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Author(English)	Nguyen Dung Dung
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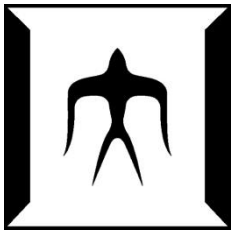

A Risk Analysis Framework for Nosocomial Influenza Infection Using Agent-Based Simulation

A Dissertation

By

Dung Minh Nguyen

Department of Computational Intelligence and Systems Science
Interdisciplinary Graduate School of Science and Engineering
Tokyo Institute of Technology

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ABSTRACT

The purpose of the research is to develop a framework to assess the risk of a highly contagious and mortal influenza-like illness infection to health care workers (HCW) in a hospital under different scenarios of infection control. The method is to build an agent-based model for simulating infection of the virus in the hospital and use an open-source software to visualize a risk graph of infection. The simulation results have shed more light on epidemiological belief of that direct patient care HCW have high risk of catching nosocomial influenza virus and that washing hand and wearing mask are effective to prevent an outbreak of the disease in the hospital. The methodologies of quantification and visualization the infection risk is a potential methodology for risk management in infection control of nosocomial infection.

A Nosocomial infection, also known as hospital-acquired infections (HAI) occurs worldwide and it represents a major source of morbidity and mortality for hospitalized patients. In recent years, with the worldwide spread of severe acute respiratory syndrome (SARS) and the 2009 influenza pandemic, research in infection prevention and control in hospitals become increasingly important. Computer simulation can be an experimental and educational tool for hospital administrators to test strategies for controlling nosocomial infections. The great advantage of simulation model is that they unable experiments which are impossible or undesirable.

Our simulation framework consists of an agent-based model for simulating nosocomial infection and a component of visualizing the contact network generated after the simulation. The advantage of agent-based model is that macro-level statistical experiment results can be achieved from micro-level evolution of agent interactions. On the other hand, network analysis can help to visualize and track micro-level contact

between agents. Since most of pathogen transmissions in healthcare settings occur via close contact, either between healthcare workers (HCW) or between HCW and patients, to visualize and detect those contacts is one of the aims of the research.

The agent-based model is developed by an agent-based simulation language called SOARS (Spot Oriented Agent Role Simulator). An agent is autonomous individual which represents a patient or a visitor, a doctor, a nurse or a hospital staff. Agent is goal-oriented and interacts with other agents in the environment that is called "spot". Virtual agent contamination level and spot contamination are calculated and they decide probability of infection. Infection protection measures taken by agent, such as wearing mask or washing hand are modeled. 4 scenarios of infection control are generated. Simulations are iterated for 30 times and in 30 days. Infection risk of doctors and nurses is observed from simulation results. The "risk graph", which is generated from simulation logs, shows close and frequent contact between doctors, nurses and inpatients. Correlation between list of infected HCW and degree of the nodes in the risk graph has been confirmed. The visualization of risk graph can be a promising method to assess infection risk of HCW in the hospital model. We can highlight and track all contacts of agents in real time. Integration with human real time tracking systems can be potential for tracking and detecting contacts between health care workers or between health care workers and patients.

Although data and knowledge for the model have been constructed based on several field works onsite, due to the lack of statistics data and impossibility of taking those experiments in a hospital, empirical validation of the model could not be conducted. Although there was no observed data fitted the simulation results, outputs are qualitatively similar to observed phenomenon in the real world.

The future work is to integrate real data collecting by sensor to the simulation framework. We have developed and used wireless tracking system to track real-time movement of humans in a building. The real data of movement of patients and health care workers in a real hospital can be achieved using the system. Changing parameters of the disease transition module can be applied to study other infectious diseases. Infection control measures can be changed in many scenarios depending on infection control resources of the hospital. The core module inherits from the current module but can be rebuilt to fit the structure of a new hospital. Simulation output shows real-time graph of the number of hospitalization, infected patient and HCW. By visualizing contact network, close and frequent contact with high-risk patients can be tracked and monitored. Variation of virtual virus contamination level of places and agents can be monitored in real time. The simulation framework could be a potential decision-making support tool for hospital administrators to evaluate nosocomial infection control and it can also be used as an educational tool to study nosocomial infection.

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CHAPTER I: Introduction

Nosocomial infections (infection acquired in hospital) occur worldwide and remain an important issue for management of health-care institutions. They constitute a major source of morbidity and mortality for hospitalized patients. In recent years, the worldwide spread of severe acute respiratory syndrome (SARS) and the 2009 influenza pandemic have highlighted the increasing importance of research in infection prevention and control in hospitals. Computer simulation can be an experimental and educational tool for hospital administrators to test strategies to control nosocomial infections. Recently, using agent-based simulation models to simulate nosocomial transmission is an emerging trend in the research field. These models exploit advantages of agent-based modeling to evaluate the efficiency of infection control measures against nosocomial infection. Although agent-based modeling is still a relatively new methodology and its application to infectious disease control is only introduced recently, it offers many advantages in integrating real data such as electronic medical record information or sensor information.

The main subject of the doctoral thesis is to develop a framework to assess the risk of a highly contagious and mortal influenza-like illness infection to health care workers in a hospital under different scenarios of infection control. The method is to build an agent-based model for simulating infection of the virus in the hospital and use open-source software to visualize a risk graph of infection. The research contributes a novel risk assessment for hospital staff to prepare for influenza pandemic in the future.

The thesis is organized as follows,

Chapter 1 is a brief introduction of the thesis and its structure.

Chapter 2 is the background of the thesis. An introduction of nosocomial infection, types of infection and infection control measure are presented. We make an exclusive review of using computer simulation and network analysis to study infection in hospitals. We briefly represent my research motivation and original approach.

In chapter 3, I represent the methodology of the research. Research objectives and research questions are established. The requirements of the simulation model and the development process are described. The method of calculating infection probability is represented here.

Full descriptions of the simulation model are represented in chapter 4. The simulation model is developed with an agent-based simulation language called SOARS. There are five types of agent, doctor agent, nurse agent, staff agent, patient agent and visitor agent. The modeling of their activity, process of infection is presented in this chapter. We use open-source software to visualize contact network that illustrates contact of agents in the hospital. Several scenarios of infection control are designed to test and evaluate efficiency of those control measures. Specifications of the simulation model, including simulation time, simulation step and other parameters can be found in this chapter. The simulation model can be rebuilt by using the simulation tool and following proper procedures. However, since a significant numbers of probability parameters were embed in the model, appropriate simulation results could only be achieved by running enough number of simulation iteration.

The simulation results and analysis are shown in chapter 5. We demonstrate simulation results by macro and microanalysis. In microanalysis, the number of infected patients and health care workers are observed. Macro analysis is performed by calculating of the amount of virus in spots and in agents. We analyze the contact network, which is

generated by interactions of agents in the simulation. Visualization of contact network, which is called "risk graph", is made to highlight and track all contacts of agents.

Chapter 6 describes data collection method and analysis techniques. Experiments of capturing human movements in a building are demonstrated.

The final chapter contents are conclusion and discussion about limitation and extension of the research. Firstly, I have built a simulation model for infection of an influenza-like illness in an artificial hospital and quantitatively assessed infection risk of the diseases. The simulation results have shed more light on epidemiological belief of that direct patient care HCW have high risk of catching nosocomial influenza virus and that washing hand and wearing mask are effective to prevent an outbreak of the disease in the hospital. Secondly, the methodologies of quantification and visualization the infection risk provided us a potential methodology for risk management in infection control of nosocomial infection. The great advantage of simulation model is that they unable experiments which are impossible or undesirable. It provides a flexibility of changing parameters to apply to other diseases rather than influenza-like illness. The real data of movement of patients and health care workers in a real hospital can be achieved by using wireless tracking systems to track real-time movement of humans. Activity pattern of people can also be collected via activity questionnaire. The simulation framework could be a potential decision-making support tool for hospital administrators to evaluate nosocomial infection control and it can also be used as an educational tool to study nosocomial infection.

CHAPTER II: Background and Literature Review

This chapter describes background of the thesis. In the first part, overview of nosocomial infection, types of infection and infection control measures are presented. The second part is an exclusive review of using computer simulation and network analysis to study infection in hospitals. In the next part of the chapter, I briefly represent my approach and its originality.

2.1 Overview of nosocomial infection

Nosocomial infections, also known as hospital-acquired infections (HAI) can be defined (WHO) [1] as,

> *An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This includes infections acquired in the hospital but appearing after discharge, and also occupational infections among staff of the facility.*

Nosocomial infections occur worldwide both developed countries and undeveloped countries and they represent a major source of morbidity and mortality for hospitalized patients. WHO has conducted a survey of nosocomial infections in 55 hospitals of 14 countries in 4 Regions (Europe, Eastern Mediterranean, South-East Asia and Western

Pacific). The results showed that an average of 8.7% of hospital patients had been infected by HAI. More than 1.4 million people in the world got infected in hospital at any time [1].

Nosocomial infections also cause financial problems for hospital administration. Estimation for the annual direct hospital cost of treating healthcare-associated infections (HAIs) in the United States has shown that overall annual direct medical costs of HAI to U.S. hospitals ranges from $28.4 to $33.8 billion [2].

Influenza A virus is among the most severe and frequent causes of hospital-acquired viral respiratory illness and infects persons in all age groups, especially in patients older than 65 years old and children [3]. Influenza can be transmitted between patients and health care workers (HCW) in the hospital settings. Contact with high-risk patients is an important potential source of influenza exposure for HCW.

2.2 Types of nosocomial influenza infection

In this study, influenza-like illness (ILI) symptoms are defined as fever (>100^{o} F) and cough or sore throat. There are three types of infection relevant to influenza are contact transmission, which are droplet transmission, and airborne transmission [4]. Traditionally, influenza viruses are believed to spread from person to person mostly through droplet transmission. These droplets travel only short distances (< 6 feet) and do not stay suspended in the air. Airborne transmission via small particle may also occur. Those particles, in contrast to droplets, can remain suspended in the air. Another indirect transmission involved with influenza infection is hand transfer from

contaminated surfaces to mucous membrane of nose or mouth. However, the relative distribution of influenza transmission by these three types has not been established yet [10].

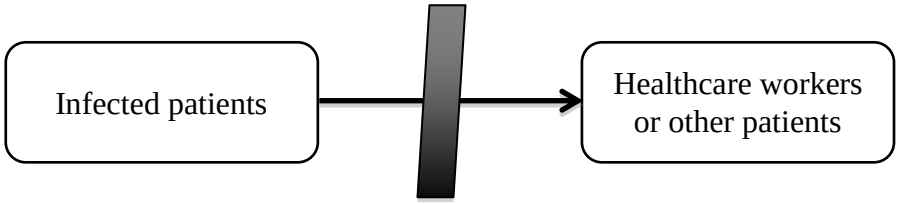
Recently emerged swine influenza (H1N1) continues to spread globally and shows a higher transmission than seasonal influenza [5]. Evidence of human to human transmission has been observed [6][7]. Highly pathogenic avian influenza (H5N1) still exists in poultry worldwide. It rarely infects humans but has mortality of over 60%. Pig is susceptible to both human and avian influenza viruses, so it could serve as a "mixing vessels" in genetic reassortment events [8]. Although the opportunity for genetic reassortment is small, the severity of such rare outcome is a big concern.

In this paper, infection process of the disease is modeled under the following assumptions.

- A novel contagious and deadly influenza-like illness emerges and spreads in a community. It causes an outbreak in the community hospital.
- The virus is transferred via both direct and indirect transmission.
- Influenza virus refers to an acute respiratory virus that causes severe influenza-like illness with cough or sore throat, plus measured fever, shortness of breath and need for hospitalization.
- Current vaccine of seasonal influenza is effective to the new disease.
- Treatment with oseltamivir within 24 hours of hospitalization reduces mortality.

2.3 Nosocomial infection control measures

Transmission of infectious virus within a healthcare setting requires three elements: a source (or reservoir), a susceptible host and a mode of virus transmission. The goal of infection control is to prevent virus transmission from infected patients (source) to healthcare workers or other patients (host).



Infection intervention

Figure 1. Intervention against nosocomial infection

Intervention against nosocomial infection consists of standard precaution and transmission-based precaution [9]. Standard precaution includes control measures which are applied to all patients, while transmission-based precaution is composed of standard precaution and precaution based on virus transmission route. There are three types of transmission-based precaution, corresponding to three types of infection route.

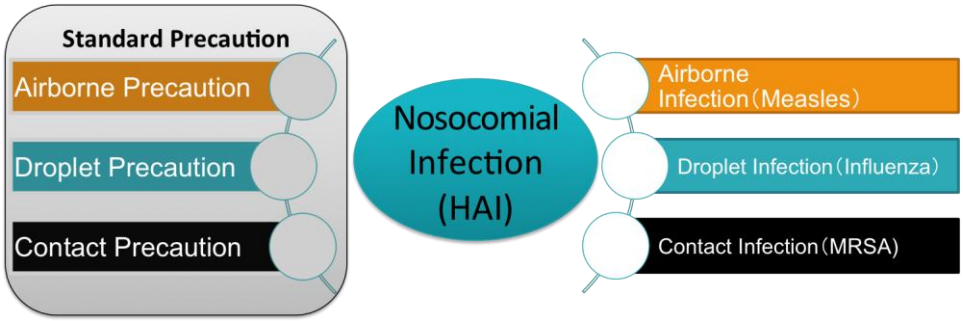


Figure 2. Type of infection, standard precaution and transmission based precaution.

Standard precaution is recommended for the care of all patients. Standard precaution contains a list of basic hygiene measures to prevent contact with moist body surfaces. Use of hand hygiene of healthcare workers is believed to be the most effective control measures of preventing nosocomial infections. It is recommended that washing hands should be taken immediately with soap and water before and after examining patients and after any contact with blood, body fluids and contaminated items. Clean, ordinary thin gloves should be worn if touching blood, body fluids, mucous membrane, and broken skin. Gloves should be changed between tasks or procedures on the same patient. Healthcare workers should wear a mask, protective eyewear and gown during any patient-care activity when there is a risk of splashes or sprays of body fluids. Routine of cleaning and disinfecting touched surfaces including handles, beds, bed rails; patient examination tables and bedside tables should be taken frequently. Clean and disinfect soiled linens should be used to avoid direct contact with items soiled with blood and body fluids. For patients whose blood or body fluids are likely to contaminate surfaces or other patients, private room, if available should be prepared to isolate them from other patients.

In addition to those standard control measures, to prevent influenza infection in health care settings, the US Center for Diseases Control (CDC) recommends vaccination prophylaxis for HCW, with particular emphasis on patient-care staff. Quarantine measures, including HCW washing hands and wearing mask, isolating patients who have symptoms of influenza from the others and restricting hospital visitors are strongly recommended [10].

2.4 Computer simulation of nosocomial infection

In recent years, with the worldwide spread of severe acute respiratory syndrome (SARS) and the 2009 influenza pandemic, research in infection prevention and control in hospitals become increasingly important. Computer simulation can be an experimental and educational tool for hospital administrators to test strategies for controlling nosocomial infections. Mathematical compartmental modeling is still the dominant method for simulating nosocomial infection. Recently, agent-based simulation models raises as a new trend of modeling infection in health care settings. This section reviews computational modeling of nosocomial infection.

Mathematical Models

An early model of spread of infectious disease in healthcare settings was proposed by Massad, *et al* (1993) [11]. Traditional SIR model was used to study spread of resistance against antibiotics in populations of bacterial pathogens. The population is divided to three groups: susceptible, infectious or recovered. The susceptible can be infected by an antibiotic-sensitive strain or a resistant strain. Cross-infection between the two strains is evaluated by an equilibrium analysis to determine which of the strain dominates the competition by the host.

A Monte Carlo simulation model was developed by Sebille, *et al* (1997) to model the spread of antibiotic-resistant bacteria in hospital units [12]. Staff–patient interactions, staff hand washing compliance, admission of colonized patients, and antibiotic use are

represented in the model. Impact of hand washing compliance on colonization has emphasized importance of hand washing in preventing colonization.

A stochastic model is developed by Cooper, *et al* (1999) to model the spread of hand-borne pathogens such in a general medical-surgical ward. The results show that increasing frequency of effective hand washing could bring endemic organisms under control. Under many scenarios, to reduce number of colonized patients appeared to be an effective control. Although to enforce surveillance activities had small effect on the introduction rate, it gave an almost linear reduction in colonized patient-days and ward-level prevalence. Higher successful introduction rates can be achieved by shortening lengths of patient stay. However, short length of stay had small effect on the other control measures unless the mean length of stay was longer than the mean time before detection of a colonized individual.

Cooper and Lipsitch (2004) presented a method for parameter estimation using structured hidden Markov models. The data to be observed is short time series of nosocomial infected patients. The authors argue that it was the first application of using hidden Markov model to study epidemic data, and it showed a high potential of fitting the data [14].

Agent-based Models

Recently, several agent-based simulation models have been used to simulate nosocomial transmission in health care settings. Agent-based simulation or agent-based modeling (ABM) is a systems approach, of which the bottom-up architecture can be used as an efficient tool to get macro-level statistical experiment results from micro-

level evolution of agent interactions. These models have exploited the advantage of agent-based modeling to evaluate the efficiency of infection control measures against nosocomial infection. Although agent-based modeling is still a relatively new methodology and its application to infectious disease control is only introduced recently, it offers many advantages in integrating real data such as electronic medical record information or sensor information. An integration of these real data with ABM shows a high potential of a novel risk assessment for infectious disease control.

