

## Cost-Effectiveness of Urgent Care for Transient Ischemic Attack: An Economic Rapid Review

Health Quality Ontario

### Context

Transient ischemic attack (TIA) can be a warning sign for immediate risk of full stroke and requires quick evaluation and start of treatment.

### Research Question

What is the cost-effectiveness of rapid access clinics versus hospital admission (to an emergency department observation unit or inpatient unit) for patients with transient ischemic attack (TIA)?

### Conclusion

Based on 1 study, 48-hour hospitalization is not cost-effective compared to care in a specialized TIA clinic.

## Context

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The Toronto Health Economics and Technology Assessment (THETA) Collaborative was commissioned by Health Quality Ontario to evaluate the cost-effectiveness and predict the long-term costs and effects of urgent care for transient ischemic attack (TIA). Published economic evaluations are reviewed, and the structure and inputs of the economic model used to estimate cost-effectiveness are summarized. The results of the economic analyses are presented for rapid access TIA clinics versus hospital admission, and the budget impact of implementing each intervention is estimated.

Health Quality Ontario conducts full evidence-based analyses, including economic analyses, of health technologies being considered for use in Ontario. These analyses are then presented to the Ontario Health Technology Advisory Committee, whose mandate is to examine proposed health technologies in the context of available evidence and existing clinical practice and to provide advice and recommendations to Ontario health care practitioners, the broader health care system, and the Ontario Ministry of Health and Long-Term Care.

**DISCLAIMER:** Health Quality Ontario uses a standardized costing method for its economic analyses. The main cost categories and associated methods of retrieval from the province's perspective are described below.

**Hospital costs:** Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency department visit, and day procedure costs for the designated International Classification of Diseases diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in the estimated costs of the diagnoses and procedures under consideration. Due to difficulties in estimating indirect costs in hospitals associated with a particular diagnosis or procedure, Health Quality Ontario normally defaults to a consideration of direct treatment costs only.

**Non-hospital costs:** These include physician services costs obtained from the Ontario Benefits for Physician Services, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible, or from the device manufacturer.

**Discounting:** For cost-effectiveness analyses, a discount rate of 5% is applied (to both costs and effects/QALYs), as recommended by economic guidelines.

**Downstream costs:** All reported downstream costs are based on assumptions of population trends (i.e., incidence, prevalence, and mortality rates), time horizon, resource utilization, patient compliance, health care patterns, market trends (i.e., rates of intervention uptake or trends in current programs in place in the province), and estimates of funding and prices. These may or may not be realized by the Ontario health care system or individual institutions and are often based on evidence from the medical literature, standard listing references, and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach.

The economic analysis represents *an estimate only*, based on the assumptions and costing methods explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

**NOTE:** Numbers may be rounded to the nearest decimal point, as they may be reported from an Excel spreadsheet.

## Objective of Rapid Review

The objective of this rapid review is to assess the cost-effectiveness of rapid access clinics for patients who have had a transient ischemic attack (TIA).

## Clinical Need and Target Population

A stroke is an event characterized by sudden neurological dysfunction caused by reduced blood flow to parts of the brain as a result of a blockage or rupture of a blood vessel. (1) Before a stroke, some people experience a TIA which causes temporary stroke-like symptoms lasting a few hours. (2, 3) A TIA can act as a warning sign of a full stroke: an attack indicates a 3.9% risk of stroke within the following 2 days and up to 9.2% within 90 days. (4) Due to the immediate risk of stroke, TIAs require quick evaluation and start of treatment using time-sensitive interventions such as antithrombotic therapy, carotid endarterectomy, tissue plasminogen activator, and modification of risk factors. (5)

Clinically, it may be ideal to hospitalize all TIA patients for assessment and treatment. However, as Warrior and Prabhakaran (5) have noted, this may not be cost-effective. In response, other strategies have been proposed, such as specialized TIA clinics called rapid access, urgent care, or same-day specialty clinics. These approaches each have pros and cons with respect to short-term and long-term costs. (5) This rapid economic evaluation was designed to determine the cost-effectiveness of rapid access clinics compared to hospitalization for the urgent assessment of TIA and initiation of treatment to reduce the risk of stroke.

# Question, Methods, and Findings

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## Research Question

What is the cost-effectiveness of rapid access clinics versus hospital admission (to an emergency department observation unit or inpatient unit) for patients with transient ischemic attack (TIA)?

