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Estimating costs and benefits of stroke management: A population-based simulation model

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ABSTRACT

The paper demonstrates how a system dynamics approach can support strategic planning of health care services and can in particular help to balance cost-effectiveness considerations with budget impact considerations when assessing a comprehensive package of stroke care interventions in Singapore. A population-level system dynamics model is used to investigate 12 intervention scenarios based on six stroke interventions (a public information campaign, thrombolysis, endovascular therapy, acute stroke unit (ASU), out-of-hospital rehabilitation, and secondary prevention). Primary outcomes included cumulative discounted costs and quality-adjusted life years (QALYs) gained, as well as cumulative net monetary benefit by 2030. All intervention scenarios result in an increase in net monetary benefit by 2030; much of these gains were realized through improved post-acute care. Findings highlight the importance of coordination of care, and affirms the economic value of current stroke interventions.

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1. Introduction

Stroke survivors with moderate to severe disability require long-term medical and social care, imposing financial and emotional burdens on patients and their families, as well as the health system. Furthermore, healthcare interventions often involve situations that are dynamically complex, characterized by long delays between cause and effect (e.g. high early costs in the short run may yield cost savings in the long term) and subject to competing interests and limited resources (Homer & Hirsch, 2006). With a rapidly aging population, it is necessary to prioritize high-value clinical interventions and implement supportive policies to optimize the use of available resources to improve patients' health outcomes. Strategic planning of care services requires an understanding of the budget impact over time arising from implementing combinations of care options. Cost-effectiveness considerations alone without consideration of cost as well as benefits over time do not provide a comprehensive picture as affordability is not taken into account and the availability of resources is not ensured. Simulation modelling of strategic choices promises

therefore to provide useful insights for health policy complementing standard health economics assessments focusing on cost-effectiveness. This paper uses simulation modelling to evaluate an extensive set of evidence-based options targeting various aspects of care across the stroke continuum in improving stroke care and informing strategic planning and practice.

Most of the literature on stroke focuses on particular interventions. The literature on clinical trials (Berkhemer et al., 2015; Hacke et al., 2008) and economic evaluations (Saka et al., 2009) typically consider one intervention at a time in a particular context. Similarly, the OR and simulation on stroke mostly investigates specific interventions; literature taking into the whole breadth of hyper-acute, acute and long-term as well as preventative care for people who have suffered a stroke is less common (Esensoy & Carter, 2018). The simulation literature on stroke care mainly comprises studies using discrete event simulation models to study specific interventions in the acute phase of stroke treatment (mostly thrombolysis to dissolve blood clots in the brain; e.g. Monks et al., 2012). There is also a

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substantive amount of work using Markov modeling to establish the cost-effectiveness of different medications to prevent strokes (Kansal et al., 2012).

Our SD model, informed by previous modeling work undertaken to support strategic planning to reduce the burden of stroke among veterans in the U.S. (Lich et al., 2014), allowed us to evaluate the social-level impact of interventions, singly and in plausible combinations, tailored to a nationwide country-level (i.e. the Singapore health system and population). Key variables of interest are epidemiological outcomes, cumulative care volumes, costs, and functional outcomes (measured in terms of quality-adjusted life years (QALYs)) from 2015 to 2030. When planning the improvement of stroke care, different time scales are important: both the hyperacute care during the first few hours after the onset of stroke as well as the long-term care of stroke sufferers has to be considered.

2. Literature review

Stroke has a major impact on human health throughout the world in terms of deaths, years lived with disability, and years of life lost (GBD 2016 Stroke Collaborators, 2019; Gorelick, 2019) as well as cost (Rajsic et al., 2019) and has received significant attention from simulation modellers. While a relative smaller number of studies has used Markov Models to examine the cost-effectiveness of treatments to manage stroke risk factors, in particular arterial fibrillation (Davidson et al., 2013; Matchar et al., 2005; Sullivan et al., 2006) most of the work has studied pathways and care processes for acute stroke care.

Typically, this work on pathways and care processes employs a discrete event simulation approach. The application of DES in stroke care spans the whole acute part of the care pathway from analysing measures to reduce the time between stroke onset and arrival in hospital (Churilov et al., 2013), measures to reduce in hospital delays (Monks et al., 2012) to understanding problems around delayed discharges (McClellan et al., 2011).

A particular interest has been the analyses of the impact of thrombolysis as well as factors preventing the use of this highly time-sensitive treatment that can only be given in a very tight time window after the onset of stroke. Stahl et al. (2003) investigated the cost-effectiveness of guidelines to reduce hospital processing times in order to increase tPA rates. Monks et al. (2012) used a DES model to show the increase in the benefit for patients which can be achieved by reduced in-hospital delays and extension of the treatment window. Further DES studies have investigated pre- or in hospital delays

preventing the administration of thrombolysis (Churilov et al., 2013; Lahr et al., 2013; Uzun Jacobson et al., 2015). Other studies have analysed the cost-effectiveness of thrombolysis using DES combined with a phase-type distribution approach to understand length of stay (Gillespie et al., 2016).

Mar et al. (Mar et al., 2010) conducted a budget impact analysis of the introduction of thrombolysis using a DES model. Their analysis showed how in terms of budget impact the cost of thrombolysis would initially outweigh the financial benefits and would only after six years financially beneficial due to the avoided long-term cost of dependency for patient who had been successfully treated with thrombolysis. Their analysis does not consider any other interventions. Discrete event simulation has previously also been employed for high level models of the overall stroke pathway (Bayer et al., 2010; Cordeaux et al., 2011).