Triola, M.M *et al*, use an agent-based, probabilistic model to simulate nosocomial infection in a small size of the medical intensive care unit population (12 patients) [15]. Nurse, patient, pathogen agent and virtual space representing the medical intensive care unit were represented in the model. Observed frequencies of nurse-patient interactions, hand-washing behavior, nursing work patterns, patient admission and discharge rates were included in the model. The model correctly estimated the numbers of patients admitted for the duration of each replication, bed occupancy, nurse-patient interaction frequencies, and hand washing compliance. Hand washing rate of 60% or greater resulted in an R0 of less than one.

An agent-based and spatially explicit epidemiological model was used to simulate the spread of influenza for nosocomial environments with high heterogeneity in interactions and susceptibilities [16]. Data of activity patterns of individuals was collected from a field survey in a ward of a local hospital. The results implied that influenza is typically transmitted through staff and less directly between patients.

Y. Meng *et al* (2007) [17] has developed an agent-based model to study spread of MRSA in a hospital. Several control measures, such as admission and repeat screening tests, shorter test turnaround time, isolation, and decolonization treatment has been

evaluated by model experimentation. The experimental results implied that the use of rapid screening tests with shorter test turnaround time. They concluded that it is the most effective policy to reduce MRSA transmission in the hospital settings.

A recent attempt to develop an agent-based model for simulating spread of influenza virus infection on a layout-based emergency department was taken by Marek Laskowski *et al* (2011) [18]. Twenty different emergency department scenarios with further simulation of four infection control strategies have been analyzed. The results suggest that within the given instance context, patient-oriented infection control tend to have a larger effect than policies that target healthcare workers.

2.5 Network Analysis of Nosocomial Infection

Another systems approach that recently gains a lot of interest in epidemiology is social network analysis [19]. A social network for contacts sufficient to transmit influenza has been constructed and analyzed [20]. The usage of contact network analysis is to capture interactions that cause the spread of diseases [21][22]. Contact network approach is relatively applied in large-scale model (countrywide or global) rather than small-scale model (community, hospital). Especially, relatively little work exists in applying contact network analysis to nosocomial infection.

2.6 Our approach and its originality

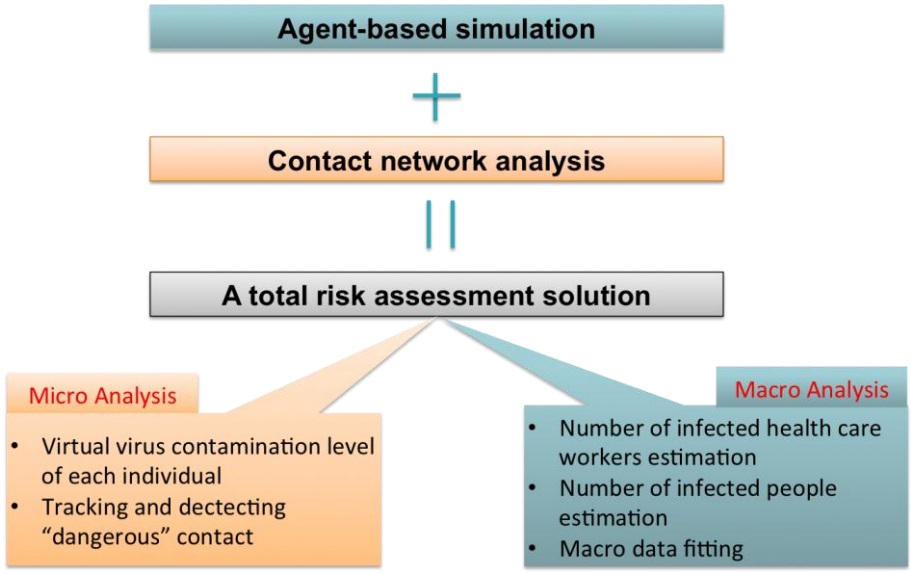


Figure 3. Imagination of the framework.

Figure 3 is an imagination of the simulation framework. There are two main components of the simulation framework: an agent-based model for simulating nosocomial infection and a component of visualizing the contact network generated after the simulation. The advantage of agent-based model is that macro-level statistical experiment results can be achieved from micro-level evolution of agent interactions. On the other hand, network analysis can help to visualize and track micro-level contact between agents. Since most of pathogen transmissions in healthcare settings occur via close contact, either between healthcare workers (HCW) or between HCW and patients, to visualize and detect those contacts is one of the aims of the research. The full description of the research methodology is represented in Chapter 3.

CHAPTER III: Methodology

In chapter 3, I represent the methodology of the research, philosophical context, preceding methodology and my research's position in the research domain. Data collection, data fitting method and analysis techniques are described in this chapter. The method of collecting real data for the simulation model is reported in this chapter. Experiments of capturing human movements in a building are demonstrated here.

3.1 Research objective and question

The research objectives are to develop a framework to assess the risk of a highly contagious and mortal influenza-like illness infection to health care workers in a hospital under different scenarios of infection control.

The research questions are

1) How to apply agent-based model to simulate influenza outbreaks in an artificial hospital?

2) How to set up artificial boundary settings to build an appropriate model of nosocomial influenza infection?

3) How to design scenarios to evaluate infection control measures of nosocomial influenza?

4) How to analyze which contacts of individuals are important factor in nosocomial influenza infection?

5) How to capture and model human activity in a hospital?

3.2 The methodology

The motivation of the research is to develop a framework that can be a decision-making support tool for hospital administrators to evaluate nosocomial infection control and it can also be used as an educational tool to study nosocomial infection. The stakeholders involved in the problem of nosocomial infection are hospital administrators, direct patient care staffs (doctor and nurse), other healthcare workers, public health officers, policy makers and so on. Since multiple-parties have different views and perspectives, to solve the problem may require the understanding of the other parties' perspectives. Therefore, the simulation framework should be a tool to promote communication among those stakeholders.

In order to be used both as a communication assistant tool and decision-making support tool for nosocomial infection control, the model must have some following properties.

- The representation of the model should be clear and easy to understand. Patient, doctor and nurse location and movement should be described properly.

- Since behavior of individuals in the hospital is heterogeneous. The model should have the capability of adapting behavior rules of individuals to the changing of their surroundings.

- Individuals' interactions, which result in infection, should be modeled completely. Since the infection control measures' purpose is to reduce the infection risk of individuals in the hospital, the effect of those control measures should be modeled properly.

- Simulations results should be presented clearly and visually. The dynamic of the epidemic should be observed from the simulations results. The efficiency of infection control measures should be interpreted from simulation results.

- Since most of pathogen transmissions in healthcare settings occur via close contact, either between healthcare workers (HCW) or between HCW and patients, visualization or tracking those contacts is a key property that the model should have.

Agent-based modeling (ABM) can meet those requirements. However, agent-based modeling is at a relatively young age of the methodology, it needs a standardized research process.

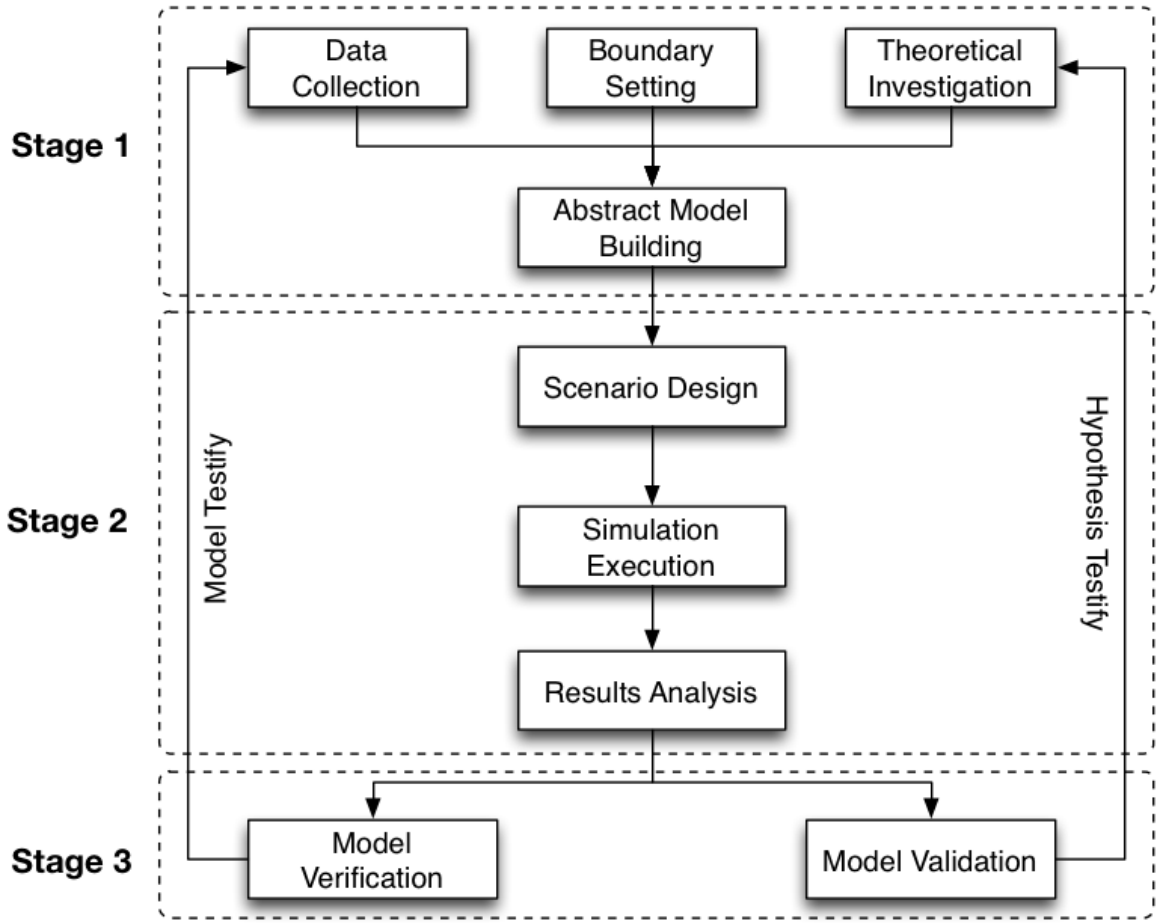


Figure 4. Research methodology and procedure.

Figure 4 illustrates the simulation development procedure. The first stage of building the model is field and theoretical investigation based on boundary setting of the research question. We conduct investigation on existing theory of nosocomial infection. Two field trips to the source (a national hospital in Vietnam, in March 2010 and April 2011) give us hints of what factors are important in the model. The model is an abstraction of a hospital in Vietnam and the scenarios, which are designed in second stage, are possible scenarios of influenza infection in the hospital. The third stage composes of model verification and validation processes. Model verification is the process of confirming that the simulation results are reasonable. On the other hand, model validation is the process of checking model's validity, that is, whether it is a

good model of what it purports to represent. The goal of model validation is to make to model useful in sense that it supports to testify the formulated hypothesis. The model verification and validation are important processes in development of agent-based models [23][24].

3.3 Preceding models

The simulation model inherits infection modeling of influenza from the following referred models [25] - [34].

The calculation of infection probability based on the interactions of agents within the environment is described below. Let's have a set of agent *i* who exits in a set of location (which is called "spot") *k*. Define Agent Virus Excretion Level (*AVEL*) of agent *i* at time *t* ($0 \leq AVEL[i](t) \leq 1$) as scale of virus excretion of the agent at the specific time. This parameter depends on the disease state of the agent. Define Agent Hazard Level of an agent *i* at time *t* ($AHL[i](t)$) as the amount of virus excretion of the agent into the environment at the specific time. Then,

$$AHL[i](t) = AVEL[i](t) \times VEP[i](t) \quad (1)$$

, where Virus Excretion Protection ($0 \leq VEP[i](t) \leq 1$) represents the effects of protection measures (e.g., mask wearing) on virus excretion of the certain infected agent. The smaller *VEP*, the more effective the protection measure is. Define Spot Contamination Level $SCL[k](t)$ as the level of virus contamination of a spot *k* at time *t*. Contamination level of the spot in the certain time *t* is the sum of total amount of virus excretion of agents in the spot and the contamination level of the spot at time $(t - 1)$.

$$SCL[k](t) = \sum_{i \in Spot[k]} AHL[i](t) + SCL[k](t-1) \times SSL[k](t) \quad (2)$$

, where Spot Sterilization Level ($0 \leq SSL[k](t) \leq 1$) represents the effects of attenuation and sterilization on the certain spot. The smaller *SSL*, the more effective the protection measure is.

Define Agent Contamination Level $ACL[i](t)$ as the amount of virus that an agent i has absorbed from the spot k where he stands at the specific time t.

$$ACL[i](t) = ACL[i](t-1) \times AF[i](t) + SCL[k](t) \times VD[k] \quad (3)$$

, where Attenuation Filter ($0 \leq AF[i](t) \leq 1$) represents the effect of attenuation protection on infection (e.g., hand washing) and Virtual Density ($0 \leq VD[k] \leq 1$) represents the density of the spot k (the bigger place, the smaller *VD*).

When an agent i at time t absorbs a significant amount of influenza virus, he will be infected and his state will change from susceptible to infected. The probability of agent i at the time t to get infected is calculated as below.

$$p[i](t) = 1 - \exp[-PC[i](t) \times ACL[i](t)] \quad (4)$$

, where $PC[i](t)$ is the Physical Condition of agent i at time t ($0 \leq PC[i](t) \leq 1$). Physical condition depends on vaccination status, heath condition, age, and sex. The healthier agent (smaller *PC*), the smaller infection probability is. If the agent is immune to the virus, *PC* is equal to 0, which means probability of infection is equal to 0.

Pathological transition of the disease is described in Figure 5. Infection levels were categorized and defined into several states below.

- State of "0" denotes pre-infection state (susceptible to infection).

- State of “1” represents state of infection. Agents stay in this state for 3 days. This is the incubation period of the disease.

- State of “2” is designated as infection state with apparent symptoms. The probability of changing state from “1” to “2” is 0.8.

- State of “2m” represents the mild case of infection. The sequence 2m→3m→5 →0i represents state transition of recovering without apparent symptoms. The sequence 2→3→5→0i describes state transition of recovering with apparent symptoms.

- State of “3s” denotes serious case of infection. The symptoms are severe influenza-like illness with cough or sore throat, plus measured fever, shortness of breath and need for hospitalization.

State of “4c” represents critically ill infection state. For patients in this state, clinical treatment in the hospital helps them to recover. The sequence 4c→4m→5→0i describes the recovering route. Inpatients at the state of “5” are recommended to discharge from hospital.

Figure 5 shows pathological state transition of influenza with clinical treatment. It is a modification of the pathological transition model presented in the paper [30] (*page 11, figure 4*).

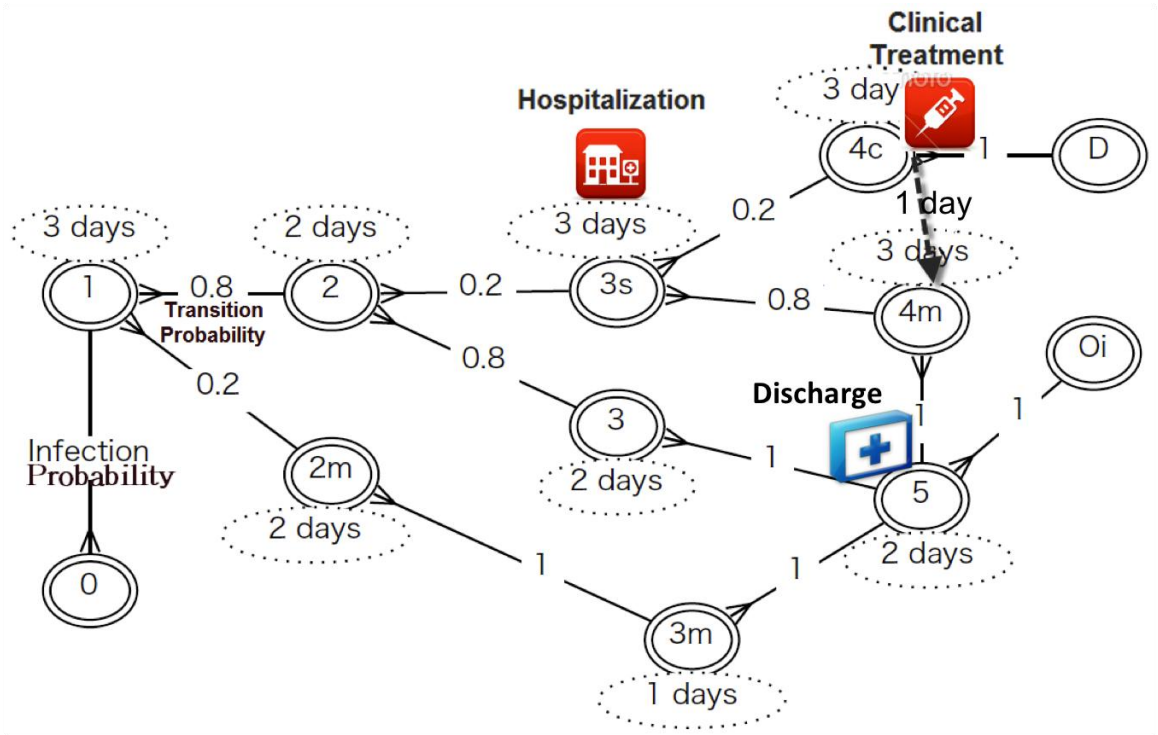


Figure 5. State transition of influenza-like illness with high contagion, high mortality and clinical pathway for infected patient.

Table 1 describes the disease states and values of Agent Virus Excretion Level (AVEL). These values are assigned in corresponding to definition of the disease states. It is believed that influenza virus can be transmitted from infected people to others from 1 day before symptoms develop and up to 5 to 7 days after becoming sick (CDC).

