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How Influenza Vaccination Policy May affect Vaccine Logistics

Tina-Marie Assi, PhD¹, Korngamon Rookkapan, PhD², Jayant Rajgopal, PhD¹, Vorasith Sornsrivichai, MD², Shawn T. Brown, PhD^{1,3}, Joel S. Welling, PhD³, Bryan A. Norman, PhD¹, Diana L. Connor, MPH¹, Sheng-I Chen, MS¹, Rachel B. Slayton, PhD¹, Yongjua Laosiritaworn, MD¹, Angela R. Wateska, MPH¹, Stephen R. Wisniewski, PhD, and Bruce Y. Lee, MD¹

¹University of Pittsburgh, Pittsburgh, PA, USA ²Prince of Songkla University, Hat Yai, Songkhla, Thailand ³Pittsburgh Supercomputing Center, Pittsburgh, PA, USA

Abstract

Background—When policymakers make decision about the target populations and timing of influenza vaccination, they may not consider the impact on the vaccine supply chains, which may in turn affect vaccine availability.

Purpose—Our goal is to explore the effects on the Thailand vaccine supply chain of introducing influenza vaccines and varying the target populations and immunization time-frames.

Methods—Utilized our custom-designed software HERMES (Highly Extensible Resource for Modeling Supply Chains), we developed a detailed, computational discrete-event simulation model of the Thailand's National Immunization Program (NIP) supply chain in Trang Province, Thailand. A suite of experiments simulated introducing influenza vaccines for different target populations and over different time-frames prior to and during the annual influenza season.

Results—Introducing influenza vaccines creates bottlenecks that reduce the availability of both influenza vaccines as well as the other NIP vaccines, with provincial to district transport capacity being the primary constraint. Even covering only 25% of the Advisory Committee on Immunization Practice-recommended population while administering the vaccine over six months hinders overall vaccine availability so that only 62% of arriving patients can receive vaccines. Increasing the target population from 25% to 100% progressively worsens these bottlenecks, while increasing influenza vaccination time - frame from 1 to 6 months decreases these bottlenecks.

Conclusion—Since the choice of target populations for influenza vaccination and the time-frame to deliver this vaccine can substantially affect the flow of all vaccines, policy-makers may want to consider supply chain effects when choosing target populations for a vaccine.

Keywords

Influenza vaccine; supply chain; immunization policy

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Corresponding Author: Bruce Y. Lee, MD MBA, University of Pittsburgh, 200 Meyran Avenue, Suite 200, Pittsburgh, PA 15213, Phone: (412) 246-6934, FAX: (412) 246-6954, BYL1@pitt.edu.

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INTRODUCTION

When policy-makers decide or make recommendations about target populations for influenza vaccination, they may not consider how they may affect vaccine supply chains (i.e., the series of steps required to get vaccines from manufacturers to patients). National supply chains need to be able to handle an immunization program as there are examples of new vaccine introduction inhibiting the supply of other vaccines[1]. Thailand and other middle-income countries are currently making such target population decisions for the influenza vaccine (e.g., whether to target individuals >65 years and when to expand to those <65 years) [2, 3]. While Thailand has well developed public health infrastructure and one of the highest-performing routine immunization programs in Southeast Asia, the influenza vaccine has historically been underutilized[4]. Previously, fewer than 100,000 doses have been distributed through the private health sector among Thailand's population of over 65 million people, covering less than 1% of the total population[5].

Therefore, the Bill and Melinda Gates Foundation-funded Vaccine Modeling Initiative (VMI) worked with the Southern Vaccine Research Team (SVRT) from the Prince of Songkla University (PSU) in Songkhla province, Thailand, to develop a computational model of the Trang province vaccine supply chain. The model was used to simulate the introduction of influenza vaccines through the routine immunization program's supply chain while varying target populations and time-frames for immunization.

METHODS

HERMES

Developed by the VMI in the Python programming language and using features provided by the SimPy package, HERMES (Highly Extensible Resource for Modeling Supply Chains) is software that can accept data on any vaccine supply chain and rapidly generate a detailed discrete-event simulation (DES) model of that supply chain to serve as a virtual laboratory. The generated model includes virtual representations of every storage location, cold room, refrigerator, freezer, transport device, vehicle, process, procedure, personnel, and vaccine vial in a supply chain. Each vial is a computational entity, which assumes various characteristics including antigen type, doses per vial, shelf-life, temperature profile, packaging size, and other presentation characteristics. Each refrigerator, freezer and transport vehicle also assumes various characteristics including storage capacity, grossing factor, and maintained temperature range. Thousands to millions of computational entities flow through various storage locations and transport vehicles in the supply chain simultaneously.

