Journal of Theoretical Biology 421 (2017) 39–50

Contents lists available at ScienceDirect

Journal of Theoretical Biology

journal homepage: www.elsevier.com/locate/jtbi

Effects of operational decisions on the diffusion of epidemic disease: A system dynamics modeling of the MERS-CoV outbreak in South Korea

Nina Shin[a], Taewoo Kwag[b], Sangwook Park[a], Yon Hui Kim[c,*]

[a] Graduate School of Business, Seoul National University 1 Gwankak-ro, Gwanak-gu, 08826, Seoul, Republic of Korea
[b] Executive Director, Healthcare R&D, G-Doc Partners 78, Donggwang-ro 27-gil, Seocho-gu, 06582, Seoul, Republic of Korea
[c] Executive Director, Business Development, Corestem Inc., 24 Pangyo-ro 255beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do, 13486 Republic of Korea

ARTICLE INFO

Article history:
Received 11 December 2016
Revised 8 March 2017
Accepted 20 March 2017
Available online 27 March 2017

Keywords:
Operational decision-based modeling
Patient-care performance
System dynamics
Health care operations planning
Korean MERS outbreak

ABSTRACT

We evaluated the nosocomial outbreak of Middle East Respiratory Syndrome (MERS) Coronavirus (CoV) in the Republic of Korea, 2015, from a healthcare operations management perspective. Establishment of healthcare policy in South Korea provides patients' freedom to select and visit multiple hospitals. Current policy enforces hospitals preference for multi-patient rooms to single-patient rooms, to lower financial burden. Existing healthcare systems tragically contributed to 186 MERS outbreak cases, starting from single "index patient" into three generations of secondary infections. By developing a macro-level health system dynamics model, we provide empirical knowledge to examining the case from both operational and financial perspectives. In our simulation, under base infectivity scenario, high emergency room occupancy circumstance contributed to an estimated average of 101 (917%) more infected patients, compared to when in low occupancy circumstance. Economic patient room design showed an estimated 702% increase in the number of infected patients, despite the overall 98% savings in total expected costs compared to optimal room design. This study provides first time, system dynamics model, performance measurements from an operational perspective. Importantly, the intent of this study was to provide evidence to motivate public, private, and government healthcare administrators' recognition of current shortcomings, to optimize performance as a whole system, rather than mere individual aspects.

1. Introduction

In 2015, Korea was faced with an unexpected yet one of the largest outbreaks, worldwide, of Middle Eastern Respiratory System (MERS). A total of 186 individuals were infected, starting with a single "index" patient (a.k.a., "patient zero"), ultimately causing 38 fatalities within a two-month time period (Choi et al., 2015). Regardless of numerous scientific journals estimation of a MERS reproduction rate < 1, implying sub-epidemic potential (Breban et al., 2013; Chowell et al., 2015), the MERS outbreak in Korea has placed historical significant impact and global recognition of the vulnerability of the present-day Korean healthcare system.

While Korea has enjoyed "top-tier" overall healthcare status, based on its placement in the Organization for Economic Cooperation and Development (OECD) rankings (Park and Jang, 2012), the recent MERS outbreak revealed shortcomings of Korean hospital and government management systems, leading to poor MERS patient care in outbreaks, as well as other ongoing patient care. Serendipitously, last year's outbreak of MERS is now being discussed as the sole responsibility of the hospital, instead of the healthcare system as a whole.

The single index patient in the 2015 Korea MERS outbreak, who returned from a trip to the Middle East, visited **Hospital A**, at which he developed a cough and fever. **Hospital A** referred the index patient to **Hospital B**. Then **Hospital B** referred inpatients, who made close contacts with the index patient, to different hospitals. Through referring process from hospital to hospital, facilities render vulnerability to a complex contagious disease, creating a MERS into a severe hospital-acquired infection (HAI). For example, Assiri et al., (2013)'s study identified the 21 of the 23 confirmed cases of MERS-CoV infection were acquired through person-to-person transmission in patient care units and three different hospital facilities in Saudi Arabia, 2013. Similarly in Korea, within 10 days between the date of symptom onset to the identification of the index patient, 28 first generation MERS cases were identified (Korea Centers for Disease Control and Prevention, 2015). Overview of the MERS spreading process across 15 hospitals (excluding unidentified cases), and 186 confirmed cases, is summarized in Fig. 1.

---

* Corresponding author.
E-mail addresses: ninaful@snu.ac.kr (N. Shin), theokwak7@gmail.com (T. Kwag), sangpark@snu.ac.kr (S. Park), yonhuisarahkim@gmail.com (Y.H. Kim).

http://dx.doi.org/10.1016/j.jtbi.2017.03.020

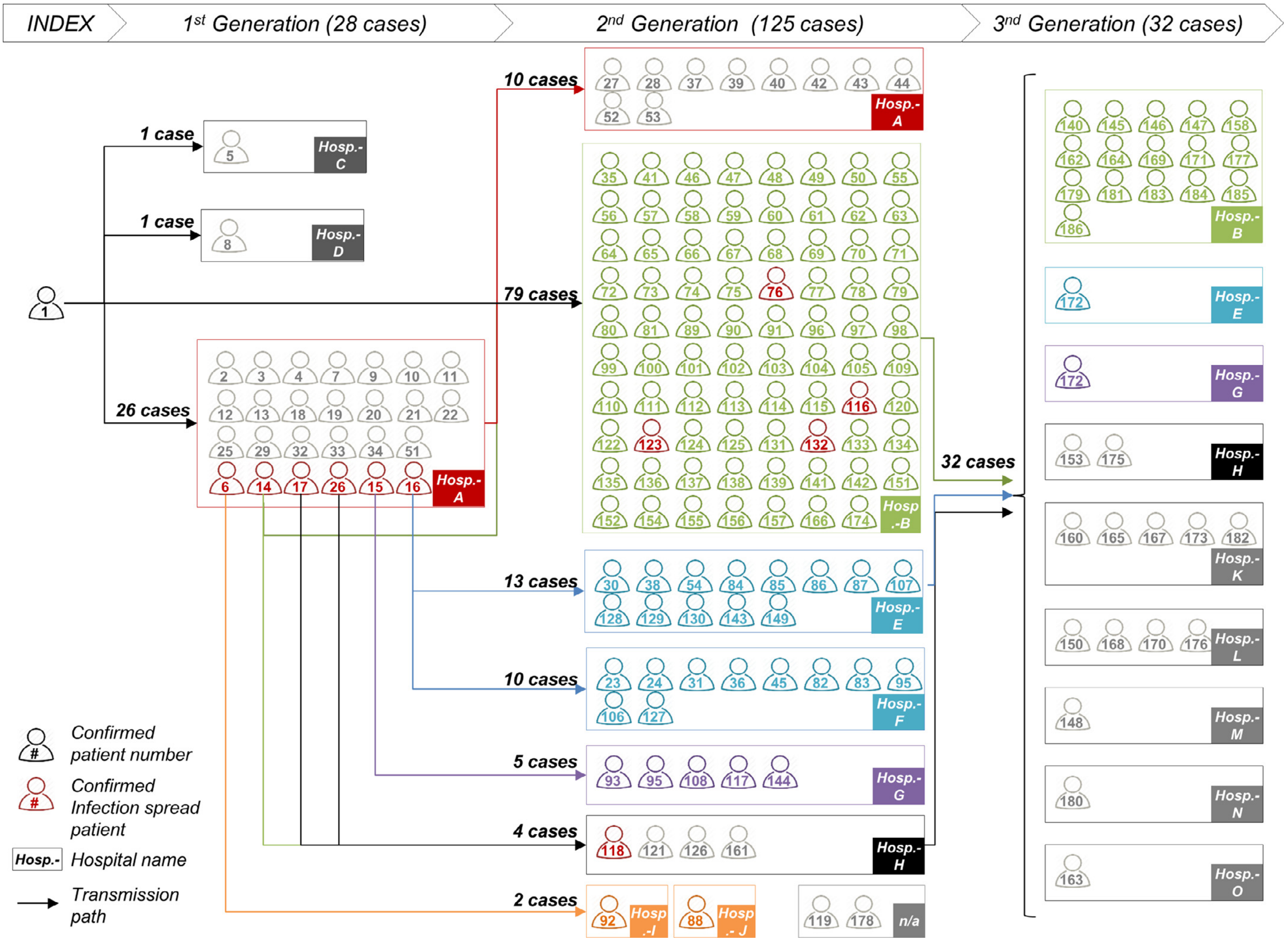

Fig. 1. Proliferation of MERS virus within 20 days in Korea.

Despite the high regard for Korea's level of medical practice, a defect in one medical specialty infectious disease was the primary catalyst for the rapid spread of MERS – ultimately causing social, economic and psychological impact nationwide (Kim, 2015b). However, a number of hypotheses were generated to explain the spread, including: excessive patients' freedom in seeking medical care at only large hospitals, inadequate quarantine, questionable government transparency, such as belated reports of infected hospital names, and the cultural social norm of visiting patients as standard etiquette (Choe, 2015a, 2015b; Korea Centers for Disease Control and Prevention, 2015). The significance of hospital operation flaws became apparent in the MERS breakout when **Hospital B** infected over 80 people, through ineffective actions and lack of protocol within emergency room (Korea Centers for Disease Control and Prevention, 2015).