Table 1. Disease state definition and value of Agent Virus Excretion Level (AVEL)

State	Definition	Fever	*AVEL*
0	Not infected	No	0.0
1	1^{st} state	Little	0.2
2	2^{nd} state	High	0.6
2m	2^{nd} mild state	Little	0.4
3	3^{rd} state	Little	0.6
3m	3^{rd} mild state	Little	0.5
3s	3^{rd} serious state	High	0.6
4c	4^{th} critical state	High	0.5
4m	4^{th} mild state	Little	0.5
5	Recovered state	No	0.0
0i	Recovered with	No	0.0
D	Death	No	0.0

CHAPTER IV: Simulation Model

Full descriptions of the simulation model are represented in this chapter. The simulation model is developed with an agent-based simulation language called SOARS (Spot Oriented Agent Role Simulator) [35][36][37]. The hospital model is a spatial representation of a hospital. There are five types of agent, doctor agent, nurse agent, staff agent, patient agent and visitor agent. Their behavior rules are modeled by a set of movement rules inside the abstracted hospital. Contacts of the agents while moving are captured and a network of contacts is generated. We use Gephi [38][39] , an open-source software for visualizing and analyzing large networks graphs, to visualize contact network. Several scenarios of infection control are designed to test and evaluate efficiency of those control measures. Specifications of the simulation model, including simulation time, simulation step and other parameters can be found in this chapter. The simulation model can be rebuilt by using the simulation tool and following proper procedures. However, because of a significant numbers of probability parameters were embed in the model, appropriate simulation results could only be achieved by running enough number of simulation iteration.

4.1 Hospital model

Representation of hospital

Figure 6 describes the organizational structure of a typical hospital. The hospital consists of a reception desk, a waiting room, a consultation room, a laboratory, a dispensary, a nurse station, a staff room, a doctor room, a locker room, 4 wards and 3 toilets. There are 18 nurses working in 3 shifts a day, 7 doctors working in rotation, 1 clerk, 1 receptionist, 1 examiner, 1 dispenser, 1 cashier and 1 cleaner staff. Agents' activity pattern is described in Figure 7.

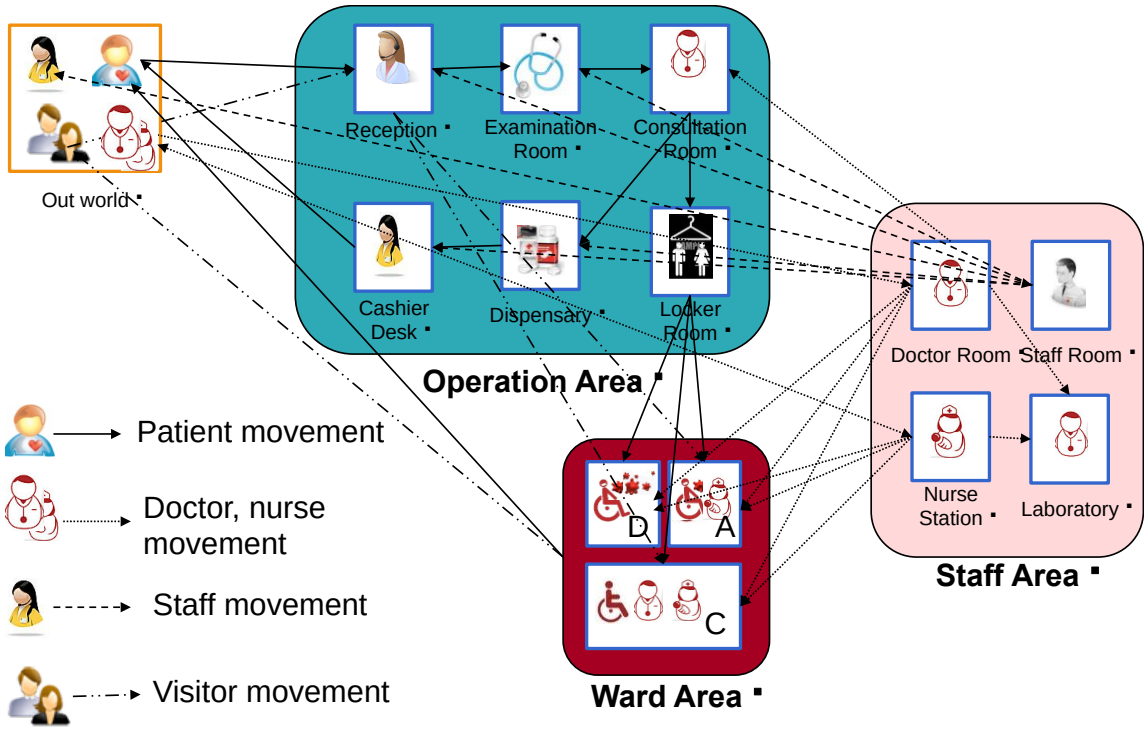


Figure 6. Structure of an artificial hospital.
Arrows illustrate movement directions of agents in hospital.

The model is built by an agent-based simulation language called SOARS (Spot Oriented Agent Role Simulator) [35][36][37]. There are three main elements in SOARS, the

“agent”, the “spot” and the “role”. These elements are described in the following sections.

Representation of spot

In SOARS, “spot” is a virtual space for agents to interact each other. Agent interacts to the others at the same spot by exchange his variables with the spot’s variables. In that manner, infected patient excretes influenza virus into the environment (the spot I he lives in) and then the other patients who are in the same spot can catch virus from the contaminated spot. The method of modeling infection process is described in 3.3 Preceding models.

Table 2 shows the variables of Ward A spot. A spot can carry a “role”, which is named “spot role” in SOARS. Spot role is a set of rules for spot behaviors. Naturally, spots cannot move, so they don’t have movement behavior like agents. As mentioned above, interactions between agents can only be made by exchanging variables between agent and spot. Therefore, spot has to carry some common variables with agent for exchanging variables. For instant, variables of AHL and AHL_temp in the table below are used to exchange data with agents. The rules of exchange data are written in spot role.

Table 2. Variables of a spot.

Basic Variables			
Name of spot			Ward A
Number			1
Initial Role			WardA_Role
Collection Variable			
agent_list			List of agents exist in the spot at the time
Number Variable			
Name	*Type*	*Value*	*Comment*
AHL	real number		Agent Hazard Level
AHL_temp	real number		Agent Hazard Level temporary variable
Num_of_Bed	integer		Number of beds
SCL	real number		Spot Contamination Level
SSL	real number		Spot Sterilization Level
VD	real number		Virtual Density for each place (Depend on size of the place, ...)

There is a special spot in the model, the “Data” spot. Table 3 describes variables of “Data” spot. The role of “Data” spot is to store parameters for experiments and to calculate output variables, as well as intermediate results of the simulation. By integrating data of the simulation in one spot, the model is more flexible in changing parameters for simulation.

Table 3. Variables of "Data" spot.

Basic Variables		
Name of spot	Data	
Number	1	
Initial Role	Data_Role	
Probability Variable		
Name	***Value***	***Comment***
Prob_Hospitalization	$Prob_Hospitalization	Probability of agents to go to hospital for health care service
Prob_Visitor	$Prob_Visitor	Probability of agent to go to hospital to visit acquaintances
List Variable		
Name		***Comment***
Contaminated_Place		The list of place where nosocomial infection occurred

HCW_Death_List	List of dead HCW by nosocomial infection
HCW_Infected_Place_List	List of spots where HCW get infected
HCW_Emergency_List	List of HCW who has high fever
Infected_HCW	List of infected HCW
Patient_DeathList	List of dead patient by nosocomial infection
Patient_Death_Place_List	List of spots where patient get infected

Keyword Variable

Name	*Value*	*Comment*
HandWashing	$HandWashing	Hand hygiene control measures. If agent use soap and water then the keyword is set to "Yes". If no treatment is being taken, then the keyword is "No". In the case of washing hand with alcohol-based hand rubs, then the keyword is "Limited".
IsolationPolicy	$IsolationPolicy	Isolation of influenza inpatients from inpatients of the other diseases. If the policy is applied then the keyword is "Yes". If is not, then "No"
Mask	$Mask	If mask is not worn then the keyword is "No". "Surgical" and "N95" stand for wearing surgical mask or N95 mask, respectively.
ReinforceSterilization	$ReinforceSterilization	Reinforce sterilization for high contaminated places (Wards and waiting room) by HPV decontamination. Keyword variables are "Yes" or "No".
SterilizationPolicy	$SterilizationPolicy	Keyword for environmental infection control. If the spot is cleaned then the keyword is "Yes". If not then "No".

Number Variable

Name	*Type*	*Value*	*Comment*
ACL_doctor_nurse	real number		Average level of contamination of doctors and nurses
ACL_doctor_nurse_temp	real number		Temporary variable for calculating ACL_doctor_nurse
ACL_patient	real number		Average level of contamination of patients
ACL_patient_temp	real number		Temporary variable for calculating ACL_patient
ACL_staff	real number		Average level of contamination of the other HCW, except doctors and nurses
ACL_staff_temp	real number		Temporary variable for calculating ACL_staff
inf_HCW	integer		Number of health care worker infected
inf_patient	integer		Number of patient infected
num_ILI	integer		Number of ILI cases diagnosed
num_dead_HCW	integer		Number of HCW dead
num_dead_patient	integer		Number of patient dead
num_discharge	integer		Number of people discharge from hospital
num_hospitalization	integer		Number of patient going in hospital
num_inpatient	integer		Number of patient staying in wards
num_inpatient_influenza	integer		Number of patient staying in wards
num_inpatient_others	integer		Number of patient staying in wards
num_visitor	integer		Number of visitors to ward
time	real number		Time (by days)
vaccine_stock	integer		Number of vaccine dose in stock

Representation of agent

Table 4 shows parameters of a patient agent. Patient agent caries a list of common variables. However, patient in different age group has different "role" variable. In SOARS, "role" is a set of behaviors of agents. An agent can only execute a role at one time. However, he can change role to another one as assigned. Role can be inherited. For instant, if I want a patient agent to wear a mask when he enters the hospital, then I can have the agent's role inherit a wearing mask role, which is a set of rules of wearing mask. In that manner, I can apply infection control measures to a group of agents all together at once. The hierarchy of agent roles is shown in Figure 8.

HCW agent and visitor agent has the same common variables, plus some special variables for their distinguished behavior. For instance, nurse agent has a time variable to set the time for routine shift or visitor agent has a list of spots that they are allowed to move in the hospital.

Table 4. Parameters of patient agent.

Basic Variables		
Name of agent	Teenager	
Number	1650	
Initial Role	Teenager_role	
Initial Spot	Outworld	
Probability Variable		
Name	***Value***	***Comment***
AttackRate	0.010	Attack Rate (Variety in age group)
ProFemale	0.48	The proportion of sex
Prob_vaccine	0.5	Probability of being vaccinated
p12	$p12	Probability of developing influenza symptoms
p23	$p23	Probability of recovery without serious symptoms
p3s4m	$p3s4m	Probability of recovery with serious symptoms

Collection Variable

agent_list	List of contact agents at the time

Keyword Variable

Name	Value	Comment
AgeGroup	Teenager	Age Group Keyword (Child, Teenager, Adolescent, Adult, Middle-aged, Elderly)
Fever	No	No or Little or High
Immunity	F	Immunity State (T,F)
Influenza_State	0	Influenza State (0,p0,0i,p0i,1,p1,....)
Job	People	Type of agent (HCW or People)
OtherDisease	F	State of being sick by other diseases (not influenza)
Pandemic_Influenza	F	Pandemic Influenza (T,F)
Sex	M	Sex (Male(M) or Female(F))

Number Variable

Name	***Type***	***Value***	***Comment***
ACL	real number		Agent Contamination Level
AF	real number		Attenuation Filter
AHL	real number		Agent Hazard Level
AVEL	real number		Agent Virus Excretion Level
FP	real number		Fitting parameter for physical condition
P	real number		Probability of Infection = 1- exp[PC*(-ACL]
PC	real number		Physical condition
SCL	real number		Spot Contamination Level (of the spot where agent exits)
VEP	real number		Virus Excretion Protection

Role Variable

Current_role	Current role

Time Variable

Name	***Value***	***Comment***
Consulting_Time	0:00	Time to consult with doctor
Examination_Result_Waiting_Time	0:00	Time to get examination result
Examination_Time	0:00	Time to have examined
Hospitalization_Time	0:00	Time spent in hospital ward
Visiting_Time	0:00	Time to visit an acquaintance in hospital

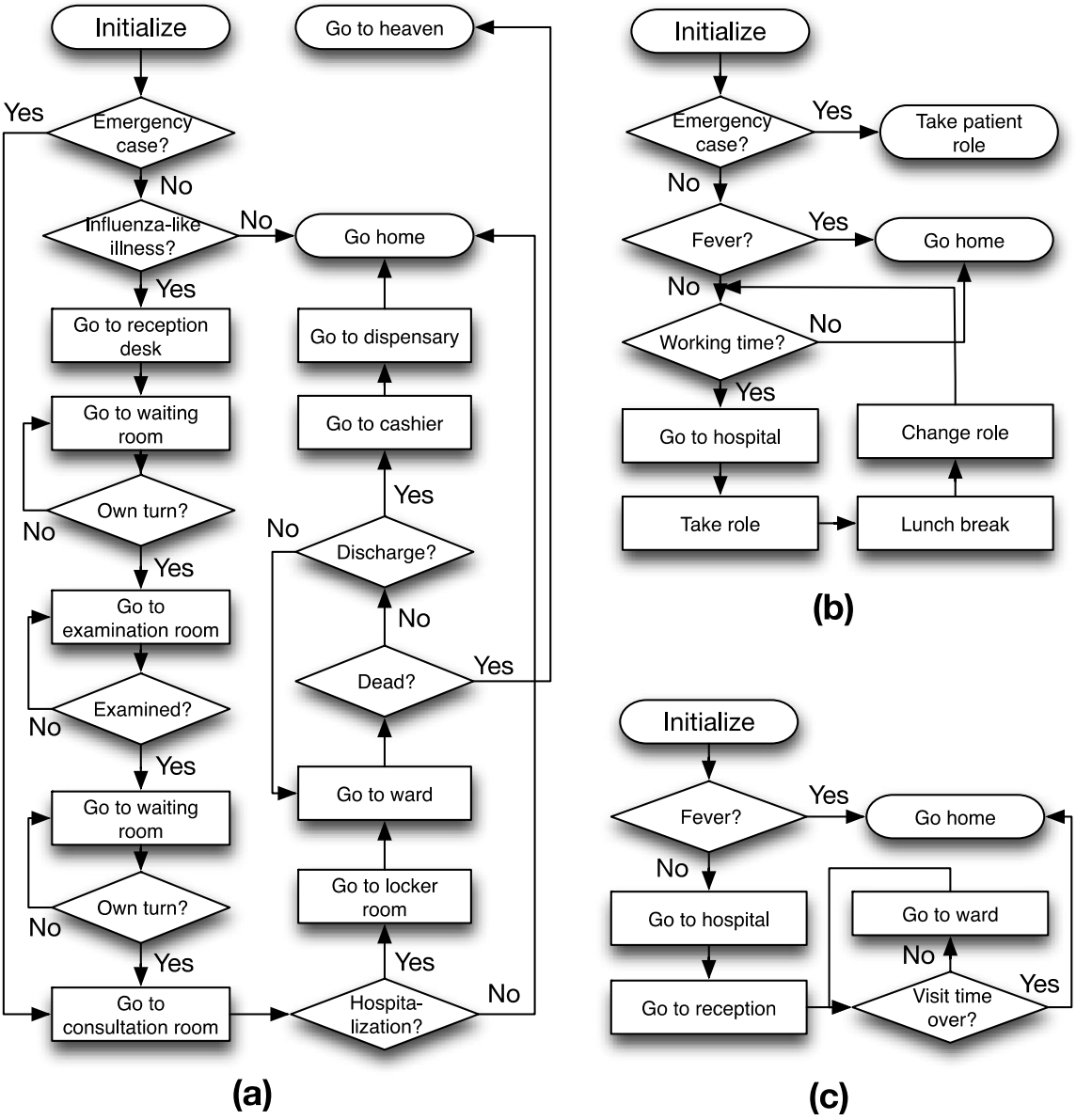


Figure 7. Flowchart of movement of patients (a), healthcare workers (HCW) (b) and visitors (c) in the hospital.