Data Collection

Members of the VMI and SVRT research teams visited National Immunization Program (NIP) sites at the central level[the Ministry of Public Health (MoPH) and Department of Disease Control (DDC)], regional and provincial stores, two district stores and two sub-district stores in the adjacent province, Hat Yai. The joint team developed a comprehensive data collection questionnaire, which was administered at every Trang province location, and used to interview nurses, public healthcare workers, and logisticians from the MoPH and the National Health Security Office (NHSO), to obtain information about operating procedures (e.g., re-order points and buffer stock policies), cold chain equipment and transportation inventory (e.g., refrigerator and truck model, and cargo capacity), and antigen-specific patient demand patterns. This collected data served as the basis for constructing the Trang province supply chain DES.

Trang Province Vaccine Supply Chain Model

In 2010, Thailand's population was 67,089,500 persons, of which 622,659 lived in Trang province; 19% in municipal areas and 81% in non-municipal areas[6, 7]. Trang province is 1 of 76 provinces in Thailand. In HERMES, vaccines flowed through the structure shown in Figure 1, which represents the Trang province NIP supply chain as of 2009. Table 1 lists all vaccines included in the NIP[8–10]. Immunizations ultimately occur at district-level [hospitals and Municipal Health Centers (MHC's)], and sub-district-level stores, where virtual people arrived each immunization day at a rate determined by geographically explicit demographic and birth data. Population demand at district locations was estimated using Trang province-specific population data from the 2000 Population and Housing Census inflated by a 1.45% annual population growth rate to 2010[6]. Arriving patients at immunization locations received age-appropriate immunizations contingent upon onsite vaccine availability. A third type of district store, the District Health Offices (DHO's) are only involved in vaccine transport and storage.

Throughout the supply chain, anytime or anywhere cold space is limited, a balanced allocation scheme, wherein complete vaccine regimens (i.e., all doses required for full immunization) are prioritized over single antigens, determines which vaccines are stored first. A 'first-in-first-out' policy dictates which vaccines are removed or introduced into a storage or transport device. Each simulation run represents a one-year time horizon. Previously-published studies present additional details on HERMES[11–13].

Supply Chain Performance Metrics

Our study reports several supply chain performance measures. Vaccine availability is the percent of children arriving at a health centre who are able to receive their requested vaccine owing to vaccine inventory availability. Vaccine availability is computed for each simulation, each vaccine type, and each vaccine administering location:

Vaccine Availability=(Number of patients receiving vaccine)÷(Number of patients arriving at a vaccine administering location) per year

Transport capacity utilization rate for each vehicle (e.g., truck, cold box or vaccine carrier) and the storage capacity utilization rate for each cold room, refrigerator and freezer are computed for each simulation run:

Transport Capacity Utilization Rate=Transport space consumed÷Total available transport space per vehicle per shipment

Storage Capacity Utilization Rate=Storage space consumed÷Total available storage space per storage device per location per storage period

Introducing the Influenza Vaccine into the NIP

Experiments consisted of introducing influenza vaccines into the NIP supply chain. Unlike routine childhood vaccines administered throughout the year and at district and sub-district facilities, influenza vaccine administration occurred only at district hospitals within a short time window from the end of the vaccine's production cycle through the influenza season. Previously, seasonal influenza vaccines were supplied in 4-dose vials. However, our experiments used single-dose vials, since the NHSO plans to introduce single-dose vials. Each individual simulated received one dose of the influenza vaccine.

Thailand is a sub-tropical country. Monsoon rains occur from May to October. The MoPH previously administered the southern hemisphere influenza vaccine between April and May[4,14,15]. Each year, WHO Influenza Collaborating Centers review circulating strains of the southern hemisphere in September and decide on variants to include in the next

season's influenza vaccine[16]. Manufacturers then have six months to develop and distribute vaccines[16]. Therefore, the earliest the influenza vaccine would be available for use in Thailand would be the following February.

