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

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**Background and Purpose**—Reducing the burden of stroke is a priority for the Veterans Affairs Health System, reflected by the creation of the Veterans Affairs Stroke Quality Enhancement Research Initiative. To inform the initiative’s strategic planning, we estimated the relative population-level impact and efficiency of distinct approaches to improving stroke care in the US 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 years) outcomes including quality-adjusted life years (QALYs) gained, strokes prevented, stroke fatalities prevented, and the number-needed-to-treat 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-type 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 number-needed-to-treat per QALY gained. *(Stroke. 2014;45:2078-2084.)*

**Key Words:** comparative effectiveness research ■ computer simulation ■ health planning ■ stroke ■ Veterans

**Stroke**

A major cause of mortality and disability, occurs in >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.12 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 poststroke.3 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, analytic 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 of the VA context. We examined the comparative impact of proposed intervention approaches on population-level health outcomes, as well as their relative efficiency. In addition, 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 stroke model for the US 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 process of model development, we engaged with experts both within 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 of the VA context. We examined the comparative impact of proposed intervention approaches on population-level health outcomes, as well as their relative efficiency. In addition, we evaluated the robustness of results given potential data uncertainties.

Data Sources
The projections of VA user demographics were based on the Veteran Population Projection Model and Decision Support Services Veteran enrollee data. Current levels of care in the VA were largely based on a study conducted by the Veterans Health Administration Office of Quality and Performance and Stroke QUERI during fiscal year 2007. 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. 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 Veteran Integrated Service Network 22 data but cross-checked against national single-factor prevalence estimates.8 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 poststroke functional status was estimated based on VA Functional Status Outcomes Database data10–12 though estimates from the literature were used in sensitivity analysis.13 Age-specific nonstroke death rates were derived from the US Census Life Tables. In the absence of data, literature review with VA source preference14–16 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.15

Intervention Scenarios
We worked with Stroke QUERI decision-makers and additional stakeholders to develop 15 distinct intervention scenarios representing the
Policy decision space (Table 1). Scenarios were organized into 3 categories: primary prevention, secondary prevention, and acute care/rehabilitation. Each intervention scenario was defined based on evidence about 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. To reduce the number of parameters that needed to be estimated, we applied the Morris method to identify the subset of parameters to which either model outputs or calibration criteria (ie, the calculated difference between additional data points and their simulated equivalent) were most sensitive (ie, contributed the most to variability in each). Next, those parameters to which calibration criteria were most sensitive were estimated (ie, calibrated) using generalized likelihood uncertainty estimation. Calculation was performed to produce >400 000 replications of the model. We selected the 1000 best-fitting parameter sets to serve as alternate baselines for uncertainty analysis. Finally, we conducted multivariate probabilistic sensitivity analysis to account for uncertainties in the 15 intervention scenarios’ effect sizes as well as in additional noncalibrated model inputs parameter values to which model outputs were sensitive. In total, 10 000 distinct model replications per intervention scenario 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. As 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, rescaling based on the likelihood estimates of the 1000 best-fitting baselines. In addition, we applied Mann–Whitney U test (2-tailed), a nonparametric 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 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. Additional data collection and rigorous estimates of it could dramatically reduce uncertainty in projected stroke outcomes.