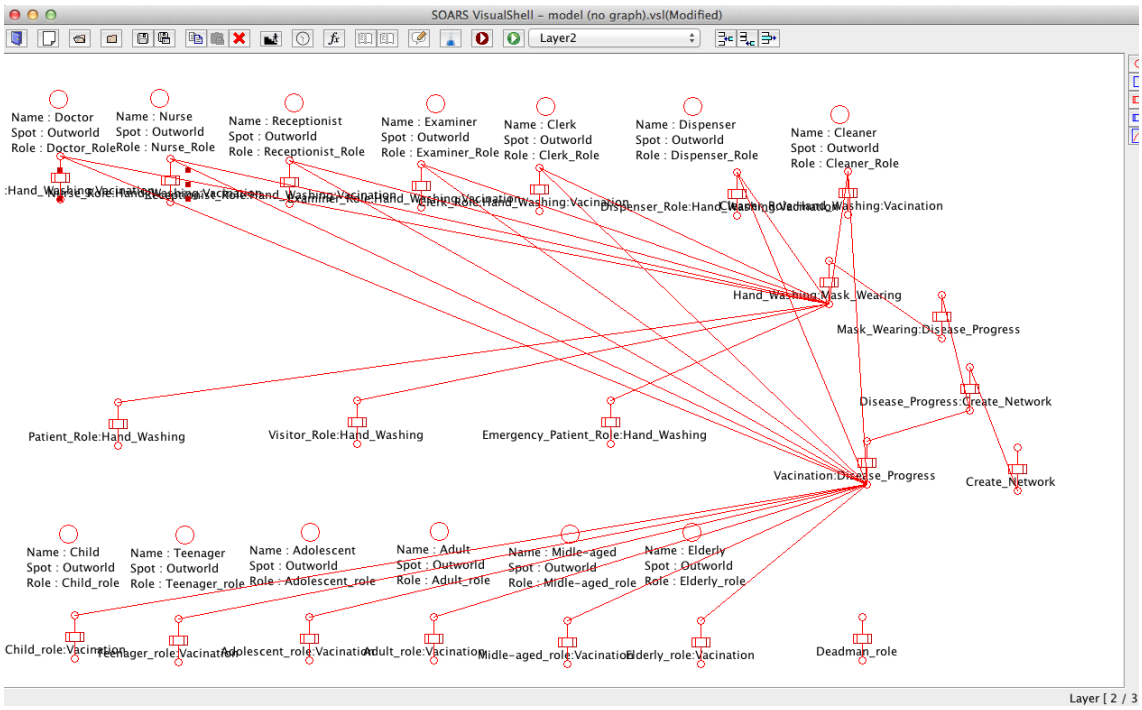


Figure 8. Agent roles and the hierarchy.

Step and stage

In SOARS, simulation procedure is executed in time step. Time step can be set from 1 second to 1 day. In each time step, the simulation executes all agent roles and spot roles at once in a sequence of "stage". There are 3 types of "stage": initial stage, main stage and terminate stage. In each stage, for each agent and spot, only one action in the set of action rules can be executed. Stage and its description are shown in Table 5.

Table 5. Stage and description.

Initial Stage		
No.	***Name of Initial Stage***	***Comment***
1	Agent_Init	Initialize agents' variables
2	WorkPlace_Init	Initialize spots' variables
3	Epidemic_Init	Initialize variables of the epidemic
4	Epidemic_Init2	Initialize variables of the epidemic
5	Vaccine_Init	Initialize variables of vaccine campaign
Main Stage		
No.	***Name of Main Stage***	***Comment***
1	Check	Check people already dead or not

2	ClearAgentList	Clear the agent list of spot and agent
3	ClearAHL	Clear agent hazard level at each step
4	Patient_Isolation	Isolate patients of severe influenza
5	Patient_Init1	Initialize variables for patient of other diseases
6	Patient_Init2	Initialize variables for influenza patient
7	Patient_Init3	Initialize variables for emergency patient
8	Visitor_Init	Create a list of visitors
9	HCW_Init	Initialize hospital health care worker
10	HealthCheck_HCW	Check health condition of HCW
11	HandWashing	Apply hand washing infection protection policies to HCWs
12	MaskWearing	Apply mask wearing infection protection policies to HCWs
13	calc_AVEL	Calculate Agent Virus Excretion Level (AVEL)
14	calc_AHL	Calculate Agent Hazard Level (AHL)
15	calc_SCL	Calculate Spot Contamination Level (SCL)
16	calc_Prob_Infection	Calculate probability of infection
17	update_ADS	Update Agent Disease State (ADS)
18	Move	Execute rules of movement of agent
19	Create_Network	Update contact list of agent and spot
20	Remedy	Medical treatment stage
21	Update_Data	Update data spot's variables
Terminate Stage		

Figure 9 is flow chart of procedures of the simulation model. At the first step of the simulation, the initialization of the agents, the hospital, and the vaccine stockpile is set for each simulation. In each following time step, the simulation runs procedures of disease progress, movement of the agents and updates epidemic data of influenza transmission within the hospital. The simulation will stop if the number of dead agent exceeds number of agent or simulation time reaches the set up time of simulation.

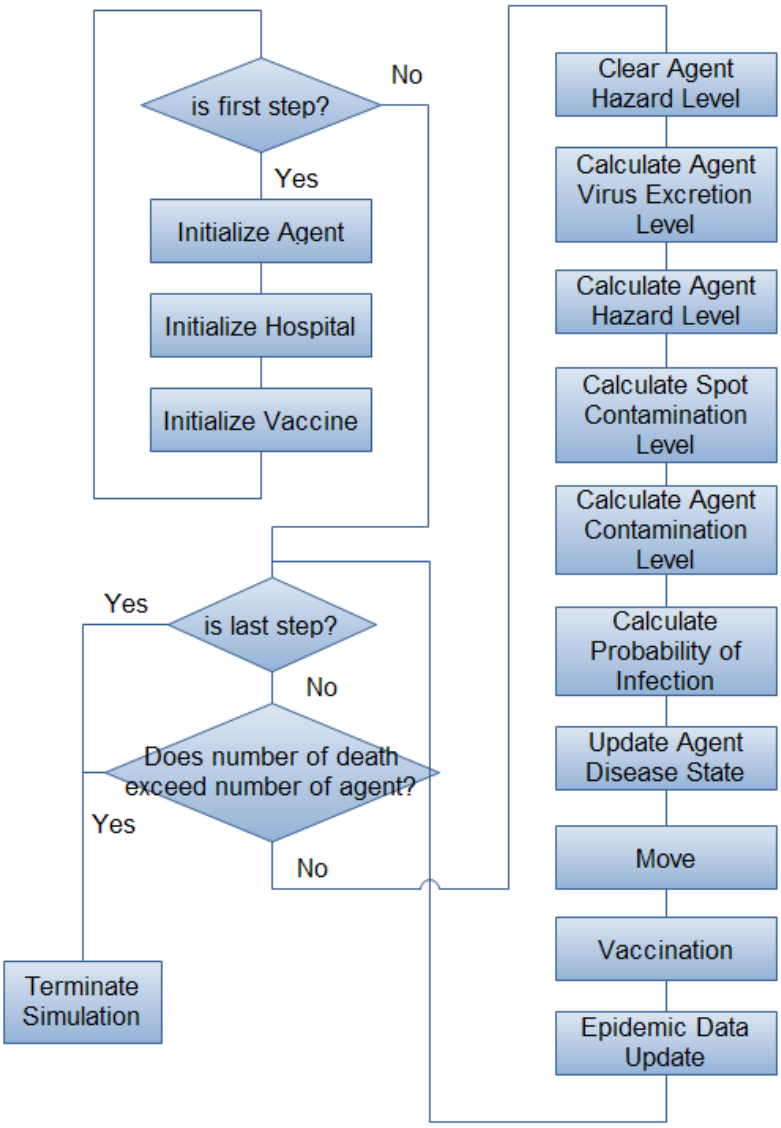


Figure 9. Step and stage in simulation

4.2 Simulation parameters

Parameters of hospital model

Simulation parameters are summarized in. Simulation is executed in 30 days. Simulation is iterated in 30 times to produce small enough standard deviation. The simulation program generated 30 files of each log files. The log files contain information on each agent and each spot at each hour. The information on each agent included name, job, disease status, immunity status, influenza virus contamination level, probability of infection, etc. The information on each spot included the level of contamination. Simulation log files also included the numbers of outpatients, inpatients, number of infected HCW, number of visitors, list of infected HCW, list of contacts of each agent, etc.

Since the model is an abstraction of a hospital in Vietnam, city population structure parameters are extracted from health and population statistic data of Vietnamese General Statistic Office [40].

Table 6.Description and value of simulation parameter

Simulation parameters		
Simulation time	30 days	
Simulation replication	30 times	
Time step	10 min	
Log time	1 hour	
City population structure		
Total population	10,000 people	
Age distribution	Proportion	% Female
Child: 0- 4 y/o	8.5	47
Teenager: 5- 14 y/o	16.5	48
Adolescent:15-19 y/o	10.2	48
Adult: 20- 34 y/o	26.0	49
Middle- aged: 35-59 y/o	29.9	51
Elderly: Over 60 y/o	8.9	60
Hospital structure		
Number of doctors	7	
Number of nurses	18	
Number of beds	28	
Number of outpatient	Average of 60/day	
Number of visitor	Average of 20/day	

Parameters of infection control measures

Preventing transmission of influenza virus within healthcare settings is important for hospital management. Spread of influenza virus can occur among patients, HCW, and visitors; in addition, HCW may acquire influenza from persons in their household or community. The fundamental elements of nosocomial influenza infection control include influenza vaccine campaign, respiratory hygiene, monitoring HCW's health, droplet precautions, hand hygiene, environment sterilization and managing visitor access and movement within the facility [41].

Values of parameters for infection control measures are shown in Table 7. Vaccinating children, adolescents, and young adults seems to be an appropriate vaccination strategy to reduce morbidity of the disease [42]. Based on studies of efficacy comparison of several hand hygiene products and masks [43][44], I set values for hand hygiene and droplet precaution control measures. Biological efficacy and rate of recontamination (parameter *SSL*) is adopted from [45][46].

Table 7. Description and value of infection control parameter

Infection control description	
Vaccination Target	(Probability of vaccination)
Child	0.30
Teenager	0.50
Adolescent	0.20
Adult	0.20
Middle-aged	0.15
Elderly	0.10
Vaccinated Population	(Percentage of population)
High	20%
Medium	10%
Low	05%
Mask wearing	(Value of *VEP*)
N95 mask	0.1
Surgical mask	0.5
No mask	1.0
Hand Hygiene	(Value of *AF*)
Soap and water	0.62
Alcohol-based hand rubs	0.73
No treatment	1.00
Environmental Infection Control	(Value of *SSL*)
After HPV decontamination	0.03
After cleaning	0.40
No cleaning	0.60
Monitor and manage ill healthcare personnel	Not to go to work, or if at work, to stop patient-care activities, leaving work
Patient isolation	Isolate critical influenza patients from patients of other diseases and from visitors
Manage visitor access	Limit visitors' access. Check visitors' temperature before entering the hospital

4.3 Scenario setting

To study the impact of infection control on nosocomial infection, I vary parameters of infection control in 4 scenarios. Parameters for the four scenarios are summarized in Table 8. High Control and High Vaccine scenario represents for the circumstance of hospital with high resource of infection control and vaccination rate in the community is high. Scenario of Low Control and Low Vaccine represents the circumstance of hospital with low level of infection control and vaccination rate in the community is low.

Table 8. Infection control parameter of four scenarios

Scenario Name	**A**	**B**	**C**	**D**
Infection Control	High Control	High Control	Medium Control	Low Control
Vaccinated Population	High Vaccine	Medium Vaccine	Low Vaccine	Low Vaccine
Hand Washing	Soap & water	Soap & water	Alcohol-based	No
Mask	N95	N95	Surgical	No
Patient Isolation	Yes	Yes	No	No
Cleaning	Yes	Yes	Yes	No
HPV Decontamination	Yes	Yes	No	No
Vaccinated Population	2000 (20%)	1000 (10%)	500 (5%)	500 (5%)

Another 3 scenarios were designed to study impact of staff washing hand and wearing mask to number of infected HCW. The parameters are shown in Table 9.

Table 9. Infection control parameter of additional scenarios.

Scenario Name	**E**	**E – washing hand**	**E – wearing**
Hand Washing	Soap & water	No	Soap & water
Mask	Surgical	Surgical	No
Patient Isolation	Yes	Yes	Yes
Cleaning	Yes	Yes	Yes
HPV	No	No	No
Vaccinated	300 (3%)	300 (3%)	300 (3%)

CHAPTER V: Simulation Results

In this chapter, simulation results are presented in two perspectives: macro-level and micro-level. In micro analysis, the number of infected patients and health care workers are observed. Macro analysis is performed by calculating of the amount of virus in spots and in agents, respectively. One of the characteristics of agent-based simulation is that macro-level statistical experiment results can be achieved from micro-level evolution of agent interactions. In this chapter, the relation between simulation results in micro-level and macro-level is discussed.

We analyze the contact network, which is generated by interactions of agents in the simulation. Visualization of contact network, which is called “risk graph”, is made to assess the risk of infection in HCW.

5.1 Macro Analysis

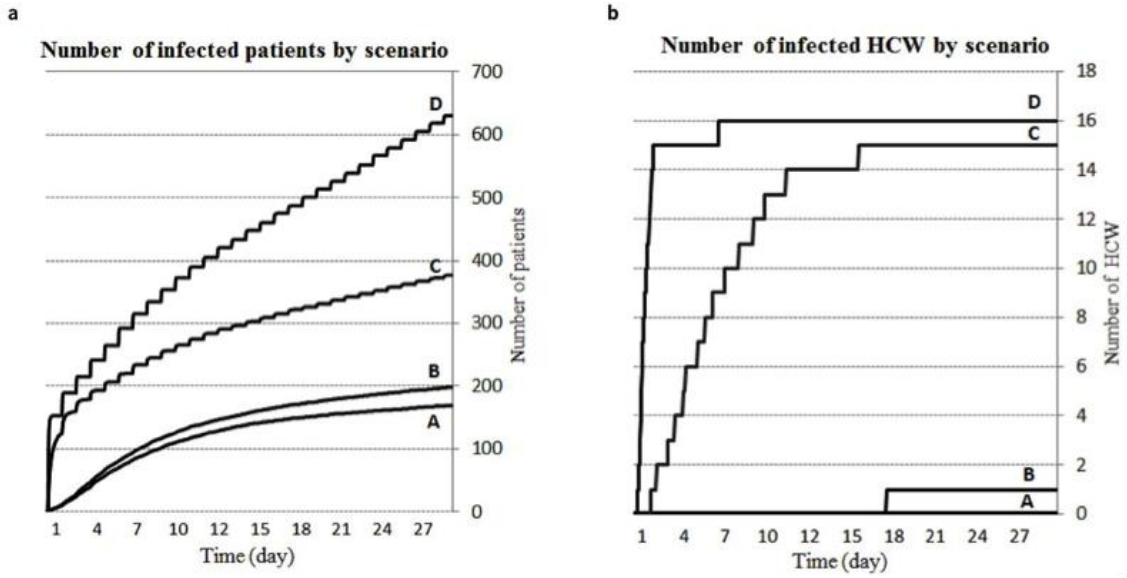


Figure 10. Variation in average number of infected patients and health care workers (HCW) over time in the four scenarios.

The aggregate number of infected patients and HCW are displayed in Figure 10a and Figure 10b, for each scenario A, B, C, D. In the Figure 10a, the number of infected patients increases rapidly from 168 in scenario A and 198 in scenario B to 377 in scenario C and to 630 patients in scenario D. The relative standard deviations differ from one scenario to another, but converge around 10% in 30 days. The number of infected patients shows an increasing trend after 30 days, however with a considerably lower speed as compared to the high increasing rate at the early stage of the simulation. The infected rate among outpatients for each scenario A, B, C, D is 9%, 11%, 24% and 39%, respectively (the average number of outpatients in scenario A, B is 1800 and in scenario C, D is 1600, respectively). Note that the simulation model counts the number

of people who get infected within the whole hospital, so these ratios indicate the infection risk level for every patient who is present at the hospital.

In the Figure 10b, the average number of infected HCW increases dramatically from 0 and 1 in scenario A and B to 15 and 16 in scenario C and D. The relative standard deviations of number of infected HCW in scenario A and B were not calculated (since the average number is between 0 and 1). The relative standard deviation of number of infected HCW in scenario C and D converges at 14% and 17%, respectively. The number of infected HCW sees an exponential increase in scenario C and D within 2 weeks but levels off afterwards. The infection rate among HCW is 0%, 3%, 50% and 53% in scenario A, B, C and D, respectively. The simulation results imply that infection control plays a significant role in protecting HCW from nosocomial influenza infection.

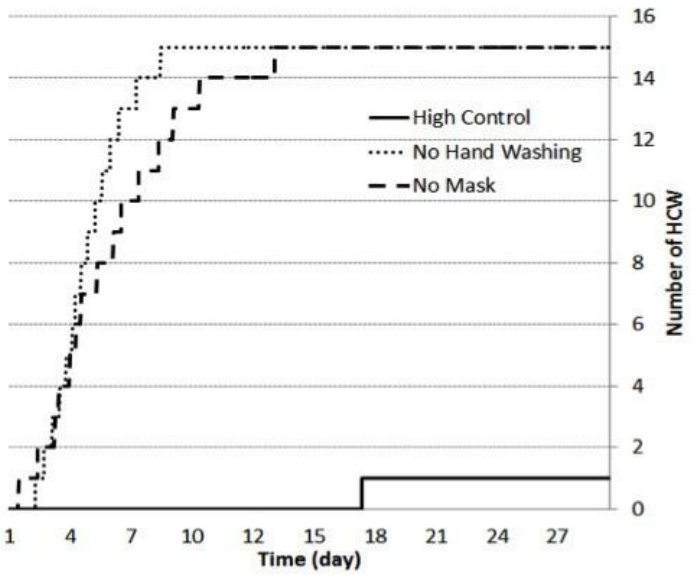


Figure 11. Variation in average number of infected health care workers (HCW) over time in scenario E, scenario E with no staff washing hand and scenario E with no staff wearing mask.

To shed more light on which infection control has the most impact on preventing nosocomial influenza in HCW, I have simulated three more scenarios. In these scenarios, same low vaccination rate (3%) was set. In scenario E, high infection control

measures were implemented. In scenario “E − washing hand” and “E − wearing mask”, staff washing hand and wearing mask were excluded, respectively (See Table 9). The number of infected HCW in each scenario is shown in Figure 11. The result shows that staff washing hand combining with wearing mask could significantly reduce the number of infected HCW.