## Methods

### Literature Search Strategy

A literature search was performed on March 4, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Embase, and Wiley Cochrane Library, to identify studies published up to March 3, 2014.

The search terms used were identical to those used in the search conducted for Health Quality Ontario's clinical evidence-based analysis on care for patients with TIA, (6) with additional search limits to restrict results to economic studies. (Appendix 1 provides details of the search strategies). As well, given the smaller number of relevant economic articles anticipated, the economic rapid review included observational studies. Titles and abstracts were reviewed by a single reviewer and, for those studies potentially meeting the eligibility criteria, full-text articles were obtained and reviewed. Reference lists were also examined for any additional relevant studies not identified through the search.

### Inclusion Criteria

- English-language full-text publications
- adults who experienced a recent TIA
- examination of the impact of a rapid access diagnostic and/or treatment service for TIA
- economic evaluations (cost-effectiveness or cost utility studies)

### Exclusion Criteria

- letters, editorials, or historical articles
- cost analyses

### Outcomes of Interest

- costs
- quality-adjusted life-years (QALY)

### Expert Panel

In November 2013, an Expert Advisory Panel on Post-Acute Community-Based Care for Stroke Patients was struck. Members of the panel included physicians, nurses, allied health professionals, and personnel from the Ministry of Health and Long-Term Care.

The role of the expert advisory panel was to provide advice on primary stroke patient groupings; review the evidence, guidance, and publications related to defined stroke patient populations; identify and prioritize interventions and areas of community-based care; advise on the development of a care pathway

model; and develop recommendations to inform funding mechanisms. The role of panel members was to provide advice on the scope of the project, the methods used, and the findings. However, the statements, conclusions, and views expressed in this report do not necessarily represent the views of the expert panel members.

### Assessment of the Quality of Evidence

To determine the usefulness of each identified study for decision-making, we applied a modified version of a methodology checklist for economic evaluations, developed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom. (7) The original checklist was used to inform the development of clinical guidelines by NICE; the wording of the questions was modified to remove references to guidelines and to make it Ontario specific. A summary of the number of studies judged to be directly applicable, partially applicable, and not applicable to the research question is presented in Appendix 2.

## Findings

The literature search identified a total of 285 citations published up to March 3, 2014: 134 articles from Ovid MEDLINE, 133 articles through Embase, and 18 articles from the Cochrane Library.

A preliminary review of titles and abstracts excluded 277 studies. Of the remaining articles, 7 were excluded because they were all cost analyses. (8-14) One study was included. (15)

In that study, a decision analytic model was constructed to evaluate the cost-effectiveness of 48-hour hospitalization versus care by urgent clinic referral of TIA patients. (15) Model inputs included the probability of stroke within 48 hours of TIA, tissue plasminogen activator (tPA) usage in hospital and in the community, utility values for each modified Rankin Score category, QALY gained per tPA treatment, and costs of hospitalization, clinic, and diagnostic imaging.

The incremental QALY gained (or lost) was calculated by multiplying the difference in probability of a stroke within 48 hours with the difference in tPA usage between the 2 treatment arms, and then multiplying this total with the QALY gained per tPA treatment. Results were presented at 1 and 30 years, as shown in Table 1.

**Table 1. Incremental cost outcomes for 48-hour hospitalization versus urgent clinic referral of TIA patients**

| Incremental Outcomes (48-Hour Hospitalization – Urgent Clinic Referral) |         |         |                   |
|-------------------------------------------------------------------------|---------|---------|-------------------|
|                                                                         | Cost    | QALY    | Cost/QALY         |
| 1 year                                                                  | \$5,573 | 0.00026 | \$21,434,615/QALY |
| 30 year                                                                 | \$5,557 | 0.0016  | \$3,473,125/QALY  |

Abbreviation: QALY, quality-adjusted life-year; TIA, transient ischemic attack  
Source: Joshi et al, 2011. (15)

Through a series of 1-way sensitivity analyses, the results were close to \$50,000 per QALY when the probability of stroke within 48 hours approached 30%. Changes to all other model parameters did not appreciably decrease the incremental cost-effectiveness ratio.

## Limitations

The study conducted by Joshi and colleagues (15) had several limitations that must be considered when interpreting the results.