While influenza cases are reported year-round, Thailand normally experiences a peak in incidence between June and October, leaving three months from the anticipated time when vaccines are received to the time of peak incidence[17]. Moreover, it takes approximately 10–14 days for a person to develop immunity following seasonal influenza vaccination, and only peaks after 4 to 6 weeks[18]. However, in previous years, reported peak activity occurred as early as January to April[17]. Other sub-tropical countries experience this variability in peak incidence, making it difficult to schedule seasonal vaccination campaigns[17].

The influenza vaccine production cycle limits the number of months available for vaccine distribution and administration[19]. Moreover, the influenza vaccine is seasonal, immunity against a particular strain is time-limited, and annual re-immunization is required to maintain protection. We therefore simulated the introduction of the influenza vaccines over one year, systematically varying vaccination time-frames from 1 to 6 months.

Influenza Vaccine Target Population Size

In recent years, fewer than 80,000 doses of influenza vaccine have been distributed which covers less than 1% of Thailand's 6.2 million inhabitants[4]. Our experiments simulated introducing enough vaccines to cover 25%, 50%, 75% and 100% of the Thai Advisory Committee on Immunization Practice (ACIP) target groups in Trang province. These target groups include: elderly >65 years, pregnant women, healthcare workers or people caring for elderly individuals, people with chronic conditions <65 years, and infants 6–23 months, as recommended by the Thai ACIP, WHO, and NHSO administrative guidelines for Thailand's influenza vaccine project in 2009, which accounts for approximately 11% of the total provincial population[2,20,21].

Sensitivity Analyses

Our baseline scenario assumed 1% inventory and shipping loss, 85% capacity utilization, and Poisson distributed monthly demand. Sensitivity analyses systematically ranged the following parameters: shipping loss rate (range: 1–3%), inventory loss rate (range: 1–3%), and storage capacity utilization (85–100%). We also varied the population demand distribution between static (fixed population arrives each month) and dynamic [number of vaccine recipients in a given month draws from a Poisson distribution with a mean of (λ)] distributions. Our previously published study has systematically varied additional parameters to test for model robustness[12]. We validated HERMES in previous studies by comparing simulation output with field observations in Thailand[22]. Each simulation was replicated and averaged over ten runs.

RESULTS

Overall Impact

Introducing influenza vaccines creates bottlenecks reducing availability of both influenza vaccines and the other NIP vaccines. Increasing the target population from 25%–100% progressively worsens these bottlenecks, while increasing influenza vaccination time -frame from 1 to 6 months decreases these bottlenecks.

Impact on Transport

Figure 2 shows bar graphs of transport capacity utilization from region to province and from province to district level across varying influenza vaccination time-frames (across the x-axis) and target population sizes (across bar shades). Regional to provincial transport capacity was slightly impacted by the introduction of the influenza vaccine but never exceeded 8% of available capacity. The average capacity utilization remained consistent across scenarios from the province to: DHOs 20% (range: 9–37%), and MHCs 15% (range: 12–20%).

However, capacity from the province to the hospitals was relatively more constrained; it increased with increasing target population sizes from 31% at baseline (range across transport vehicles at this level: 21–44%), wherein only NIP vaccines are distributed, to 49% (range: 22–344%), 69% (range: 22–652%), 89% (range: 22–960%) and 109% (range: 22–1268%) for target population sizes 25%, 50%, 75% and 100%, respectively. Capacity utilization above 100% indicates routes in which vehicle capacities are insufficient to transport entire shipments, resulting in portions of vaccine requisitions being unmet and potentially missed vaccination opportunities.

Increasing the vaccination time-frame from 1 to 6 months reduced transport capacity utilization resulting in fewer overfilled routes between the province and district-level hospitals. For example, introducing influenza vaccines over longer time-frames reduced transport capacity utilization to an average across routes of 151% (range: 22–1268%) for a 1-month campaign to 90% (range: 22–655%), 70% (range: 22–450%), 59% (range: 22–347%), 53% (range: 22–286%) and 49% (range: 22–245%) for campaign time-frames of 2, 3, 4, 5, and 6 months, respectively.