Although system dynamics has been widely used in health care settings to study many strategic policy and planning questions (Atkinson et al., 2015) the use of system dynamics in the area of stroke care is limited. Esensoy and Carter (Esensoy & Carter, 2018) have used system dynamics to develop a whole-system patient flow model for stroke patients. They investigate the routes of different types of patients through the system and consider the relevant capacities in the system. Lich and colleagues (Lich et al., 2014) reported on the use of a comprehensive system dynamics model to compare the effectiveness of different stroke interventions. This comparison used Numbers Needed to Treat per Quality Adjusted Life Year gained as comparator measure, but did not consider the cost of different interventions. Both these system dynamics studies were carried out to inform decision makers planning stroke care service across a comprehensive healthcare system (the province of Ontario and the US Veterans' administration respectively).

3. Case study

3.1. Stroke and treatments for stroke patients

Stroke can be the consequence of a blood clot in the brain (ischemic stroke) or of a bleed (haemorrhagic stroke); both of which reduce the blood supply to parts of the brain. Effective hyper-acute therapies to reduce the likely level of long-term disability exist for ischemic stroke, but not for haemorrhagic stroke for which these interventions would be dangerous. It is crucial to distinguish between these types of stroke based on a brain scan very quickly since the dissolution of the blood clot with medication (thrombolysis; tPA) (Jauch et al., 2013) or the mechanical removal of the blood clot (endovascular

therapy; EVT) (Powers et al., 2015) can only be carried out with acceptable risk within a short period of time after the onset of the stroke (4.5 h for thrombolysis, 6 h for endovascular therapy). Delays in seeking care or in-hospital delays can make patients ineligible for treatment. Rehabilitation after the acute phase can reduce the level of disability for stroke survivors (Winstein et al., 2016). Survivors of stroke are at a high risk for further strokes; secondary prevention of further strokes due to the control of risk factors such as high-blood pressure, arterial fibrillation and high cholesterol is therefore also important (Kernan et al., 2014).

One intervention of particular interest is the evaluation of treating patients in an acute stroke unit (ASU). An ASU is a designated area or ward where acute stroke patients are treated by a multi-disciplinary team including nurses, physiotherapists, dietitians, and patient educations (Ministry of Health of Singapore, 2009). Meta-analyses of trials comparing the management of acute stroke patients in a specialized ward with a general medical ward have shown that treatment in an ASU have been associated with a reduction in mortality, disability and institutionalization through better coordination of acute care, as well as, in some cases, post-acute rehabilitation and secondary prevention management (Claesson et al., 2000; Launois et al., 2004; Saka et al., 2009; Te Ao et al., 2012). However, as mentioned previously, most trials typically evaluate such treatments as standalone interventions; in reality, patients are administered a package of interventions, each of which can have synergistic and inter-related impacts on health and cost outcomes. As such, our model evaluates the impact of treatment in a stroke unit alone (termed here ASU) and in combination with other interventions which would be naturally promoted through an ASU (termed here Comprehensive Acute Stroke Unit (CASU)).

3.2. Modelling context and approach

In response to the growing burden of stroke in Singapore, the Stroke Services Improvement (SSI) team was set up by the Ministry of Health (MOH) in October 2014, with the mandate of improving stroke care on a national level in Singapore. We collaborated with the SSI, as well as clinicians and other academic experts, in developing a population-level systems dynamics (SD) model to examine the system-wide impact of reorganizing and improving stroke care management in Singapore in relation to health and cost outcomes. Throughout the model development the modelling team was in regular dialogue with representatives from the SSI and the MOH. We discussed structural assumptions,

parameter estimates, and policy options with stakeholders. Preliminary findings were presented to the stakeholders at several occasions and the modelling team refined the work based on the feedback received.

The concern of the stakeholders in Singapore, the Ministry of Health and the Stroke Services Improvement Initiative, was broader than just the acute part of the care journey and was not focused on the details of care provision for individual patients. Instead the concerns were of a more strategic nature. Of interest was the resource allocation for health and long-term care services for all stroke sufferers across the healthcare system. We have chosen a system dynamics approach over a DES approach since system dynamics is particularly suitable for high-level problems where factors such as the cumulative effect of the probabilistic delays or individual patient level differences are not of significance. In this work we could draw on prior work that had been conducted using a system dynamics approach to support strategic planning to reduce the burden of stroke among veterans in the U.S. (Lich et al., 2014).

The interest of our stakeholders in resource allocation across the system was different from what could be addressed in typical health economic analyses of cost-effectiveness for a closed treatment cohort. We opted for an open cohort approach as is recommend for budget impact analysis (S. D. Sullivan et al., 2014). This allowed us to examine resource use (and care volumes) which would be experienced by Singapore under alternative stroke policy options over the coming years. We also took a wide scope and included a large range of relevant services and intervention since this allows for a consistent the evaluation of technologies across the whole pathway and especially also for the knock-on effects between interventions (Pilgrim et al., 2009).

