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Cost-effectiveness of a real-time spatiotemporal mapping surveillance system for meticillin-resistant *Staphylococcus aureus* prevention

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SUMMARY

Objectives: An infection surveillance system based on a hospital's digital twin [4D-Disease Outbreak Surveillance System (4D-DOSS)] is being developed in Singapore. It offers near-real-time infection surveillance and mapping capabilities. This early economic modelling study was conducted, using meticillin-resistant *Staphylococcus aureus* (MRSA) as the pathogen of interest, to assess the potential cost-effectiveness of 4D-DOSS.
Methods: A Markov model that simulates the likelihood of MRSA colonization and infection was developed to evaluate the cost-effectiveness of adopting 4D-DOSS for MRSA surveillance from the hospital perspective, compared with current practice. The cycle duration was 1 day, and the model horizon was 30 days. Probabilistic sensitivity analysis was conducted, and the probability of cost-effectiveness was reported. Scenario analyses and a value of information analysis were performed.
Results: In the base-case scenario, with 10-year implementation/maintenance costs of 4D-DOSS of \$0, there was 68.6% chance that 4D-DOSS would be cost-effective. In a more pessimistic but plausible scenario where the effectiveness of 4D-DOSS in reducing MRSA transmission was one-quarter of the base-case scenario with 10-year implementation/maintenance costs of \$1 million, there was 47.7% chance that adoption of 4D-DOSS would be cost-effective. The value of information analysis showed that uncertainty in MRSA costs made the greatest contribution to model uncertainty.
Conclusions: This early-stage modelling study revealed the circumstances for which 4D-DOSS is likely to be cost-effective at the current willingness-to-pay threshold, and identified the parameters for which further research will be worthwhile to reduce model

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uncertainty. Inclusion of other drug-resistant organisms will provide a more thorough assessment of the cost-effectiveness of 4D-DOSS.

Introduction

Healthcare-associated infections (HAIs) increase the risk of mortality and incur healthcare costs [1]. Infection surveillance is a cornerstone of HAI control [2]. A robust HAI surveillance and outbreak detection system increases the likelihood that infection clusters will be contained effectively. In Singapore, most hospitals employ a traditional approach for HAI surveillance. When infection clusters are detected, relevant datasets are extracted and aggregated, and epidemiological linkages are mapped manually to gain insights into sources and routes of infection transmission [3,4]. The manual nature of these investigations means that there is often substantial lag between outbreak occurrence and response. This approach is also highly reliant on staff observational skills, and complex transmission patterns with wide spatiotemporal separation can be missed.

Digital twins are virtual representations of a physical asset with bidirectional data connections [5]. In the context of infection surveillance and outbreak investigations, digital twins provide a comprehensive view of a facility's infection control measures and allow automated mapping of the spread of infection [5]. Real-time patient, staff or asset movement can be tracked using 'Internet of Things' devices to uncover hidden routes of infection transmission. Machine learning algorithms can be incorporated to parse large volumes of data to conduct predictive modelling and simulate the impact of potential interventions.

In Singapore, a digital twin with real-time surveillance and outbreak mapping capabilities, termed the '4-Dimensional Disease Outbreak Surveillance System' (4D-DOSS), is being developed in a tertiary hospital. It was hypothesized that the adoption of 4D-DOSS will translate to improved outbreak response timeliness, which will, in turn, reduce the spread of infection. The adoption of 4D-DOSS is also expected to reduce the workload of infection prevention and control (IPC) practitioners. This early health economic study was conducted to evaluate the cost-effectiveness of the decision to adopt 4D-DOSS compared with current practice, using meticillin-resistant *Staphylococcus aureus* (MRSA) as the nosocomial pathogen of interest [6]. MRSA was selected as it is a major multi-drug-resistant organism (MDRO) associated with HAIs in Singapore hospitals (58.1% of *S. aureus* associated with HAIs were meticillin-resistant), and remains endemic in most healthcare settings despite extensive control efforts [7,8]. The goal of this study was not to make a definitive conclusion on the adoption of 4D-DOSS, but to provide some insights to local hospital decision-makers regarding the investment of scarce resources and areas for further research [6].