Although washing hand and wearing mask control measures were recommended worldwide, the extent to which these measures can help prevent influenza transmission has not been firmly established. Recent studies have evaluated the efficiency of those control measures [47][48]. The authors agree with the suggestion that use of masks should always be paired with regular hand washing. In the circumstance of limited vaccine availability, using surgical mask and washing hand with soap, which are relatively inexpensive and practical, could be a good strategy in nosocomial influenza infection.

5.2 Micro Analysis

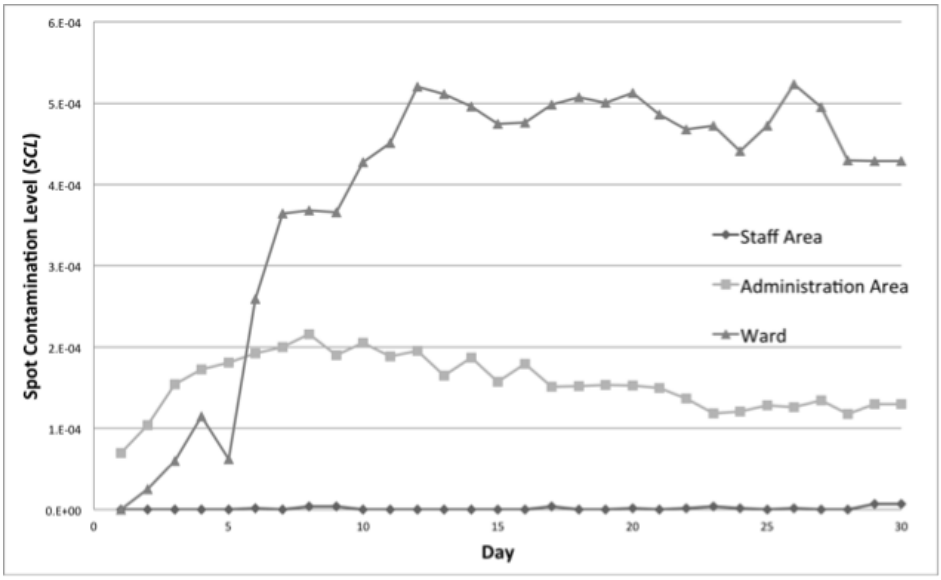


Figure 12. Variation of Virus Contamination of areas in the hospital in scenario A

In page 18, I have demonstrated the algorithm to calculate the amount of virtual influenza virus existing in spot and agent. Spot Contamination Level (*SCL*) at the certain time t is the sum of total amount of virus excretion of agents in the spot and the contamination level of the spot at time ($t - 1$). It depends on the number and the disease condition of infected agents existing in the spot. Figure 12 shows the average contamination level of Ward area, Administration area and Staff area in scenario A of High Control and High Vaccine. The results show that the Ward area is the most contaminated area. The Administration area ranks the second while the Staff area is almost clean. The result implies that wards in hospital are likely contaminated with influenza virus when an outbreak of influenza emerges in the community.

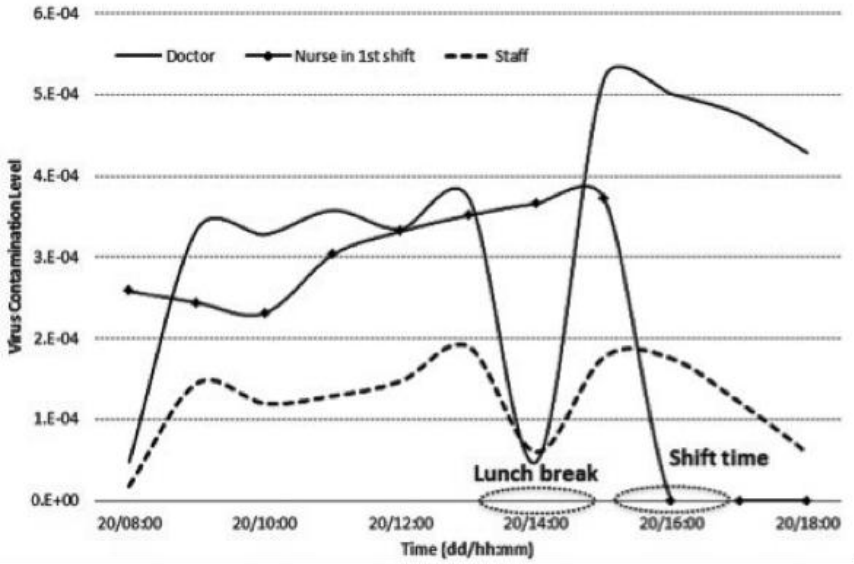


Figure 13. Variation of virus contamination level of HCW in a working day in scenario A

Agent Contamination Level $ACL[i](t)$ is the amount of virus that an agent i has at the specific time t. The Figure 7 describes the average virus contamination level of doctors, nurses and other staff in working time in 20th day when the number of inpatients reaches its peak in the scenario of A [High Control High Vaccine]. The average virus contamination level of doctors and nurses are higher than those of other staff. This could be explained by the fact that doctors and nurses work in ward area more than other staff. Sharp drops recorded in the contamination level among HCW strongly correlate with daily routines of the HCW concerned. The virus contamination levels of doctors and other staff falls to their troughs at the time of lunch break (from 13:00 to 14:00). The virus contamination level of nurses also decreases rapidly when they change their shift and leave the hospital.

The conclusion of micro analysis is that doctors and nurses, who provide direct care to influenza patients, have higher risk of catching influenza virus within the hospital. This conclusion supports long-standing belief in hospital infection control that annual

influenza vaccination should be required for every health care worker who has direct contact with patient.

5.3 Contact Network Analysis

We analyze the contact network, which is generated by interactions of agents in the simulation of scenario D. We assume that once two agents come into a same spot, one contact is made between them. Figure 14 shows the structure of the contact network. Each agent carries a contact list of agents who are in the same spot with him at the time *t*. The weight of the contact is calculated be multiply contact time with contact density. In this research, I assume that the contact density is uniform in every spot.

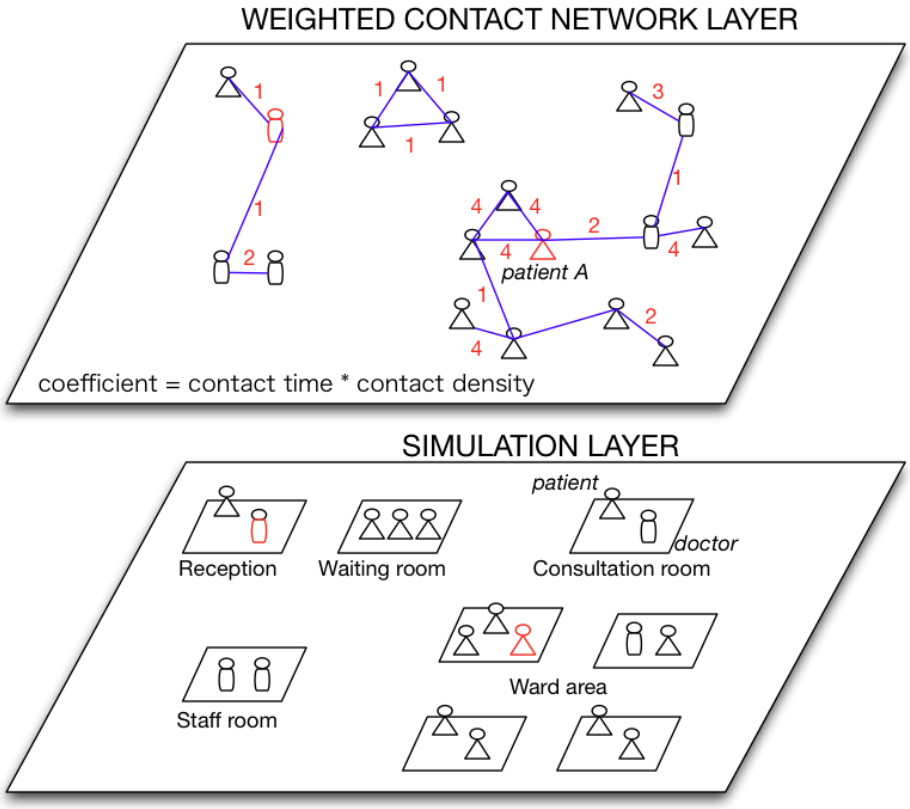


Figure 14. Contact network of agent after simulation

The contact lists vary by time when agents are moving inside the hospital. When an agent comes into a spot, he inserts him on the top of the agent_list of the spot. The spot then copies the agent_list of the spot back to the agent. In that manner, the agent_list of the agent is the list of agents who exist in the same spot with him (including himself). The agent_list of agent and spot is deleted at every time step, in order to keep the agent_list up to simulation time. The method of insert and copy agent_list is illustrated in Figure 15.

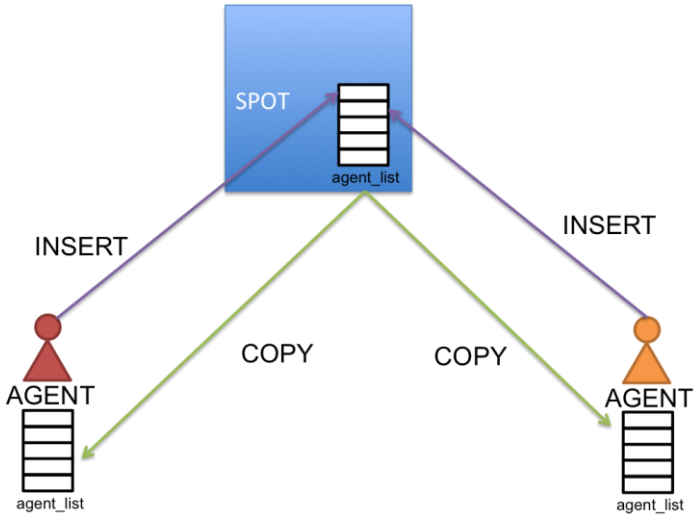


Figure 15. The method of update agent_list variables of agent and spot

The simulation log of agent_list in scenario D is converted to .csv file and is imported to Gephi [38], an open source graph visualization software.

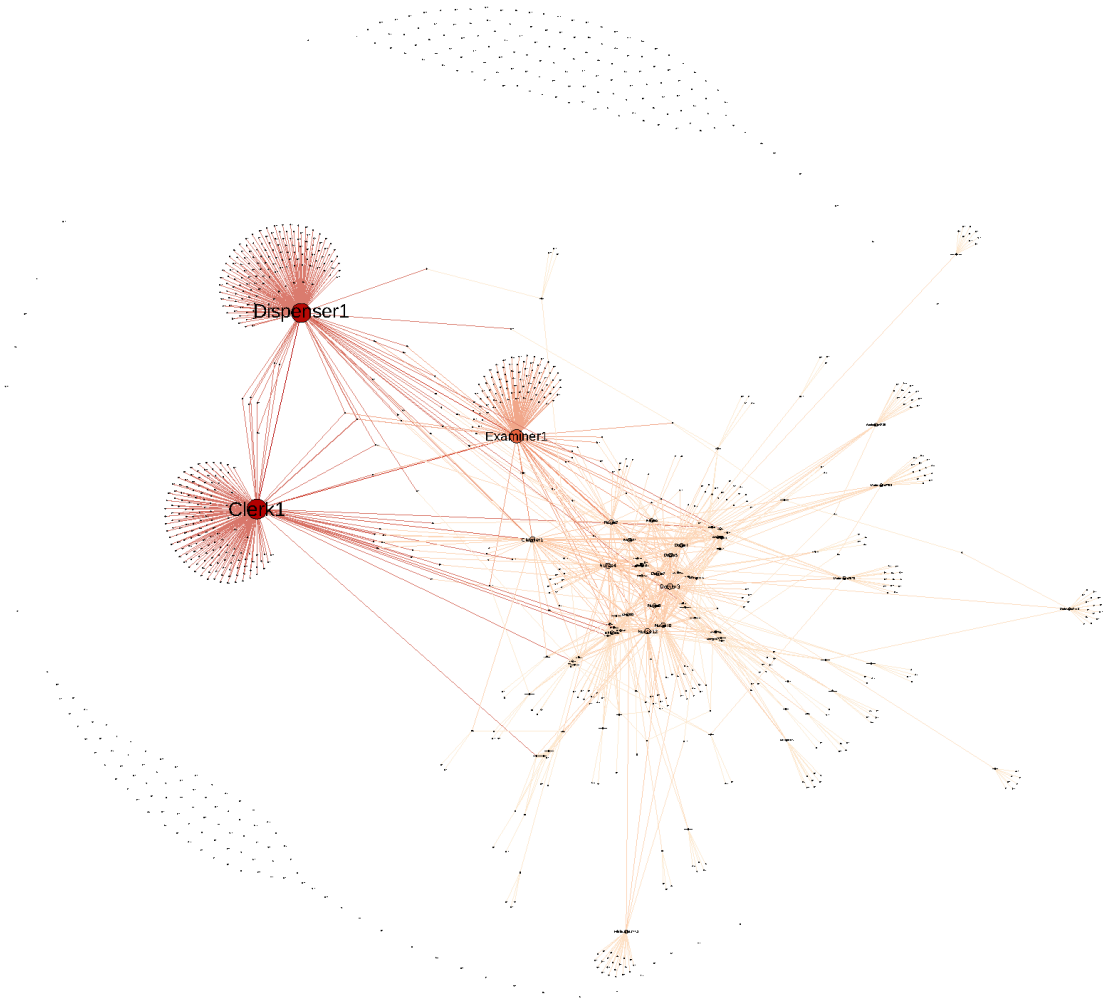


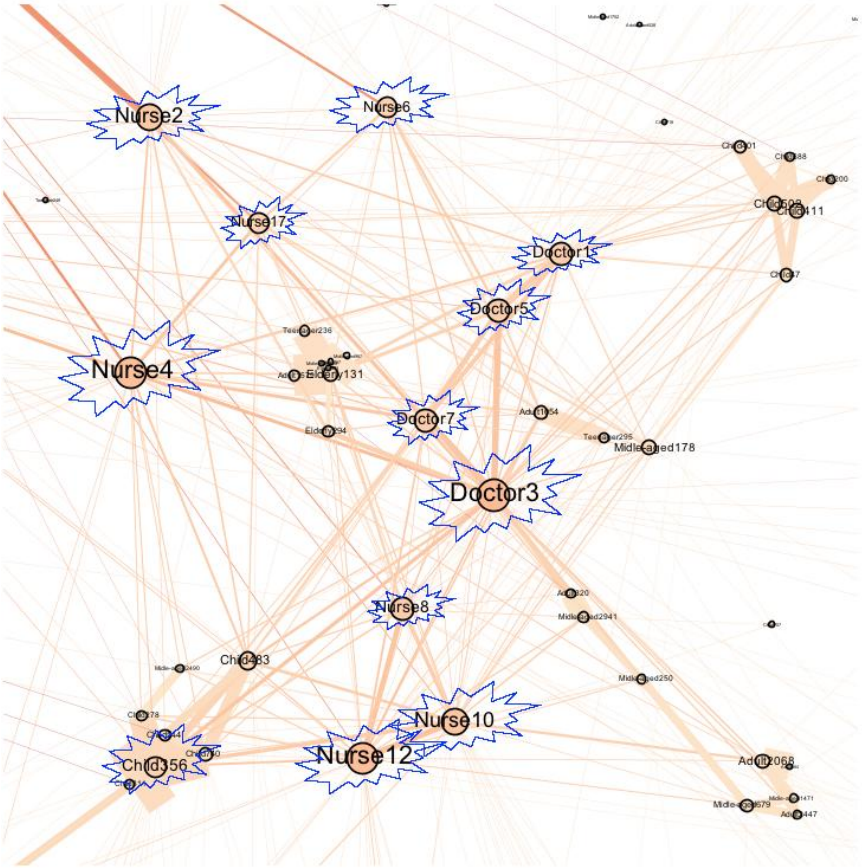
Figure 16. Visualization of contact network in scenario D

Figure 16 illustrates the visualization of contact network, which is called ”risk graph”. Each node in the graph represents an agent in the simulation model. Lines in the graph illustrate aggregate of contact between agents the simulation of scenario D. The thicker the line, the more frequent contact between the agents has been made. The size of the node is proportional to the degree, which indicates amount of contact that he had made. The layout of the graph is Force Atlas [39], in which the connected nodes are attracted into the center of the graph and unconnected nodes are pushed out off the outside.

Visual conclusions of the risk graph:

- The dispenser, the clerk and the examiner (there is only one dispenser, one clerk and one examiner in the hospital) nodes are the three biggest nodes (in degree). It implies that the three heath care workers have made the most contact with patients. However, most of the contacts were made with outpatients, so the nodes represent them are pulled out off center of the graph.

- Nodes that represent nurses, doctors and inpatients are attracted into the center of the graph (See Figure 17). It implies that frequent close contacts were made between them.