4. Model development

We developed an age- and sex- structured, population-level SD stroke model for Singaporeans and permanent residents (PRs). The simulation period was from 2015 to 2030 reflecting the time horizon the decision makers were interested. We used a two-year ramp-up period to implement various packages of interventions aimed at individuals with acute stroke based on an estimate how long it would take to change clinical practice. The SD model simulates the transition of stroke patients and survivors (stocks), stratified by a system of stroke specific disability categories via flows over time. These categories describe the degree of long-term disability of stroke suffers and are based on the commonly used

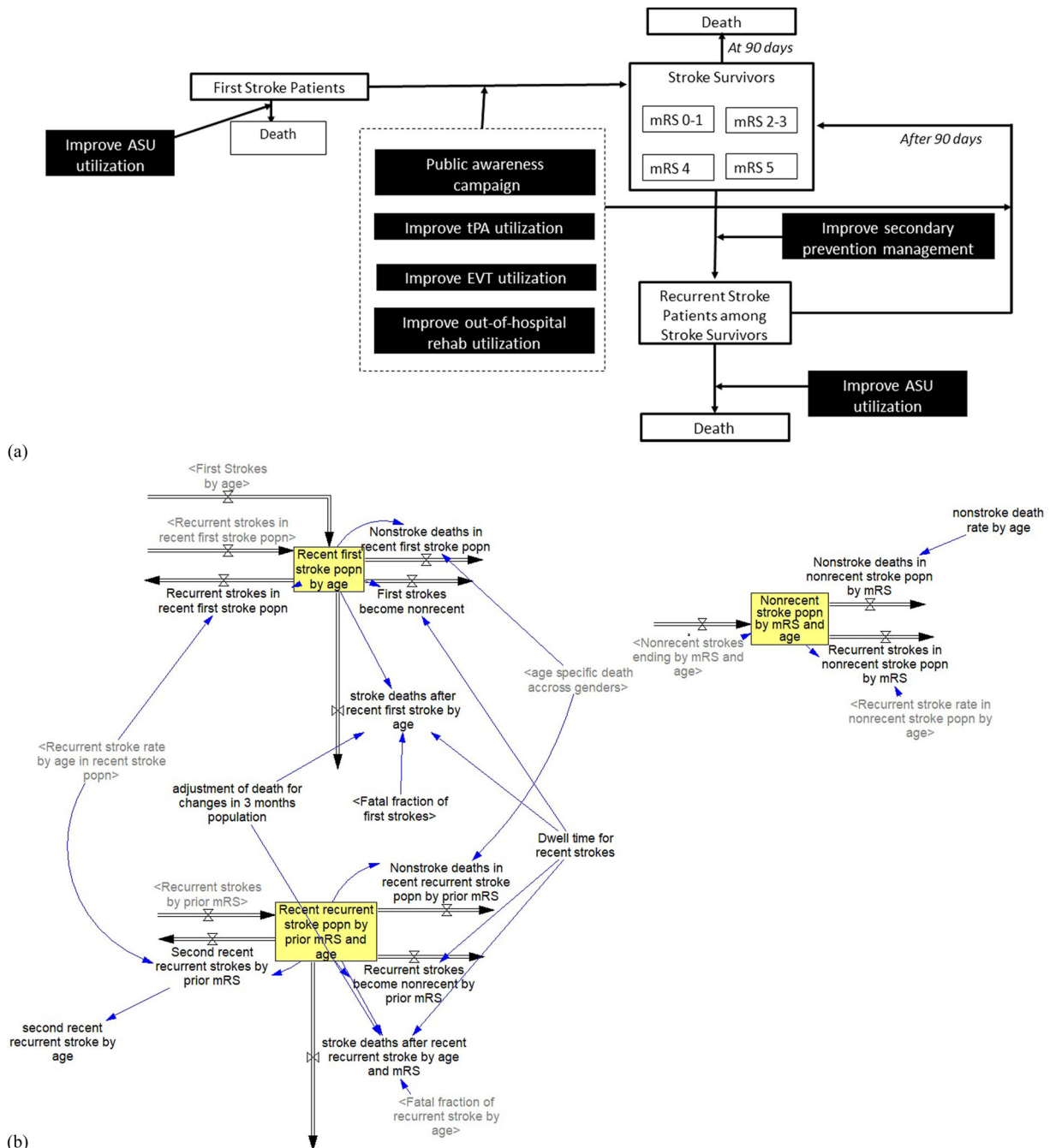


Figure 1. (A) Schematic representation of the Singapore stroke model; (B) Stock-flow diagram of the stroke population module.

modified Rankin Scale (mRS). Once Singaporeans and Singapore permanent residents (PRs) experience their first stroke (calculated based on age and gender specific incidence rates), they enter a stock of First Stroke Patients. Some patients die due to stroke-attributable or non-stroke-attributable causes within the first 90 days of the onset of stroke while some survive. These first stroke survivors are accumulated in the stock Stroke Survivors, which accounts for the individuals with a history of stroke in the community. If these stroke survivors have a recurrent stroke, they enter the stock, Recurrent Stroke Patients among Stroke Survivors; those who survive within 90 days from their most recent stroke

move back into Stroke Survivors (again stratified by mRS group). The model simulates the effect of different intervention scenarios on the risk of death or a recurrent stroke, and the distribution of stroke survivors by mRS group (Figures 1A and 1B).

Vensim DSS was used for model construction, parameterization, calibration, and evaluation (Ventana Systems, 2015). The model was structured in a number of modules (table 1). See in the appendix the data sources for the model.

The starting point of our modelling efforts, the simulation of the age and gender specific incidences and deaths from first strokes based on a population model, was calibrated against data from the local

Table 1. Module description.