Methods

Target setting and population

Singapore General Hospital is the largest acute care hospital in Singapore, with 1939 inpatient beds [9]. In 2021, the hospital had 72,492 visits [9]. The hospital's MRSA control policies follow the national infection prevention and control guidelines [3]. MRSA screening is conducted for all non-MRSA-positive inpatients at admission and fortnightly. Contact precautions are implemented for MRSA-positive patients. MRSA decolonization is conducted for all MRSA carriers [10]. Outbreak investigation is initiated if two or more epidemiologically-linked MRSA cases are observed. Investigation procedures include: extraction of relevant data; manual mapping of patient movements with cross-analysis with clinical/laboratory data for epidemiological linkages; environmental screening; and screening of healthcare workers [3]. The target population is all hospital inpatients.

Intervention

4D-DOSS is a real-time spatiotemporal mapping digital twin surveillance system, developed in collaboration with Axomem Pte Ltd. Its concept is borrowed from the way that gamers interact with the virtual world/space, and comprises a virtual hospital map built within game-development software and updated via the hospital data cloud with near-real-time clinical, laboratory and patient movement information [11]. Detailed surveillance algorithms are incorporated to perform prospective infection cluster detection and risk prediction. In the event of a suspected MRSA outbreak, 4D-DOSS can be tasked to perform epidemiological linkage analysis using environmental, movement, clinical and laboratory parameters. This negates the need for manual epidemiological linkage analysis, and reduces the IPC workload compared with current practice. The adoption of 4D-DOSS can also be expected to increase timeliness of the MRSA outbreak response as the system will expedite the most time-consuming step in a traditional outbreak investigation. Consequently, this will reduce the likelihood of onward MRSA transmission.

Ethical approval

This study was exempted from ethics review by the SingHealth and National University of Singapore Institutional Review Board.

Study perspective and design

This study followed the CHEERS guidelines [12]. A decision analytic Markov model was used to compare the decision to adopt 4D-DOSS with the current standard of care from the hospital perspective. The cycle duration was 1 day, and the model horizon was 30 days. Three health states were considered: no MRSA colonization or infection; MRSA colonization; and MRSA infection (Figure 1). Patients could enter the model with no colonization or infection, or with colonization. MRSA colonization was defined as patients with positive MRSA screening cultures but without positive clinical cultures. MRSA infection occurred when a patient developed positive clinical

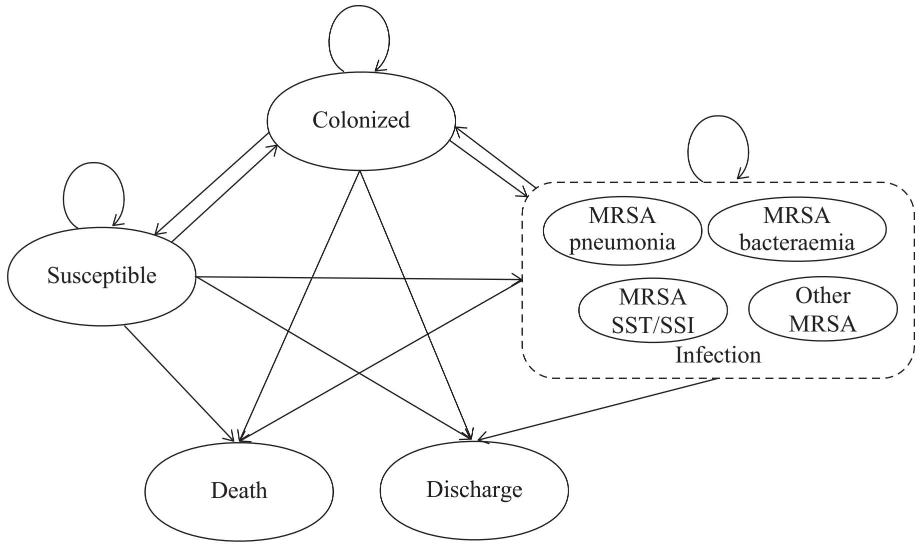

Figure 1. Markov model showing transition states for inpatients admitted to the hospital. The model simulates the natural history of possible meticillin-resistant *Staphylococcus aureus* colonization and infection for each inpatient within a single hospital admission, using a sequence of daily transitions. MRSA, meticillin-resistant *Staphylococcus aureus*; SSI, surgical site infections; SST, skin and soft tissue infections.

culture(s) for MRSA. Patients could transit between the three health states, or to the terminal states of discharge or death. Patients were assumed to move from 'infected' to 'colonized' when MRSA treatment was completed. Patients were assumed to move from 'colonized' to 'no colonization' when MRSA decolonization was completed.