Impact on Vaccine Storage

Figure 3 shows bar graphs of storage capacity utilization across varying influenza vaccination time-frames (across the x-axis) and target population sizes (across bar shades) at the provincial level and district levels. The Trang province supply chain has ample storage capacity at all levels to accommodate the influenza vaccine across the evaluated scenarios. Vaccine storage at the regional store, MHCs, DHOs and sub-districts never exceed 4% of the available space, and never exceed 6% at hospitals across all Thai ACIP target population sizes and vaccination time-frames. Conversely, the provincial store is more space constrained, where capacity utilization increases across target population sizes, but decreases across vaccination time-frames from 14% at baseline to 33%, 50%, 67%, and 84% (1-month time-frame), 25%, 34%, 42% and 50% (2-month time-frame), 22%, 28%, 34% and 39% (3-month time-frame), 21%, 25%, 29% and 34% (4-month time-frame), 20%, 23%, 27% and 30% (5-month time-frame), and 19%, 22%, 25% and 28% (6-month time-frame) for target population sizes 25%, 50%, 75% and 100%, respectively. Reducing the effective storage space from 100% to 85% further increases space utilization in refrigerators and limits the remaining available space to store other temperature-sensitive products.

Impact on Vaccine Availability

Transport bottlenecks ultimately have substantial impacts on vaccine availability at the service delivery level. While influenza vaccine availabilities increase with time-frame from 1 to 5 months, this effect is minimized as the size of target populations increase from 25% to 100% of the Thai ACIP influenza target group. However, because other NIP vaccines are administered at all district and sub-district locations, impacts on their availability are minimal.

At baseline, vaccine availabilities for the tuberculosis, diphtheria-tetanus-pertussis (DTP), oral polio, Japanese encephalitis, hepatitis-B (HepB), DTP-HepB, and measles vaccines are 95%, 95%, 97%, 94%, 94%, 96% and 95%, respectively. Initial vaccine availabilities are not 100% because in these scenarios, we assume 1% loss along each transport route and storage node. Additionally, the ordering policy in Trang province prescribes ordering vaccines based on the previous month's demand which may not be a perfect representation of the next month's demand. Finally, open vial waste may result in wasted vaccines, which reduces the availability of doses towards the end of a set of immunization sessions. Introducing influenza vaccines across increasing vaccination time-frames decreased the vaccine availabilities of NIP vaccines slightly from 95% at baseline to an average of 94% (range across Thai ACIP target population sizes and influenza vaccination time-frames: 91–97%).

Conversely, the influenza vaccine availability increases as the vaccination time-frame increases. Figure 4 shows bar graphs of vaccine availabilities for the influenza vaccine across varying vaccination campaign time-frames (across the x-axis) and Thai ACIP target population sizes (across bar shades). Introducing the influenza vaccine in a one-month campaign resulted in vaccine availabilities of 53%, 43%, 37% and 32% for Thai ACIP target population sizes of 25%, 50%, 75% and 100%, respectively. Increasing the vaccination time-frame for Thai ACIP target population sizes of 25%, 50%, 75% and 100%, respectively increased influenza vaccine availabilities to 69%, 54%, 49%, and 45% (2-month time-frame), 80%, 62%, 54%, and 49% (3-month time-frame), 89%, 68%, 59% and 54% (4-month time-frame), 96%, 74%, 64%, and 58% (5-month time-frame), and 96%, 80%, 68% and 62% (6-month time-frame).

The reductions in availabilities of influenza vaccines were largely driven by five hospitals which serve the largest Thai ACIP target population segments. The remaining four hospitals did not experience vaccine shortages in any scenario. Even in the 100% Thai ACIP target group and 1-month vaccination time-frame scenario, providing additional transport capacity at the five districts which experience transportation bottlenecks improves the average NIP vaccine availability from 94% at baseline to 95%, and the vaccine availability of the influenza vaccine from 32% to 95%.

Considering that patients whom have never received influenza vaccinations require two doses of the seasonal influenza vaccine, storage and transport capacities and vaccine availabilities may be further strained.

Sensitivity Analyses

Sensitivity analyses demonstrated that varying the patient demand, shipping and inventory loss rates, and storage capacity utilization did not significantly affect the pattern of results ($p < 0.05$ using unpaired t-tests). However, the model was not robust to 3% shipping and inventory loss rates ($p < 0.05$).

