Strategic Planning to Reduce the Burden of Stroke among Veterans: Using Simulation Modeling to Inform Decision Making

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Abstract

Background and Purpose—Reducing the burden of stroke is a priority for the Veterans Affairs (VA) Health System, reflected by the creation of the VA Stroke Quality Enhancement Research Initiative (QUERI). To inform the initiative's strategic planning, we estimated the

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relative population-level impact and efficiency of distinct approaches to improving stroke care in the United States Veteran population to inform policy and practice.

Methods—A System Dynamics stroke model of the Veteran population was constructed to evaluate the relative impact of 15 intervention scenarios including both broad and targeted primary and secondary prevention and acute care/rehabilitation on cumulative (20-year) outcomes including quality-adjusted life years (QALYs) gained, strokes prevented, stroke fatalities prevented and the number-needed-to-treat (NNT) per QALY gained.

Results—At the population level, a broad hypertension control effort yielded the largest increase in QALYs (35,517), followed by targeted prevention addressing hypertension and anticoagulation among Veterans with prior cardiovascular disease (27,856) and hypertension control among diabetics (23,100). Adjusting QALYs gained by the number of Veterans needed to treat, thrombolytic therapy with tissue plasminogen activator was most efficient, needing 3.1 Veterans to be treated per QALY gained. This was followed by rehabilitation (3.9) and targeted prevention addressing hypertension and anticoagulation among those with prior cardiovascular disease (5.1). Probabilistic sensitivity analysis showed that the ranking of interventions was robust to uncertainty in input parameter values.

Conclusions—Prevention strategies tend to have larger population impacts, though interventions targeting specific high-risk groups tend to be more efficient in terms of NNT per QALY gained.

Keywords

strategic planning; comparative effectiveness; simulation model; special populations; Veterans

Introduction

Stroke, a major cause of mortality and disability, occurs in more than 610,000 people and accounts for $38.6 billion in direct and indirect medical costs annually in the United States.[1] Opportunity for improvement in stroke prevention and stroke care is broadly acknowledged.[1,2] Significant stroke burden and opportunity for improvement also exists in the Veterans Affairs (VA) health system. The VA Stroke Quality Enhancement Research Initiative (QUERI) was created to translate evidence into system-wide practice to reduce stroke risk, improve patient care, and to help Veterans reach the best possible outcomes post stroke.[3]

In order to prioritize their efforts, the Stroke QUERI executive committee recognized the need for quantitative impact estimates of investment alternatives in research and implementation to reduce stroke burden. Given the Stroke QUERI's extensive charge, including primary prevention, acute care and rehabilitation, secondary prevention, and the need to accommodate a wide range of stakeholder involvement, the executive committee sought a systematic, analytical approach to strategic planning.

In close collaboration with stroke experts and QUERI decision-makers, we built and analyzed a population-level System Dynamics stroke model for Veterans to estimate the relative impact of 15 intervention scenarios for supporting decision-making. Given the need

to guide research and practice to improve stroke outcomes VA-wide, the project was intended to focus on classes of interventions of particular importance to VA leadership. Through literature review and engagement of a diverse team of stroke experts, we sought to ground simulated intervention scenarios in current practice in VA facilities, and plausible changes based on understanding the VA context. We examined the comparative impact of proposed intervention approaches on population-level health outcomes, as well as their relative efficiency. Additionally, we evaluated the robustness of results given potential data uncertainties.

Methods

Decision Model Overview

To better understand trade-offs between alternate stroke care improvement targets, we built a population-level System Dynamics (SD) stroke model for the United States VA enrollee population. Throughout the process of model development, we engaged with experts both within VA and more broadly to integrate their understanding of stroke and stroke care. Vensim DSS 5.11[4] was used for model construction, parameterization, calibration and evaluation. We initiated the model in 2010 with a population of 4.14 million VA users, defined as Veteran enrollees who utilized VA primary care service in the past 12 months. This subpopulation of enrollees, considered reachable by VA-based intervention, comprised 48% of all Veteran enrollees (based on 2007 data from Veterans Administration Desert Pacific Healthcare Network/VISN 22 databases). The model introduced a fraction of the VA enrollee non-user population each year, who become VA users following an incident transient ischemic attack (TIA) or stroke.