First, the underlying assumption in the decision analytic model was that only differences between the 2 treatment options were the cost of 48-hour hospitalization compared to the clinical cost and the difference in tPA usage in hospital versus in a community setting. Beyond that, the authors did not consider any further clinical or cost difference between the 2 treatments. Additional studies on long-term effects need to be conducted to determine whether this assumption is correct.

Second, although the authors did not explicitly describe the hypothetical patient that their model was based on, it appears to be a generally typical TIA patient presenting at the emergency department. They did not explore possible subgroups of TIA patients who may benefit more from one intervention versus another. Rather, the choice in the decision model was for all TIA patients to receive hospitalization or referral to the urgent clinic. However, the most cost-effective treatment protocol may be patient specific. For instance, while high-risk patients may benefit from hospitalization, patients at low risk can be referred to a health care setting equipped with adequate resources to be further evaluated in a timely fashion.

Third, Joshi and colleagues did not fully explore the uncertainty in the model parameters. Although the 1-way sensitivity analyses conducted by the authors suggests that the results were robust, it is likely that, if conducted, a probability sensitivity analysis that considered the uncertainty surrounding the model parameters (especially the costs and QALY inputs) would produce highly uncertain results.

Fourth, the model inputs in this study originated from different jurisdictions. Although this is commonly done in economic modelling due to a lack of data, papers often state the country to which the model is most applicable. Since the paper was published in the journal of the American Academy of Neurology and both authors are affiliated with institutions in the United States, it might be assumed that this study is most applicable to the American health care system. However, the clinical outcomes in the model were based on sources from the United States and the United Kingdom, and the costs were based on a study from Denmark. This makes it difficult to contextualize the results to the Ontario population.

Fifth, there may be a discrepancy in one of the inputs provided to the model. The study used to extract the value for QALY improvement with tPA usage for this model reported 2 numbers. Joshi and colleagues (6) used the number reported in the text (0.531), but another number appeared in the table (0.751). Using this other value would not change the final results appreciably, but the difference should be noted.

Despite these limitations, this study constitutes the only evidence evaluating the cost-effectiveness of rapid assessment of patients with TIA, according to this rapid review. The results should be contextualized to Ontario and interpreted with caution.

## Conclusions

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According to 1 study identified through this rapid review, 48-hour hospitalization for urgent assessment and initiation of treatment for patients experiencing a transient ischemic attack does not appear to be cost-effective compared to care in a specialized TIA clinic.

# Acknowledgements

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| Dr. Leanne K. Casaubon | Toronto Western Hospital; University of Toronto            | Assistant Professor-Division of Neurology, Stroke Program                 |

# Appendices

## Appendix 1: Research Methods

### Search Results

**Search date:** March 4, 2014

**Databases searched:** Ovid MEDLINE 1946 to February Week 3 2014, Ovid MEDLINE In-Process and Other Non-Indexed Citations March 03, 2014