Baseline and transition probabilities

The baseline incidence of MRSA colonization at admission was provided by the hospital's infection prevention and epidemiology (IPE) department (Table I). Transition probabilities in the model were time-dependent and were derived from patient data (Supplementary Figure A1, see online supplementary material) [13]. Time-dependent transition probabilities were used instead of time-fixed transition probabilities as the likelihood of MRSA colonization and infection was reported to be dependent on length of hospital stay [14]. The 'etm' package in R software was used to derive the transition probabilities [13].

Costs

All costs were adjusted to 2022 Singapore Dollars (1 SGD = 0.75 USD) (Table I) [15]. As it was not possible to ascertain the implementation/maintenance cost of 4D-DOSS for MRSA surveillance accurately at this early stage, a figure for baseline implementation/maintenance cost of $0 was input and implementation/maintenance cost was varied in the scenario analyses. The costs of MRSA surveillance were obtained from the hospital's IPE department – it was estimated by the department that the adoption of 4D-DOSS would result in sustained manpower savings of one full-time IPC nurse compared with current practice. Diagnosis and treatment costs were obtained from the hospital's pathology and pharmacy departments, respectively, and were specific to infection types. As the time horizon for the model was only 30 days, discounting for costs was not applicable.

Efficacy and outcomes

As the effectiveness of reducing MRSA transmission due to the adoption of 4D-DOSS is not known at this early stage, estimates from the published literature were used, and effectiveness was varied in the scenario analyses [16]. Worby *et al.* modelled the combined effect of an MRSA management bundle (MRSA screening, cohorting of MRSA-positive patients, and decolonization treatment) in a teaching hospital, and found that it reduced MRSA transmission by 64% (relative risk = 0.36) [16]. The outcome evaluated in the model was the number of life-years gained. Quality-adjusted life-years was not used because the impact of MRSA infections is usually short-lived and less likely to cause long-term changes in quality of life. Life-years were discounted at 3% per year.

Analytical approach

Economic analysis was performed using Excel 2022 (Microsoft Corp., Redmond, WA, USA). A Monte Carlo simulation of 1,000 iterations was conducted based on statistical distributions to represent uncertainty from the model parameters. Mean costs and life-years saved per 10,000 patient days with 95% uncertainty intervals were reported. In addition, the incremental net monetary benefit at a willingness to pay of $45,000 per life-year saved, which is the threshold used to inform decisions on subsidy of medical technologies in Singapore, was reported [17]. Alongside the base-case scenario, 11 scenario analyses were conducted to describe the changes in cost-effectiveness when the implementation/maintenance costs of 4D-DOSS and effectiveness in reducing MRSA transmission were varied simultaneously. Specifically, 10-year implementation/maintenance costs of $1 million, $2 million and $3 million were considered; and effectiveness in reducing MRSA transmission of one-half (relative risk of MRSA colonization/infection from susceptible state = 0.68) and one-quarter (relative risk of MRSA colonization/infection from

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Table I
Input parameters for the Markov model