Accounting for heterogeneous stroke or TIA risk, the model stratified VA users into 11 mutually exclusive stocks (depicted as solid rectangles in Figure 1) representing individuals with similar natural history and response to treatment (e.g., history of recent diagnosed TIA). Veteran users without prior TIA or stroke were segmented by stroke risk factors: age (<45, 45-64, 65-75, >75), hypertension and systolic blood pressure (<140 mmHg, 140 mmHg-159 mmHg, >160 mmHg), atrial fibrillation (AF), diabetes mellitus type 2, smoking, and cardiovascular disease (CVD). The post-TIA population was disaggregated by diagnosis (diagnosed versus undiagnosed) and time since last TIA event; the post-stroke population was categorized by time since most recent stroke and functional independence via modified Rankin Scale (mRS).

The SD model simulated the transitions between health states (stocks) via flows over time. Typical of SD models, movements among health states were governed by processes with multiple influences, nonlinearity, accumulation, delay, and feedback.[5] Input parameters (omitted from Figure 1 for simplification) include time delays, constants, rates, and time series inputs. More information on model assumptions can be found at http://vastrokemodel.weebly.com.

Data Sources

The projections of VA user demographics were based on The Veteran Population Projection Model (VetPop)[6] and Decision Support Services (DSS) Veteran enrollee data. Current levels of care in the VA were largely based on a study conducted by the Veterans Health Administration (VHA) Office of Quality and Performance (OQP) and Stroke QUERI during FY 2007.[7] A Framingham-based risk calculator was used to determine relative stroke rates as the pre-event population changed with time either based on exogenous factors or through intervention.[8] To achieve this, the pre-event population was stratified into 256 risk groups reflecting relevant combinations of key stroke risk factors; the prevalence of each risk factor and risk factor combination was based on VISN 22 data but cross-checked against national single-factor prevalence estimates.[6,8,9] The risk calculator used was selected as the best match to available risk data and specific prevention interventions considered in the model. The distribution of post-stroke functional status was estimated based on VA Functional Status Outcomes Database (FSOD) data[10-12], though estimates from the literature were used in sensitivity analysis.[13] Age-specific non-stroke death rates were derived from the U.S. Census Life Tables. In the absence of data, literature review with VA source preference[14-16] was conducted to inform assumptions. For example, while national sources were compared, the initial prevalence of TIA and stroke were estimated from a study on large administrative VA medical databases.[14]

Intervention Scenarios

We worked with Stroke QUERI decision makers and additional stakeholders to develop 15 distinct intervention scenarios representing the policy decision space; each improving current practice denoted as "current levels of care" (Figure 2). Scenarios were organized into 3 categories: primary prevention, secondary prevention, and acute care/rehabilitation. Each intervention scenario was defined based on evidence concerning specific interventions within the categories, current VA levels of care (what proportion of eligible individuals are receiving the intervention), projected level of care with plausible effort, and expected intervention effectiveness.

Sensitivity Analysis, Model Calibration, and Uncertainty Analysis

Given the breadth of the model and gaps in VA data, it was important to conduct a rigorous sensitivity analysis to identify key uncertain parameters, model calibration to estimate these parameter values given additional data, and uncertainty analysis to assess robustness of findings given existing uncertainty. [29] To reduce the number of parameters that needed to be estimated, we applied the Morris method[30] to identify the subset of parameters to which either model outputs or calibration criteria (i.e., the calculated difference between additional data points and their simulated equivalent) were most sensitive (i.e., contributed the most to variability in each). Next, those parameters to which calibration criteria were most sensitive were estimated (i.e., "calibrated") using generalized likelihood uncertainty estimation.[31] Calibration was performed to produce more than 400,000 replications of the model. We selected the 1,000 best- fitting parameter sets to serve as alternate baselines for uncertainty analysis. Finally, we conducted multivariate probabilistic sensitivity analysis to account for uncertainty in the 15 intervention scenarios' effect sizes as well as in additional non-

calibrated model inputs parameter values to which model outputs were sensitive. In total, 10,000 distinct model replications were simulated to represent uncertainty in model input parameter values.