**Limits:** English, Humans

**Filters:** Economic evaluation filter

| #  | Searches                                                                                                                                                                                                                                                                                                                                                      | Results |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| 1  | exp Ischemic Attack, Transient/                                                                                                                                                                                                                                                                                                                               | 17459   |
| 2  | (tia? or transient isch?emic attack*).ti,ab.                                                                                                                                                                                                                                                                                                                  | 12605   |
| 3  | 1 or 2                                                                                                                                                                                                                                                                                                                                                        | 25283   |
| 4  | exp Time Factors/                                                                                                                                                                                                                                                                                                                                             | 982702  |
| 5  | exp Emergency Medical Services/                                                                                                                                                                                                                                                                                                                               | 93157   |
| 6  | exp Hospitalization/                                                                                                                                                                                                                                                                                                                                          | 154639  |
| 7  | exp Outpatient Clinics, Hospital/                                                                                                                                                                                                                                                                                                                             | 15399   |
| 8  | exp Risk Assessment/                                                                                                                                                                                                                                                                                                                                          | 170656  |
| 9  | (tia? clinic* or transient isch?emic attack* clinic*).ti,ab.                                                                                                                                                                                                                                                                                                  | 78      |
| 10 | (special* adj4 (tia or transient isch?emic attack*).ti,ab.                                                                                                                                                                                                                                                                                                    | 29      |
| 11 | ((immediate or rapid or early or urgent or delay* or prompt) adj2 (evaluation or diagnosis or treatment or assessment or access or care)).ti,ab.                                                                                                                                                                                                              | 139585  |
| 12 | 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11                                                                                                                                                                                                                                                                                                                        | 1473908 |
| 13 | economics/ or exp "costs and cost analysis"/ or economics, dental/ or exp "economics, hospital"/ or economics, medical/ or economics, nursing/ or economics, pharmaceutical/ or (economic\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$ or (expenditure\$ not energy) or (value adj1 money) or budget\$.ti,ab. | 575561  |
| 14 | ((energy or oxygen) adj cost) or (metabolic adj cost) or ((energy or oxygen) adj expenditure)).ti,ab.                                                                                                                                                                                                                                                         | 19379   |
| 15 | 13 not 14                                                                                                                                                                                                                                                                                                                                                     | 571127  |
| 16 | 3 and 12 and 15                                                                                                                                                                                                                                                                                                                                               | 149     |
| 17 | Animals/ not (Animals/ and Humans/)                                                                                                                                                                                                                                                                                                                           | 3791961 |
| 18 | 16 not 17                                                                                                                                                                                                                                                                                                                                                     | 147     |
| 19 | exp Case Reports/ or exp letter/ or exp editorial/ or exp Comment/ or historical article/                                                                                                                                                                                                                                                                     | 3074470 |
| 20 | 18 not 19                                                                                                                                                                                                                                                                                                                                                     | 144     |
| 21 | limit 20 to english language                                                                                                                                                                                                                                                                                                                                  | 134     |
| 22 | remove duplicates from 21                                                                                                                                                                                                                                                                                                                                     | 134     |

**Search date:** March 4, 2014

**Databases searched:** Embase 1980 to 2014 Week 09

**Limits:** English, Humans

**Filters:** Economic evaluation filter

| #  | Searches                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Results |
|----|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| 1  | exp transient ischemic attack/ or (tia? or transient isch?emic attack*).ti,ab.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 33132   |
| 2  | exp Delayed Diagnosis/ or exp time/ or exp emergency health service/ or exp Hospitalization/ or exp outpatient department/ or exp Risk Assessment/ or (tia? clinic* or transient isch?emic attack* clinic* or (special* adj4 (tia or transient isch?emic attack*)) or ((immediate or rapid or early or urgent or delay* or prompt) adj2 (evaluation or diagnosis or treatment or assessment or access or care))).ti,ab.                                                                                                                                                                                                   | 1318407 |
| 3  | ((Cost adj effectiveness).ab. or (Cost adj effectiveness).ti. or (Life adj years).ab. or (Life adj year).ab. or Qaly.ab. or ((Cost or costs).ab. and Controlled Study/ or (Cost and costs).ab.) and ((health economics/ or exp economic evaluation/ or exp health care cost/ or exp pharmaco-economic\$ or (econom\$ or cost or costs or costly or costing or price or prices or pricing or pharmaco-economic\$).ti,ab. or (expenditure\$ not energy).ti,ab. or (value adj2 money).ti,ab. or budget\$.ti,ab.) not ((metabolic adj cost) or ((energy or oxygen) adj cost) or ((energy or oxygen) adj expenditure)).ti,ab.) | 141328  |
| 4  | 1 and 2 and 3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 143     |
| 5  | Animals/ not (Animals/ and Humans/)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 1412538 |
| 6  | 4 not 5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 143     |
| 7  | exp case report/ or exp letter/ or exp editorial/                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 3133553 |
| 8  | 6 not 7                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 143     |
| 9  | limit 8 to english language                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 136     |
| 10 | remove duplicates from 9                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 133     |