Variables	Estimate (SD)	Prior distribution	Reference
Costs (2022 SGD)			
4D-DOSS implementation	0		Assumption
Manpower for MRSA surveillance and outbreak management under current standard of care (per patient)	0.31 (0.17)	Gamma (3.31, 0.09)	Data provided by hospital's infection prevention and epidemiology team
Manpower for MRSA surveillance and outbreak management with 4D-DOSS (per patient)	0.15 (0.08)	Gamma (3.31, 0.05)	
Contact precautions (for MRSA colonized/ infected patients only – per day)	82.36 (15.48)	Gamma (28.29, 2.91)	
Daily cleaning and disinfection (for MRSA colonized/infected patients only – per day)	5.57 (1.39)	Gamma (16.00, 0.35)	
Terminal cleaning and disinfection (for MRSA colonized/infected patients only – per patient)	26.53 (6.63)	Gamma (16.00,1.66)	
MRSA decolonization (for MRSA colonized/ infected patients only – per course)	36.24 (6.04)	Gamma (36.00, 1.01)	
MRSA surveillance swab (per test)	257.30 (36.35)	Gamma (82.47, 3.12)	Data provided by hospital's pathology department
Diagnosis (for MRSA infected patients only – per day)			
Pneumonia	67.96 (14.02)	Gamma (23.48, 2.89)	
Bacteraemia	52.60 (9.84)	Gamma (28.57, 1.84)	
SST/SSI	48.49 (9.58)	Gamma (25.59, 1.89)	
Other	48.49 (9.58)	Gamma (25.59, 1.89)	
Treatment (for MRSA infected patients only – per day)			Data provided by hospital's pharmacy department
Pneumonia	11.92 (1.99)	Gamma (36.00, 0.33)	
Bacteraemia	44.08 (7.35)	Gamma (36.00, 1.22)	
SST/SSI	46.27 (7.89)	Gamma (34.35, 1.35)	
Other	44.08 (7.35)	Gamma (36.00, 1.22)	
Bed-day	838.36 (282.17)	Gamma (8.83, 94.97)	[26]
Efficacy			
Relative risk of MRSA colonization or infection from susceptible with 4D-DOSS	0.36 (0.11)	Log-normal (0.36, 0.11)	[15]
Other input parameters			
Probability of MRSA colonization at admission	0.08 (0.20)	Beta (14.64, 168.36)	Data provided by hospital's infection prevention and epidemiology team
Probability of each infection type			
Pneumonia	0.09 (0.01)	Dirichlet (70.67, 0.01)	
Bacteraemia	0.19 (0.01)	Dirichlet (173.11, 0.01)	
SST/SSI	0.45 (0.02)	Dirichlet (619.10, 0.01)	
Other	0.28 (0.03)	Dirichlet (118.90, 0.01)	
Lifespan of 4D-DOSS (years)	10	Fixed	[18]
Life expectancy (years)	84 (13.92)	Gamma (36.00, 2.32)	[27]
Mean age at admission	59 (9.95)	Gamma (36.00, 1.66)	Data provided by the hospital's infection prevention and epidemiology team
Effective population	640,665	Fixed	[8]

SGD, Singapore Dollars; 4D-DOSS, 4D-Disease Outbreak Surveillance System; MRSA, meticillin-resistant *Staphylococcus aureus*; SSI, surgical site infection; SST, skin and soft tissue infection; SD, standard deviation.

susceptible state = 0.84) of that in the published literature were considered in a two-way analysis [16].

A value of information analysis was conducted to estimate the population expected value of perfect information (pEVPI) and population expected value of partial perfect information (pEVPPI). The pEVPI is the expected monetary value in making the best economic decision if all uncertainties in the model are eliminated, while the pEVPPI identifies the expected monetary value of resolving uncertainty around the set of related parameters [18]. To determine the effective population, the effective lifespan of 4D-DOSS was assumed to be 10 years [19]. For the pEVPPI analysis, specific parameters/groups of parameters were evaluated: surveillance costs, comprising manpower costs for MRSA surveillance and costs of MRSA surveillance swabs; environmental cleaning costs, comprising costs of daily and terminal cleaning; costs of contact precautions, comprising

Table II

Summary of results per 10,000 patient days based on a Monte Carlo simulation of 1000 iterations