List of node (in descending order of degree) and time the agent get infected

Agent Name	Degree	Infected Day/Time
Clerk1	186	
Dispenser1	180	
Examiner1	122	11/17:00
Doctor3	47	15/11:00
Cleaner1	46	13/10:00
Nurse4	45	13/14:00
Nurse12	45	24/00:00
Nurse10	38	18/21:00
Nurse2	36	10/14:00
Nurse8	31	11/20:00
Doctor1	31	3/15:00
Doctor5	31	4/15:00
Doctor7	31	14/15:00
Child356	28	2/11:00
Nurse6	27	3/12:00
Nurse17	26	3/12:00

Figure 17. Center of the risk graph and list of infected health care workers in scenario D

Figure 17 shows the center of the risk graph, in which close contacts between doctors, nurses and inpatients are illustrated. The nodes, which are marked by blue explosion shapes, represent health care workers who have been infected during the simulation. We can see that those agents are at the center of the risk graph and are have frequent contacts with inpatients. The nodes, which represent doctors, and nurses who have been infected during the simulation arose on top of the list of nodes in descending order of degree. However, the dispenser and the clerk were not infected; even though nodes represent them have a high degree. It can be explained that most of the contacts they made were with outpatients, so their risk of infection were low. The risk can also be evaluated by Spot Contamination Level of the place that the two staff was working in (See Figure 12). The Figure shows that staff area and administration area where the two staff works are less contaminated than ward area. It means that infection risk of those staff is lower than risk infection of nurses who almost work with inpatient in ward area.

Several conclusions can be drawn from analysis on risk graph are:

- Two nodes are spatially closer if they have a close and frequent contact.
- Close and frequent contacts between agents will attract them into center of the graph.
- Risk of infection can be assessed not only by the degree of the nodes but also by the amount of close contacts.

(See APPENDIX B: Supplemental Material *for more information about the risk graph)*

5.4 Summary

Simulation result analysis is summarized as below,

- Significant variation in number of infected patients and number of infected HCW in the four scenarios A, B, C, D has been observed from simulation results.

- Staff washing hand combining with wearing mask resulted in significant reduction of number of infected HCW in the three additional scenarios.

- In scenario A, average of Spot Contamination Level (*SCL*) of Ward area was the highest, administration area ranks the second, while the staff area's average *SCL* was significantly small.

- The average virus contamination level of doctors and nurses were higher than those of other staff in a day of simulation. The virus contamination level of HCW reflected their activity in the hospital.

- In the visualization of the risk graph, hospital staffs were at the outside of the graph, while doctors and nurses were attracted into the center of the graph. Doctors, nurses and inpatients node are spatially close and weights of the edges that connect them are significant high.

5.5 Model verification and validation

Model verification is the process of confirming the simulation is working as initially planned. The process includes debugging, and test the model at the extremes to ensure that the simulation results are reasonable. On the other hand, model validation is the process of checking model's validity, that is, whether it is a good model of what it purports to represent.

In the model verification process, while debugging is not mentioned here, I have done analyses on variances of several simulation outputs. The results found out that 30 replication is enough to make relative standard deviations small enough. In Figure 13, Virus Contamination Level of HCW reflects the activity pattern of the workers which implies that activity pattern of HCW has been modeled as initially planned. Analyses on Spot Contamination Level show that the places (except wards) are more contaminated in the workday and almost clean of influenza virus at night. This indicates that infection process has been modeled as initially described.

The purposes of the model are to assess risk of nosocomial influenza infection in HCW. The simulation results have validated that HCW can be infected and direct patient-care HCW (doctors and nurses) have higher possibility of catching nosocomial influenza virus compared to other staff. The simulation results of several infection control scenario has shed more light on efficiency of those on preventing an outbreak of influenza in the hospital. Because of lack of statistics data and impossibility of taking those experiments in a hospital, empirical validation of the model could not be conducted. Although data and knowledge for the model has been perceived from three

field works onsite, the lack of precise data of HCW and patients activity is the limitation of the model. In the next chapter, in preparation for collecting real data for the model, experiments of capturing human's real activity are described.

CHAPTER VI: Experiments of Capturing Human Movement

This chapter describes data collection method and analytical technique for capturing human's real movement in a building. P2P wireless cards are divided into 2 groups. Devices in group 1 are set up to be "tag" that positions are fixed. Devices in group 2 are set up to be "antenna" that human carrying during the experiments. Antenna records signal strength of tags that is near to its position. By analyzing antenna signal, we can track its location that is location of the human who is carrying it. Comparing to consumer-grade GPS device that positional accuracy is approximately 10 meters [49], we can expect for positional accuracy of less than dozens of centimeters [50].

6.1 Introduction of P2P sensor

Figure 18. P2P wireless card

Figure 18 shows the aspect of the P2P wireless card. Specification of the card is described in Table 10 [50].

Table 10. Specifications of P2P wireless card.

Name of device	Wireless Peer to Peer Card (under development)
Size	Pocket-size
Communication system	P2P
Memory	16K flash memory
Data format	ID, start time, end time of contact, intensity
Signal strength	Integer between 0 and 255. Default is 154
Contac intensity	Percentage

Contact range	Dozens of cm up to 10m
Simultaneous recognition	up to 10 - 30 cards
Battery life	2-3 days
Interface	USB
Data transfer rate	2.4kbps

6.2 Experiment 1: Test signal intensity

The purpose of the experiment is to test signal intensity of the cards. Although they are made with same specifications, individual errors are not exceptional. In order to observe the correlation between signal intensity and distance of wireless cards, I conduct the experiment as below.

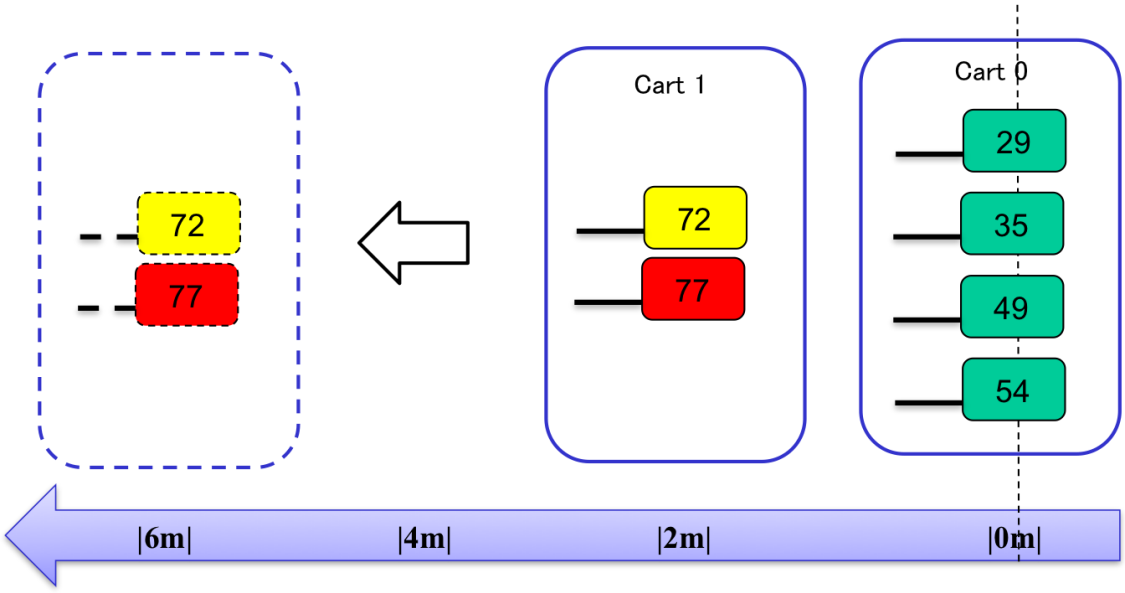


Figure 19. Experiment 1 setting

An experiment 1 setting is illustrated in Figure 19. We take a sample of wireless cards randomly (6 cards). Four cards is set up to be tags, while the other two are antennas.

Tag ID 29, 35, 49, 54 are fastened on cart 0. Cart 1 carries antenna ID 72 and 79. Antenna card ID 72 signal power is set up to 0. Antenna card ID 77 signal power is set up to default 154 (signal power is an integer between 0 and 255). We moves cart 1 far away from cart 0 each 2m, in each 30 seconds. Signal intensity of tags 29, 35, 49 and 54 was recorded in memory of antennas 72 and 77.

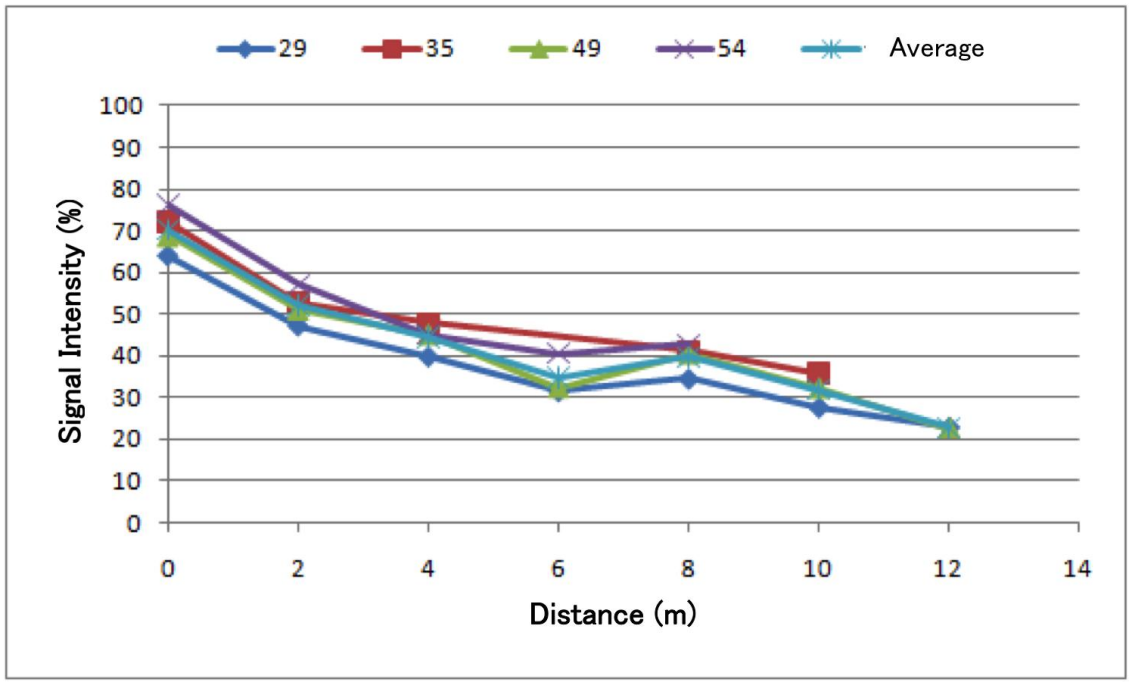


Figure 20. Recorded signal intensity of tags in antenna number 77

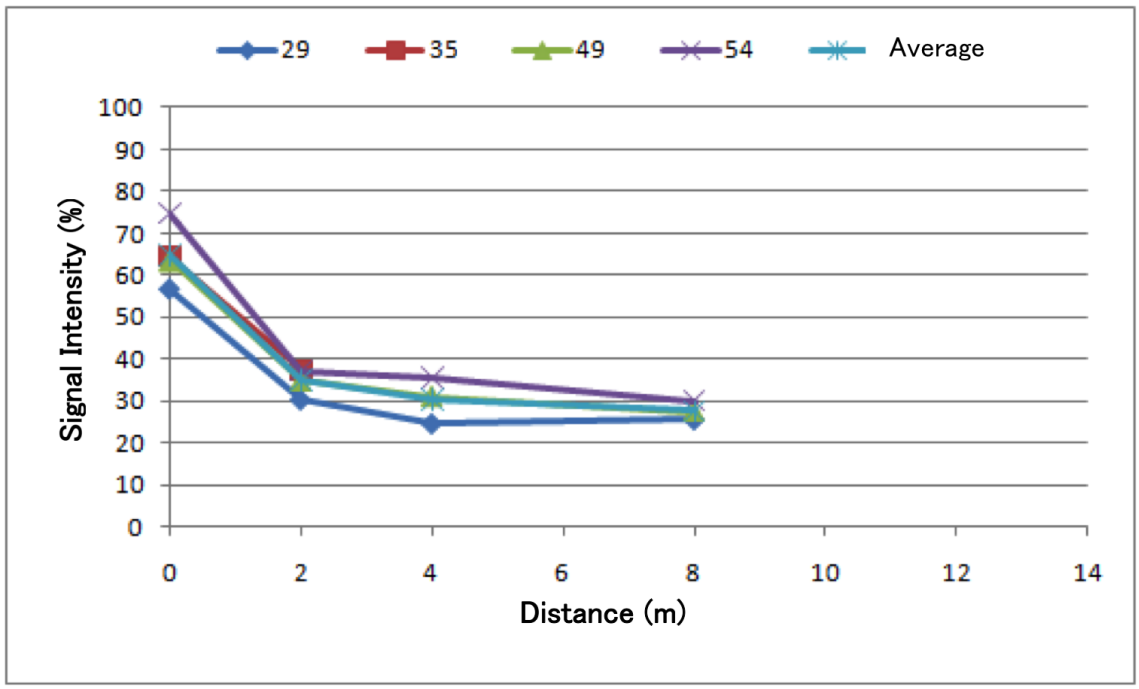


Figure 21. Recorded signal intensity of tags in antenna number 72

Figure 20 and Figure 21 show correlation between signal intensity of antennas and distance between them and tags. Variation in recorded signal intensity can be observed from the graphs. In Figure 20, average signal intensity of tags decreases gradually from 70% at distance of 0m to 20% at distance of 12m. In Figure 21, average signal intensity falls rapidly from 70% to 35% at distance of 2m, and then gradually declines to 30% at the distance of 8m.

Since an antenna record all signal from tags in its surroundings, to distinguish which tag is nearest to the antenna needs an recognized difference in signal intensity of the tags. In the case of antenna number 72, change in distance between 0m and 2m can be observed in the change of signal intensity. However, with distance of more than 2m, since the change in intensity is very small compared to change in distance, it is hard to estimate the distance between the antenna and the tags. In another word, antenna 72 , which signal power is set up to 0, can only distinguish tags in short distance of less than 2m.

Meanwhile, antenna 77, which signal power is set up to default 154, can identify tags in the range up to 12m.

In experiment 1, I have found out suitable signal power for tags and antennas in order to identify and distinguish each others. In the next 2 experiments, I use tags and antennas with appropriate power settings to capture human's movement in a building.

6.3 Experiment 2: Capture human movement in clinic settings

The purpose of the experiment is to simulate human movement in a clinic setting. An experiment setting is described in Figure 22 .

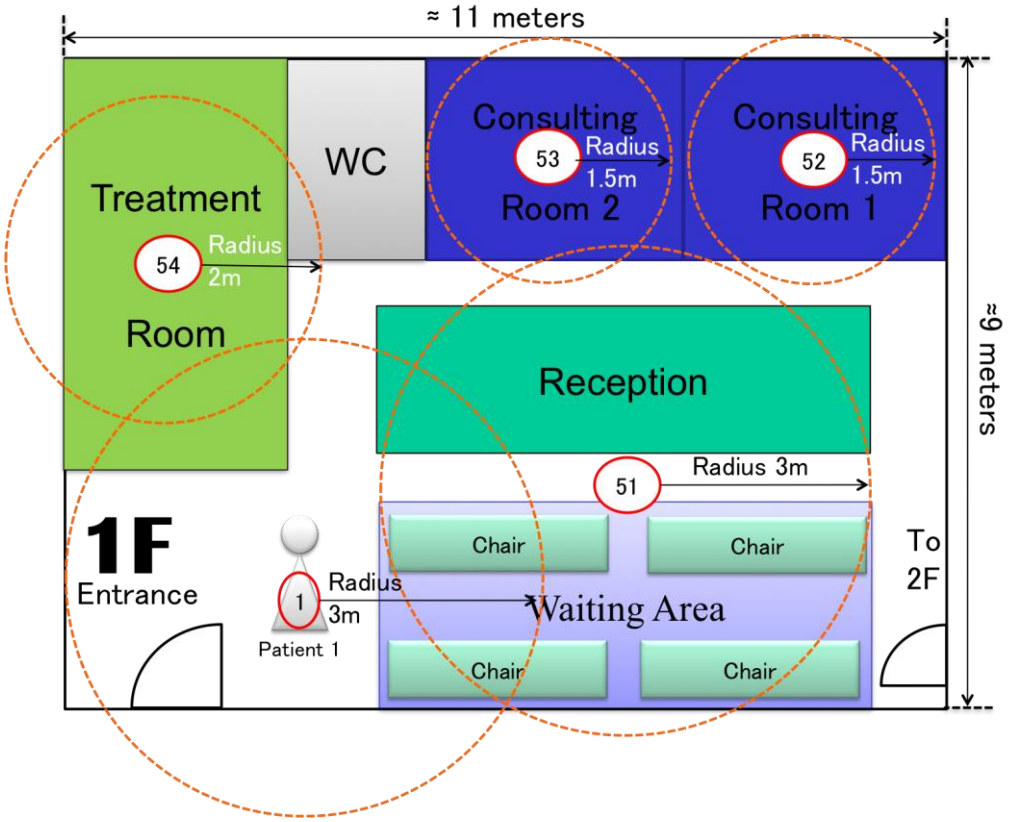


Figure 22. Experiment of capturing human movement in a clinic setting

A person carried antenna ID number 1 and walk around in a virtual clinic. Tag ID 51, 52, 53, 54 were set up at waiting area, consulting room 1, consulting room 2 and treatment room, respectively. Signal power of card ID 1, 51 was set to default of 154. Card ID 52, 53 and 54's signal power were 0. Signal intensity of tags 51, 52, 53, 54 was recorded in memory of antenna 1. Based on results of experiment 1, distance between tag and antenna is estimated by signal intensity between them. Tag 1's memory (in .csv format) was processed by cutting small values of signal intensity. Then the processed data was converted to data format of SOARS Animator [51]. The Figure 23 illustrates the animation of the person's movement in the virtual clinic.

