

The Appropriate Use of Neuroimaging in the Diagnostic Work-Up of Dementia: OHTAC Recommendation

Ontario Health Technology Advisory Committee

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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.

About Health Quality Ontario

Health Quality Ontario (HQO) is an arms-length agency of the Ontario government. It is a partner and leader in transforming Ontario's health care system so that it can deliver a better experience of care, better outcomes for Ontarians, and better value for money.

Health Quality Ontario strives to promote health care that is supported by the best available scientific evidence. The Evidence Development and Standards branch works with advisory panels, clinical experts, developers of health technologies, scientific collaborators, and field evaluation partners to provide evidence about the effectiveness and cost-effectiveness of health interventions in Ontario.

To conduct its systematic reviews of health interventions, the Evidence Development and Standards branch examines the available scientific literature, making every effort to consider all relevant national and international research. If there is insufficient evidence on the safety, effectiveness, and/or cost-effectiveness of a health intervention, HQO may request that its scientific collaborators conduct economic evaluations and field evaluations related to the reviews. Field evaluation partners are research institutes focused on multicentred clinical trials and economic evaluation, as well as institutes engaged in evaluating the safety and usability of health technologies.

About the Ontario Health Technology Advisory Committee

The Ontario Health Technology Advisory Committee (OHTAC) is a standing advisory subcommittee of the Board of Directors of Health Quality Ontario. Based on the evidence provided by Evidence Development and Standards and its partners, OHTAC makes recommendations about the uptake, diffusion, distribution, or removal of health interventions within the provincial health system. When making its recommendations, OHTAC applies a unique decision-determinants framework that takes into account overall clinical benefit, value for money, societal and ethical considerations, and the economic and organizational feasibility of the health care intervention in Ontario.

Publishing Health Quality Ontario Research

When the evidence development process is nearly completed, draft reviews, reports, and OHTAC recommendations are posted on HQO's website for 21 days for public and professional comment. For more information, please visit: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/professional-and-public-engagement-and-consultation>.

Once finalized and approved by the Board of Directors of Health Quality Ontario, the research is published as part of the *Ontario Health Technology Assessment Series*, which is indexed in MEDLINE/PubMed, Excerpta Medica/Embase, and the Centre for Reviews and Dissemination database. Corresponding OHTAC recommendations and associated reports are also published on the HQO website. Visit <http://www.hqontario.ca> for more information.

When sufficient data are available, OHTAC tracks the ongoing use of select interventions it has previously reviewed, compiling data by time period and region. The results are published in the Ontario Health Technology Maps Project Report.

Disclaimer

This report was prepared by the Evidence Development and Standards branch at Health Quality Ontario or one of its research partners for the Ontario Health Technology Advisory Committee and was developed from analysis, interpretation, and comparison of scientific research. It also incorporates, when available, Ontario data and information provided by experts and applicants to HQO. The analysis may not have captured every relevant publication and relevant scientific findings may have been reported since the development of this recommendation. This report may be superseded by an updated publication on the same topic. Please check the Health Quality Ontario website for a list of all publications: <http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations>.

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Background

Overuse, underuse, and misuse of interventions are important concerns in health care and lead to individuals receiving unnecessary or inappropriate care. In April 2012, under the guidance of the Ontario Health Technology Advisory Committee's Appropriateness Working Group, Health Quality Ontario (HQO) launched its Appropriateness Initiative. The objective of this initiative is to develop a systematic framework for the ongoing identification, prioritization, and assessment of health interventions in Ontario for which there is possible misuse, overuse, or underuse.

For more information on HQO's Appropriateness Initiative, visit our website at www.hqontario.ca.

The Evidence Development and Standards branch at Health Quality Ontario (HQO) conducted an evidence-based analysis (1) to answer the following research questions:

- What is the prevalence and reversibility of potentially reversible (treatable) causes of dementia?
- What are the indications for a structural imaging investigation for dementia diagnosis?
- What is the clinical utility or adjunctive value of neuroimaging for diagnosis?
- When structural imaging is indicated, which modality should be used (computed tomography [CT] or magnetic resonance imaging [MRI])?
- What is the diagnostic accuracy of neuroimaging for discriminating dementia types?

In addition, HQO commissioned the Toronto Health Economic and Technology Assessment (THETA) Collaborative to evaluate the cost-effectiveness of offering structural imaging to all patients with mild to moderate dementia, compared with offering structural imaging according to clinical criteria outlined by the 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia (CCC). (2) Using estimates of diagnostic accuracy from the clinical evidence, the economic evaluation also examined which modality (CT or MRI) is most cost-effective, where structural imaging is indicated. (3)

Conclusions

Conclusions of the evidence-based analysis:

- With the exception of vascular disease, prevalence of potentially treatable dementias is low (< 10%), and improvement after treatment of the underlying etiology is less than 1% (GRADE: Very low).
- Prediction rules and individual clinical indications do not reliably predict abnormalities or influence diagnosis or treatment (GRADE: Very low).
- The clinical utility of structural neuroimaging is:
 - high for patients with potentially mixed dementia
 - high for patients where there is uncertainty for 2 years or more about the type of dementia
 - low for patients with Alzheimer disease clinically diagnosed by follow-up over time (e.g., 1 year)
 - low for patients where vascular dementia has been clinically excluded (GRADE: Low)
- For the detection of a vascular component to dementia, there is a lack of evidence that MRI is superior to CT (GRADE: Low).
- In terms of diagnostic accuracy, structural neuroimaging has low to moderate sensitivity and high specificity for discriminating Alzheimer disease, Creutzfeldt-Jakob disease, and clinically ambiguous cases (GRADE: Low to Very low).