Outcomes

Each intervention was simulated sequentially in each replication of the model, and results were calculated by taking the difference in cumulative quality-adjusted life years (QALYs), incident strokes, and stroke fatalities during a 20-year time period. While these results inform relative population-level impacts of each intervention, they do not capture differences in resources required to achieve these impacts. A clinically and operationally-relevant surrogate for actual resource utilization and efficiency, we calculated the number-needed-to-treat (NNT) to achieve a 1-unit change in QALY during a 20-year period. A discount rate of 3% was applied to all outcomes.

Because the simulated outcomes were highly skewed, we reported the median of each outcome across the 10,000 replications, with 95% uncertainty bounds for each intervention. Uncertainty bounds were derived from the cumulative distribution function of each output prediction, re-scaling based on the likelihood estimates of the 1,000 best-fitting baselines. In addition, we applied Mann-Whitney U test[32] (two-tailed), a non-parametric test, to assess the statistical significance of differences in NNT per QALY gained across all possible pairs of intervention scenarios across replications. We tested a set of null hypotheses that there is no difference between each pair of intervention scenarios.

RESULTS

The Morris method[30] reduced the complexity of the model calibration by identifying 36 parameters (out of 60) to which calibration criteria or model outputs were most sensitive. It is worth noting that the most influential parameter across all the outputs is the stroke rate per thousand in the pre-event VA user population per year. Further data collection and rigorous estimates of it could dramatically reduce uncertainty in projected stroke outcomes.

Table 1 presents simulated outputs across the 15 intervention scenarios in a descending order with respect to QALYs gained over 20 years. Improving hypertension control for all VA users from baseline (73%) to a plausibly achievable level (between 87% and 95%) yielded the largest benefits in 20-year QALYs gained, strokes prevented, and stroke fatalities prevented. Carotid endarterectomy (CEA) for individuals with prior stroke had the lowest improvement in QALYs. Because of the small number of eligible individuals relative to other interventions, thrombolytic therapy with tissue plasminogen activator (tPA) for acute stroke had a relatively small impact at the population level but was the most efficient strategy in terms of NNT per QALY gained (3.1). Increasing eligible strokes receiving rehabilitation service from baseline (30%) to 60% ranked second in terms of NNT per QALY gained (3.9). At current tPA administration levels, system-wide effort to increase the fraction of individuals arriving at the hospital within 60 minutes of stroke symptom onset was the least efficient strategy evaluated.

A box plot illustrating the expected NNT per QALY gained and estimated uncertainty, grouped by intervention category, is shown in Figure 3. Within each category, interventions are ordered from lowest NNT per QALY to highest. Though hypertension control for all VA users yields the greatest population-level benefit among primary prevention interventions, it is the least efficient in this category. More efficient were: targeted primary prevention focusing on specific high risk groups including VA users with severe hypertension, diabetes, prior CVD, or AF, as well as targeted hypertension and anticoagulation treatment for VA users with prior CVD and AF. Among secondary prevention interventions, the top 3 efficient interventions regarding NNT per QALY gained are management of recently diagnosed TIA (6.0), accurate and timely TIA diagnosis (9.0), and CEA post-TIA (9.4). Comparing intervention impacts across replications, the Mann-Whitney U test revealed that all pairs of these 15 interventions were statistically significantly different from each other in terms of NNT per QALY gained at a significance level of $P < 0.001$.

DISCUSSION

In this paper, we describe a computer model of stroke incidence and outcomes in the VA population and present analyses offering the Stroke QUERI a systematic foundation for understanding the impact of implementing alternate strategies for stroke prevention and treatment under consideration. From this project, we learned that several interventions have both large cumulative benefits to the Veteran population and are also relatively efficient in terms of NNT per QALY gained, including targeting individuals with a history of CVD for treatment of hypertension and AF and rehabilitation after acute stroke. This finding is being used by the Stroke QUERI to focus research and implementation efforts.