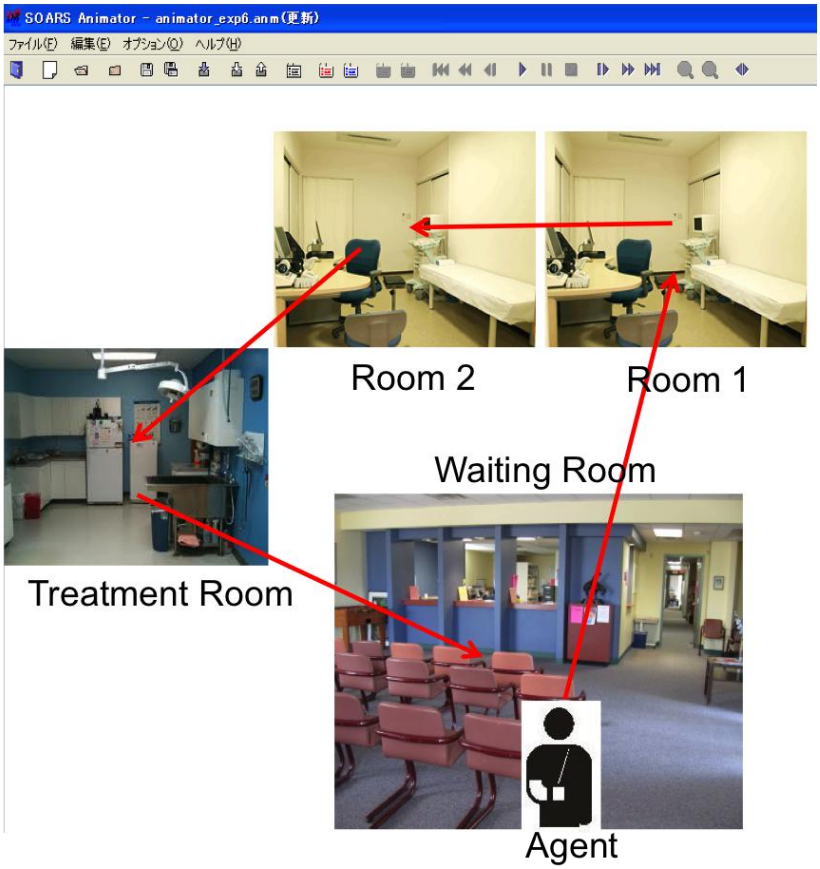


Figure 23. Animation of movement of human in clinic setting

In that manner, real movement of the human was captured by combining the wireless card systems and SOARS Animator. However, since the model was built in Visual Shell module of SOARS, the data from wireless card systems needed to be converted to Visual Shell data format. The next experiment demonstrates the procedure of converting the data.

6.4 Experiment 3: Capture human movement in clinic settings

The purpose of the experiment is to simulate human movement in a hospital setting. Experiment settings is described in Figure 24

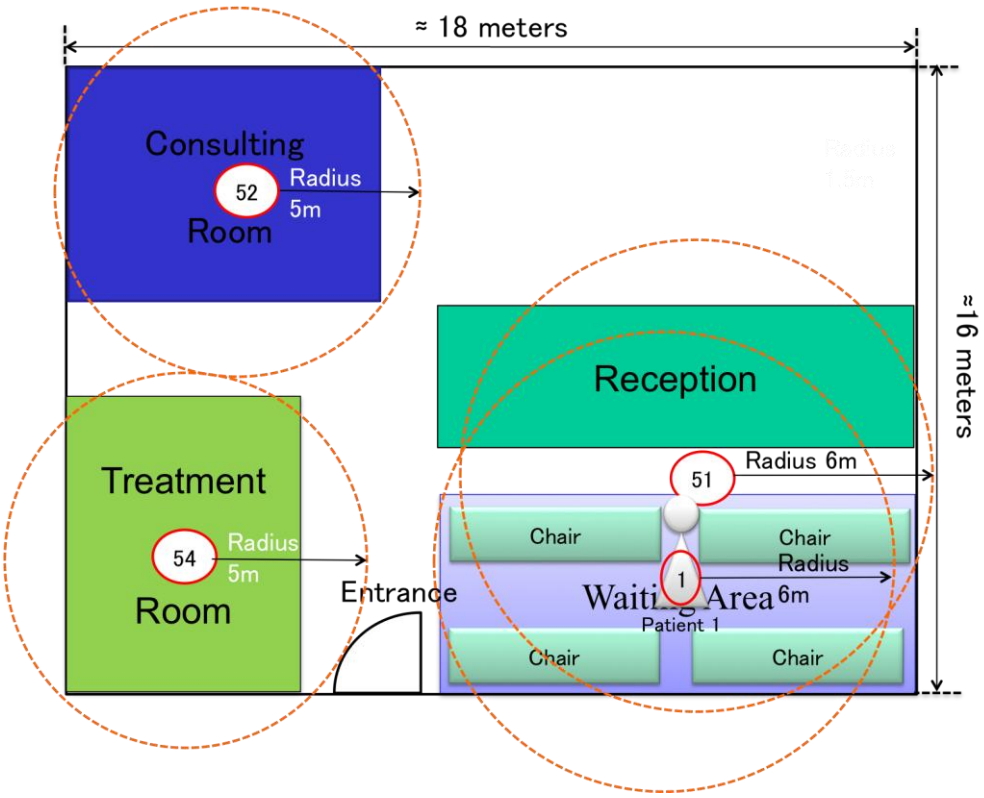


Figure 24. Experiment of capturing human movement in a hospital setting

A person carried antenna ID number 1 and walk around in an area of a virtual hospital. Tag ID 51, 52, 54 were set up at waiting area, consulting room and treatment room, respectively. In order to cover a larger area of the hospital settings, the power of all wireless cards were set up to max power of 254. Recorded signal intensity of tags 51, 52, 54 in memory of antenna 1 (in .csv format) was processed and converted to Visual Shell format (.vsl). The data of the human movement was import into agent role in SOARS Visual Shell [51]. The SOARS model is illustrated in Figure 25.

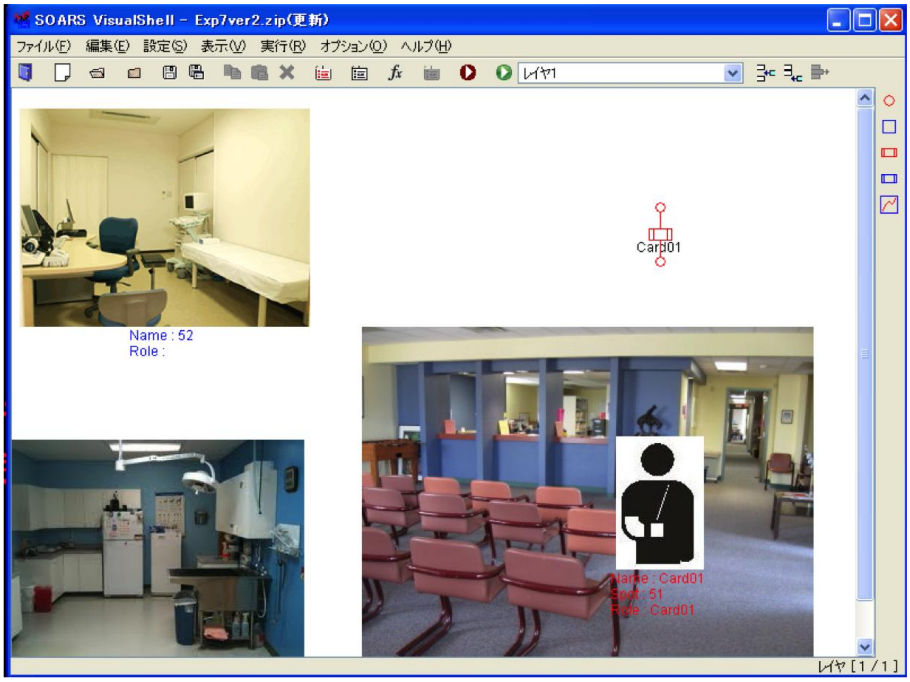


Figure 25. SOARS model of human activity in an area of a virtual hospital.

6.5 Summary

Three experiments with the wireless card system was conducted. The first experiment purpose is to test performance of an sample of wireless cards. The results showed the correlation between signal intensity and distance between tags and antenna. Based on the results in experiment 1, experiment 2 and 3 were conducted to capture a human movement in a small virtual clinic and a bigger area in a virtual hospital. The human movement was simulated by using SOARS Visual Shell and SOARS Animator [51]. The conclusion is that the wireless card system can be used to capture movement of human under a appropriate setting of tags and antennas. The data of the card system can be processed and imported into SOARS. In that way, real data of human movement in a hospital can be imported to the hospital model which is described in 4.1 Hospital model.

CHAPTER VII: Conclusions

We have built a simulation model for infection of an influenza-like illness in an artificial hospital and quantitatively assessed infection risk of the diseases. The simulation results have shed more light on epidemiological belief of that direct patient care HCW have high risk of catching nosocomial influenza virus and that washing hand and wearing mask are effective to prevent an outbreak of the disease in the hospital. The methodologies of quantification and visualization the infection risk have been demonstrated. The original approach has provided us a potential methodology for risk management in infection control of nosocomial infection.

The great advantage of simulation model is that they unable experiments which are impossible or undesirable. It provides a flexibility of changing parameters to apply to other diseases rather than influenza-like illness. The computation of dynamical change of virtual influenza virus can assess the risk of infection quantitatively and visually. Even though the computational effort of the modeling method is hard, with the evolution of computing, time execution of the simulation model is constantly reduced.

The methodology of categorizing infection levels into detailed disease states can be used to apply to other pathogens like smallpox, measles and so on by changing state period and state transition probability. Comparing to traditional SIR model, in which population is roughly divided in three groups of susceptible, infectious and recovered individuals; our methodology provides a better modeling of infection process.

The visualization of risk graph demonstrated above can be a valid method to assess infection risk but it is not completed. The nature of contact that transmit virus cannot be

seen from the graph. However, thanks to the development of large networks graphs visualization software, such as Gephi, we can highlight and track all contacts of agents in real time. Integration with human real time tracking systems can be potential for tracking and detecting contacts between health care workers or between health care workers and patients.

Although data and knowledge for the model have been constructed based on several field works onsite, due to the lack of statistics data and impossibility of taking those experiments in a hospital, empirical validation of the model could not be conducted. Although there was no observed data fitted the simulation results, outputs are qualitatively similar to observed phenomenon in the real world.

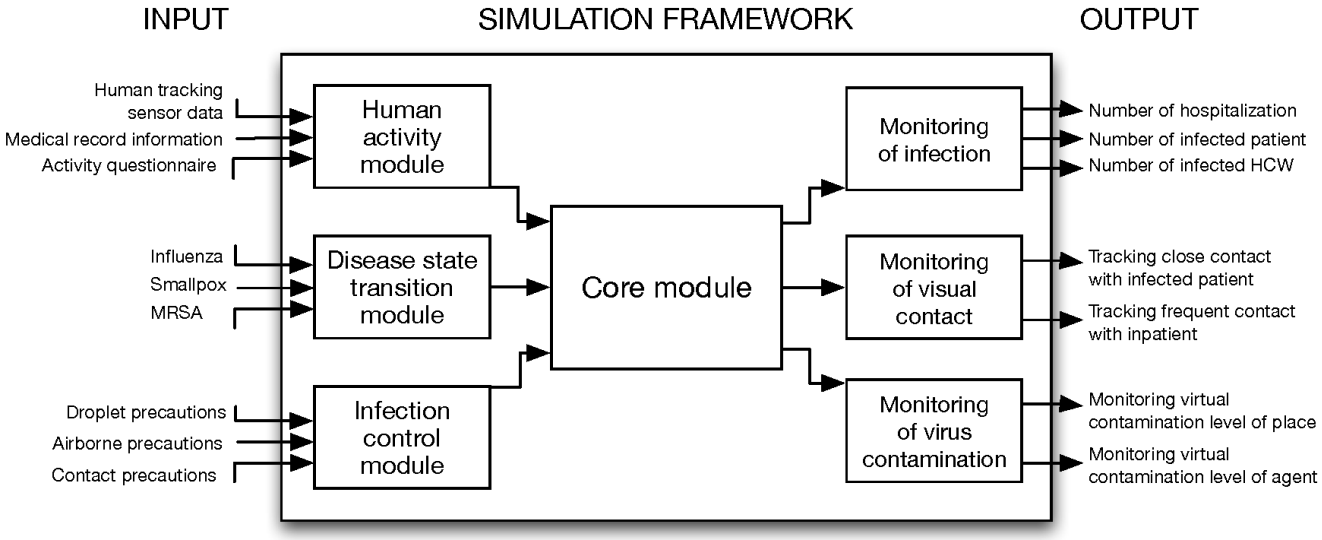


Figure 26. Structure of the simulation framework

The future work is to integrate real data collecting by sensor to the simulation framework. The structure of the simulation framework is illustrated in Figure 26. We have developed and used wireless tracking systems to track real-time movement of humans in a building. The real data of movement of patients and health care workers in

a real hospital can be achieved. Activity pattern of people can also be collected via activity questionnaire. Changing parameters of the disease transition module can be applied to study other infectious diseases. Infection control measures can be changed in many scenarios depending on infection control resources of the hospital. The core module inherits from the current module but can be rebuilt to fit the structure of a new hospital. Simulation output shows real-time graph of the number of hospitalization, infected patient and HCW. By visualizing contact network, close and frequent contact with high-risk patients can be tracked and monitored. Variation of virtual virus contamination level of places and agents can be monitored in real time. The simulation framework could be a potential decision-making support tool for hospital administrators to evaluate nosocomial infection control and it can also be used as an educational tool to study nosocomial infection.

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APPENDIX A: Field Works

This section includes materials of field trips to Vietnam in order to collect information and data for the simulation model. The figures and pictures in this section are not allowed to be copied or distributed.

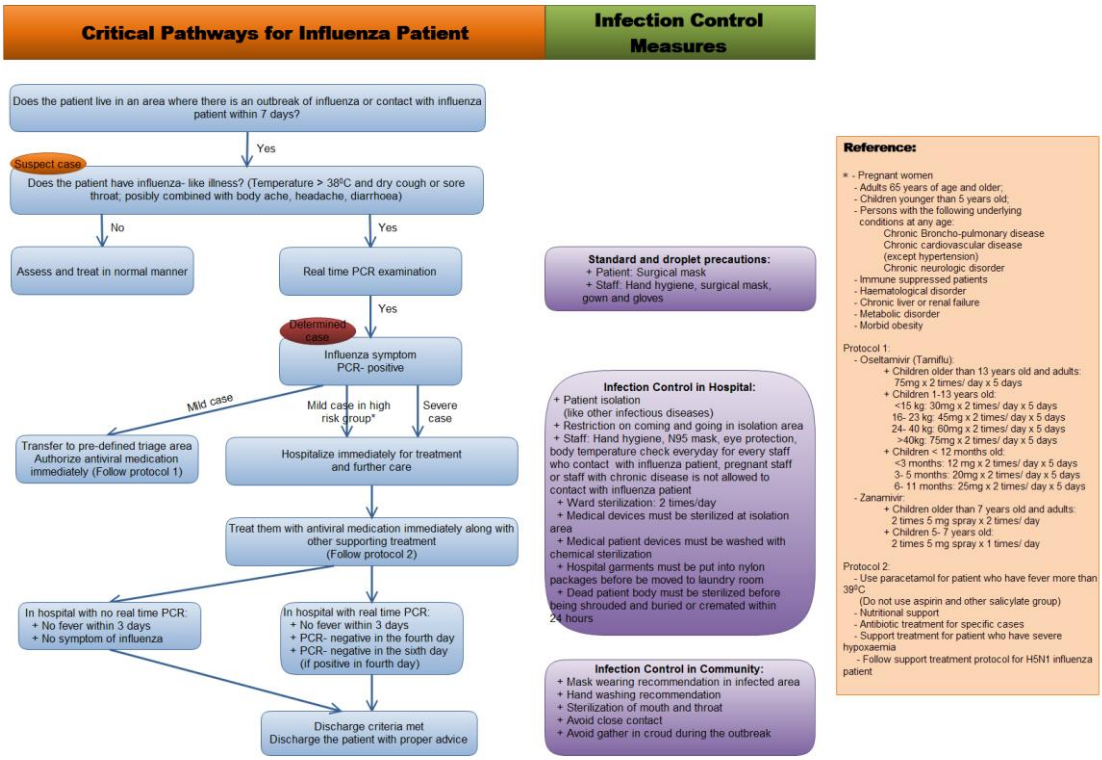

Figure 27. Critical pathways for influenza patient in Vietnam

Reference: Vietnam Ministry of Public Health, Available at : http://www.moh.gov.vn/homebyt/vn/upload/info/attach/1249300232187_Huong_dan_chan_doan_dieu_tri_cum_dai_dich_H1N12009.doc. Accessed August, 2009.