Module	Module description
Stroke Population	The main module of the model (see Figure 1B) is accounting for the population of recent (within 3 months) and non-recent stroke survivors distinguished according to dependency categories (mRS) and age.
Singapore population	This module captures demographic change over time, which influences the incidence of first strokes.
Stroke – fatal & survived	This module calculates the number of people who suffer fatalities within three months of the stroke or survive a first or recurrent strokes based on demographic factors taking into account stroke type (ischemic vs. non-ischemic)
Recurrent stroke rates	Calculates recurrent stroke rates taking into account the fraction of the survivors of a first stroke which receive adequate risk factor management.
Fatal fraction of strokes	Calculates the fatal fraction of strokes based on the quality of acute care/stroke unit care.
tPA and EVT by mRS for first strokes	This module estimates the disability effect of first strokes given the hyperacute treatment received (tPA and/or EVT) and taking into account treatment availability and likely delays between stroke onset and hospital arrival (which influences both eligibility for treatment and treatment outcomes).
tPA and EVT by mRS for recurrent strokes	This module calculates the disability effect of recurrent strokes similarly to the previous module, but also considering the prior mRS status due to the first stroke.
Strokes by mRS	Calculates the long-term dependency status: modifying the status achieved after the hyperacute treatment by the effect of stroke unit treatment and rehabilitation.
Stroke interventions	Calculates the effect of a publicity campaign on the onset to arrival times in hospital as well as the fractions of medically eligible stroke sufferers receiving different forms of treatment.
Care volumes	This model counts the number of different treatments given over time.
Cost	Calculates overall costs including cost of treatment and long-term care costs as well as the cost of a public information campaign to encourage people to seek early treatment.

stroke registry. The modelling team then reviewed the relevant literature on the management of stroke. Choices about which interventions to include as well as local clinical practice were discussed with the local stakeholders. For each intervention we build model equations reflecting the impact on mortality rate and disability which were calibrated against the effects seen in clinical trials. We assumed an additive effect of combined interventions (e.g. thrombolysis and rehab). The model was then calibrated against local historical data for secondary stroke and reviewed by the stakeholders.

4.1. Stroke interventions

We considered six different interventions to improve stroke care: a public information campaign to raise awareness of stroke symptoms and urgency, thrombolysis with tissue plasminogen activator (tPA), endovascular therapy (EVT), treatment in an ASU, out-of-hospital rehabilitation, and secondary prevention.

Efficacy of each stroke care intervention and its associated cost was estimated from various sources, including literature reviews, primary and secondary data, and expert opinion. For each intervention, we estimated the effect of the intervention on the distribution of disability.

The public campaign was projected to increase the proportion of patients arriving at hospital within 210 min from the onset of stroke by 3% and between 210 and 300 min from the onset of stroke by 1%, based on results from a study of the effect of raising stroke awareness in Canada (Hodgson et al., 2007).

The impact of tPA, EVT and out-of-hospital rehabilitation on functional outcome of stroke patients, was measured using the modified Rankin

Scale (mRS) (Berkhemer, et al., 2015; Hacke et al., 2008; Koh et al., 2014a; The National Institute of Neurological Disorders & Stroke rt-PA Stroke Study Group, 1995) We conceptualised these interventions as shifts in the expected long-term disability for stroke survivors (expressed as mRS; see [Appendix, Supplementary material Tables A2-A4](#)). Based on the literature and discussion with medical experts we took into account that the effect of interventions would depend on the severity of the stroke (which correlates with the likely long-term disability outcome in absence of an interventions). The combination of interventions can then be understood as repeated shifts of the expected long-term disability. This approach allowed to use data from randomised controlled trials to parameterise individual interventions (by selecting parameters which minimise the mean squared deviation between the long-term disability distribution of shifted control group and the long-term disability distribution of the intervention group in the trial). We have chosen this approach since data for the effect of combined interventions is not available.

Treatment in an ASU was projected to reduce mortality risk due to stroke by 13% (Sun et al., 2013), while secondary prevention (including anti-hypertensive medication, anticoagulants, antiplatelet, and statin) was projected to reduce stroke survivors' risk of recurrent stroke by 75%, based on extant literature (Hackam & Spence, 2007).

4.1.1. Stroke care interventions: Current and desired level of care

The current proportion of eligible patients receiving tPA or EVT was derived from published reports of the Singapore Stroke Registry between 2006 and 2012 (National Registry of Disease Office, 2014). The Registry was also used to estimate the number

Table 2. Stroke care interventions considered in the model: current vs. desired level of care.

Intervention	Impact	Current Status	Desired Status	Effect size
Campaign to raise awareness of stroke symptoms and urgency	Increase the number of stroke patients arriving at hospital	≤210 min: 54.7% 210-300 min: 7.2%	57.7% 8.7%	3.0% 1.5%
Increase tPA administration efficiency of hospital process	Increase the proportion of eligible patients receiving tPA	34.8%	70.0%	35.2%
Increase EVT administration efficiency of hospital process	Increase the proportion of eligible patients receiving EVT	First Strokes: 9.9% Recurrent Strokes: 1.2%	20.0% 3.0%	10.1% 1.8%
Increase utilization of ASU	Increase the proportion of stroke patients managed in ASU	50.4%	80.0%	29.6%
Increase utilization of out-of-hospital rehabilitation	Increase the proportion of eligible patients receiving out-of-hospital rehabilitation (day rehab centres and home rehab sessions)	50.0%	70.0%	20.0%
Increase proportion of eligible people under appropriate secondary prevention	Increase the proportion of eligible people with history of stroke receiving secondary prevention	50.0%	75.0%	25.0%

tPA, tissue plasminogen activator; EVT, endovascular therapy; ASU, acute stroke unit.

of stroke patients who have been admitted to ASU between July and September 2014 for at least one night (National Registry of Disease Office, 2014). Local estimates of the current proportion of eligible patients receiving out-of-hospital rehabilitation (home or day rehabilitation centres) was calculated as the proportion of referred stroke patients attending at least one out-of-hospital rehabilitation session within 90 days from the date of discharge (Agency for Integrated Care, 2015).

The SSI team then identified performance targets under a plausible improvement regimen. (see Table 2).