This study also revealed that broad-based prevention, such as improving hypertension management for all Veterans, was powerful in terms of cumulative benefits to the population, though not always as efficient as other intervention approaches since larger numbers of individuals must be treated for each unit of benefit. For example, considering QALY gains in Table 1, targeted prevention focused on hypertension and anticoagulation **for individuals with AF** amongst the subset of VA users with prior CVD achieves 78% of the gains that improving hypertension control for all users achieves. Echoing the guidelines for primary prevention of stroke[33], our study suggested that more efficient primary prevention should target high risk subgroups of veterans either with more severe condition (e.g. severe hypertension with SBP>160 mmHg) or with elevated risk in the presence of multiple stroke risk factors (e.g. prior history of CVD and hypertension).

A crucial feature of this exercise is that it was performed to address the VA decision context and results may differ in non-VA populations. For example, the efficacy of tPA will be dependent on local context, such as the proportion of people with stroke arriving soon after symptom onset and baseline rates of tPA use. Results also depend on the framing of key questions, for example if acute interventions were consolidated under a stroke unit.

This work is based on available data; as such, one limitation is that several of the model inputs are uncertain. However, guided by sensitivity analysis, we identified where uncertainty in inputs most affected outputs and focused our literature review, data analysis,

and consultation with the Stroke QUERI advisory committee on those inputs. We addressed remaining uncertainties through rigorous probabilistic sensitivity analysis and demonstrated that the strategic conclusions presented here are robust to these uncertainties.

A second limitation is that costs are not included directly, due to the complexity of cost estimation in this broad model and the variability in costs across facilities; instead we used the surrogate of NNT as an indicator of efficiency. This allows general comparisons of similar interventions (e.g., lifetime medication and clinical management for prevention) but is less relevant in comparing across the three broad intervention categories. We found the NNT analysis a useful reference point for Stroke QUERI discussion of the relative cost, feasibility, and sustainability of specific interventions; NNT provided decision makers a way to visualize the number of people who would need to receive the intervention in order to achieve one QALY.

A third limitation is that the benefits of prevention are underestimated in this study. For instance, hypertension control not only reduces the risk of stroke, but also lowers the risk of myocardial infarction, heart failure and chronic kidney disease whose benefits are not explicitly included in our results given the focus on stroke. Accounting for this secondary effect would only reinforce the estimated cumulative benefits of prevention.

The SD Stroke model presented here serves as a tool for policy makers to focus research on crucial points of uncertainty in order to improve decision making.[34] This framework has been used by the VA Stroke QUERI in discussions about how to move forward in strategic planning and goal development to improve the quality of stroke care in the VA system.[35] In response to results of the model, the Stroke QUERI has expanded its allocation of research and implementation on prevention, including new efforts to improve secondary prevention among Veterans post TIA or stroke, and improved integration with other QUERIs addressing hypertension in high-risk individuals. The model has potential to be applied to other contexts, particularly other managed health systems; the structure of the model can be adapted, accounting for local data, resources, and constraints. Further, it provides an example of how modeling can be applied to address clinical and public health policy problems to promote positive action.