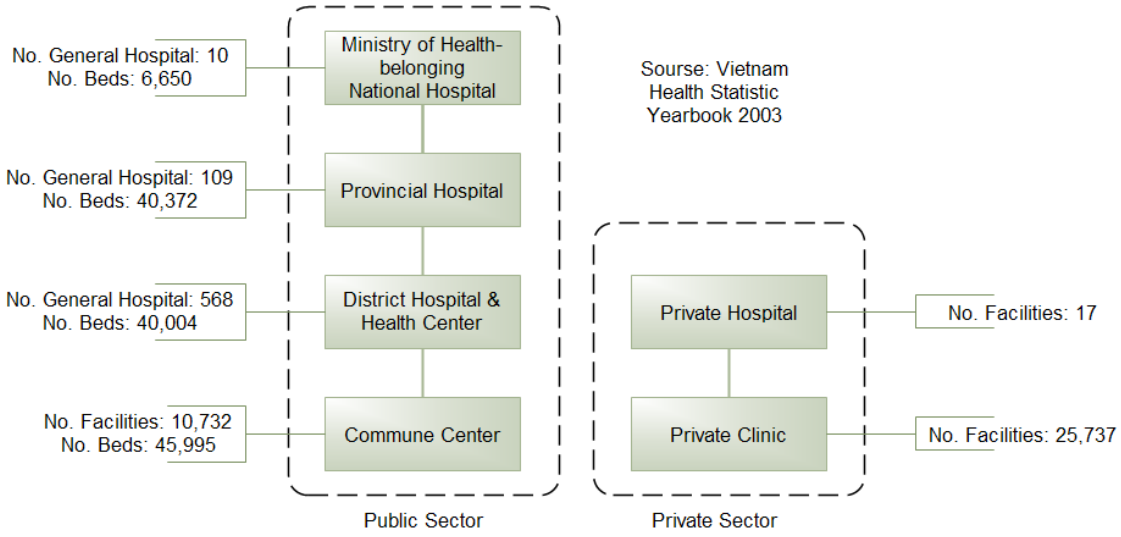

Figure 28. Hospital system in Vietnam

APPENDIX B: Supplemental Material

This section includes supplemental results of additional simulations.

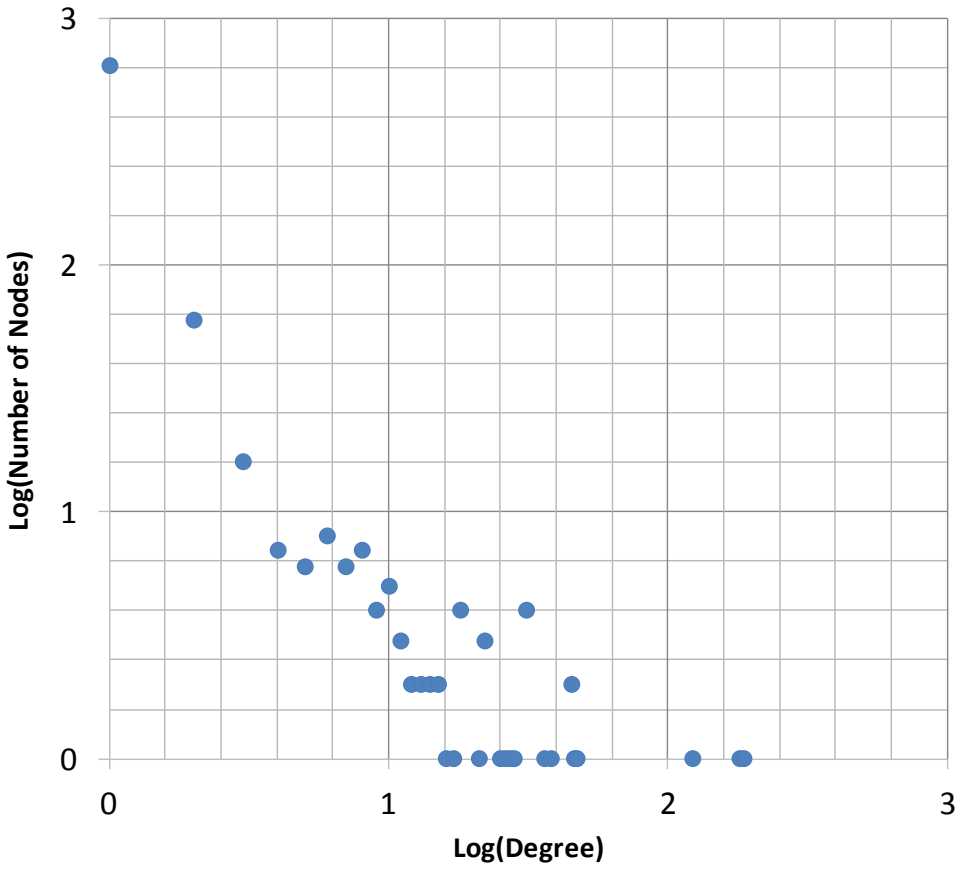

Figure 29. Degree distribution of the risk graph. Average Degree: 2.313

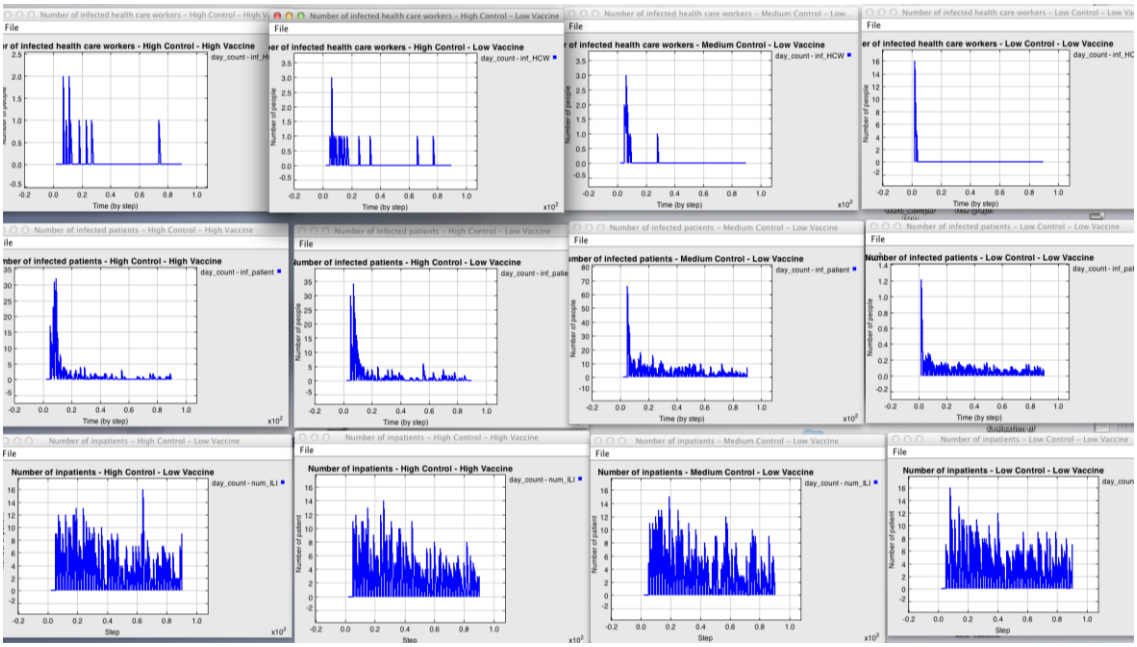

Figure 30. Simulation charts on SOARS main console.
Simulation time: 3 months. Scenarios number: 4

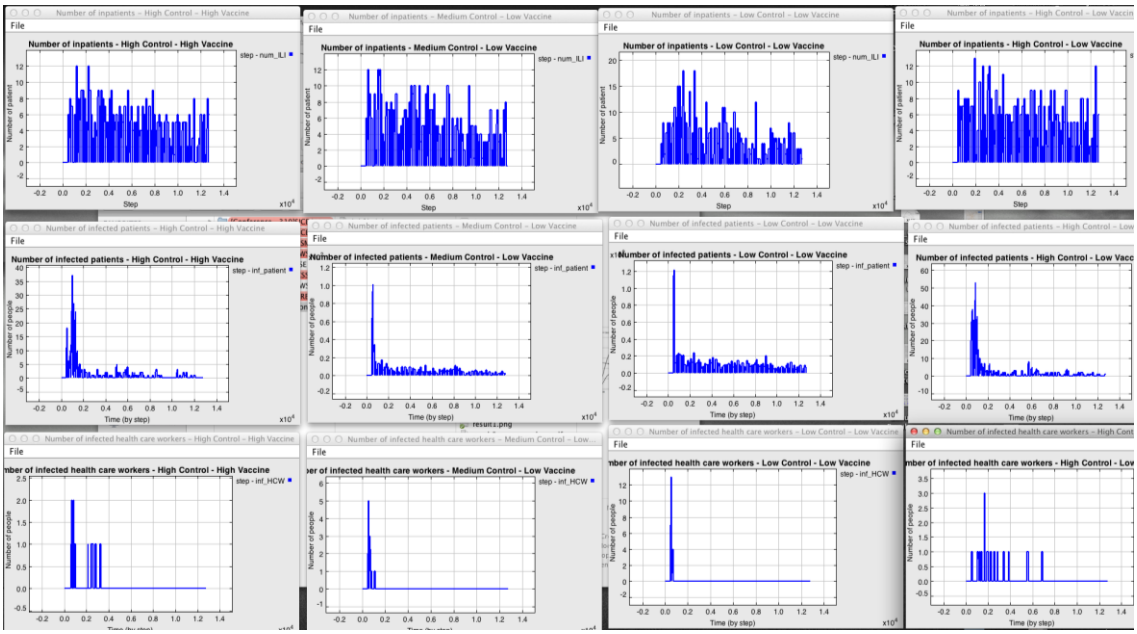

Figure 31. Simulation charts on SOARS main console.
Simulation time: 12 months. Scenarios number: 4

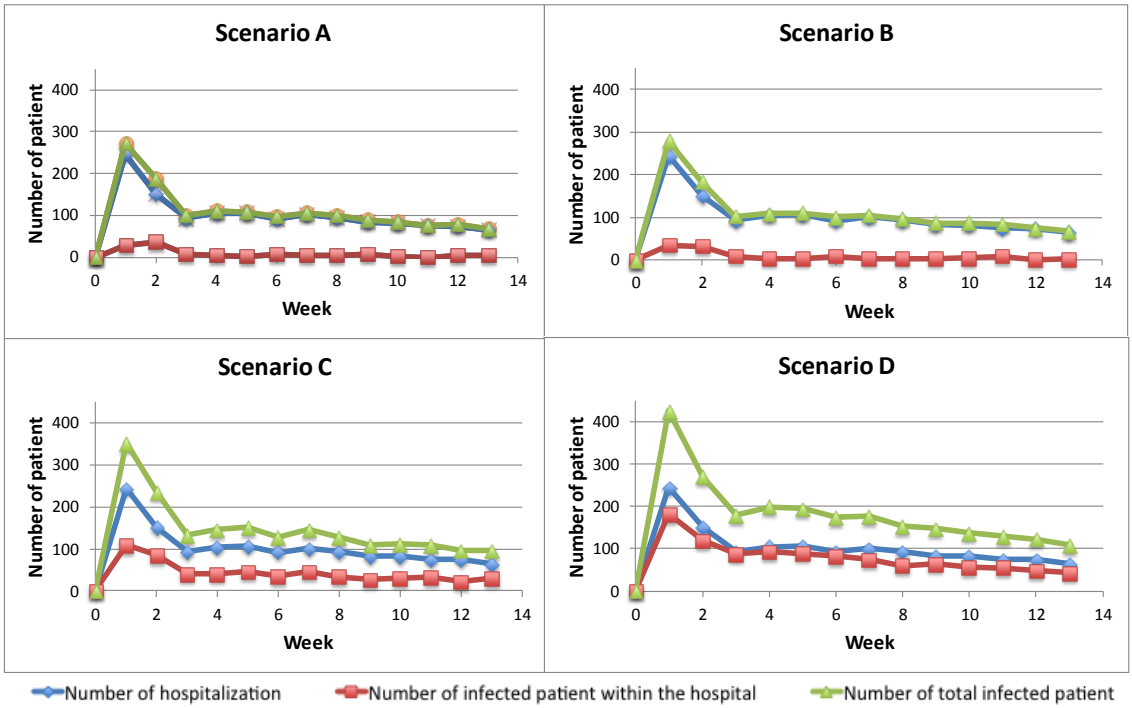

Figure 32. Variations in number of hospitalization, number of nosocomial infected patient and number of total infected patient in the four scenarios. Simulation time: 14 weeks. Scenarios number: 4

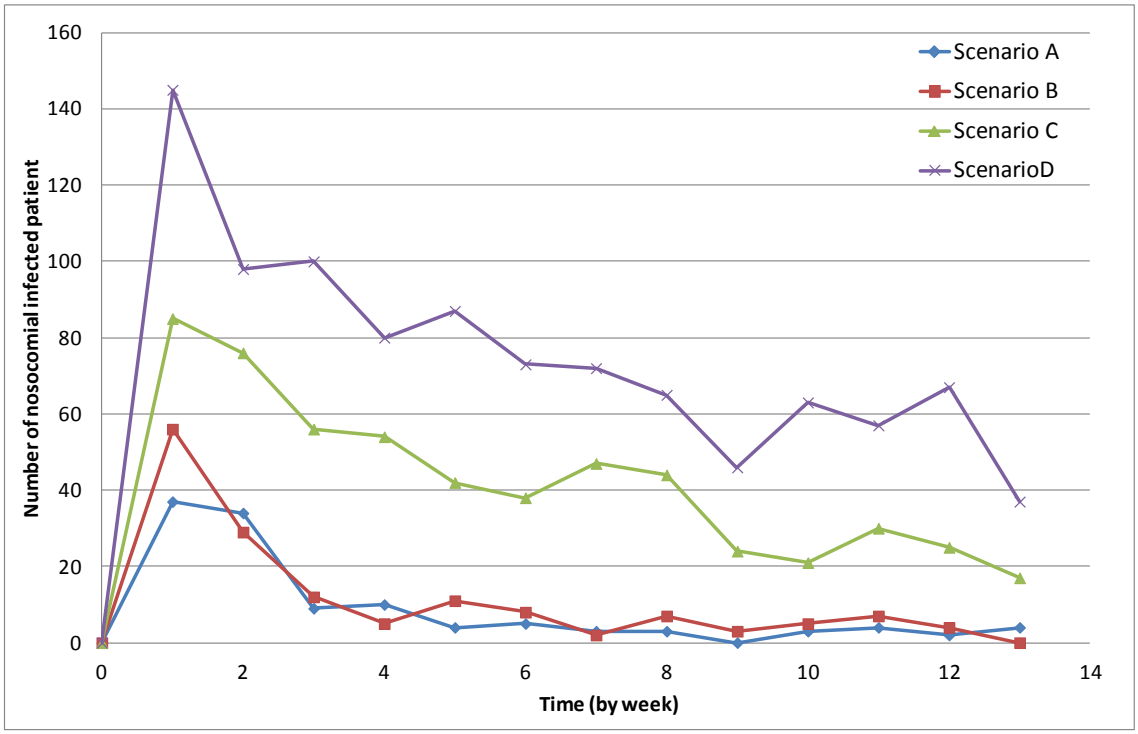

Figure 33. Variations in number of nosocomial infected patient in the four scenarios. Simulation time: 14 weeks. Scenarios number: 4

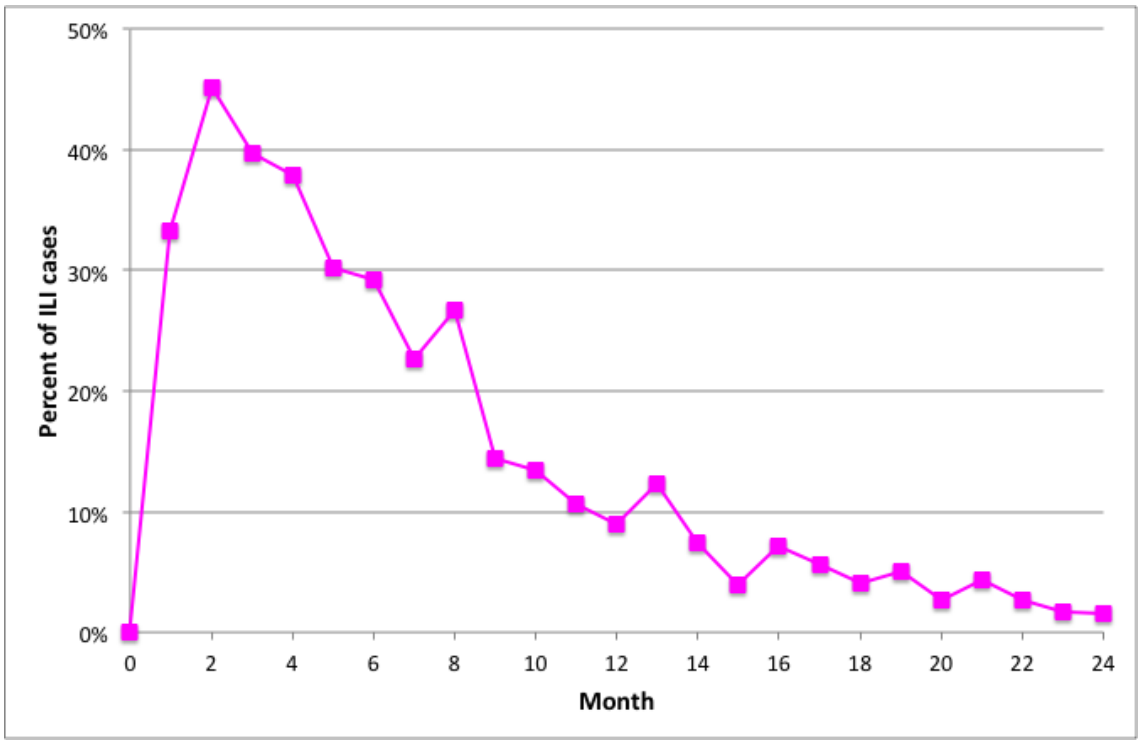

Figure 34. Variations in percentage of ILI cases in scenario D. Percentage of ILI cases is counted by dividing number of ILI cases to number of hospitalization. Simulation time: 2 years.