Consequently, due to healthcare system shortcomings, there is a strong need for operational review of the MERS outbreak, and we undertook this study to contribute to "preventive" epidemiological efforts in forestalling infectious disease spread, in parallel to "cure" efforts from epidemiologists and/or hospital physicians and staff. Our study aimed to address the following research objectives: (i) systematic examination and measurement of the flaws of existing healthcare operation that hypothetically affected the MERS outbreak, and (ii) development and provision of operational guidelines that can alleviate future outbreaks as continuous improvement efforts.

The study is organized as follows. The next section presents the background of MERS as an HAI, followed by a methodology section that describes both the qualitative and quantitative approaches we undertook, followed by the results and discussion. Finally, we conclude with a summary to show the needs for current shortcomings in Korean healthcare system and to optimize performance as a whole system, rather than mere individual aspects.

2. Hospital acquired-infection and overcrowding of hospital rooms

Hospital-acquired infections (HAIs) or healthcare-acquired infections (HCAIs) issues have been quantified as a 1 in 10 hospitalized patients acquiring infection after admission (Graves, 2004). Hand hygiene has been acknowledged as the most common source of infection transmission from one patient to another (Allegranzi and Pittet, 2009) and as the foundation of healthcare associated infection preventions (Kretzer and Larson, 1998; Pittet et al., 2006). However, Korea currently practices controversial healthcare settings for patients with infectious diseases, e.g., excess installation of multi-patient beds per rooms and encouragement of family visitor caregiving for infected patients.

2.1. Single-patient rooms versus multi-patient rooms

As a part of the Korean healthcare system's efforts to provide citizens with complete medical care, the system is also under pressure to lower medical costs. The Korean government has been trying to optimize patient room design by increasing numbers of “multi-patient rooms” rather than “single-patient rooms”, in order to minimize overall healthcare cost for its citizens, as announced at the 2015 Health Insurance Policy Review Committee Conference in Seoul. Consequently, the existing system neglects operational perspectives and raises concerns by allowing 50% of hospital rooms to have more than four beds per room (Ki, 2015). Under another global view, the Canadian Standards Association argued that expansion of single patient rooms is no longer an option but a necessary decision (Stall, 2012), highlighting the relationship between patient room design and increased hand-touch dimensions within specific, patient-proximal areas. Stall (2012) reported risks of infections (such as *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and vancomycin-reistant *Enterococcus*) increased by 10–11% with new exposure to hospital roommate. Therefore, noted that with an increasing deadly threat of nosocomial infections, rooms with four or more beds expose patients to potential infections and, thus, the installation of single patient rooms is vital. Thus, infection control activities have been emphasized, such as the isolation of high-risk patients or patient with epidemiologically significant pathogens (Huang and Platt, 2003; Marshall et al., 2004). Furthermore, Bootsma et al. (2006) developed rapid diagnostic testing (RDT) for prediction of MRSA (methicillin-resistant Staphylococcus aureus) to a below 1%, using Monte Carlo simulation model. While prevention of HAIs has been previously studied and applied elsewhere, its need for application in Korean policy remains unaddressed.

2.2. *Frequent family visit and caregiving*

Family visiting and caregiving is a culturally active norm in the Korean healthcare system. However, the active family care has increased the risks of disease transmission, through frequent contacts with patients and hand-touch areas. Hand-touch sites are pathways to transmit pathogens from patient to patient, healthy visitors, caregivers, and/or hospital staff (Oelberg et al., 2000; Rheinbaben et al., 2000). Even though ward cleaners are given specific cleaning specifications of general areas and bathrooms, these do not cover all hand-touch sites that are specifically near patients, such as bed rails and nurse call buttons (Dancer, 2004; Dancer et al., 2008; White et al., 2008). Consequently, frequent hand-sites provide imminent risks for patients and visitors, especially the sites that are closely situated beside patients. Bhalla et al. (2004) performed a two-week experiment using organisms such as vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus* to examine the frequency of hand acquisition of pathogens, after contact with surfaces near patients, and found that “hand imprint cultures were positive for one or more of the pathogens after contacting surfaces in 53% of occupied patient rooms, and 24% of rooms that had been cleaned after patient discharge.” Their research concluded that the environment could play a significant role in the contamination of medical staff. Korea, where families are obligated to provide partial patient caregiving as a social norm (Ki, 2015), is in dire need for social education in the negative influence of frequent visits, and excessive care of patients, leading to HAIs.

2.3. *Lack of operational perspective of infection control*

Besides the hand hygiene and excessive family contact frequencies as the main causes of HAIs, inadequate systems for quarantine, public health emergencies, and patient referral have been identified as critical causes of the MERS outbreak in Korea (Kim, 2015a). Under global standards, infection control needs to be applied throughout the hospital management structure, to ultimately change behavior and culture to prevent further spread of, and better treatment of, infected patients (Brannigan et al., 2009). The importance of an infection control standard of protocols is emphasized in Friesema et al. (2009) study, describing that the establishment of a speedy protocol is equally effective as the enhancement of hygienic measures. Similarly, Koopmans (2009) concluded that ineffective control of outbreaks raises the overall financial burden on both the patient and the healthcare facilities and administration (e.g., added costs for cleaning, disinfection, closure of wards including intensive care units, and postponement of surgery).

In another example, Lee and Ki (2015) reported a high-quality operational management as a requirement for an effective 4-step epidemiologic investigation, whose objective was to verify and quantitatively measure the size of an outbreak through the following steps: (1) Identification of suspected (or confirmed) cases; (2) case definition of initial case (or index patient) and estimation of the number of total cases; (3) decision of outbreak public announcement, based on the expected number of cases; and (4) determination of the appropriate response(s). Additional examples of applicable methodologies for preventing and controlling infections have been developed for real-time patient-tracking technologies, which can ultimately aid epidemiology from local to national settings (Pearson, 2009), in addition to using routine sampling techniques from the food industry for initiating environmental screens as a preventive measure for outbreaks (Griffith, 2006).

Within the simulation domain, Cooke et al. (2010) identified causes for poor patient treatment delays, using system dynamics modeling, and discovered a need for robust and long-term solutions (rather than local solutions), for understanding the underlying dynamics of the system. While system dynamics model does not aim to reflect the consequences of short-term variability, or specific answers to policy changes at the tactical level, its essence lies in providing effective aids for a variety of research objectives in the healthcare industry (Wolstenholme, 1993).

Healthcare system modeling studies are generally partitioned into two categories: (1) a macro-level, which mainly uses system dynamics model for high-level modeling; and (2) a micro-level, which incorporates discrete-event simulation and queuing analysis, for in-depth modeling of specific healthcare functions and patient pathways (Rohleder et al., 2013). Using a macro-level system dynamics modeling approach, our study intends to investigate the effect of operational decisions, such as patient-room design, occupancy control at emergency room and patient-visitor management, on the patient-care performance, such as number of infected patients (secondary infections) and financial burden on patients.

3. Methodology

We identified comprehensive constructs of stocks and flows, in accordance with Sterman’s (2000) suggestions for high-level model building, based on a semi-structured interview process. Then, we referenced previous transmission dynamics studies of Severe Acute Respiratory Syndrome (SARS), which reflects similar pertinent variables such as infectivity rate, the likelihood of an outbreak, and the impact of control measures (e.g., Anderson et al., 2004; Lipsitch et al., 2003; Riley et al., 2003). Lastly, based on Wolstenholme’s (1993) thinking system approach, we took efforts to sequence customized epidemiology investigation, specifically MERS-CoV case management, to systematically identify the status of each patient (i.e., susceptible or infected).

3.1. *Semi-structured interview*

We adopted a qualitative analysis, derived from Bhakoo & Choi (2013)’s semi-structured interview protocol, to build our sys-

Table 1
Representative quotation related to MERS outbreak.

Categories	Cases	Illustrative quotes and examples from healthcare administrators
Human resources	Lack of nurses	*"Although it may vary depending on the regions, nurses are most likely to be understaffed in most of the hospitals at the moment"* *"Despite the increase in hospital revenues, most of the hospitals are facing difficulties in fulfilling appropriate numbers of nurses"*
	Lack of ward cleaners	*"Hospital cleaning roles and responsibilities are outsourced, and their expertise and quality control management level are questionable. There is a limitation in enforcing standardized quality level specifics"*
Knowledge and skills	Lack of knowledge in nosocomial viruses	*"Current overall perceptions of nosocomial viruses are critically low. Thus, except for a few large hospitals, the rest of hospitals do not have the proper resources in place"*
	Lack of training	*"Prior to MERS outbreak, hospitals including small local hospitals lacked understandings and trainings in how to deal with potential respiratory infection viruses"*
Equipment and technology	Limited equipment for isolation in case of outbreak (quarantine)	*"Only a limited number of hospitals carry appropriate equipment and isolation capability for infection prevention"*
Financial	Lack of government support	*"Government does not provide sufficient incentives for hospitals that install special equipment for infection prevention."*
	Excessive government requirement	*"Government provides too much guideline and policy in cooperating with healthcare insurance (i.e., reconstructing patient-room design to expand multi-patient rooms for overall cost down)"*
Information	Lack of information sharing between hospitals	*"Hospitals are extremely sensitive to reputation. With a high sensitivity to negative image, they are generally reluctant to share information to public and extremely careful in sharing information with other hospitals"*