Scenario no.	Description of scenario [15]	Incremental costs per 10,000 patient days (2022 SGD)	Incremental outcomes per 10,000 patient days (life-years)	NMB	ICER	Likelihood of cost-effectiveness
1 (base-case)	No implementation/maintenance costs AND effectiveness as reported in published literature	-1630 (-2185—1074)	0.08 (0.06—0.10)	5134 (4165—6103)	Dominant	68.6%
2	No implementation/maintenance costs and one-half as effective as reported in published literature	-767 (-1327—208)	0.04 (0.03—0.07)	2168 (1716—3646)	Dominant	56.7%
3	No implementation/maintenance costs AND one-quarter as effective as reported in published literature	-524 (-1081—34)	0.03 (0.01—0.05)	2000 (999—3002)	Dominant	54.0%
4	Implementation/maintenance costs of $1M over technology lifespan AND effectiveness as reported in published literature	712 (150—1275)	0.07 (0.05—0.09)	2388 (1441—3335)	10,337	55.4%
5	Implementation/maintenance costs of $1M over technology lifespan AND one-half as effective as reported in published literature	1591 (1049—2133)	0.03 (0.02—0.05)	-126 (-1091— 839)	48,873	49.9%
6	Implementation/maintenance costs of $1M over technology lifespan AND one-quarter as effective as reported in published literature	1894 (1343—2445)	0.02 (0.00—0.03)	-1123 (-2087—159)	110,524	47.7%
7	Implementation/maintenance costs of $2M over technology lifespan AND effectiveness as reported in published literature	2793 (2247—3340)	0.09 (0.07—0.11)	1208 (214—2201)	31,418	50.5%
8	Implementation/maintenance costs of $2M over technology lifespan AND one-half as effective as reported in published literature	3463 (2905—4020)	0.03 (0.01—0.05)	-2143 (-3085—1202)	118,124	43.8%
9	Implementation/maintenance costs of $2M over technology lifespan AND one-quarter as effective as reported in published literature	4670 (4146—5195)	0.03 (0.01—0.04)	-3564 (-4530—2598)	189,988	39.4%
10	Implementation/maintenance costs of $3M over technology lifespan AND effectiveness as reported in published literature	5262 (4720—5804)	0.08 (0.06—0.10)	-1720 (-2644—796)	66,860	41.9%
11	Implementation/maintenance costs of $3M over technology lifespan AND one-half as effective as reported in published literature	6044 (5513—6574)	0.02 (0.01—0.04)	-4982 (-5933—4031)	256,045	35.4%
12	Implementation/maintenance costs of $3M over technology lifespan AND one-quarter as effective as reported in published literature	6406 (5852—6960)	0.02 (0.00—0.04)	-5387 (-6342—4432)	282,952	34.3%

SGD, Singapore Dollars; NMB, net monetary benefit; ICER, incremental cost-effectiveness ratio.

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costs of contact precautions and costs of MRSA decolonization; unit costs of a bed-day; diagnosis costs; treatment costs; probability of MRSA colonization at admission; and relative risk of MRSA colonization or infection with 4D-DOSS.

Results

Base-case results

The changes in costs and outcomes from adopting 4D-DOSS in the base-case analysis are shown in Table II. For 10-year implementation/maintenance costs of $0, 4D-DOSS resulted in cost savings and better health outcomes compared with the current standard of care. At willingness to pay of $45,000 per life-year saved, there was 68.6% and 57.1% chance that 4D-DOSS would be cost-effective and cost-saving, respectively (Figure 2).

Scenario analyses

The changes to costs and outcomes in the scenario analyses are shown in Table II and illustrated in Supplementary Figure A2 (see online supplementary material). When the effectiveness of 4D-DOSS was similar to that in the published literature with 10-year implementation/maintenance costs of $2 million (Scenario 7), the decision to adopt 4D-DOSS would likely be cost-effective (50.5% chance of cost-effectiveness). However, in the more pessimistic scenario where the effectiveness was one-half of that in the published literature with 10-year implementation/maintenance costs of 4D-DOSS of $2 million (Scenario 8), the decision to adopt 4D-DOSS would unlikely be cost-effective (43.8% chance of cost-effectiveness). In the most pessimistic scenario where the effectiveness was one-quarter of that in the published literature with 10-year implementation/maintenance costs of 4D-DOSS of $3 million (Scenario 12), there was only 34.3% chance that the adoption of 4D-DOSS would be cost-effective.

Value of information analysis

At willingness to pay of $45,000 per life-year saved, the pEVPI was $3,455,173 (Figure 3). Across the different parameters, the unit costs of a bed-day had the highest pEVPPI, followed by surveillance costs and environmental cleaning costs.

Discussion

This early-stage study modelled the circumstances for which 4D-DOSS is likely to be cost-effective for MRSA surveillance in a Singapore hospital. For implementation/maintenance costs of $0, 4D-DOSS was cost-saving, improved patient outcomes and was the economically dominant strategy. The value of information analysis showed that uncertainty in the economic model arose mainly from the four main cost parameter groups: surveillance costs; environmental cleaning costs; costs of contact precautions and isolation; and unit costs of a bed-day. Future research targeted at these parameters may be warranted to reduce model uncertainty.