4.1.2. Outcome measures

Our work took a health perspective and focused on health related outcomes and costs. Primary outcome measures used to compare the impact of each intervention scenario were cumulative discounted costs (measured in SGD), cumulative quality-adjusted life years (QALYs) gained based on a mapping of long-term disability measured in mRS to quality of life (Rivero-Arias et al., 2010), and cumulative net monetary benefit. Costs and QALYs were discounted at 3% per annum. Net monetary benefit were calculated as the difference between cumulative monetary value of QALYs gained and cumulative costs between the status quo and each intervention scenario (Hartwell et al., 2011); in absence of an official cost-effectiveness threshold for Singapore we used the gross domestic product per capita, SGD 70,000, to represent the approximate willingness-to-pay threshold for 1 QALY gained (World Health Organization, 2003).

Secondary outcome measures included the number of first and recurrent stroke episodes and corresponding number of fatalities, and difference in cumulative care volumes between status quo and each intervention scenario by 2030.

4.1.3. Model calibration and sensitivity analysis

Model parameters regarding stroke epidemiology and the number of patients receiving tPA or EVT

were calibrated against data from Singapore Stroke Registry from 2006 to 2013.

In order to test the robustness of the model against uncertainty in parameter estimates we tested the sensitivity of the model to all parameters using one way sensitivity analysis (see also Appendix, Supplementary material Tables B1 and B2). We examine clinical outcomes (number of stroke survivors by disability as well as fatalities from first and secondary stroke) as well as cost.

Since the interventions are likely to have synergistic effects (e.g. the awareness campaign increases the effectiveness of an expansion in thrombolysis provision) we additionally conducted multivariate probabilistic sensitivity analyses in which parameters characterizing all the stroke interventions were varied in order to understand the combined effect of uncertainty in interventions. Parameters were varied by $\pm 10\%$, assuming a random uniform distribution. The model was run for 1000 simulations per variable for one-way sensitivity analyses and 10,000 simulations for probabilistic sensitivity analyses, respectively. The sensitivity analysis supports the robustness of the model.

5. Results

We simulated 12 different intervention scenarios (Table 3) based on the six different stroke interventions singly or in plausible combinations.

5.1. Stroke epidemiology from 2015 to 2030

At baseline, the annual number of first stroke episodes is projected to grow by almost 70% from 5,596 in 2015 to 9,446 in 2030 (Figure 2A), while the number recurrent stroke episodes is projected to rise by 80%, all factors remaining unchanged (Figure 2C). Intervention scenarios that include secondary prevention result in 9,918 (or 18%) fewer cumulative recurrent stroke episodes by 2030, compared to baseline (Figure 2C).

Table 3. List of intervention scenarios.

	Model Scenario Name	Model Scenario Description
1	Status Quo	Current practice of care
2	tPA Only	Increase the proportion of eligible patients receiving tPA
3	Campaign & tPA	Increase the number of patients arriving to hospital early within 300 minutes <i>and</i> the proportion of eligible patients receiving tPA
4	EVT Only	Increase the proportion of eligible patients receiving EVT
5	tPA & EVT	Increase the proportion of eligible patients receiving tPA and/or EVT
6	Campaign, tPA, & EVT	Increase the number of patients arriving at hospital early <i>and</i> the proportion of eligible patients receiving tPA and/or EVT
7	Rehab only	Increase the proportion of eligible patients receiving out-of-hospital rehabilitation
8	Secondary prevention only	Increase the proportion of stroke survivors receiving secondary prevention
9	CASU	Increase the proportion of eligible patients managed in an ASU and receiving out-of-hospital rehabilitation, while also increasing the proportion of stroke survivors receiving secondary prevention
10	CASU & tPA	Increase the proportion of eligible patients receiving tPA, being managed in an ASU and receiving out-of-hospital rehabilitation, while also increasing the proportion of stroke survivors receiving secondary prevention.
11	CASU, tPA & EVT	Increase the proportion of eligible patients receiving tPA and/or EVT, being managed in an ASU and receiving out-of-hospital rehabilitation, while also increasing the proportion of stroke survivors receiving secondary prevention.
12	Everything combined	Increase the number of patients arriving to hospital early within 300 minutes, tPA and/or EVT, being managed in an ASU and receiving out-of-hospital rehabilitation, while also increasing the proportion of stroke survivors receiving secondary prevention.

tPA, tissue plasminogen activator; EVT, endovascular therapy; ASU, acute stroke unit; CASU; comprehensive acute stroke unit.

In terms of mortality, the number of first and recurrent stroke-related fatalities is projected to rise by more than 80% from 975 in 2015 to 1,785 in 2030, at baseline levels. However, we found that providing a care package combining treatment in an ASU with post-acute care (out-of-hospital rehabilitation and secondary prevention) (referred to in this paper as a “comprehensive ASU” [CASU]) resulted in the lowest number of stroke fatalities by 2030 compared to the status quo (a cumulative reduction of 2,141 stroke fatalities or 10% from the status quo); this is due to the reduced risk of a recurrent stroke episode (by secondary prevention), and corresponding mortality (through treatment in an ASU) (Figure 2B and 2D).

5.1.1. Differences in cumulative care volumes by 2030

Under the status quo, 9,989 episodes received only tPA, 1,154 episodes received only EVT and 216 episodes received both, cumulatively by 2030. 107,453 stroke episodes were treated in an ASU, while 64,152 stroke episodes receiving out-of-hospital rehabilitation, cumulatively by 2030, at baseline. The number of stroke survivors under secondary prevention was 37, 515 by 2030.