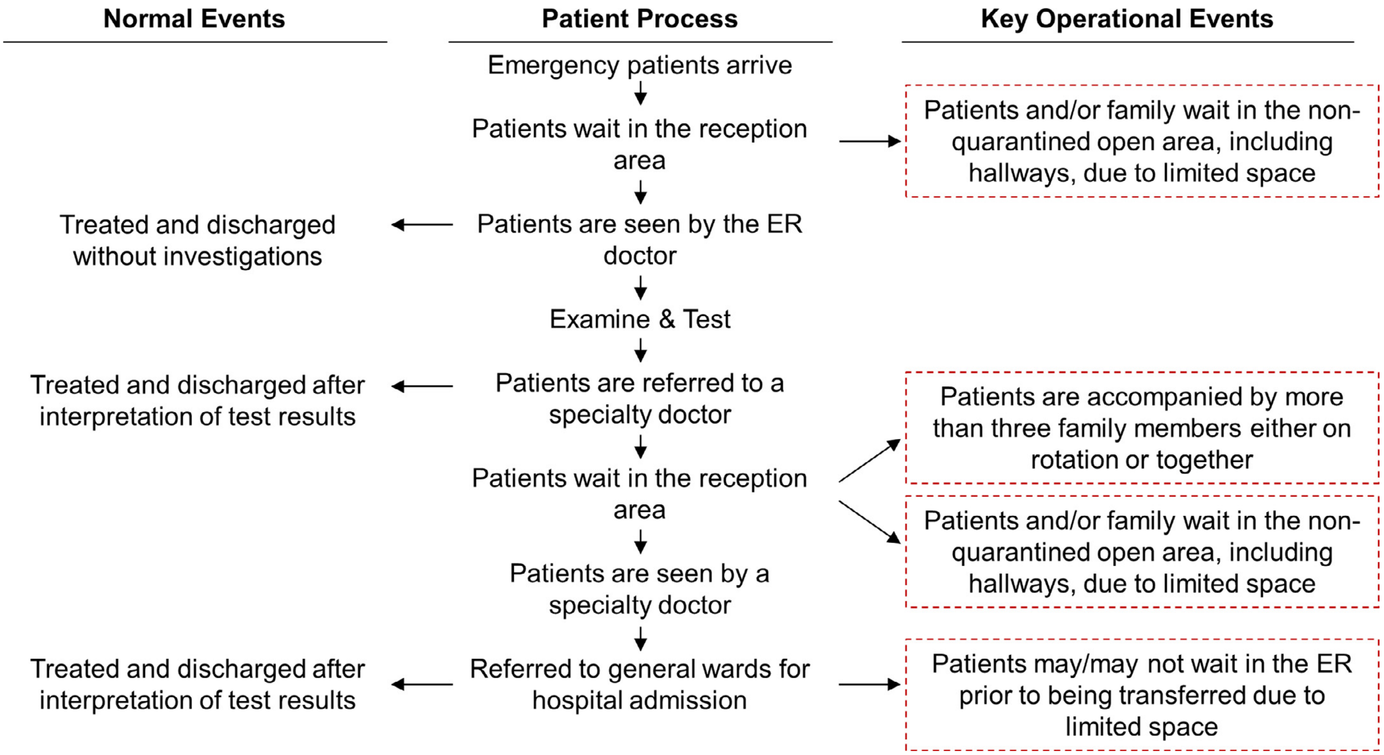

Fig. 2. Schematic representation of ER elements, processes, and pathways considered for system dynamics model.

tem dynamics model, as follows: (1) initial interview questionnaires; (2) discussions of operational variables of patient care process**,** followed by collaborative design of a system model, and modification to questionnaires; (3) additional discussion until no new key operational aspects are discovered; and lastly (4) confirmation of the system model that represents dynamic hypotheses relevant to the case study. The final interview questionnaire is shown in **Appendix A**.

We next compiled a comprehensive list of quotes from official investigators of the Korean MERS outbreak, Korea healthcare system experts, and reports based on hospital staff and patients who were involved in the outbreak (Bae, 2015; Choi et al., 2015; Kang, 2015). Table 1 illustrates representative quotes relevant to the study analysis.

Finalized key operational factors that affected 2015 Korea MERS outbreak in emergency room have been summarized in Fig. 2.

3.2. Data collection and initial analysis

We combined the abovementioned qualitative findings with quantitative findings from the case of MERS outbreak in Korea, in order to finalize the model in preparation for quantitative analysis.

3.2.1. Data collection

Our accumulated data of infection cases was based on a publicly available site, jointly operated by the Ministry of Health and Welfare and Korean Centers for Disease Control and Prevention, and peer-reviewed articles (Table 2).

Table 2
References for data collection.

Category	Provided data	Reference
Demographics and characteristics of infected cases	Patient number, gender, age, admission/confirmed date, infected location, infection route, existing illness	(Central MERS Management Headquarter, 2016; Ki, 2015; Kim et al., 2015b; Korea Centers for Disease Control and Prevention, 2015)

Table 3
Summary of confirmed cases of MERS outbreak in Korea 2015 (n = 186).

Classifications		Number of Patients	% of Total
Infection generation	Index patient	1	.5
	1st	28	15.1
	2nd	125	67.2
	3rd	32	17.2
Infected patient	Existing patient	113	60.8
	Visitors & caregivers	32	17.2
	Medical staffs	40	21.5
	Unidentified	1	.5
Infected location	Same room	27	14.5
	Same ward	69	37.1
	Emergency room	82	44.1
	Others	5	2.7
	Unidentified	3	1.6
Patients with existing illness	Yes	15	8.1
	No	171	91.9

Table 3 summarizes the classifications of 186 MERS confirmed cases by the infection generation, infected patient type, infected location, and possession of preexisting illnesses. With a single index patient (generation zero), a total of 3 generations of secondary infections occurred: 1st generation of 28 patients infected by the index patient, 2nd generation of 125 patients infected by the 1st generation, 3rd generation of 32 patients infected by of 2nd generation. Not only was the infection transmitted between patients (60.8%) and visitors (17.2%), MERS also infected medical staff members, including doctors, nurses, and even ambulance drivers (21.5%). Moreover, various outbreak locations showed a clear indication of nosocomial infection with a significant spread rate in patient rooms (14.5%), emergency rooms (44.1%), and patient wards (37.1%).

3.2.2. Initial data analysis

Table 4 summarizes the characteristics of the various infected generations of 183 confirmed cases (excluding two unidentified cases and the index patient) by infection location and patient type. The center of infection spread was general wards for the 1st and 3rd generation (with 20 cases and 16 cases, respectively), and emergency room for 2nd generation (with 73 cases). The majority of infected personnel were inpatients (61%), followed by medical staffs (22%), and visitors (17%).

3.3. System dynamics model and input variables

System dynamics modeling was chosen to visually demonstrate the stock and flow perspective of the susceptible and potential infected patients. Using Vensim PLE 6.3G modeling software, we illustrated a stock and flow system, with patients representing the flow, to aid in designing appropriate disease control action plans for varying environmental hospital settings.

The model illustrated in Fig. 3 depicts a high-level overview dynamics model of causal relationships between operational decisions (patient room designs, occupancy control at emergency room, patient-visitor management) and patient care performance (number of infected patients and average cost per patient). The aim of this model was to applicably aid decision processing, addressing dire needs for evaluating overall causal relationships and system design. We chose exogenous and endogenous variables in the simplest form, rather than trying to accurately mimic the MERS outbreak. Thus, the sole purpose of the study was to simulate different results dependent on different operational decisions, and to close the gaps among epidemiologists, policy makers, and healthcare operation experts in understanding the MERS outbreak. While an actual outbreak prediction model, representing the actual event, would have been ideal, such an endeavor exceeds the scope of this study.

We followed Cooke et al.'s (2010) processing scheme, prior to finalizing the model. First, we performed the discussion among the healthcare operation management experts. After the discussion, the model was modified with information representing the opinions of various groups. Second, we consulted systems engineering consultants to finalize the logic of the healthcare model. Lastly, we then developed two models, mainly focused on overcrowding variables and patient room design, to evaluate changes in the infection spread rate. The listed exogenous variables for the system were set up such as to represent general hospital settings in Korea (Table 5).

Input variables were estimated based on the representative cases of **Hospital A** and **Hospital B. Hospital A**, the representative setting of the general ward (GW) environment, is where the index patient stayed on both the 7th and 8th floors. A total of 929 (263 patients, 389 caregivers, and 277 medical staff members) subjects were exposed to MERS transmission (Kim et al., 2015b). As we discovered during the interview process, each floor supports an average of 40 beds, and the occupancy rate of GW (α) was about 85%. **Hospital B**, the representative setting of the emergency room (ER) environment, was where one of the super spreaders (who transmitted the infection to more than four patients) Patient 14 stayed, supporting an average of 60 beds in the ER. The occupancy rate of ER (α) was 111% which placed within top 10 overcrowded national university hospitals in Korea (avg. = 105%, low = 79%, high = 182%).

Table 4
Number of confirmed cases excluding unidentified cases (percentile) (n = 183).