Acknowledgments

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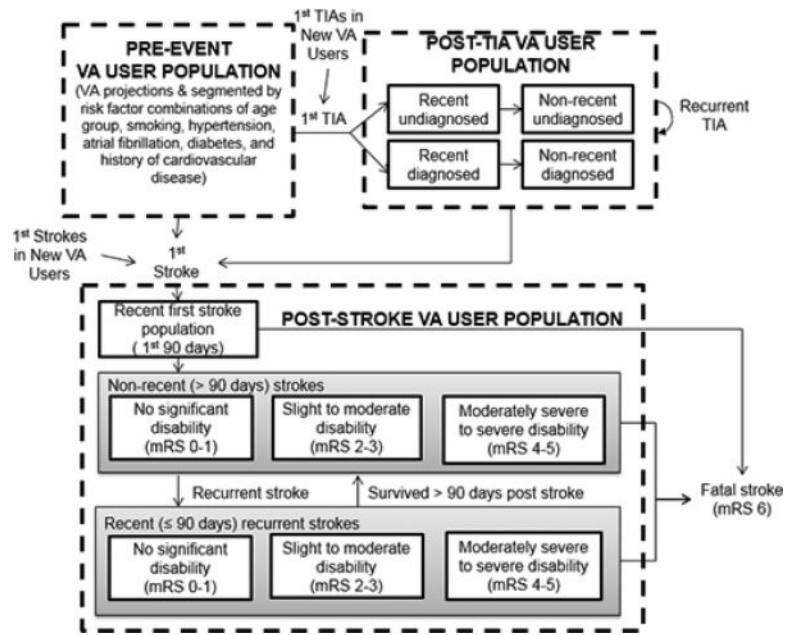
Figure 1.
Depicted in the diagram are the stocks (solid rectangles) and flows (arrows), which capture the states and changes in health status of the Veteran enrollee population over time. The dashed rectangles show the descriptive segmentation of the Veteran population based on history of TIA or stroke. The flows in the model manipulate the transitions between stocks which shift individuals between states over time and ultimately affect modeled outcome variables. "VA users without prior TIA or stroke" are not tracked as a stock, but rather a flow into indicated stocks.

Description of Intervention Scenarios	Target subpopulation among VA Users	Current Level of Care†	Projected Achievable Level of Care	Estimated Effect Size‡
Pre-event primary prevention				
Improve hypertension control for all VA users with SBP≥140mmHg	All pre-event users with 140mmHg≤SBP<160mmHg	73% with SBP<140mmHg	91% with SBP<140mmHg (87%-95%)	19% stroke RRR for movement from 140mmHg<SBP<160mmHg to SBP<140mmHg and 31% for movement from >160mmHg to <140mmHg[17]
Improve hypertension control for VA users with SBP≥160 mmHg	All pre-event users with SBP≥160mmHg	4% with SBP>160mmHg	2% with SBP>160mmHg (1.5%-2.5%)	31% RRR of stroke[17]
Improve hypertension control for VA users with DM	All pre-event users with DM and HTN	90% with SBP<140mmHg	97% with SBP<140mmHg (95%-98%)	18% stroke RRR for movement from 140mmHg<SBP<160mmHg to SBP<140mmHg and 31% for movement from >160mmHg to <140mmHg[17]
Improve ischemic stroke prevention for all eligible VA users with AF(Antiplatelet/Anticoagulation therapy)	All pre-event users with AF	34% with TTR≥60%	60% (40%-80%)	66% stroke RRR for anticoagulation[18,19]
Improve hypertension control and/or management of AF for VA users with prior cardiovascular disease	All pre-event users with CVD HTN and/or AF	No AF: 73% SBP<140mmHg AF: 78% SBP<140mmHg and 34% with TTR≥60%	No AF: 89% SBP<140mmHg (85%-93%) AF: 91% SBP<140mmHg (88%-94%) 60% TTR≥60% (40%-80%)	19% stroke RRR for movement from 140mmHg<SBP<160mmHg to SBP<140mmHg and 31% for movement from >160mmHg to <140mmHg[17] 66% stroke RRR for anticoagulation[18,19]
Secondary prevention				
Improve accuracy/timeliness of TIA diagnosis in VA users by increasing awareness/symptom recognition	All incident TIAs among VA users	71% of TIAs diagnosed* (Range 70%-80%)	81% (81%-85%)	Greatest stroke risk in first week after TIA; diagnosed can receive prevention
Improve the immediate management of TIA through expedited evaluation and risk factor management	All diagnosed TIAs	39% managed well* (Range 39%-53%)	80% (61.3%-83.8%)	40% reduction in risk of stroke for highest-risk period* (90 days post-TIA; Range 40%-72%)[20]
Improve the rate of CEA for eligible individuals post-TIA	All eligible VA users post-diagnosis of TIAs	15% of diagnosed TIA eligible; 35% of these receive CEA	60% (40%-75%)	Average of 37.5% RRR of recurrent TIA or stroke[21]
Increase % of stroke patients receiving guideline concordant stroke care for secondary prevention	All incident strokes among VA users	30%*	60% (50%-70%)	40% reduction in risk of stroke for next 90 days* (Range 40%-72%)[20]
Improve the rate of CEA for eligible individuals following acute ischemic stroke	All eligible VA users post-stroke	15% of strokes eligible, of these 35% receive CEA	60% (40%-75%)	Average of 37.5% RRR of recurrent stroke[21]
Acute Treatment /Rehabilitation				
Increase % of acute stroke ED arrival within 60 minutes of symptom onset	All incident strokes among VA users	18% of acute strokes ED arrival within 60 minutes	35% (27.5%-53.8%)	Increases percentage of individuals eligible for tPA[22,23]
Improve the use of thrombolytic therapy with tPA within the VA health care system	Incident strokes eligible for tPA among VA users	33% of Veterans arriving on time are medically eligible for tPA; of these, 11% of receive tPA	44% (18%-48%)	36% RRR in functional loss for tPA within 3 hours and 5% RRR of death during the acute period (corresponding to a 0.6 percentage point absolute risk reduction)[25,26]
Increase the % of ischemic stroke patients receiving proper deep venous thromboembolism prophylaxis	All incident strokes among VA users	79%	91% (81%-94%)	12.5% RRR of death during the acute period (corresponding to a 1.4 percentage point absolute risk reduction)[26]
Increase the % of acute ischemic stroke patients receiving dysphagia screening upon admission	All incident strokes among VA users	23%	84% (50%-88%)	3.3% RRR of death within the acute period[27]
Increase % of eligible stroke patients receiving guideline concordant rehabilitation services	All eligible VA users post-stroke	30%	60% (55%-73%)	35% reduction in risk of ending in mRS 4-5 and mRS 2-3, ending in mRS 2-3 and mRS 0-1, respectively[28]