Our Markov model captured the effect of reducing the IPC workload and reducing MRSA transmission on costs and outcomes. A strength of this model was the use of time-dependent transition probabilities to simulate the likelihood of MRSA colonization and infection, which is in contrast to previous MRSA modelling studies [20,21]. A recent study by Chow *et al.* demonstrated a dose—response relationship between length of stay and odds of MRSA acquisition [22]. Hence, the use of aggregated time-fixed transition probabilities will oversimplify the likelihood of MRSA colonization and infection within a hospital admission, and can result in over- or underestimation of disease progression [23].

As this was an early-stage study, inputs were based on best-available evidence, and scenario analyses were conducted for the parameters with the greatest uncertainty. The effectiveness measure was derived from the published literature because a prospective trial to determine the effectiveness of

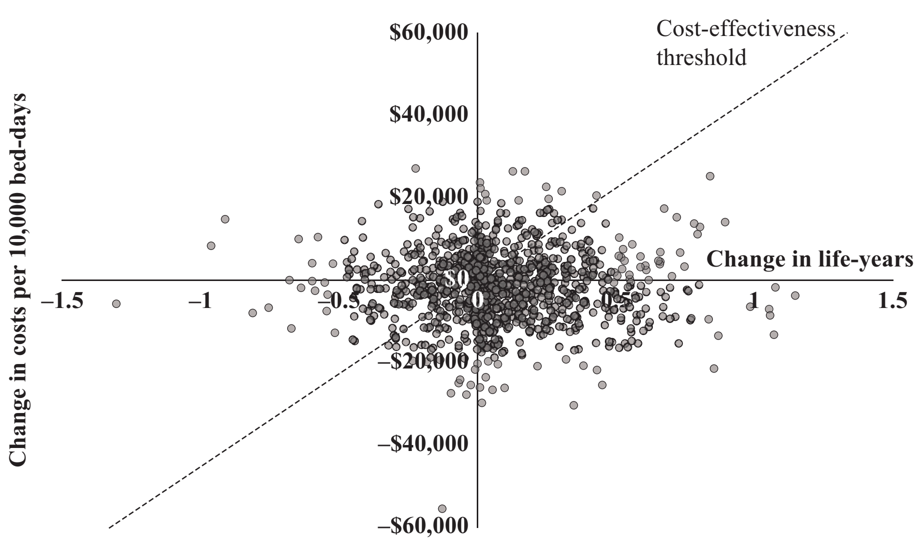

Figure 2. Expected change to costs and health benefits from implementation of the 4D-Disease Outbreak Surveillance System (4D-DOSS) per 10,000 bed-days in base-case analysis. At willingness to pay of $45,000 per life-year saved, 4D-DOSS has 68.6% chance of being cost-effective.

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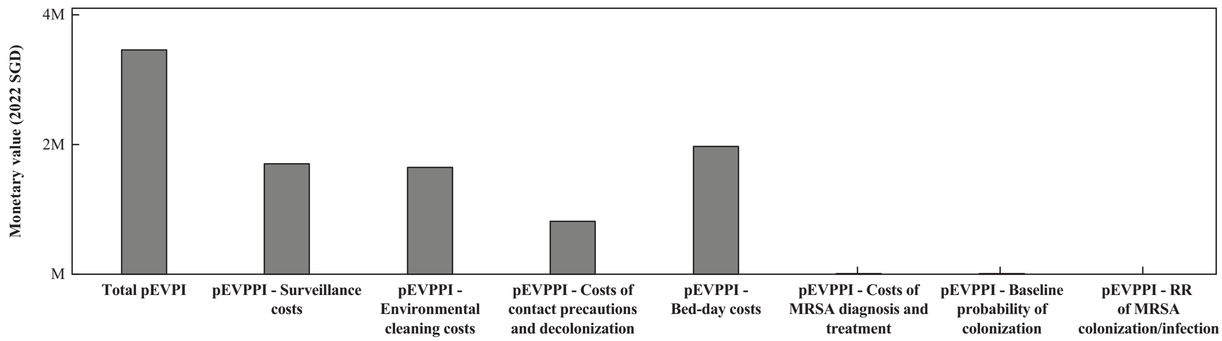

Figure 3. Value of information analysis at willingness to pay of $45,000 per life-year saved. Of the different parameter groups, bed-day cost had the highest expected value of partial perfect information. MRSA, meticillin-resistant *Staphylococcus aureus*; pEVPI, population expected value of perfect information; pEVPPI, population expected value of partial perfect information; RR, relative risk; SGD, Singapore Dollars.

