim could be up to 3 days for the experiments described in Chapter 5.

Combining contact networks and the simulation model, we discuss our experiments on evaluating the combination of school closure and workforce shift in Chapter 5. By examining the impacts of temporal factors in school closure, workforce shift and their combinations, together with sensitivity analysis on $R_0$, we found that under the given settings, the effect of school closure and workforce shift are saturated at 6 and 8 weeks respectively. All-school closure excels at suppressing peak incidences and class closure is more useful to lessen attack rates. The combination of all-school closure and workforce shift outperforms each individual measure only if duration is longer than 6 weeks or
school closure is triggered as late as 5% threshold. Combined interventions may be more effective if school closure starts first when duration is less than 4 weeks or workforce shift starts first when duration is longer than 4 weeks.

After all, we conclude that invention simulations are critical and practical for helping policy makers to make wise decisions on containing and mitigating the spread of infectious diseases. Simulating various “what-if” scenarios in the Singapore contact network is the start of increasing the quantitative evaluation to support the local administration in the battle of confronting the threat of infectious diseases in the future.

6.2 Future Work

Our contact network based framework for infectious disease intervention comprises three parts: contact network generation, intervention-oriented simulation and intervention evaluation. Accordingly, our plans for future work can be categorized into those three parts as well.

6.2.1 Contact Network

Our current contact network models the social structures by their size in terms of number of people who visit regularly. Although we leverage on population indices to manifest the proximity tendency between individuals, there is the lack of spatial representation in the contact network generation. Incorporating the spatial coordinates into social structures could enable the distance-based selection of candidate populations for the respective social structures as well as distance-based interventions, such as closing down the schools within 5km to the school with an on-going outbreak, which could be more cost-effective and less stressful to our public health system.

Moreover, the contact network captures mainly the regular contacts. It is rational because regular contacts tend to take place more frequently and in close distance (people tend to keep large distance to a stranger if they could). However, irregular contacts or dynamic contacts may also contribute a non-trivial fraction of infections, especially for those diseases with high infectivity. How to model the dynamic contacts in a static network structure would be a challenge. Introducing weights to the edges to differentiate regular and dynamic contacts is one plausible way, but it may suffer from the substantial increase of edges. Another alternative is contacts switching between the connected nodes.
Travelling through public transport is part of the daily routine of many people. Cabins of trains and buses are the perfect locations to get infected because of 1) closed environment and 2) shorter interpersonal distance when crowded. Our current transport model implies the transmissions take place in the railway stations or bus stops and does not capture in-cabin transmissions.

Lastly, we notice that churches and nightclubs were hot-spots in 2009 H1N1 pandemic in Singapore [127] but had not been modelled in our contact network. There is also a lack of modelling on visitors/tourists, private-school students, college students, army recruits, and etc. Incorporating more social structures will undoubtedly improve the reality of the contact networks, and lead to more accurate epidemiological analysis and simulations results ultimately.

6.2.2 Intervention Simulation

Human response to an epidemic outbreak may contribute substantially to the transmission dynamics of infectious disease. In our simulations, we model the self-protection mechanism by uniformly reducing the effective transmissibility for symptomatic infectious agents. It is noted that the extent of human response to an epidemic outbreak often depends on the fear of infection. Such fear could be modelled as diffusion spreading from the symptomatic agents to the rest of the contact network through the chain of contacts. Incorporating the model of fear diffusion and spontaneous human response into our simulation could further improve the extent of reality of our model.

6.2.3 Intervention Evaluation

In Chapters 4 and 5, we mainly focus on the temporal parameters of interventions (trigger and duration). We investigate the combinations of different triggers and durations to discover the patterns of intervention effectiveness with respect to temporal variations. Other than temporal parameters, target, efficacy and cycle could also be interesting subjects for further investigation. Scale refers to the percentage of contacts affected by the intervention. Varying scale could result in diverse outcomes of interventions as well as different amounts of cost, e.g. vaccination. Efficacy represents the response or compliance to interventions. Different levels of efficacy could directly affect the outcome of interventions. For example, school closure might turn out to be ineffective if most of the students still hang out together during the period of closure. Cycle defines the
characteristics of cyclic interventions. It would be interesting to know how much impact arise from changing lengths of *interval* and *period*.