Classifications		1st generation	2nd generation	3rd generation	Total
Infected location	Patient room	8 (.04)	16 (.09)	3 (.02)	27 (.15)
	General ward	20 (.11)	33 (.17)	16 (.09)	69 (.37)
	Emergency room	–	73 (.40)	9 (.05)	82 (.45)
	Others	–	1 (.01)	4 (.02)	5 (.03)
Total		*28 (.15)*	*123 (.67)*	*32 (.17)*	*183 (1.0)*
Infected patients' profile	Existing patient	13 (.07)	86 (.47)	13 (.07)	112 (.61)
	Family or visitor	11 (.06)	16 (.09)	4 (.02)	31 (.17)
	Medical staff	4 (.02)	21 (.11)	15 (.09)	40 (.22)
Total		*28 (.15)*	*123 (.67)*	*32 (.18)*	*183 (1.0)*

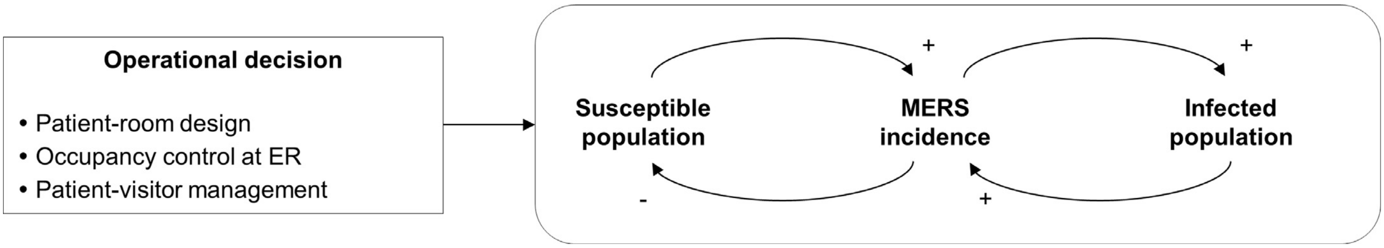

Fig. 3. General diagram of the model.

Table 5
Exogenous variables for system dynamics model.

Variables	Description
BEDS	Number of beds in the ER and general ward, including single-patient and multi-patient rooms.
α	Daily occupancy rate of ER and general ward, including single-patient and multi-patient rooms.
β	Average number of persons who physically visited and/or cared for the patient, partially carrying out the responsibility of caregiving.
CONTACT	Average number of daily contacts that occurred for a single patient in the corresponding area including wards, lobby, kitchen, and ER.
λ	Probability of secondary infection caused by the index patient.

Table 6
Parametric specifications of GW and ER settings.

Input variable	GW setting	ER setting
Number of beds (*BEDS*)	40	60
Occupancy rate (α)	.85	.79 *low*; 1.82 *high*
Number of visitors (β)	3	1 *low*; 3 *base*; 5 *high*
Number of contacts (*CONTACT*)	7	
Infectivity rate (λ)	.01 *low*; .05 *base*; .10 *high*	

Table 7
Results of 1st secondary infection cases and simulation result.

Input variable	Patient 1 (GW Setting)	Patient 14 (ER Setting)
Duration (days)*	10	9
Number of close contacts*	626	594
Contacts made per patient per day*	63	66
Attack rate (infectivity rate)*	.04	.14
Occupancy rate*	.85	1.11
Actual number of infected patients*	27	78
Simulated number of infected patients	25	77

* Actual value for variables adopted from the Korea Centers for Disease Control and Prevention (2015)

Table 8
Numbers of infected patients on day 10.

Number of visitor(s)	$\beta = 1$		$\beta = 3$		$\beta = 5$		
ER occupancy rate	Low	High	Low	High	Low	High	Mean
Low infectivity	1.7	3.3	1.7	3.3	1.7	3.3	2.5
Base infectivity	10.8	98.9	11.1	116.0	11.2	122.8	61.8
High infectivity	22.6	201.3	24.4	318.6	25.0	383.3	162.5

Additional details for involved hospitals and MERS infectivity rate are as follows:

- The number of visitors (β) was conservatively estimated, with a minimum of three visitors per patient in the GW, and three visitors per patient in the ER. The cultural norm allows for family members' participation in caregiving to the patient, regardless of the availability of nurses and other professional caregivers.
- The contact frequency (*CONTACT*) was estimated based on the provided number of close contacts by the Korean Centers for Disease Control and Prevention (2015). Based on contact investigations of Patient 176, average of 7 direct contacts with family members and visitors per day have been estimated.
- The infectivity rate (λ) was estimated based on Drosten et al. (2014) finding of a 5% secondary transmission rate among household contacts of patients with MERS-CoV. While Kim et al.'s (2015) study estimated 3.9% attack rate (or infection rate) at the residence of the index patient, they also found range of 1.4%–14.3% attack rate without significant pattern in its environmental settings or infection spread patients' characteristics. Thus, while considering 5% as our base infectivity rate, we also examined effects of different infectivity rates further in this study.

The comprehensive parametric settings of the initial model are demonstrated in Table 6. Collecting and developing more detailed input variables that lead to accurate prediction of the infection spread should be the aim of future studies, but goes beyond our goal.

3.3.1. General transmission dynamics model

Fig. 4 shows the first secondary infected population model in this study. In brief, first, total population is the summation of patients' arrival dependent to occupancy rate at the interested environmental setting, and number of visitors dependent to number of patient arrival. Total population is established as a susceptible population contributing to the estimation of probability of contact with infected patient, arising of a single infected patient. Second, cumulative estimation of the first secondary infected patients, as of day 1, is calculated based on the function of the infectivity of MERS and the contacts between infected and susceptible population. Lastly, model is ran and observed for the number of interested days or until no susceptible population is available. Positive sign (+) indicate whether the origin event/population positively contributes to the next event/population. The parametric settings of (i) number of patients and visitors are estimated based on patient's hospital information, and (ii) number of contacts made per day, infectivity rate of MERS and occupancy rate are presented in Table 7.

We performed "white box" analysis, also known as structure-based validation, for verifying the model (Brailsford et al., 2004; Lane et al., 2000), using information from official investigators of the MERS outbreak, to ensure the accuracy of the model's representation in Fig. 4. The objectives of this test were to gain qualitative insight into the system, and to include the appropriate perceptions of the actual processes in "real world" settings.

The comparison of Fig. 4 simulation result with the actual data of Patient 1, within general ward (GW), and actual data of Patient 14 within emergency room (ER) are shown in Table 8. Simulation results of infected patients are shown as 25 and 77, respectively to

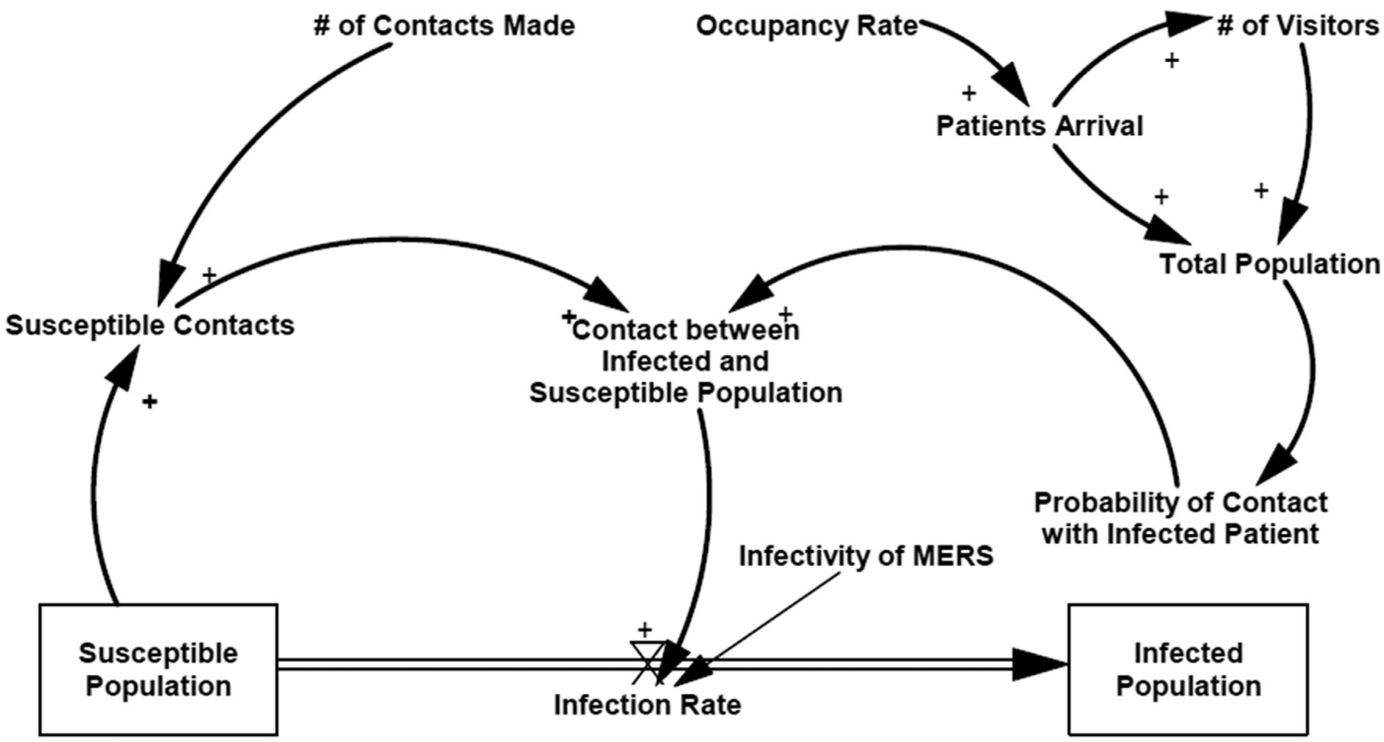

Fig. 4. First secondary infection model for Patient 1 and Patient 14.