4D-DOSS in reducing MRSA transmission has yet to be conducted [16]. However, it is recognized that the effectiveness measure in published studies may not be representative of the effectiveness of 4D-DOSS, given differences in base MRSA prevalence, MRSA surveillance processes and MRSA infection control policies in different countries and study settings. Hence, a pessimistic approach was adopted for the scenario analyses, with effectiveness of one-half and one-quarter of that reported in the literature considered [16]. Scenario analyses were also conducted for the implementation/maintenance costs of 4D-DOSS because use-cases for 4D-DOSS are yet to be fully ascertained. For accurate determination of the implementation/maintenance costs of 4D-DOSS for MRSA surveillance, there is a need to identify all the functions of 4D-DOSS accurately, and apportion the overall implementation/maintenance costs based on function-specific utilizations [19,24]. Hence, while no definitive recommendations on the adoption of 4D-DOSS can be made at present, these scenario analyses will be useful in the future when use-cases for 4D-DOSS are fully described, or when a prospective trial to determine the efficacy of 4D-DOSS in reducing MRSA transmission has been conducted.

The value of information analysis showed that the single parameter of bed-day costs made the greatest contribution to model uncertainty. The study findings indicated that further research to value bed-day costs will be most helpful to eliminate uncertainty around decision-making. Of importance, research on bed-day costs should be aimed at determining the opportunity costs instead of the accounting costs. This because accounting costs are intended for expenditure recovery and will inevitably include fixed and sunk costs. Study designs that include micro-costing methods to calculate direct variable costs, or contingent valuations to determine the decision-maker's willingness to pay, will be more useful in estimating the opportunity costs of bed-days in Singapore [25,26].

This study has limitations. First, it was assumed in the Markov model that patients move from 'colonized' to 'no colonization' when MRSA decolonization was completed. This assumption was made because swabs to check for MRSA colonization status after decolonization therapy are not taken routinely in the study hospital. However, it is acknowledged that this assumption may not be fully valid because some patients may remain colonized with MRSA despite receiving MRSA decolonization therapy, and likely depends on the decolonization protocol used [27]. Second, this study relied on retrospective data from hospital databases and expert input for some parameters, which could have introduced bias. For instance, positive clinical MRSA cultures were used as a surrogate for the presence of MRSA clinical infections; while this is likely accurate for most patients, a small proportion may have positive clinical MRSA cultures without symptoms of infection, and will not require antibiotic treatment. Hence, it is proposed that the model should be updated with stronger evidence from prospective studies when available. Third, this model applies to the average inpatient and does not differentiate between intensive care and general wards. If different surveillance strategies for 4D-DOSS were implemented for different ward types in the future, this cannot be accommodated in the model. Finally, this study focused solely on MRSA as the nosocomial pathogen of interest. While MRSA is the most prevalent MDRO associated with HAIs in Singapore, this is likely an underestimate of the benefits associated with the use of 4D-DOSS for infection surveillance as the system can be expanded for the surveillance of other MDROs with marginal cost [7]. As the Markov model used in this study can easily be adapted for other major MDROs, it is suggested that expansion of the current economic analysis to other MDROs of interest in future studies may provide a more thorough assessment of the cost-effectiveness of 4D-DOSS for infection surveillance.

In conclusion, early health economic models provide insight into the potential cost-effectiveness of an innovation at an early stage, and highlight uncertain parameters for future research. This early modelling study identified the circumstances for which the adoption of 4D-DOSS for MRSA surveillance in a Singapore tertiary hospital is likely to be cost-effective. Moving forwards, accurate estimates on the implementation/maintenance costs of 4D-DOSS and prospective studies to determine the effectiveness of 4D-DOSS in preventing MRSA transmission are needed to guide the decision to adopt 4D-DOSS.

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Conflict of interest statement
None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2023.09.010.

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