Promotion of hyper-acute interventions, tPA and EVT, led to an approximate 11,267 (or almost 100%) increase in numbers treated with either or both, cumulatively by 2030, compared to baseline; combining hyper-acute interventions with a public information campaign led to a 14, 060 (or 127%) increase in numbers treated with acute care by 2030 compared to baseline, due the latter’s impact on reducing onset-to-door time.

In addition to, and as a result of, improving functional outcomes, implementing hyper-acute interventions reduced patients requiring post-acute

rehabilitation and long-term care; for example, increasing the proportion of patients receiving tPA and EVT, all other interventions left unchanged, reduced the cumulative number of stroke incidences requiring rehabilitation by 230 by 2030.

Promotion of secondary prevention, holding all other interventions at baseline levels, led to an approximate 650 (or 6%) reduction in patients requiring tPA and/or EVT by 2030, and 3,392 (or 5%) reduction in patients requiring rehabilitation; this is due to the favorable impact secondary prevention had on the likelihood of a recurrent stroke.

5.1.2. Differences in cumulative discounted costs from 2015 to 2030

Based on the care volumes above, the additional implementation costs of each intervention compared to status quo were measured between 2015 and 2030. Increasing the proportion of eligible patients receiving acute care (tPA and EVT) resulted in a cumulative cost increase of SGD 22 million (or 0.3%) compared to the status quo. In fact, improving the proportion of eligible strokes receiving tPA (holding all other interventions constant) resulted in an actual savings in costs of SGD 1 million, compared to baseline; this is because increasing the proportion of stroke patients receiving tPA improves functional outcomes in the simulated population, thereby reducing post-acute-care costs, particularly long-term care. Increasing the proportion of those treated in a CASU (inclusive of rehabilitation and secondary prevention) resulted in a cumulative increase of SGD 305 million (or 4%) compared to the status quo. All six interventions combined resulted in a cumulative cost increase of approximately SGD 336 million (or 5%) in comparison to status quo by 2030 (Figure 3A).

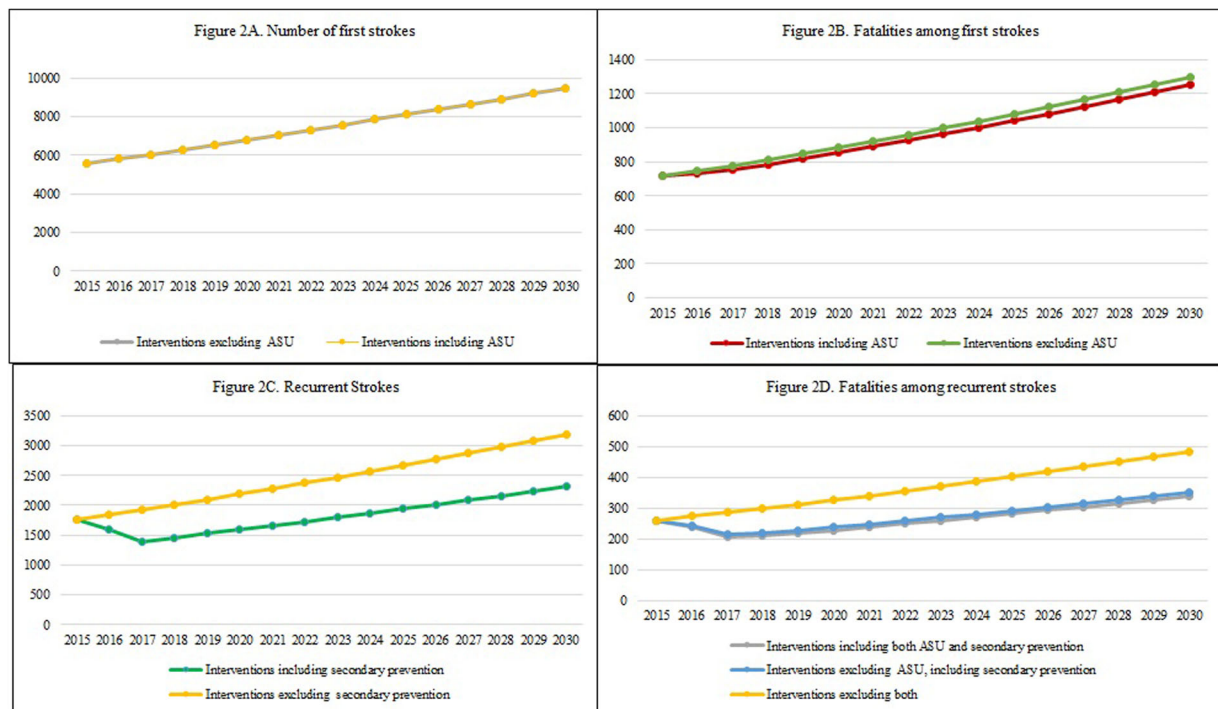


Figure 2. Strokes and stroke fatalities.

5.1.3. Cumulative discounted QALYs gained in 2030

When considering single interventions only, promoting secondary prevention resulted in the highest QALYs gained (3,893 or 0.7%), closely followed by rehabilitation (3,760). Combining the increased proportion of eligible strokes receiving hyper-acute treatment (tPA and EVT) with a public information campaign resulted in a higher number of QALYs gained (compared to status quo) (2,121) compared with the sum of implementing these interventions individually (1,941) (Figure 3B), illustrating a synergistic effect. Increasing the proportion of those treated in a CASU resulted in a cumulative gain of 7,381 QALYs (or 1.3%) compared to the status quo. As expected, the intervention scenario in which all of the six stroke interventions are included resulted in the highest gain in QALYs (9,411 or 2%) from the status quo.