Patient 1 and 14, in finding to the actual number of 27 and 78 are very similar to the model.

4. Operational decision-based modeling, analysis, and results

The finalized system dynamics models of a single hospital (Figs. 5 and 7) illustrate feedback loops dependent on operational decision variables (patient-room design, ER occupancy control, patient-visitor management), which also drive the system behavior represented by the total number of infected patients (secondary infection). While the abovementioned general transmission dynamics model illustrates a causal loop diagram of first secondary infection model, this section constructs and analyzes models that incorporate operational decision variables and closely observe secondary infection outcomes. The right-hand side of the model represents increasing population infected with MERS, while the left-hand side of the model represents a decreasingly susceptible population. The nature of the loop does not account for the cure rate, but solely focuses on the sensitivity of the change in the exogenous variable.

We performed two main scenario-based simulations and evaluated (1) the effect of ER overcrowding on secondary infection outcomes; and (2) the effect of patient room design on total patient-care performance.

4.1. Effects of ER occupancy rate and number of visitors on secondary infection outcome

To demonstrate the effect of ER occupancy rate on the patient care performance, we evaluated varying potential numbers of infected patients by the ER occupancy rate ($\alpha_{low}=.79$, $\alpha_{high}=1.82$), the number of visitors per patient ($\beta_{low}=1$, $\beta_{base}=3$, $\beta_{high}=5$), and the infectivity rate ($\lambda_{low}=.01$, $\lambda_{base}=.05$, $\lambda_{high}=.07$) as shown in Fig. 5. Briefly, the first secondary infected population model, added the emergency occupancy rate and number of contacts made in the ER within the model). We specifically focused on day 10 in accordance with the super spreaders' average exposed duration of 10 days (Korea Centers for Disease Control and Prevention, 2015). Table 8 summarizes the estimated number of infected patients on day 10.

Table 9
Rate of secondary infection transmission in high (vs. low) ER occupancy circumstance.

Number of visitor(s)	$\beta=1$	$\beta=3$	$\beta=5$
Low infectivity	x1.9	x1.9	x1.9
Base infectivity	x9.2	x10.4	x10.9
High infectivity	x8.9	x13.1	x15.3

Under all infectivity scenarios, the numbers of infected patients appeared insensitive to the low ER occupancy- (no. infected patients avg. $=1.7\pm0$ *low*; $11.1\pm.2$ *base*; 24.0 ± 1.3 *high*) compared to the high ER occupancy- circumstance (no. infected patients avg. $=3.3\pm0$ *low*; 112.6 ± 12.3 *base*; 201.1 ± 92.3 *high*). Consequently, these results highlight the importance of ER overcrowding management as a preventive measure for outbreaks.

Table 9 demonstrates how the number of visitors, per patient, increased the speed of secondary infections in high (compared to low) ER occupancy circumstance. The change in the secondary infection speed between low- and high occupancy circumstances becomes apparent by comparing low infectivity (x1.9 to x1.9) and high infectivity (x8.9 to x15.3) scenarios. Specifically, under base infectivity scenario, allowing 5 visitors per patient (vs. 1 visitor) contributed to an estimated 23.4 (27%) more infected patients.

Fig. 6 (A) and (B) visually confirm a sharp increase in the numbers of infected patients under the high occupancy- (Fig. 6 (B)) vs. low occupancy-circumstances (Fig. 6 (A)). Moreover, the increased number of visitors, per patient, affected overall secondary infection outcome more severely, in both high- (min. $=201.3$, max. $=383.3$) and low-occupancy circumstances (min. $=22.6$, max. $=25.0$).

Lastly, Fig. 6 (C) illustrates the comparison of the two extreme worst and best case scenarios under base infectivity scenario. The worst case scenario represents high ER occupancy, with high num-

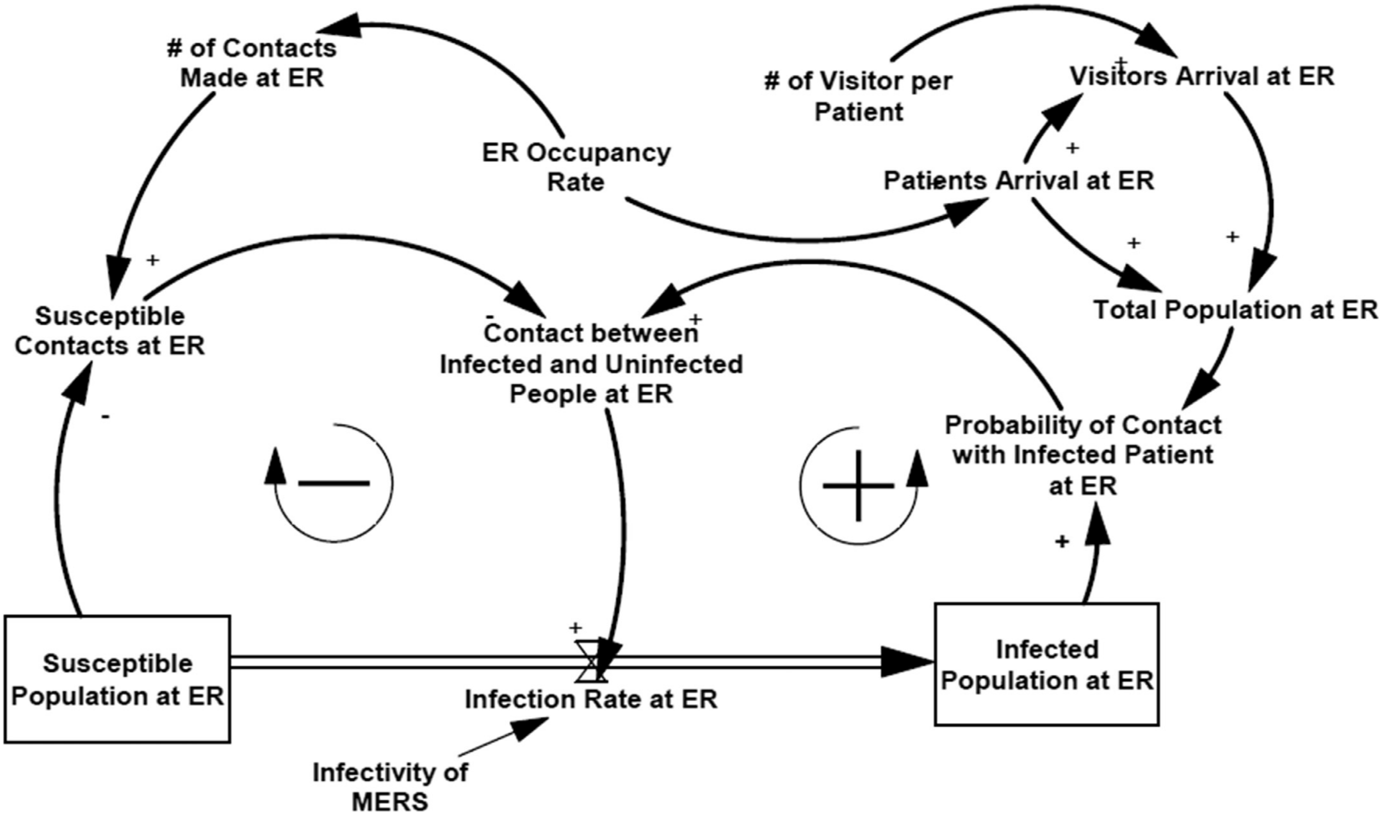

Fig. 5. System dynamics model of emergency room.

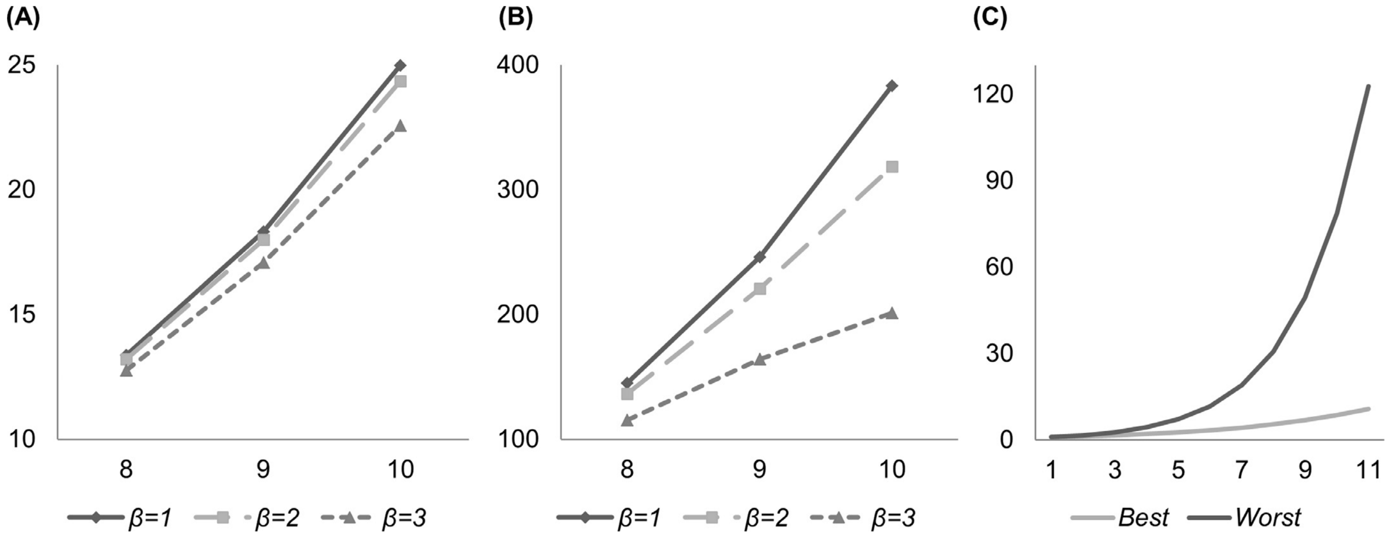

Fig. 6. Potential number of infected patients (y-axis) and number of days (x-axis).

bers of visitors per patient, and vice-versa for the best case scenario. Consequently, the visible gap in secondary infection outcome starts widening on day 5, reaching its maximum of estimated 122.8 infected patients, on day 10.