**Search date:** March 4, 2014

**Databases searched:** Cochrane Database of Systematic Reviews: Issue 3 of 12, March 2014

**Limits:** English, Humans

**Filters:** Economic evaluation filter

| ID  | Search                                                                                                                                                                                                             | Hits  |
|-----|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------|
| #1  | MeSH descriptor: [Ischemic Attack, Transient] explode all trees                                                                                                                                                    | 515   |
| #2  | tia? or transient isch?emic attack*:ti,ab,kw (Word variations have been searched)                                                                                                                                  | 391   |
| #3  | #1 or #2                                                                                                                                                                                                           | 775   |
| #4  | MeSH descriptor: [Time Factors] explode all trees                                                                                                                                                                  | 48228 |
| #5  | MeSH descriptor: [Emergency Medical Services] explode all trees                                                                                                                                                    | 2736  |
| #6  | MeSH descriptor: [Hospitalization] explode all trees                                                                                                                                                               | 11493 |
| #7  | MeSH descriptor: [Outpatient Clinics, Hospital] explode all trees                                                                                                                                                  | 617   |
| #8  | MeSH descriptor: [Risk Assessment] explode all trees                                                                                                                                                               | 7107  |
| #9  | tia? clinic* or transient isch?emic attack* clinic*:ti,ab,kw (Word variations have been searched)                                                                                                                  | 184   |
| #10 | special* n4 (tia or transient isch?emic attack*):ti,ab,kw (Word variations have been searched)                                                                                                                     | 0     |
| #11 | ((immediate or rapid or early or urgent or delay* or prompt) n2 (evaluation or diagnosis or treatment or assessment or access or care)):ti,ab,kw (Word variations have been searched)                              | 56    |
| #12 | #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11                                                                                                                                                                     | 65972 |
| #13 | MeSH descriptor: [Economics] this term only                                                                                                                                                                        | 54    |
| #14 | MeSH descriptor: [Costs and Cost Analysis] explode all trees                                                                                                                                                       | 21477 |
| #15 | MeSH descriptor: [Economics, Dental] this term only                                                                                                                                                                | 3     |
| #16 | MeSH descriptor: [Economics, Hospital] explode all trees                                                                                                                                                           | 1590  |
| #17 | MeSH descriptor: [Economics, Medical] this term only                                                                                                                                                               | 37    |
| #18 | MeSH descriptor: [Economics, Nursing] this term only                                                                                                                                                               | 15    |
| #19 | MeSH descriptor: [Economics, Pharmaceutical] this term only                                                                                                                                                        | 231   |
| #20 | (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic*) or (expenditure* not energy) or (value near/1 money) or budget*:ti,ab,kw (Word variations have been searched) | 41878 |
| #21 | #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20                                                                                                                                                               | 41961 |
| #22 | ((energy or oxygen) near cost) or (metabolic near cost) or ((energy or oxygen) near expenditure):ti,ab,kw (Word variations have been searched)                                                                     | 2157  |
| #23 | #21 not #22                                                                                                                                                                                                        | 41477 |
| #24 | letter or editorial or historical article:pt (Word variations have been searched)                                                                                                                                  | 5991  |
| #25 | #23 not #24                                                                                                                                                                                                        | 41396 |
| #26 | MeSH descriptor: [Animals] explode all trees                                                                                                                                                                       | 6516  |
| #27 | MeSH descriptor: [Humans] explode all trees                                                                                                                                                                        | 1125  |
| #28 | #26 not (#26 and #27)                                                                                                                                                                                              | 5391  |
| #29 | #25 not #28                                                                                                                                                                                                        | 41233 |
| #30 | #3 and #12 and #29                                                                                                                                                                                                 | 18    |