DISCUSSION

Our results indicate that introducing seasonal influenza vaccines through the routine immunization supply chain in Trang province, Thailand, not only affects vaccine availabilities of the influenza vaccine, but also impacts the availabilities of all other routine vaccines for arriving patients. Increasing the length of the influenza vaccine administration time-frame improves the availability of the influenza vaccine, allowing for more arriving patients to be vaccinated. However, longer vaccination time-frames and larger target population sizes can have negative impacts on other routine vaccines in the supply chain, and may also negatively impact the epidemiology of the spread of influenza. Therefore,

Trang province, and other parts of Thailand, may consider augmenting their transport capacity (e.g., more or larger trucks) before introducing influenza vaccines.

Determining appropriate target populations and identifying coverage goals for preparedness plans are equally important and should be done in tandem with evaluations of their impacts on existing vaccine supply chain resources. Regardless of the number of doses supplied to or within a country, if vaccines cannot reach their target populations through appropriate channels, they cannot be effective.

Moreover, the current lag between egg-based vaccine production and roll-out requires time for strain identification and preparation, optimization of virus growth conditions, bulk manufacturing operations, quality control, and vaccine filling and release, limiting the available immunization time-frame to 6 or 7 months out of the year[23]. With the potential adoption of cell-based vaccine production technology, public health decision-makers may be able to increase the time-frame for vaccine administration, and thereby minimize the impact of surges in vaccine requirements on the supply chain[24]. Therefore, considering the length of the vaccination time-frame when developing seasonal influenza preparedness plans can help public health programs reach their target vaccine coverage rates without compromising overall vaccine distribution.

Previous studies show that Thailand's vaccine supply chain is well-functioning[4]. Previous studies also show that there are other countries, such as Niger, that have less well-functioning supply chains[13,25]. Therefore, identifying obstacles with influenza vaccine introduction in Thailand suggest that other countries may experience similar or even greater challenges.

Our study highlights the utility of models in identifying effects of decisions not immediately evident. Models have long been used to help decision making in other industries, including meteorology[26], manufacturing[27], transportation[28], aerospace[29], and finance[30], and sports and rehabilitation[31]. Alternatively, their use to date in public health has not been as extensive[32,33]. Models have assisted responses to the spread of infectious disease such as the 2009 H1N1 influenza pandemic and health-care associated infections[34–37], however much of their potential remains untapped.

Limitations

By definition, all models are simplified representations of real life. Therefore, they cannot capture every potential factor, event, or outcome. The model is based on data up to June 2010 and does not represent future changes that may occur. Actual demand may vary from estimated demand, which was drawn from cross-sectional census data. Constructing our model involved substantial data collection from various sources including records and interviews at different locations. As a result, parameter values may vary in accuracy and reliability, although sensitivity analyses demonstrated that model outcomes are robust under a wide variety of circumstances. The exception is when shipping and inventory loss rates above 3%, which have not been found to be reported above 1%.

CONCLUSION

Even when the target coverage is fairly low, introducing the seasonal influenza vaccine into the Trang province vaccine supply chain, results in transportation bottlenecks from the provincial to district levels, limiting the availability of influenza vaccines and all other routine vaccines for arriving patients. In order to prevent this eventuality, Thailand may need to augment existing storage and transport capacity. This is an example of why supply

chain considerations may be an important component of influenza immunization target population decisions.