5.1.4. Difference in cumulative net monetary benefit between each intervention scenario and status quo in 2030

Each QALY gained was valued at 1 times gross domestic product (GDP) per capita (SGD 70,000) based on recommendations to assign the value of 1 to 3 times GDP per capita (World Health Organization, 2002), to estimate the cumulative net monetary benefit from these interventions until 2030. While in the short-term, ramp-up of interventions led to initial net monetary loss compared to the status quo, within a 15-year timeframe, all interventions resulted in a positive cumulative net monetary benefit, compared to the status quo. This

finding is understandable, given time delays between costs incurred and full benefits realized. As expected, in 2030, the intervention scenario with all six interventions combined had the highest net monetary (SGD 323 million). As a single intervention strategy, post-acute care, namely rehabilitation, followed by secondary prevention, had the highest gain in net monetary benefit by 2030 (SGD 227 million and SGD 180 million, respectively), compared to hyper-acute interventions such as tPA and EVT; this is an important finding as it reaffirms the value of a CASU in providing not only acute service, but also improved coordination of post-acute care. (Figure 4).

6. Discussion

Our analysis indicates that all interventions combined (public information campaign, increasing the proportion of strokes receiving acute interventions as well as out-of-hospital rehabilitation and secondary prevention), synergistically produced more benefits by 2030 and resulted in the largest net monetary gain at the end of the simulation period. Furthermore, given that post-acute care, namely rehabilitation, followed by secondary prevention, had the highest gain in net monetary by 2030 reaffirms the value of a CASU in providing improved coordination of post-acute care.

Among single improvements in stroke care, increasing the number of stroke patients receiving out-of-hospital rehabilitation resulted in the largest gain in net monetary benefit compared to status quo over the 15-year simulation ramp-up period.

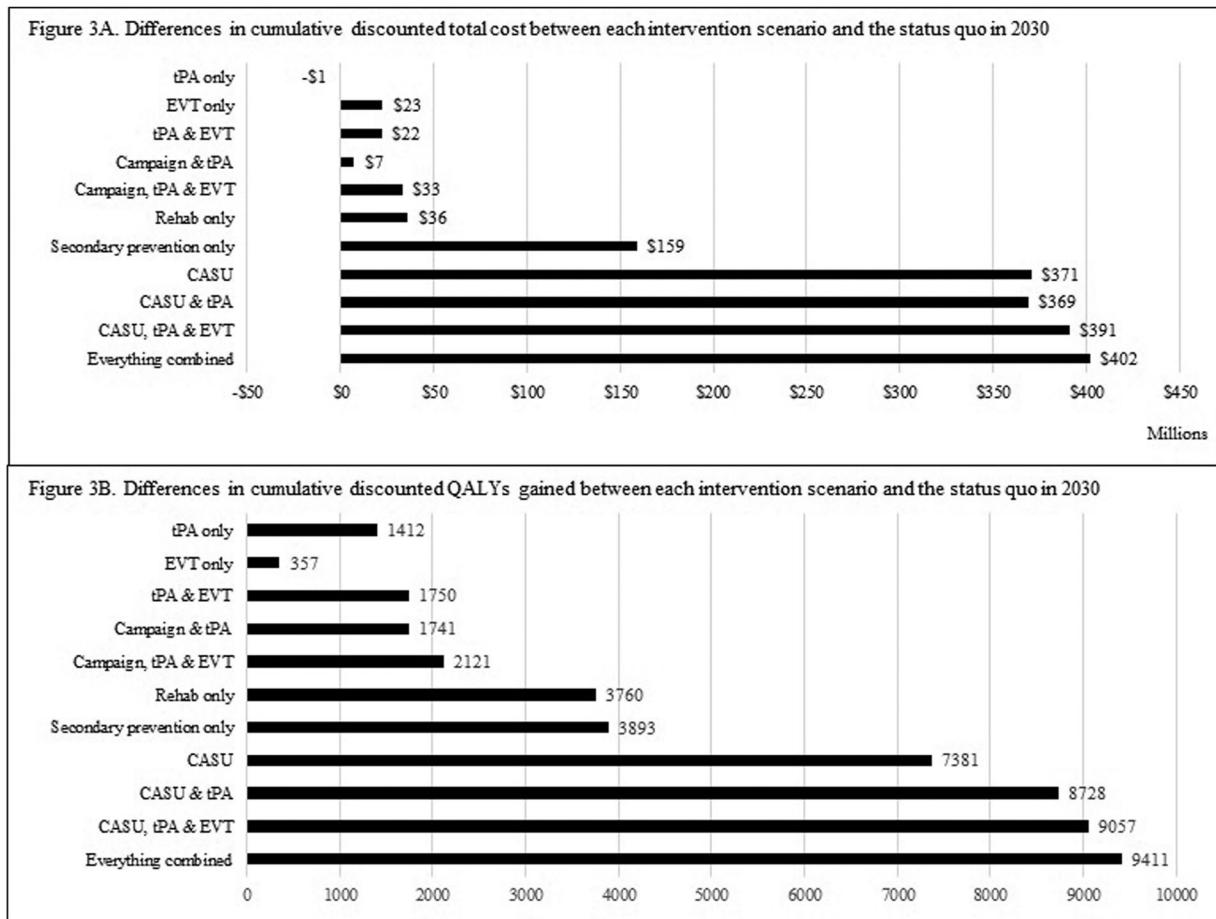


Figure 3. Cumulated costs and QALYs.