Table 2 presents simulated outputs across the 15 intervention scenarios in a descending order with respect to QALYs gained for 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 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-type plasminogen activator 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 tissue-type plasminogen activator 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 2. 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 mellitus, 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 on NNT per QALY gained are management of recently diagnosed TIA (6.0), accurate and timely TIA diagnosis (9.0), and carotid endarterectomy 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 article, 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 because larger numbers of individuals must be treated for each unit of benefit. For example, considering QALY gains in Table 2, targeted prevention focused on hypertension and anticoagulation for individuals with AF among the subset of VA users with prior CVD achieves 78%
<table>
<thead>
<tr>
<th>Description of Intervention Scenarios</th>
<th>Target Subpopulation Among VA Users</th>
<th>Current Level of Care*</th>
<th>Projected Achievable Level of Care</th>
<th>Estimated Effect Size†</th>
</tr>
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<tr>
<td><strong>Pre-event primary prevention</strong></td>
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<tr>
<td>Improve hypertension control for all VA users with SBP &gt;140 mm Hg</td>
<td>All pre-event users with 140 mm Hg &lt; SBP &lt; 160 mm Hg</td>
<td>73% with SBP &lt; 140 mm Hg</td>
<td>91% with SBP &lt; 140 mm Hg (87%–95%)</td>
<td>19% stroke RRR for movement from 140 mm Hg &lt; SBP &lt; 160 mm Hg to SBP &lt; 140 mm Hg and 31% for movement from &gt; 160 mm Hg to &lt; 140 mm Hg17</td>
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<tr>
<td>Improve hypertension control for VA users with SBP &gt; 160 mm Hg</td>
<td>All pre-event users with SBP &gt; 160 mm Hg</td>
<td>4% with SBP &gt; 160 mm Hg</td>
<td>2% with SBP &gt; 160 mm Hg (1.5%–2.5%)</td>
<td>31% RRR of stroke17</td>
</tr>
<tr>
<td>Improve hypertension control for VA users with DM</td>
<td>All pre-event users with DM and HTN</td>
<td>90% with SBP &lt; 140 mm Hg</td>
<td>97% with SBP &lt; 140 mm Hg (95%–98%)</td>
<td>18% stroke RRR for movement from 140 mm Hg &lt; SBP &lt; 160 mm Hg to SBP &lt; 140 mm Hg and 31% for movement from &gt; 160 mm Hg to &lt; 140 mm Hg17</td>
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<tr>
<td>Improve ischemic stroke prevention for all eligible VA users with AF (antiplatelet/ anticoagulation therapy)</td>
<td>All pre-event users with AF</td>
<td>34% with TTR &gt; 60%</td>
<td>60% (40%–80%)</td>
<td>66% stroke RRR for anticoagulation18,19</td>
</tr>
<tr>
<td>Improve hypertension control and management of AF for VA users with prior cardiovascular disease</td>
<td>All incident TIAs among VA users</td>
<td>71% of TIAs diagnosed‡ (range 70%–80%)</td>
<td>81% (81%–85%)</td>
<td>Greatest stroke risk in first week after TIA; diagnosed can receive prevention</td>
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<tr>
<td><strong>Secondary prevention</strong></td>
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<tr>
<td>Improve accuracy/timeliness of TIA diagnosis and VA users by increasing awareness/symptom recognition</td>
<td>All diagnosed TIs</td>
<td>39% managed well‡ (range 39%–53%)</td>
<td>80% (61.3%–83.8%)</td>
<td>40% reduction in risk of stroke for highest risk period‡ (90 days post-TIA; range 40%–72%)35</td>
</tr>
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<td>Improve the immediate management of TIA through expedited evaluation and risk factor management</td>
<td>All eligible VA users post-diagnosis of TIs</td>
<td>15% of diagnosed TIA eligible; 35% of these receive CEA</td>
<td>60% (40%–75%)</td>
<td>Average of 37.5% RRR of recurrent TIA or stroke31</td>
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<tr>
<td>Improve the rate of CEA for eligible individuals post-TIA</td>
<td>All eligible VA users poststroke</td>
<td>15% of strokes eligible, of these 35% receive CEA</td>
<td>60% (40%–75%)</td>
<td>Average of 37.5% RRR of recurrent stroke31</td>
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<td>Increase % of patients with stroke receiving guideline concordant stroke care for secondary prevention</td>
<td>All incident strokes among VA users</td>
<td>30%‡</td>
<td>60% (50%–70%)</td>
<td>40% reduction in risk of stroke for next 90 d‡ (range 40%–72%)32</td>
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<td>Improve the rate of CEA for eligible individuals following acute ischemic stroke</td>
<td>All incident strokes among VA users</td>
<td>18% of acute strokes ED arrival within 60 min</td>
<td>35% (27.5%–53.8%)</td>
<td>Increases percentage of individuals eligible for tPA22,23</td>
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<td>Acute treatment/rehabilitation</td>
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<tr>
<td>Increase % of acute stroke ED arrival within 60 min of symptom onset</td>
<td>All incident strokes among VA users</td>
<td>33% of veterans arriving on time are medically eligible for tPA; of these, 11% of receive tPA</td>
<td>44% (18%–48%)</td>
<td>36% RRR in functional loss for tPA within 3 h and 5% RRR of death during the acute period (corresponding to a 0.6 percentage point absolute risk reduction)24,25</td>
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<td>Improve the use of thrombolytic therapy with tPA within the VA health care system</td>
<td>All incident strokes among VA users</td>
<td>79%</td>
<td>91% (81%–94%)</td>
<td>12.5% RRR of death during the acute period (corresponding to a 1.4% point absolute risk reduction)26</td>
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(Continued)
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 (eg, severe hypertension with systolic blood pressure >160 mm Hg) or with elevated risk in the presence of multiple stroke risk factors (eg, prior history of stroke).33 The strategic conclusions presented are robust to these uncertainties.

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 tissue-type plasminogen activator will be dependent on local context, such as the proportion of people with stroke arriving soon after symptom onset and baseline rates of tissue-type plasminogen activator 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, because of 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.

### Table 2. Median and 95% Uncertainty Bounds for Key Stroke Outcomes for Each Stroke Intervention Scenario Compared With Current Level of Care for 20 Years

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<td>Increase % of eligible patients with stroke receiving guideline concordant rehabilitation services</td>
<td>All eligible VA users poststroke</td>
<td>30%</td>
<td>60% (55%–73%)</td>
<td>35% reduction in risk of ending in mRS 4–5 and mRS 2–3, ending in mRS 2–3 and mRS 0–1, respectively28</td>
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Fifteen stroke intervention scenarios are defined, with each including a target subpopulation, current and projected level of care, and estimated effectiveness of the intervention. AF indicates atrial fibrillation; CEA, carotid endarterectomy; CVD, cardiovascular disease; DM, diabetes mellitus; ED, emergency department; HTN, hypertension; mRS, modified Rankin Scale; RRR, relative risk reduction; SBP, systolic blood pressure (measured in mm Hg); TIA, transient ischemic attack; tPA, tissue-type plasminogen activator; TTR, time in therapeutic range; and VA, Veterans Affairs.

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*Baseline (the comparator and current level of care); †workgroup consensus; and ‡calibrated within the model.

A 3% discount rate is used in all calculations. AF indicates atrial fibrillation; CEA, carotid endarterectomy; CVD, cardiovascular disease; DVT, deep vein thrombosis; NNT, number-needed-to-treat; PP, primary prevention; QALY, quality-adjusted life year; SBP, systolic blood pressure (measured in mm Hg); SP, secondary prevention; TIA, transient ischemic attack; TR/R, treatment/rehabilitation; and VA, Veterans Affairs.
This allows general comparisons of similar interventions (e.g., lifetime medication and clinical management for prevention) but is less relevant in comparing across the 3 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 1 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 to improve decision-making. 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. 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. Furthermore, it provides an example of how modeling can be applied to address clinical and public health policy problems to promote positive action.

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Disclosures

None.

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