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REFERENCES

1. de Oliveira LH, et al. Rotavirus vaccine introduction in the Americas: progress and lessons learned. *Expert Rev Vaccines*. 2008; 7(3):345–353. [PubMed: 18393604]
2. WHO. Global Alert and Response. Geneva, Switzerland: World Health Organization; 2009. Pandemic influenza preparedness and response.
3. Payaprom Y, et al. Understandings of influenza and influenza vaccination among high-risk urban dwelling Thai adults: a qualitative study. *J Public Health (Oxf)*. 2010; 32(1):26–31. [PubMed: 19706649]
4. Simmerman JM, et al. Influenza in Thailand: a case study for middle income countries. *Vaccine*. 2004; 23(2):182–187. [PubMed: 15531035]
5. Simmerman JM, et al. The cost of influenza in Thailand. *Vaccine*. 2006; 24(20):4417–4426. [PubMed: 16621187]
6. TNSO. The 2000 Population and Housing Census. In: TNSO. , editor. Data and Statistics. Bangkok, Thailand: Thailand National Statistical Office; 2010.
7. TNSO. [cited 2011 07 May 2011] Statistical Data: Table Searching. 2011. Available from: <http://web.nso.go.th/en/stat.htm>.
8. World Health Organization. [cited 2010 September] Vaccine volume calculator. 2009. Available from: http://www.who.int/immunization_delivery/systems_policy/logistics/en/index4.html.
9. WHO. [cited 2010] WHO Prequalified Vaccines. 2010. Available from: http://www.who.int/immunization_standards/vaccine_quality/PQ_vaccine_list_en/en/index.html.
10. VMI. (VMI). , editor. Thailand Seasonal Influenza Vaccine Packaged Volume Information. Bangkok: Department of Disease Control; 2011.
11. Assi TM, et al. Impact of changing the measles vaccine vial size on Niger's vaccine supply chain: a computational model. *BMC Public Health*. 2011; 11:425. [PubMed: 21635774]
12. Lee BY, et al. Replacing the measles ten-dose vaccine presentation with the single-dose presentation in Thailand. *Vaccine*. 2011; 29(21):3811–3817. [PubMed: 21439313]
13. Lee BY, et al. Impact of Introducing the Pneumococcal and Rotavirus Vaccines Into the Routine Immunization Program in Niger. *Am J Public Health*. 2011
14. CDC. [cited 2010 03 January] Seasonal influenza (Flu): The flu season. 2010. Available from: <http://www.cdc.gov/flu/about/season/flu-season.htm>.
15. Thawatsupha P, et al. Isolation and identification of influenza virus strains circulating in Thailand in 2001. *Southeast Asian J Trop Med Public Health*. 2003; 34(1)
16. Gerdil C. The annual production cycle for influenza vaccine. *Vaccine*. 2003; 21(16):1776–1779. [PubMed: 12686093]
17. Simmerman JM, et al. Incidence, seasonality and mortality associated with influenza pneumonia in Thailand: 2005–2008. *PLoS One*. 2009; 4(11):e7776. [PubMed: 19936224]

18. Cox RJ, Brokstad KA, Ogra P. Influenza Virus: Immunity and Vaccination Strategies. Comparison of the Immune Response to Inactivated and Live, Attenuated Influenza Vaccines. *Scandinavian Journal of Immunology*. 2004; 59(1):1–15. [PubMed: 14723616]
19. Policy Recommendation Paper: Strategy for Establishing the Human Vaccine Plant. Vol. Chapter 5. Thailand: Bangkok: International Health Policy Program; 2010.
20. Policy Recommendations on Thailand Strategy for Pandemic Influenza. Thailand: Bangkok: International Health Policy Program; 2010.
21. Administrative guideline for influenza vaccine project. Bangkok: Thailand National Health Security Office; 2009.
22. Lee BY, et al. Maintaining vaccine delivery following the introduction of the rotavirus and pneumococcal vaccines in Thailand. *PLoS One*. 2011; 6(9):e24673. [PubMed: 21931805]
23. WHO. Global Alert and Response (GAR). Switzerland: World Health Organization Geneva; 2009. Pandemic influenza vaccine manufacturing process and timeline.
24. Rappuoli R. Cell-culture-based vaccine production: Technological options. *The Bridge*. 2006; 36(3):17–24.
25. Assi T-M, et al. Impact of changing the measles vaccine vial size on Niger's vaccine supply chain: a computational model. *BMC Public Health*. 2011; 11(1):425. [PubMed: 21635774]
26. Klingberg J, et al. Comparison of modelled and measured ozone concentrations and meteorology for a site in south-west Sweden: implications for ozone uptake calculations. *Environ Pollut*. 2008; 155(1):99–111. [PubMed: 18063256]
27. Lee, et al. Multi-agent systems applications in manufacturing systems and supply chain management: a review paper. Vol. Vol. 46. London, Royaume-Uni: Taylor & Francis; 2008. p. 33
28. Borndorfer R, Lobel A, Weider S. A bundle method for integrated multi-depot vehicle and duty scheduling in public transit. *Computer-aided Systems in Public Transport*. 2008; 600(Part 1):3–21.
29. Moormann, et al. Object-oriented computational model building of aircraft flight dynamics and systems. Paris, FRANCE: Elsevier; 1999. p. 79
30. Fouque J-P, Papanicolaou G, Sircar K. Financial Modeling in a Fast Mean-Reverting Stochastic Volatility Environment. *Asia-Pacific Financial Markets*. 1999; 6(1):37–48.
31. Neptune RR. Computer modeling and simulation of human movement. Applications in sport and rehabilitation. *Phys Med Rehabil Clin N Am*. 2000; 11(2):417–434. viii. [PubMed: 10810769]
32. Trochim WM, et al. Practical challenges of systems thinking and modeling in public health. *Am J Public Health*. 2006; 96(3):538–546. [PubMed: 16449581]
33. Epstein, JM. Generative social science: Studies in agent-based computational modeling. Princeton, NJ: Princeton University Press; 2006.
34. Cooley P, et al. Protecting health care workers: a pandemic simulation based on Allegheny County. *Influenza Other Respi Viruses*. 2010; 4(2):61–72. [PubMed: 20167046]
35. Lee BY, et al. Vaccination deep into a pandemic wave potential mechanisms for a "third wave" and the impact of vaccination. *Am J Prev Med*. 2010; 39(5):e21–e29. [PubMed: 20965375]
36. Lee BY, et al. Simulating school closure strategies to mitigate an influenza epidemic. *J Public Health Manag Pract*. 2010; 16(3):252–261. [PubMed: 20035236]
37. Lee BY, et al. A computer simulation of employee vaccination to mitigate an influenza epidemic. *Am J Prev Med*. 2010; 38(3):247–257. [PubMed: 20042311]