4.2. Effect of patient room design on total patient-care performance

To capture the effect of the patient room design on the total estimated number of infected patients on day 10 in GW setting, we assigned fractions of susceptible contacts made at each room (e.g., CONTACT = 1 for single-room, 4 for 4-patients room, and 6 for 6-patients room) as shown in Fig. 7. Briefly, the first secondary infected population model, added the fractions of single patients, four patients and to six patients.

Details of patient room design, costs, and estimated number of infected patients are shown in Table 10 under the parametric settings of the number of beds ($BEDS = 40$), the occupancy rate ($\alpha = .85$), the number of visitors per patient ($\beta = 3$), and the infectivity rate ($\lambda_{low} = .01$, $\lambda_{base} = .05$, $\lambda_{high} = .07$). Number of patients' arrival, patient capacity, and beds are assumed equal across varying design types (A through F), while number of rooms will differ (i.e., design A may offer 6 single-patient rooms when design F offer a single room with 6 beds). We estimated costs of private rooms and multi-patient rooms, based on the data of representative three hospitals

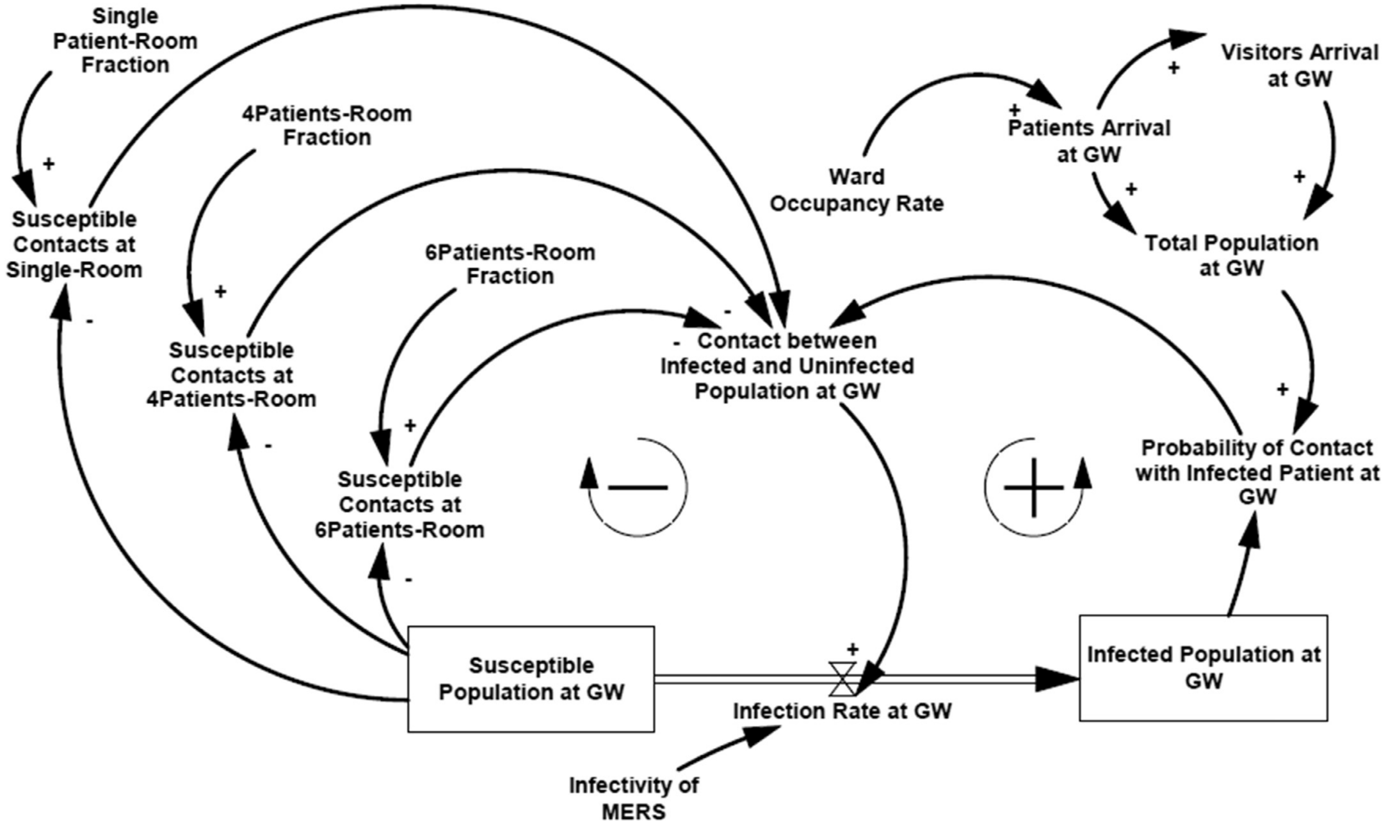

Fig. 7. System dynamics model of general ward.

Table 10
Details of patient room design, number of infected patients, patient charge on day 10.

	Economic design	←		→		*Optimal design*
Design type	**F**	**E**	**D**	**C**	**B**	**A**
Fractions of patient room						
Single patient room	-	10%	25%	50%	80%	100%
4-patients room	-	10%	25%	25%	10%	-
6-patients room	100%	80%	50%	25%	10%	-
Number of infected patients						
Low infectivity	1.8	1.7	1.5	1.3	1.2	1.1
Base infectivity	13.1	10.1	6.7	4.0	2.4	1.6
High infectivity	29.0	21.3	12.8	6.6	3.3	2.0
Expected patient charge (USD)						
Total	333	1,667	3,667	6,917	10,767	13,333
Average per patient	8	42	92	173	269	333

in Seoul, as publicly provided on the National Health Insurance Review and Assessment Service website (Health Insurance Review and Assessment Service, 2016). The patient charge of private rooms was significantly higher than multi-patient rooms, as private rooms are not covered by national healthcare insurance. Thereby, the average costs of single-, 4-, and 6-patient rooms were estimated to be 400,000KRW (approx. 333 USD), 20,000 KRW (approx. 16 USD), and 10,000 KRW (approx. 8 USD), respectively.

While the average expected cost per patient could be as low as 8 USD, based on a 100% 6-patient room economic design, a maximum of 29.0 infected patients from one-hospital model were estimated in high infectivity situations. By merely increasing the fraction of total beds of single-patient rooms to 25% and reducing 6-patient rooms to 50%, the newly changed patient room design effectively lowered the number of infected patients by more than 50%, for an additional $83 USD per patient in both base and low infectivity scenarios.

Table 11
Reduced percentage of number of infected patients, reference to economic design F.

Design type	F	E	D	C	B	A
Low infectivity	0%	6%	15%	25%	33%	38%
Base infectivity	0%	23%	49%	69%	82%	88%
High infectivity	0%	27%	56%	77%	89%	93%

While the decrease in numbers of infected patients seemed invariable in both the low and base infectivity cases (Fig. 8), the decrease in proportion of infected patients is significant (Table 11).

By considering design type C in placement of type F, the simulation result shows 25% and 69% decrease in total number of infected patients in low and base infectivity scenarios, respectively. Additionally, in high infectivity scenario, both the curvature and rapid increase in percentages clearly indicate significant effect of

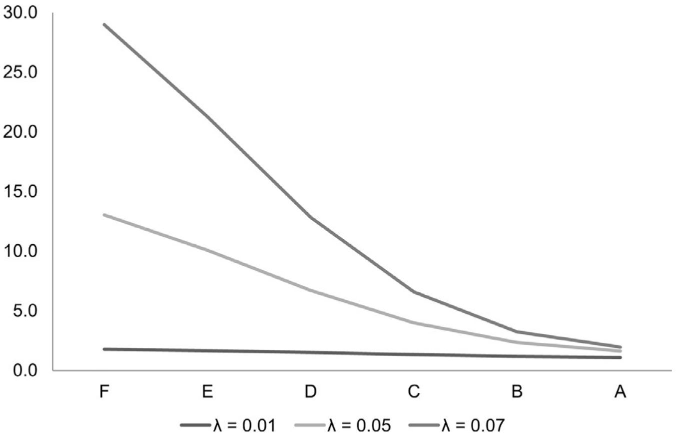

Fig. 8. Numbers of potentially infected patients (y-axis) by patient-room design (x-axis).

design type on secondary infection outcome. Overall, the estimated number of infected patients sharply decreased as the total cost of the patient rooms increased by multiples of, and total costs of, patient rooms.

5. Discussion

5.1. Summary of the main findings

Our system dynamics model was built to incorporate and minimize the gap among perspectives of epidemiologists, policy makers, and healthcare operation experts in Korea. It is essential to examine the means to lower viral infectivity rates and the need for operational examination became inevitable, as shown in our study.