Apart from all sorts of intervention parameters that we would like to examine combinatorial, we are also interested to measure the effectiveness of intervention strategies in terms of cost. Such cost includes morbidity and mortality, hospitalization and etc due to the diseases, as well as the costs incurred from implementing interventions. Instead using three measurements (*attack rate*, *peak incidence* and *peak day*) in the current analysis, translating all those into a definite dollar value is more straightforward for comparison between the strategies. More importantly, public health resources are often limited so that utilizing such limited resources in a cost-effective manner is far more critical and practical for policy makers.
Reference


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Appendix A Questionnaire

You are invited to participate in a research. This information sheet provides you with information about the research. The Principal Investigator (PI, the person in charge of this research) or his/her representative will also describe this research to you and answer all of your questions. Read the information below and ask questions about anything you don’t understand before deciding whether or not to take part.

What is the project about?

In this project, a large-scale epidemic simulation model of Singapore will be constructed by taking demographic, social contact, and geographic factors into consideration. People, in the course of carrying out their daily activities, move between different locations, exposing themselves to infectious agents within these locations and meanwhile transporting the agents between different locations as well. We represent these processes by a large complex network model, representing the whole Singapore population and their social inter-activities that are pandemic related. The research is composed of three parts:

- Data collections, such that later simulations and analyses can have a reliable starting point.
- Simulations and modelling, where infectious disease spreading and intervention strategies will be modelled and simulated.
- Strategy developments for epidemic control and recovery. Essential information obtained from the simulation model will help health agency develop effective containment strategies in advance of a pandemic infectious disease.

What is the duration of the project?

We hope to recruit 5,000 subjects for this study. Anyone who is residing in Singapore or visiting Singapore for >24 hours can participate in this research. The duration of this research project is 2 years. But the duration of your participation is limited to the amount of time you take to fill in the questionnaire form.

Your decision to participate in this research is voluntary and is completely up to you. You can also withdraw any time.

What do I need to do to participate in the project?

A participant only has to fill in an anonymous survey questionnaire on his social contact pattern (such as how many people he meets in a typical day, their age, their sex, and location of meeting) and basic demographic information (e.g., his age, sex, town of residence, race, occupation).

No research data will be retrieved from any medical records. No biological sample will be taken. No identification information will be collected. No one in the project will have any information on your identity. There will be no physical discomfort.

What benefit do I get for participating in the project?
There will be no reimbursement for participation. There is no direct benefit to you by participating in this research. The knowledge gained will benefit the public in the future.

**Whom can I call if I have questions or problems with this project?**

Please contact the Principal Investigator (Attn: Wong Limsoon at telephone 6516-2902 or email wongs@comp.nus.edu.sg) for all research-related matters and in the event of research-related injuries.

For an independent opinion regarding the research and the rights of research participants, you may contact a staff member of the National University of Singapore Institutional Review Board (Attn: Mr Chan Tuck Wai, at telephone 6516 1234 or email at irb@nus.edu.sg).

**Part I Basic Data**

Explanation notes: Please provide the following basic information about yourself. If you have more than one residence place (for example, you may live in a dormitory during weekdays and go home weekends), all the different places should be taken into record.

**Part II: Typical Weekday (Mon-Fri)**

The typical activities taken during weekdays including the morning (1), afternoon (2), evening activities (3) (when, where, the number of people you contact with)

**Part III: Typical Weekend Days (Sat-Sun)**

The typical activities taken during weekend days including the morning (1), afternoon (2), evening (3) activities (when, where, the transportation mode, the number of people you contact with)

**Part IV: Typical Day in Hospitalization**

The number of people you are in contact with during your stay in hospital ward if applicable

**Definition on Contact:**

(i) stay in the same flat after work; or
(ii) stay in the same office or any other not-so-large closed space such as lift, air-con corridor, etc.; or
(iii) stay within 1-meter range in open space;
(iv) stay within 5-meter range in large closed space, e.g., MRT station or conference hall.
Part 1: Basic Data