## Appendix 2: Critical Appraisal of Studies Given Full-Text Review

**Table A1: Applicability of Reviewed Studies**

| <b>Question:</b> What is the cost-effectiveness of rapid access clinics versus hospital admission (emergency department observation unit or inpatient admission) for patients with transient ischemic attack? |                                                                 |                                                                                                                                                                               |                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|
| <b>Lead Author, Year</b>                                                                                                                                                                                      | <b>Is the study population appropriate to the question?</b>     | <b>Are the interventions appropriate to the question?</b>                                                                                                                     | <b>Are all relevant interventions compared?</b>                                                                       |
| Gubitz G, 1999 (8)                                                                                                                                                                                            | Yes                                                             | No                                                                                                                                                                            | No                                                                                                                    |
| Jackson D, 2009 (9)                                                                                                                                                                                           | Yes                                                             | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Joshi JK, 2011 (15)                                                                                                                                                                                           | Yes                                                             | Partly                                                                                                                                                                        | Partly                                                                                                                |
| Luengo-Fernandez R, 2009 (10)                                                                                                                                                                                 | Yes                                                             | Partly                                                                                                                                                                        | No                                                                                                                    |
| Martinez-Martinez MM, 2013 (11)                                                                                                                                                                               | Yes                                                             | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Nahab F, 2012 (12)                                                                                                                                                                                            | Yes                                                             | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Ross MA, 2007 (13)                                                                                                                                                                                            | Yes                                                             | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Wu CM, 2009 (14)                                                                                                                                                                                              | Yes                                                             | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| <b>Lead Author, Year</b>                                                                                                                                                                                      | <b>What country was this study conducted in?</b>                | <b>Is the health care system in which the study was conducted sufficiently similar to Ontario with respect to this question/ topic? Explain the ways in which they differ</b> | <b>Are estimates of relative treatment effect the same as those included in the clinical evidence-based analysis?</b> |
| Gubitz G, 1999 (8)                                                                                                                                                                                            | Canada                                                          | Yes                                                                                                                                                                           | NA                                                                                                                    |
| Jackson D, 2009 (9)                                                                                                                                                                                           | UK                                                              | Yes                                                                                                                                                                           | NA                                                                                                                    |
| Joshi JK, 2011 (15)                                                                                                                                                                                           | Unclear                                                         | Unclear                                                                                                                                                                       | No                                                                                                                    |
| Luengo-Fernandez R, 2009 (10)                                                                                                                                                                                 | UK                                                              | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Martinez-Martinez MM, 2013 (11)                                                                                                                                                                               | Spain                                                           | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| Nahab F, 2012 (12)                                                                                                                                                                                            | US                                                              | No                                                                                                                                                                            | Yes                                                                                                                   |
| Ross MA, 2007 (13)                                                                                                                                                                                            | US                                                              | No                                                                                                                                                                            | Yes                                                                                                                   |
| Wu CM, 2009 (14)                                                                                                                                                                                              | Canada                                                          | Yes                                                                                                                                                                           | Yes                                                                                                                   |
| <b>Lead Author, Year</b>                                                                                                                                                                                      | <b>Are costs measured from a health care payer perspective?</b> | <b>Are non-direct health effects on individuals excluded?</b>                                                                                                                 | <b>Are both costs and health effects discounted at an annual rate of 5%?</b>                                          |
| Gubitz G, 1999 (8)                                                                                                                                                                                            | Unclear                                                         | No                                                                                                                                                                            | NA                                                                                                                    |
| Jackson D, 2009 (9)                                                                                                                                                                                           | Yes                                                             | No                                                                                                                                                                            | NA                                                                                                                    |
| Joshi JK, 2011 (15)                                                                                                                                                                                           | Yes                                                             | No                                                                                                                                                                            | No                                                                                                                    |
| Luengo-Fernandez R, 2009 (10)                                                                                                                                                                                 | Yes                                                             | Yes                                                                                                                                                                           | No                                                                                                                    |
| Martinez-Martinez MM, 2013 (11)                                                                                                                                                                               | Yes                                                             | Yes                                                                                                                                                                           | No                                                                                                                    |

| Lead Author, Year               | Are costs measured from a health care payer perspective?                                                            | Are non-direct health effects on individuals excluded?     | Are both costs and health effects discounted at an annual rate of 5%?                                    |
|---------------------------------|---------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| Nahab F, 2012 (12)              | Yes                                                                                                                 | Yes                                                        | No                                                                                                       |
| Ross MA, 2007 (13)              | Yes                                                                                                                 | Yes                                                        | No                                                                                                       |
| Wu CM, 2009 (14)                | Yes                                                                                                                 | Yes                                                        | No                                                                                                       |
| Lead Author, Year               | Do the estimates of resource use differ from that which would be expected in an Ontario context?                    | Is the value of health expressed in terms of QALYs?        | Are changes in health-related quality of life (HRQOL) obtained directly from patients and/or caregivers? |
| Gubitz G, 1999 (8)              | No                                                                                                                  | No                                                         | NA                                                                                                       |
| Jackson D, 2009 (9)             | No                                                                                                                  | NA                                                         | NA                                                                                                       |
| Joshi JK, 2011 (15)             | Yes                                                                                                                 | Yes                                                        | Patients                                                                                                 |
| Luengo-Fernandez R, 2009 (10)   | No                                                                                                                  | No                                                         | No                                                                                                       |
| Martinez-Martinez MM, 2013 (11) | No                                                                                                                  | No                                                         | No                                                                                                       |
| Nahab F, 2012 (12)              | No                                                                                                                  | No                                                         | No                                                                                                       |
| Ross MA, 2007 (13)              | No                                                                                                                  | No                                                         | No                                                                                                       |
| Wu CM, 2009 (14)                | No                                                                                                                  | No                                                         | No                                                                                                       |
| Lead Author, Year               | Has the valuation of changes in HRQOL (utilities) been obtained from a representative sample of the general public? | Overall Judgement (Directly, partially, or not applicable) | Other Comments                                                                                           |
| Gubitz G, 1999 (8)              | NA                                                                                                                  | Not applicable                                             | Costing study                                                                                            |
| Jackson D, 2009 (9)             | NA                                                                                                                  | Not applicable                                             | Costing study                                                                                            |
| Joshi JK, 2011 (15)             | No                                                                                                                  | Partially applicable                                       | Applicable in the comparison of urgent clinic assessment versus acute hospitalization                    |
| Luengo-Fernandez R, 2009 (10)   | No                                                                                                                  | Not applicable                                             | Costing study as part of an RCT                                                                          |
| Martinez-Martinez MM, 2013 (11) | No                                                                                                                  | Not applicable                                             | Cost analysis included in an observational study                                                         |
| Nahab F, 2012 (12)              | No                                                                                                                  | Not applicable                                             | Cost study of the intervention                                                                           |
| Ross MA, 2007 (13)              | No                                                                                                                  | Not applicable                                             | 90-day cost study of intervention                                                                        |
| Wu CM, 2009 (14)                | No                                                                                                                  | Not applicable                                             | Cost analysis of an intervention                                                                         |