The comparison of economic and optimal patient room design scenarios showed that under the low infectivity scenario, patient room designs did not show significant number of infected patients, over a 10-day of period. However, under the all infectivity case scenarios, the financial savings of economic design were offset by the increased proportion of infected patients, thus worsening patient care outcome. While it is impractical to advocate exclusive single-patient room installations, alternative designs to current economic designs are necessary.

Secondly, excessive ER occupancy rates, at a 182% maximum, based on a recent report on overcrowding in Korea hospitals (Oh, 2016), has become an imminent problem in Korea. While the secondary infection outcomes under low ER occupancy circumstance showed a minimal effect, high ER occupancy circumstance displayed maximum of 92.3 infected patient differences. The restriction of occupancy rates appeared significantly dependent on number of visitors, per patient, under base and high infectivity scenarios

Lastly, frequent visits from families and friends highly affected the infection spread-rate. Korean cultural tradition encourages social etiquette for families to act as caregivers when their immediate family member is hospitalized. Consequently, more than 20 percent of the confirmed infected cases in the Korean 2015 MERS outbreak were family members of inpatients, and it became clear that family caregivers could have transmitted pathogens to other inpatients within the same hospital environments. In support of the Korean healthcare organization's statement that the cultural tendency of frequent visits to patients needs to be reassessed (Choe, 2015b), our simulation result demonstrated that a decrease in number of visitors from 5 to 1 resulted in a dramatic decrease in the potential number of infected patients. Moreover, comparing the best- and worst-case scenarios illustrated a gap of approximately 122.8 patients, by day 10.

While optimal patient care-centric hospital designs may place financial burdens on individual patients, successfully decreasing the number of total potentially infected patients, from the entire system's perspective. While operational decisions may not have directly mitigated the MERS infectivity rate, it could significantly improve patient-care quality by alleviating rate of spread within medical centers (Vincent et al., 2008). It is important for healthcare management and healthcare participants to consider optimizing overall system's benefit over individual's healthcare benefit.

5.2. Managerial implications

A lack of systematic guidelines in handling infectious disease outbreaks, across different hospital tiers, represents vulnerability in Korean healthcare operations. No specific guidelines were provided for the transfer of patients from one facility to another, causing misplacement of critical information. Besides environmental factors, intrinsic factors, such as lack of knowledge of infectivity, proper guidelines, prior to patient admission or transfer, could also effectively minimize the rate of infection transmission.

We further showed that by pairing thorough interviews with healthcare professionals, in addition to the use of simulation tools (e.g., stock and flow charts and causal loop diagrams), integrative efforts will contribute to the development of a comprehensive qualitative model of prevention. Kim et al. (2015a) reported comprehensive infection control measures and recommendations for healthcare facilities highlighting procedures for hand hygiene and use of personal protective equipment (hand hygiene), testing procedure of radiological examination and diagnostic collection, packaging, transportation (laboratory management), following with isolation procedure for outpatient, emergency room patient, and visitors (patient management) for the recommendation. Study includes surgery procedure and postoperative removal procedure (surgery on suspected or infected patient) in guideline to improve emergency response to outbreaks and to prevent of MERS CoV. Our study adds the values in the operational factors as an importance of patient room design (layout management) and family caregiving and visit frequencies (occupancy control management), consequently adding additional values to previously reported guidelines.

6. Conclusions and future directions

The objective of this endeavor was to understand the effect of operational decisions on the infection spread process, which could potentially halt or reduce deadly outbreaks. Built upon discussions with representatives of MERS outbreak researchers and Korean healthcare system experts, we designed an applicable initial model that incorporates fundamental perspectives of healthcare operations. The healthcare industry, made up of different tiers of organizations with different objectives, can truly benefit from the application of system dynamics models, which effectively consider different participants and multitudes of interactions. In our view, this approach can effectively close the gap between understanding and preferred solutions by different disciplinary experts, for overall healthcare quality management.

Future studies on the investigation of optimal healthcare operations management could benefit by integrating other key determinants of hospital-acquired infections provided by Kim et al. (2015a) (i.e., contact control via personal protective equipment, disinfection, and environmental cleaning). Second, the model used in this research currently assumes the hospital is able to provide equal number of beds whether they are economic design (all 6-patients room) or optimal design (all single patient room) through the unrestricted ward capacity. Following assumption could impact the economic assumption, thus, future studies should consider the inclusion of financial perspective for the healthcare operational cost optimization. Lastly, future building of system dynamics model in healthcare should consider the addition of "black box" testing as part of the model validation process (Brailsford et al., 2004). While we did consider black box testing, which quantitatively measures and compares the simulation result with data from the actual event, we found that such analysis was beyond the purview of our current study. However, researchers, whose main objectives are to closely model the actual outbreak, could benefit from adopting such validation processes.

Conflict of interest

The authors declare no conflicts of interest regarding the contents of this manuscript.

Author contributions

All authors contributed to the discussions and design of the framework. Nina Shin and Yon Hui Kim designed and developed the research. Taewoo Kwag conducted the interview and contributed the analysis. Nina Shin and Sangwook Park conceived, developed, and analyzed the system dynamics model. Nina Shin and Yon Hui Kim wrote the manuscript. Sangwook Park and Yon Hui Kim contributed materials and analysis tools. All authors read and approved the final manuscript.

Acknowledgement

The authors thank the Institute of Management Research at Seoul National University for supporting this research. Note that the interpretation and conclusions contained herein do not represent those of Ministry of Health and the Korean Centers for Disease Control. All of the data used within the study were from public sources.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jtbi.2017.03.020.

References

Allegranzi, B., Pittet, D., 2009. Role of hand hygiene in healthcare-associated infection prevention. J. Hosp. Infect. 73, 305–315. doi:10.1016/j.jhin.2009.04.019.

Anderson, R.M., Fraser, C., Ghani, A.C., Donnelly, C.A., Riley, S., Ferguson, N.M., Leung, G.M., Lam, T.H., Hedley, A.J., 2004. Epidemiology, transmission dynamics and control of SARS: the 2002-2003 epidemic. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 359, 1091–1105. doi:10.1098/rstb.2004.1490.

Assiri, A., McGeer, A., Perl, T.M., Price, C.S., Al Rabeeah, A., a, Cummings, D.A.T., Alabdullatif, Z.N., Assad, M., Almulhim, A., Makhdoom, H., Madani, H., Alhakeem, R., Al-Tawfiq, J., a, Cotten, Watson, S.J., Kellam, P., Zumla, A.I., 2013. Hospital outbreak of Middle East respiratory syndrome coronavirus. N. Engl. J. Med. 369, 407–416. doi:10.1056/NEJMoa1306742.

Bae, J.-M., 2015. "The Duty to Prevent" during an epidemic situation like 2015 Korean MERS outbreak. Epidemiol. Health 37. doi:10.4178/epih/e2015037.

Bhakoo, V., Choi, T., 2013. The iron cage exposed : institutional pressures and heterogeneity across the healthcare supply chain. J. Oper. Manage. 31, 432–449. doi:10.1016/j.jom.2013.07.016.

Bhalla, A., Pultz, N.J., Gries, D.M., Ray, A.J., Eckstein, E.C., Aron, D.C., Donskey, C.J., 2004. Acquisition of nosocomial pathogens on hands after contact with environmental surfaces near hospitalized patients. Infect. Control Hosp. Epidemiol. 25, 164–167. doi:10.1086/502369.

Bootsma, M.C.J., Diekmann, O., Bonten, M.J.M., 2006. Controlling methicillin-resistant Staphylococcus aureus: quantifying the effects of interventions and rapid diagnostic testing. Proc. Natl. Acad. Sci. U.S.A. 103, 5620–5625. doi:10.1073/pnas.0510077103.

Brailsford, S.C., Lattimer, V.A., Tarnaras, P., Turnbull, J.C., 2004. Emergency and on-demand health care: modelling a large complex system. J. Oper. Res. Soc. 55, 34–42. doi:10.1057/palgrave.jors.2601667.

Brannigan, E.T., Murray, E., Holmes, A., 2009. Where does infection control fit into a hospital management structure. J. Hosp. Infect. 73, 392–396. doi:10.1016/j.jhin.2009.03.031.

Breban, R., Riou, J., Fontanet, A., 2013. Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk. Lancet 382. doi:10.1016/S0140-6736(13)61492-0, 694–699.

Central MERS Management Headquarter, 2016. Press Releases [WWW Document]. URL http://www.mers.go.kr (accessed 4.18.16).

Choe, S.-H., 2015a. Experts Fault South Korean Response to MERS Outbreak [WWW Document]. New York Times. URL http://nyti.ms/1dCznMzASIA (accessed 4.15.16).

Choe S.-H., 2015b. MERS Virus's Path: One Man, Many South Korean Hospitals [WWW Document]. New York Times. URL http://nyti.ms/1FMCo3p (accessed 4.15.16).

Choi, J.H., Yoo, B., Lee, S.Y., Lee, E.G., Ki, M., Lee, W., Jung, J.R., Chang, K., 2015. Epidemiological Investigation on the 119th Confirmed MERS-CoV Case with the Indefinite Mode of Transmission in Pyeongtaek Outbreak. Korea. Epidemiol Health e2015054 doi:10.4178/epih/e2015054.