Figure 2.

15 stroke intervention scenarios are defined, with each including a target subpopulation, current and projected level of care and estimated effectiveness of the intervention.

Footnote:*Calibrated within the model; †Baseline (the comparator, "current level of care"); ‡ Workgroup consensus. SBP: Systolic Blood Pressure (measured in mmHg); DM: Diabetes Mellitus; HTN: Hypertension; AF: Atrial Fibrillation; TIA: Transient Ischemic Attack; ED: Emergency Department; tPA: Tissue plasminogen activator; TTR: Time in Therapeutic Range; RRR: Relative Risk Reduction; CEA: Carotid Endarterectomy; mRS: Modified Rankin Scale
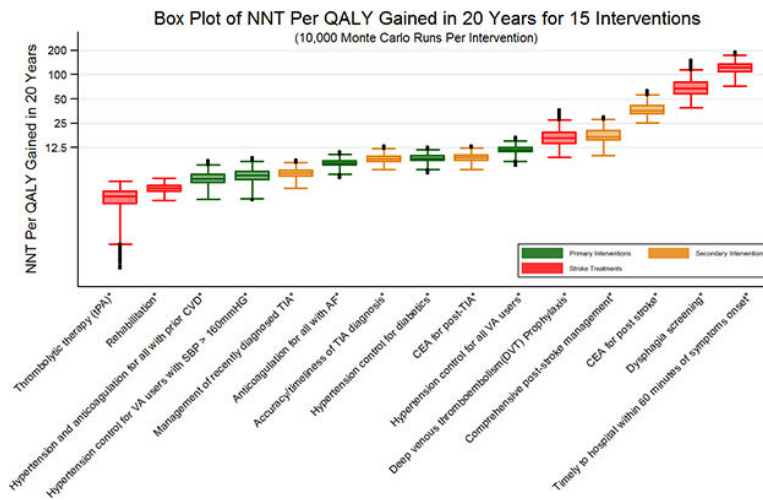
Figure 3.