Abbreviations: NA, not applicable; QALY, quality-adjusted life-year; RCT, randomized controlled trial; UK, United Kingdom; US, United States.

**Table A2: Quality of Applicable Studies**

| Lead Author, Year: Joshi JK, 2011 (15) <sup>a</sup>                                                                                                                                                       |                              |                                                                                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-----------------------------------------------------------------------------------------------------|
| Item                                                                                                                                                                                                      | Yes/Partly/<br>No/Unclear/NA | Comments                                                                                            |
| Does the model structure adequately reflect the nature of the health condition under evaluation?                                                                                                          | Yes                          |                                                                                                     |
| Is the time horizon sufficiently long to reflect all important differences in costs and outcomes? (e.g., if the rate of mortality differs between interventions, does the model take a lifetime horizon?) | Yes                          | 30-year time horizon                                                                                |
| Are all important and relevant health outcomes included?                                                                                                                                                  | Yes                          | Based on long-term estimates of QALY gained per tPA treatment; no other potential benefits included |
| Are the estimates of relative treatment effects obtained from best available sources?                                                                                                                     | Yes                          | Based on a prior cost-effectiveness model                                                           |
| Do the estimates of relative treatment effect match the estimates contained in the clinical evidence-based analysis?                                                                                      | No                           | Treatment effect is QALY                                                                            |
| Are all important and relevant (direct) costs included in the analysis?                                                                                                                                   | No                           | Only included initial hospitalization costs                                                         |
| Are the estimates of resource use obtained from best available sources?                                                                                                                                   | Yes                          | Based on several studies that analyzed resource utilization                                         |
| Are the unit costs of resources obtained from best available resources?                                                                                                                                   | Yes                          | Based on several studies that analyzed resource utilization, cost analysis, and cost-effectiveness  |
| Is an appropriate incremental analysis presented or can it be calculated from the reported data?                                                                                                          | Yes                          |                                                                                                     |
| Are all important and uncertain parameters subjected to appropriate sensitivity analysis?                                                                                                                 | No                           | Only 1-way sensitivity analyses presented; results presented in a confusing manner                  |
| Is there a potential conflict of interest?                                                                                                                                                                | No                           |                                                                                                     |
| <b>Overall assessment (minor/potentially serious/very serious limitations)</b>                                                                                                                            |                              | <b>Potentially serious limitations</b>                                                              |
| Other comments: Acute hospitalization resulted in a huge ICER. However, the overall uncertainty in the results is unknown because of the lack of probabilistic sensitivity analysis.                      |                              |                                                                                                     |

Abbreviations: ICER, incremental cost-effectiveness ratio; NA, not applicable; QALY, quality-adjusted life-year; tPA, tissue plasminogen activator.

<sup>a</sup>Checklist is used for studies judged to be directly or partially applicable to the research question.

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## Conflict of Interest Statement

All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

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