1. Age: □ 0 – 14 □ 15 – 24 □ 25 – 34 □ 35 – 44 □ 45 – 54 □ 55 – 64 □ 65+

2. Gender: □ Male □ Female

3. Profession: □ student □ working □ not working

4. Ethnicity: □ Chinese □ Malay □ Indian □ Others

5. Number of people living in the same house:
□ 1 □ 2 □ 3 □ 4 □ 5 □ 6 □ 7 □ Others: ___

5.1. For all the people living in the same house as you, please indicate their relationship with you and their age:

<table>
<thead>
<tr>
<th>Relationship with you</th>
<th>Age (If you do not know the exact age, give your best estimation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td></td>
</tr>
</tbody>
</table>

6. Are you under a medical insurance covering outpatient benefit?
□ Yes □ No □ Don’t know

7. What transport do you regularly use to go from home to workplace/school? (Can choose more than one)
□ Bus □ Bus and MRT □ MRT □ Car □ Shuttle
□ Walking □ Motorcycle

8. How much time do you take to go to workplace/school?
□ Less than 30 min □ 30 – 44 min □ 45 – 59 min □ 60 – 89 min □ 90 min or more

9. Where do you stay?
□ Postcode_________ □ east □ west □ north □ south □ central
10. Where is your workplace/school?
☐ Postcode_________ ☐ east ☐ west ☐ north ☐ south ☐ central
Everyone falls sick from time to time. Questions 11 to 15 ask you about what you usually do when you have flu.

11. What action did you take when the flu illness start?
☐ Self-medication ☐ General Practitioner (e.g., neighbourhood clinic) ☐ Polyclinic
☐ A & E ☐ Hospital

12. After how many days do you take action after the first symptom of flu (e.g., fever)?
☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ more than 3 days

13. How many days do you go to work/school when you have a fever in the daytime.
☐ 0 day ☐ 1 day ☐ 2 days ☐ 3 days ☐ 4 days or more

14. Do you go shopping with a fever?
☐ Yes ☐ No ☐ Sometimes

15. Do you take preventive measures when people surrounding caught fever?
☐ Yes ☐ No ☐ A little bit

16. Do you still remember the SARS outbreak in 2003? During the SARS outbreak, did you avoid the following public places?

<table>
<thead>
<tr>
<th></th>
<th>No</th>
<th>Totally avoid</th>
<th>Reduce frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Large shopping centre</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>b. Big supermarket</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>c. Bus</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>d. MRT</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

17. How often do you go to the following places?

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>once</th>
<th>twice</th>
<th>3 times</th>
<th>4 times</th>
<th>Others, pls specify</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. shopping in town</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>b. shopping nearby</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
<tr>
<td>c. supermarket</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td></td>
</tr>
</tbody>
</table>
d. exercise places in one week ☐ ☐ ☐ ☐ ☐ ☐

e. places of worship in one month ☐ ☐ ☐ ☐ ☐ ☐

f. hospital in one month ☐ ☐ ☐ ☐ ☐ ☐

18. Which is your most frequently visited MRT stations if you regularly travel by MRT?
   a. The MRT station you usually get on: _______________________
   b. The MRT station you usually alight: _______________________

Part 2: Typical Weekday

In this section, questions 1 to 12 ask you about how you spend your time in a typical weekday (Mon to Fri).

In the morning
1. In the morning, what time do you depart for work/school?
   ☐ Before 6am ☐ 6am – 7am ☐ 7am – 8am ☐ 8am – 9am ☐ 9am – 10am
   ☐ 10am or later ☐ Others: _______

2. During departure to work/school, what is the estimated number of people you are in contact with?
   ☐ Less than 5 ☐ 5 – 14 ☐ 15 – 29 ☐ 30 – 44 ☐ 45 or more

3. How long is your work/school hour?
   ☐ 8 hr ☐ Others: _______

4a. What is the estimated number of people you are regularly in contact with in your office/class?
   ☐ Less than 5 ☐ 5 – 14 ☐ 15 – 29 ☐ 30 – 44 ☐ 45 or more

4b. For students only: When you are in school, what is the estimated number of people you are in contact with outside class?
   ☐ Less than 5 ☐ 5 – 14 ☐ 15 – 29 ☐ 30 – 44 ☐ 45 or more

5. Where do you go for lunch?
   ☐ Somewhere nearby and within walking distance
   ☐ Go out somewhere by bus, MRT, car
   ☐ In office
   ☐ Back to home
   ☐ Others: ______________________
   ☐ In school
6. During lunch, what is the estimated number of people you are in contact with?