Chowell, G., Abdirizak, F., Lee, S., Lee, J., Jung, E., Nishiura, H., Viboud, C., 2015. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. BMC Med. 13, 210. doi:10.1186/s12916-015-0450-0.

Cooke, D., Rohleder, T., Rogers, P., 2010. A dynamic model of the systemic causes for patient treatment delays in emergency departments. J. Model. Manage. 5, 287–301. doi:10.1108/17465661011092650.

Dancer, S.J., 2004. How do we assess hospital cleaning? A proposal for microbiological standards for surface hygiene in hospitals. J. Hosp. Infect. 56, 10–15. doi:10.1016/j.jhin.2003.09.017.

Dancer, S.J., White, L., Robertson, C., 2008. Monitoring environmental cleanliness on two surgical wards. Int. J. Environ. Health Res. 18, 357–364. doi:10.1080/09603120802102465.

Drosten, C., Meyer, B., Müller, M.a, Corman, V.M., Al-Masri, M., Hossain, R., Madani, H., Sieberg, A., Bosch, B.J., Lattwein, E., Alhakeem, R., Assiri, A., Hajomar, W., Albarrak, A., Al-Tawfiq, J., Zumla, A., Memish, Z., 2014. Transmission of MERS-coronavirus in household contacts. N. Engl. J. Med. 371, 828–835. doi:10.1056/NEJMoa1405858.

Friesema, I.H.M., Vennema, H., Heijne, J.C.M., de Jager, C.M., Morroy, G., van den Kerkhof, J.H.T.C., de Coster, E.J.M., Wolters, B.a, ter Waarbeek, H.L.G., Fanoy, E.B., Teunis, P.F.M., van der Linde, R., van Duynhoven, Y.T.H.P., 2009. Norovirus outbreaks in nursing homes: the evaluation of infection control measures. Epidemiol. Infect. 137, 1722–1733. doi:10.1017/S095026880900274X.

Graves, N., 2004. Economics and preventing hospital-acquired infection. Emerg. Infect. Dis. 10, 561–566. doi:10.3201/eid1004.020754.

Griffith, C., 2006. HACCP and the management of healthcare associated infections: are there lessons to be learnt from other industries. Int. J. Health Care Qual. Assur. Inc. Leadersh. Health Serv. 19, 351–367. doi:10.1108/09526860610671409.

Health Insurance Review and Assessment Service, 2016. Uninsured Medical Examination Fee [WWW Document]. URL http://www.hira.or.kr/eng/index.html (accessed 6.24.16).

Huang, S.S., Platt, R., 2003. Risk of methicillin-resistant Staphylococcus aureus infection after previous infection or colonization. Clin. Infect. Dis. 36, 281–285. doi:10.1086/345955.

Kang, Y., 2015. An Interview of MERS Epidemic Investigator. Pressian.

Ki, M., 2015. 2015 MERS outbreak in Korea : hospital-to-hospital transmission. Epidemiol. Health 37, 4–7. doi:10.4178/epih/e2015033.

Kim, D.-H., 2015a. Structural factors of the Middle East respiratory syndrome coronavirus outbreak as a public health crisis in Korea and future response strategies. J. Prev. Med. Public Heal. 48, 265–270. doi:10.3961/jpmph.15.066.

Kim, J.S., 2015b. Lessons learned from new emerging infectious disease, Middle East respiratory syndrome coronavirus outbreak in Korea. Epidemiol. Health 37, e2015051. doi:10.4178/epih/e2015051.

Kim, J.Y., Song, J.Y., Yoon, Y.K., Choi, S.-H., Song, Y.G., Kim, S.-R., Son, H.-J., Jeong, S.-Y., Choi, J.-H., Kim, K.M., Yoon, H.J., Choi, J.Y., Kim, T.H., Choi, Y.H., Kim, H.Bin, Yoon, J.H., Lee, J., Eom, J.S., Lee, S.-O., Oh, W.S., Choi, J.-H., Yoo, J.-H., Kim, W.J., Cheong, H.J., 2015a. Middle East respiratory syndrome infection control and prevention guideline for healthcare facilities. Infect. Chemother. 47, 278–302. doi:10.3947/ic.2015.47.4.278.

Kim, K.M., Ki, M., Cho, S.-I., Sung, M., Hong, J.K., Cheong, H.-K., Kim, J.-H., Lee, S.-E., Lee, C., Lee, K.-J., Park, Y.-S., Kim, S.W., Choi, B.Y., 2015b. Epidemiologic features of the first MERS outbreak in Korea: focus on Pyeongtaek. St. Mary's Hosp. Epidemiol. Health 37, e2015041. doi:10.4178/epih/e2015041.

Koopmans, M., 2009. Noroviruses in healthcare settings: a challenging problem. J. Hosp. Infect. 73, 331–337. doi:10.1016/j.jhin.2009.06.028.

Korea Centers for Disease Control and Prevention, 2015. Middle East respiratory syndrome coronavirus outbreak in the Republic of Korea, 2015. Osong Public Heal. Res. Perspect. 6, 269–278. doi:10.1016/j.phrp.2015.08.006.

Kretzer, E.K., Larson, E.L., 1998. Behavioral interventions to improve infection control practices. Am. J. Infect. Control 26, 245–253. doi:10.1016/S0196-6553(98)80008-4.

Lane, D.C., Monefeldt, C., Rosenhead, J,V, 2000. Looking in the wrong place for healthcare improvements: a system dynamics study of an accident and emergency department. J. Oper. Res. Soc. 51, 518–531. doi:10.1057/palgrave.jors.2600892.

Lee, C., Ki, M., 2015. Strengthening epidemiologic investigation of infectious diseases in Korea: lessons from the Middle East respiratory syndrome outbreak. J. Korean Med. Assoc. 58, 706–713. doi:10.5124/jkma.2015.58.8.706.

Lipsitch, M., Cohen, T., Cooper, B., Robins, J.M., Ma, S., James, L., Gopalakrishna, G., Chew, S.K., Tan, C.C., Samore, M.H., Fisman, D., Murray, M., 2003. Transmission dynamics and control of severe acute respiratory syndrome. Science (80-.) 300, 1966–1970. doi:10.1126/science.1086616.

Marshall, C., Wesselingh, S., McDonald, M., Spelman, D., 2004. Control of endemic MRSA - what is the evidence? A personal view. J. Hosp. Infect. 56, 253–268. doi:10.1016/j.jhin.2004.02.001.

Oelberg, D.G., Joyner, S.E., Jiang, X., Laborde, D., Islam, M.P., Pickering, L.K., 2000. Detection of pathogen transmission in neonatal nurseries using DNA markers as surrogate indicators. Pediatrics 105, 311–315.

Oh, J., 2016. Severity of ER Overcrowding at University Hospitals (KOREAN). MediSobiza.

Park, E.C., Jang, S.I., 2012. The diagnosis of healthcare policy problems in Korea. J. Korean Med. Assoc. 55, 932–939. doi:10.5124/jkma.2012.55.10.932.

Pearson, A., 2009. Historical and changing epidemiology of healthcare-associated infections. J. Hosp. Infect. 73, 296–304. doi:10.1016/j.jhin.2009.08.016.

Pittet, D., Allegranzi, B., Sax, H., Dharan, S., Pessoa-Silva, C.L., Donaldson, L., Boyce, J.M., 2006. Evidence-based model for hand transmission during patient care and the role of improved practices. Lancet Infect. Dis. 6, 641–652. doi:10.1016/S1473-3099(06)70600-4.

Rheinbaben, F.V., Schunemann, S., Grob, T., Wolff, M.H., 2000. Transmission of viruses via contact in a household setting: experiments using bacteriophage ??X174 as a model virus. J. Hosp. Infect. 46, 61–66. doi:10.1053/jhin.2000.0794.

Riley, S., Fraser, C., Donnelly, C.A., Ghani, A.C., Abu-Raddad, L.J., Hedley, A.J., Leung, G.M., Ho, L.-M., Lam, T.-H., Thach, T.Q., Chau, P., Chan, K.-P., Lo, S.-V., Leung, P.-Y., Tsang, T., Ho, W., Lee, K.-H., Lau, E.M.C., Ferguson, N.M., Anderson1, R.M., 2003. Transmission dynamics of the etiological agent of SARS in Hong Kong: impact of public health interventions. Science (80-.) 300, 1961–1966. doi:10.1126/science.1086478.

Rohleder, T.R., Cooke, D., Rogers, P., Egginton, J., 2013. Coordinating health services: an operations management perspective. In: Handbook of Healthcare Operations Management. Springer, pp. 421–445.

Stall, N., 2012. Private rooms: a choice between infection and profit. Can. Med. Assoc. J. 184, 24–25. doi:10.1503/cmaj.109-4077.

Sterman, J.D., 2000. Business Dynamics: Systems Thinking and Modeling for A Complex World. Irwin/McGraw-Hill, Boston.

Vincent, C., Aylin, P., Franklin, B.D., Holmes, A., Iskander, S., Jacklin, A., Moorthy, K., 2008. Is health care getting safer. BMJ 337, a2426–a2436. http://dx.doi.org/10.1136/bmj.a2426.

White, L.F., Dancer, S.J., Robertson, C., McDonald, J., 2008. Are hygiene standards useful in assessing infection risk? Am. J. Infect. Control 36, 381–384. doi:10.1016/j.ajic.2007.10.015.

Wolstenholme, E.F., 1993. A case study in community care using systems thinking. J. Oper. Res. Soc. 44, 925. doi:10.2307/2584184.