HIGHLIGHTS

- We develop a discrete-event simulation model to represent vaccine distribution in Thailand.
- We model the distribution of influenza vaccines through the routine immunization program.
- We vary vaccine target population sizes and time-frames for vaccine distribution.
- Larger target population sizes create supply chain bottlenecks and reduce vaccine availability.
- Increasing distribution time-frames alleviate bottlenecks and improved vaccine availability.

Figure 1.

Trang Province Vaccine Supply Chain Network

*Districts-level stores serve approximately 60% of patients seeking vaccination in Trang Province, which vaccinate 1 to 4 days per month

**Sub-district-level stores serve approximately 40% of patients seeking vaccination in Trang Province, which vaccinate 1 day per month

***Patients arrive at these locations for vaccine administration. Other locations are only involved in vaccine storage. The number of vaccines ordered by vaccine administering sites is governed by their previous month's vaccine demand without ordering additional buffer stock.

Figure 2.

Average Transport Capacity Utilization across Varying Influenza Vaccination time-frames and Target Population Sizes

Figure 3.
Average Storage Capacity Utilization across Varying Influenza Vaccination time-frames and Target Population Sizes

Figure 4.

Average Influenza Vaccine Availability across Varying Vaccination Campaign time-frames and Target Population Sizes

Table 1

Vaccine Characteristics in the Trang Province Routine Immunization Program

Description (units)	Dose(s) /person	Packed volume/dose (cm ³)	Packed volume of diluent/dose (cm ³)	Storage preference	Target population	Source
<i>Vaccine type</i>						
Bacille Calmette Guerin (BCG) (10 doses/vial)	1	1.2	0.7	Refrigerator	Newborn	8,9
Hepatitis B (HB) (2 doses/vial)	2	0.5	-	Refrigerator	<1 year	8,9
Diphtheria-tetanus-pertussis (DTP) (10 doses/vial)	5	3.0	-	Refrigerator	<5 years	8,9
Diphtheria-tetanus-pertussis-hepatitis B (DTP-HB) (10 doses/vial)	3	0.5	-	Refrigerator	<1 year	8,9
Oral Polio Virus (OPV) (20 doses/vial)	5	1.0	-	Freezer	<5 years	8,9
Measles (M) (10 doses/vial)	1	3.5	4.0	Refrigerator	<1 year	8,9
Japanese Encephalitis (JE) (2 doses/vial)	3	0.5	11.5	Refrigerator	<3 years	8,9
Measles-mumps-rubella (MMR) (10 doses/vial)	1	0.5	0.5	Refrigerator	7 years	8,9
Diphtheria-tetanus (dT) (10 doses/vial)	2	0.5	-	Refrigerator	7, 12 years	8,9
Seasonal Influenza * (1 dose/vial)	1	5.3	-	Refrigerator	25%, 50%, 75%, and 100% of Trang province ACIP target groups	10

*. Packaged volume of seasonal influenza vaccine provided through personal communication between the SVRT and Department of Disease Control in Thailand.