The median number-needed-to-treat (NNT) per quality-adjusted life year (QALY) gained across 10,000 replications of the model is indicated by the line inside each box. The box spans the first to third quartiles, and the whiskers include the maximum and minimum values of NNT per QALY gained, excluding outliers. Outliers are depicted by solid circles. The vertical axis is on a logarithmic scale.

Footnote:$*P$-value < 0.001 when Mann–Whitney U test is applied to examine whether NNT per QALY gained for each intervention is significantly different from each other intervention. NNT: numbers-needed-to-treat; QALY: quality-adjusted life year

Table 1

Median and 95% Uncertainty Bounds for key Stroke Outcomes for each Stroke Intervention Scenario Compared to "Current Level of Care" over 20 Years

	QALYs Gained	Strokes Prevented	Stroke Fatalities Prevented	NNT Per QALY Gained
Hypertension control for all VA users[PP]	35,517 (27,302, 48,540)	20,940 (15,637, 29,413)	2,440 (1,547, 3,919)	11.8 (9, 14.2)
Hypertension control and anticoagulation for those with prior CVD[PP]	27,856 (19,493, 40,131)	16,479 (11,290, 24,368)	1,911 (1,123, 3,208)	5.1 (3.6, 7)
Hypertension control for diabetics[PP]	23,100 (16,990, 32,481)	13,688 (9,756, 19,805)	1,585 (9,86, 2,609)	9.2 (7.1, 11)
Rehabilitation[TR/R]	18,974 (12,845, 27,872)	210 (−71, 664)	73 (15, 164)	3.9 (3, 4.8)
Management of recently diagnosed TIA[SP]	10,838 (6,391, 17,304)	6,382 (4,043, 9,665)	727 (405, 1,243)	6.0 (4.5, 7.5)
Anticoagulation for all with AF[PP]	9,568 (2,553, 18,205)	5,643 (1,521, 11,096)	642 (163, 1,422)	8.1 (6.2, 9.7)
Comprehensive post-stroke management[SP]	6,315 (2,970, 10,985)	10,283 (6,095, 15,879)	1,340 (743, 2,246)	17.0 (12.3, 26.4)
Dysphagia screening[TR/R]	2,574 (1,239, 4,994)	−119 (−207, −63)	645 (344, 1,150)	67.8 (45.1, 110.4)
Hypertension control for VA users with SBP>160[PP]	2351 (1,762, 3,221)	1,385 (997, 1,963)	161 (100, 260)	5.7 (3.7, 7.7)
DVT Prophylaxis[TR/R]	2,001 (565, 4,690)	−94 (−193, −28)	509 (151, 1,078)	16.3 (10.8, 26.5)
Thrombolytic therapy[TR/R]	1,180 (405, 2,213)	0 (−11, 27)	31 (10, 65)	3.1 (1.1, 4.4)
CEA for post-TIA[SP]	748 (194, 1,434)	449 (116, 801)	51 (13, 106)	9.4 (7.4, 11.4)
Timely to hospital within 60 minutes of symptoms onset[TR/R]	733 (342, 1,270)	0 (−6, 16)	19 (9, 37)	122.3 (84.4, 158.3)
Accuracy/timeliness of TIA diagnosis[SP]	723 (190, 2,555)	440 (121, 1,545)	51 (14, 207)	9.0 (7.3, 11.3)
CEA for post stroke[SP]	344 (87, 747)	655 (170, 1,222)	84 (22, 170)	35.6 (28.2, 55.5)

A 3% discount rate is used in all calculations.

PP: Primary Prevention; SP: Secondary Prevention; TR/R: Treatment/Rehabilitation; NNT: numbers-needed-to-treat; QALY: quality-adjusted life years; CVD: Cardiovascular Disease; TIA: Transient Ischemic Attack; AF: Atrial Fibrillation; SBP: Systolic Blood Pressure (measured in mmHg); DVT: Deep Vein Thrombosis; tPA: Tissue plasminogen activator; CEA: Carotid Endarterectomy