☐ Less than 5  ☐ 5 – 14  ☐ 15 – 29  ☐ 30 – 44  ☐ 45 or more

**In the afternoon**

7. In the afternoon, what time do you go home from work/school?

☐ 4pm – 5pm  ☐ 5pm – 6pm  ☐ 6pm – 7pm  ☐ 7pm – 8pm  ☐ 8pm or later  ☐ Others: ___

8. During your travel from work/school to home, what is the estimated number of people you are in contact with?

☐ Less than 5  ☐ 5 – 14  ☐ 15 – 29  ☐ 30 – 44  ☐ 45 or more

9. Where do you have your dinner?

☐ Have dinner at home  ☐ Package from food court and take home  
☐ Dinner at food court  ☐ others: __________________________

10. During dinner time, what is the estimated number of people you are in contact with?

☐ Less than 5  ☐ 5 – 14  ☐ 15 – 29  ☐ 30 – 44  ☐ 45 or more

**In the evening**

11. In the evening, what are your activities? (can choose more than one)

12. For every activity you selected, indicate the estimated number of people you are in contact with.

<table>
<thead>
<tr>
<th>Less than 5</th>
<th>5 – 14</th>
<th>15 – 29</th>
<th>30 – 44</th>
<th>45 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Go shopping</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Exercise</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Pub</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Cinema</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Stay at home</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>☐ Others: ☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

**Part 3: Typical Weekend**

In this section, questions 11 to 15 ask you about how you spend your time in a typical weekend (Sat to Sun).
9. How do you travel to these places?
☐ MRT  ☐ MRT and bus  ☐ Bus  ☐ Car  ☐ Taxi  ☐ Walk  ☐ Stay at home

10. During your traveling time, what is the estimated number of people you are in contact with?
☐ Less than 5  ☐ 5 – 14  ☐ 15 – 29  ☐ 30 – 44  ☐ 45 or more

**In the evening**

11. In the evening, what time do you have outdoor activities? (Choose all the time slots that you have outdoor activities)
☐ 5pm – 6pm  ☐ 6pm – 7pm  ☐ 7pm – 8pm  ☐ 8pm – 9pm  ☐ Others: ______

12. In the evening, what are the regular activities you do? (You can choose more than one)
☐ Shopping in town
☐ Shopping nearby
☐ Market
☐ Swimming pool
☐ Place of worship
☐ Stay at home
☐ Others: ______
☐ Gathering with friends/relatives

13. For every activity you selected, indicate the estimated number of people you are in contact with.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Less than 5</th>
<th>5 – 14</th>
<th>15 – 29</th>
<th>30 – 44</th>
<th>45 or more</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shopping in town</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shopping nearby</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Market</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swimming pool</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Place of worship</td>
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<td></td>
</tr>
<tr>
<td>Stay at home</td>
<td></td>
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<td></td>
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<tr>
<td>Others: ______</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gathering with friends/relatives</td>
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</tr>
</tbody>
</table>

14. How do you travel to these places?
☐ MRT  ☐ MRT and bus  ☐ Bus  ☐ Car  ☐ Taxi  ☐ Walk  ☐ Stay at home

15. During your traveling time, what is the estimated number of people you are in contact with?
☐ Less than 5  ☐ 5 – 14  ☐ 15 – 29  ☐ 30 – 44  ☐ 45 or more
Part 4: Typical Day in Hospitalization

In this section, questions 1 to 3 ask you about how you are in contact with other patients in a typical day when you are admitted to a ward of hospital or specialty centre.

1. Have you ever been admitted to a ward of hospital or specialty centre in Singapore?

☐ Yes  ☐ No

2. If applicable, please indicate the estimated number of patients you are in contact with in your ward.

☐ Less than 5  ☐ 6 – 10  ☐ 15 – 29  ☐ 30 – 44

3. If applicable, please indicate the estimated number of patients you are in contact with outside your ward.

☐ Less than 5  ☐ 6 – 10  ☐ 15 – 29  ☐ 30 – 44

Thank You! 😊