This is primarily due to the estimated improvement in functional outcome in the long-term. With the exception of tPA, other interventions incurred a net increase in cumulative costs (including long-term care) by 2030. Often clinical interventions can be exclusively available to only a subgroup of stroke patients due to contraindication; for tPA and EVT, the most stringent eligibility criterion is onset-to-door time. Thus, we observed that the intervention scenario in which a public information campaign to raise awareness of stroke symptoms is launched increases the proportion of eligible strokes receiving these acute clinical interventions, thus producing a synergistic effect in the number of QALYs gained than implementing these interventions individually.

In distinction to conventional cost-effectiveness analyses in which a cohort of individuals is followed over time (a “closed” cohort), this modelling approach generates estimates of the impact from year to year over the entire population (an “open” cohort). This allows an estimate of the year to year impact at the societal level, as well as the cumulative impact over a defined time horizon (here to 2030). For this reason, net monetary benefit – related to the incremental cost-effectiveness ratio – is the most natural metric for value. This study contributes to the expanding literature, e.g. Kunc

and Kazakov (2013), that demonstrates the possible savings in healthcare costs using SD models.

Methodologically our SD approach to strategic planning of the comprehensive stroke care complements the operational DES simulation studies more prominent in the stroke area and the cost-effectiveness studies focused on single interventions and examining closed cohorts. In this project, we had to consider interventions, outcomes and costs as well as take into account very different time scales (minutes and hours in the hyperacute phase to months (rehabilitation) and years (long-term care), different outcomes. Moreover, we knew that implementation of some of the improvements would happen over time. Considerable effort had to be invested in assembling and reconciling the evidence from different sources necessary for an analysis of how the combination of changes in the implementation in the interventions would over time change outcomes. System dynamics modelling allowed us to integrate evidence from the medical literature, local data and expert opinion to enable the analysis of the entire system of care provided for people who have suffered a stroke. It was in particular possible, to arrive at reasoned estimates of the effect combination of interventions even though RCT typically only report on the effect of interventions in

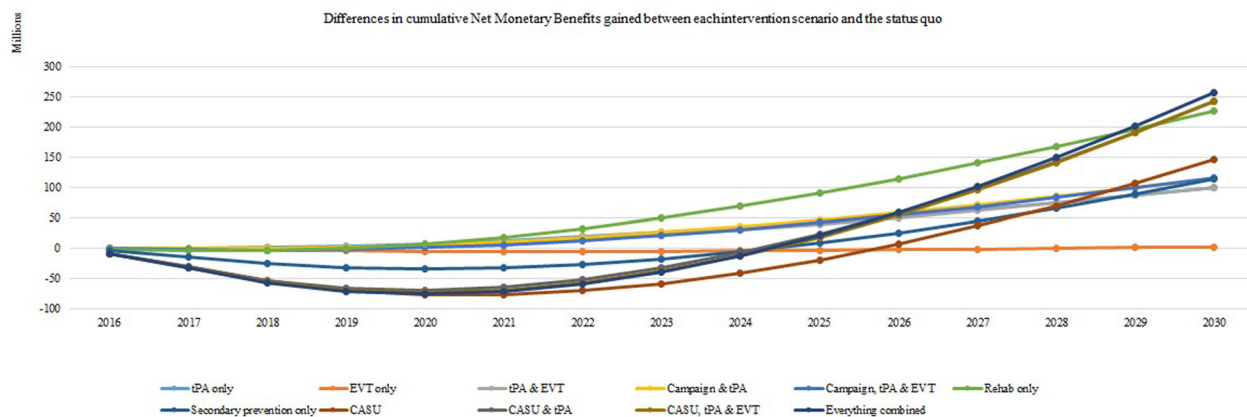


Figure 4. Difference in cumulative Net Monetary Benefit gained between each intervention scenario and status quo.

isolation. The modelling approach did not only allow the integration of evidence from different sources, but also supported the communication among team and our stakeholders with both medical and administrative and policy responsibilities and backgrounds.

7. Conclusions

In our study, we built a model of stroke for Singapore representing the health and cost impact of various interventions to improve stroke care. As a population-level model, this provides projections of outcomes over time, accounting for dynamic phenomena such as changing demographics. The process of building this simulation model allowed various stakeholders to convene and share their understanding of the current stroke management and exchange ideas for better informed planning. The study findings will inform and improve current stroke services delivery in Singapore.

One limitation of the study is the uncertainty of several model parameters due to the lack of data. We addressed this by determining these parameters through consultation with the SSI team and calibration. We addressed remaining uncertainties through rigorous one-way and probabilistic sensitivity analyses; by varying key parameters within a 10% margin, we demonstrated that conclusions presented in this paper were robust to these uncertainties.

Another limitation is that intervention costs per episode treated were assumed to remain the same, irrespective of the scale of the intervention; it is likely that increasing the scale of intervention beyond a certain threshold would involve certain fixed or sunk costs (such as the cost of new equipment, purchase of additional land or buildings). The monetary cost of productivity losses among patients and their caregivers were also excluded, as well as costs of associated conditions of stroke such as, vascular dementia, and their morbidities. However, such underestimation of costs may be, to a certain

extent, offset by the underestimation of the additional benefits that interventions such as secondary prevention can have on other medical conditions and co-morbidities such as the risk of heart failure, myocardial infarction, and chronic kidney disease.

The results from this model are being used for stroke services planning in Singapore, and this stroke SD model will be updated periodically to help policymakers with their informed decision-making. This SD model may be utilized by other countries and healthcare providers to explore local specific cost considerations and to assist with healthcare systems planning and projections.

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Disclosure statement

Dr. Koh owns equity in a private tele-rehabilitation company, T-Rehab Private Limited. The other authors report no conflicts.

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