Conclusions of the economic analysis:

- The lack of a “gold standard” test for diagnosing dementia makes it difficult to compare competing methods and modalities.
- Given the published clinical evidence, CCC with CT (followed by MRI for patients suspected of having a space-occupying lesion) is the most effective and least costly strategy for distinguishing causes of mild to moderate dementia.
- However, if we assume that MRI with clinical assessment represents the gold standard, then imaging everyone with MRI is the most cost-effective strategy.
- The cost-effectiveness model does not take into account the “value of knowing” that patients, carers, and their physicians may place on diagnostic information.
- Given the many limitations in the clinical evidence base, the model best serves as a framework for exploring key areas of uncertainty in this issue.

Decision Determinants

OHTAC has developed a decision-making framework that consists of 7 guiding principles for decision making and a decision determinants tool. When making a decision, OHTAC considers 4 explicit main criteria: overall clinical benefit, consistency with expected societal and ethical values, value for money, and feasibility of adoption into the health system. For more information on the decision-making framework, please refer to the *Decision Determinants Guidance Document* available at: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/decision-making-framework>.

Appendix 1 provides a summary of the decision determinants for this recommendation.

Based on the decision determinants criteria, OHTAC weighted in favour of the societal and ethical considerations, specifically, the importance of certainty in making a definitive diagnosis for patients, families, and clinicians. OHTAC also considered the uncertainty around the evidence given its low quality.

OHTAC Recommendations

Based on the available evidence:

- OHTAC supports the current guideline (2) that patients with suspected dementia who present with certain special clinical features¹ should undergo neuroimaging with CT or MRI.
- OHTAC recommends that acquisition and reporting of diagnostic imaging for dementia be standardized to ensure quality.
- OHTAC recommends a mega-analysis² on dementia.

¹Age < 60 years; rapid unexplained decline in cognition or function; duration < 2 years; unexplained neurological symptoms; history of cancer; use of anticoagulants or history of bleeding disorder; history of urinary incontinence and gait disorder early in the course of dementia; any new localizing signs; unusual or atypical symptoms or presentation; gait disturbance.

²A broad examination and comparison of the safety, efficacy, effectiveness, and cost-effectiveness of multiple interventions for a given disease state or health condition to assist decision making. (For details see: <http://www.hqontario.ca/evidence/evidence-process/evidence-review-process/types-of-evidence-based-analysis-reports>.)

Appendices

Appendix 1: Decision Determinants

Table A1: Decision Determinants for Imaging for Dementia

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology to result in high, moderate, or low overall benefit?	Effectiveness How effective is the health technology likely to be (taking into account any variability)?	Research Questions <ul style="list-style-type: none"> What is the clinical utility or adjunctive value of neuroimaging for diagnosis? When structural imaging is indicated, which modality (CT or MRI) should be used? What is the diagnostic accuracy of neuroimaging for discriminating dementia types? <p><u>Clinical Utility</u></p> <p>Imaging has the most clinical utility in cases where mixed dementia is potentially present or there is uncertainty as to the type of dementia despite follow-up over time. Clinical utility is low for clinically diagnosed Alzheimer disease or clinically excluded vascular dementia (GRADE: Low).</p> <p><u>Diagnostic Accuracy:</u></p> <ul style="list-style-type: none"> MRI compared to CT: There is a lack of evidence that MRI is superior to CT for the detection of cerebrovascular disease in dementia patients (GRADE: Low). Discriminating dementia types: CT and MRI have low to moderate sensitivity and high specificity for correctly identifying patients with Alzheimer disease, Creutzfeldt-Jakob disease, and clinically ambiguous dementias (GRADE: Low to Very low). <p>Many studies evaluated CT or MRI 10 or more years ago; thus, it is unknown if there may be differences in the utility of scans using state-of-the-art machines and imaging sequences.</p>
	Safety How safe is the health technology likely to be?	CT involves exposure to a small effective dose of radiation (estimated 2–4mSv). MRI is contraindicated for patients with implanted ferromagnetic devices.
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology?	Research Question <ul style="list-style-type: none"> What is the prevalence and reversibility of potentially reversible (treatable) causes of dementia? <p>With the exception of vascular disease, a very small proportion of cases are reversible or treatable (GRADE: Very low). Almost 750,000 Canadians were living with cognitive impairment and dementia in 2011 and prevalence is projected to nearly double in the next 2 decades. (4)</p>
	Need How large is the need for this health technology?	Research Question <ul style="list-style-type: none"> What are the indications for a structural imaging investigation for dementia diagnosis? <p>Neither individual nor sets of clinical indications reliably select the subset of patients who will likely benefit from neuroimaging (GRADE: Very low).</p>

Decision Criteria	Subcriteria	Decision Determinants Considerations
Consistency with expected societal and ethical values^a How likely is adoption of the health technology to be congruent with societal and ethical values?	Societal values How likely is the adoption of the health technology to be congruent with expected societal values? Ethical values How likely is the adoption of the health technology to be congruent with expected ethical values?	The diagnosis of dementia is a terminal one, and an understanding of the underlying illness is important for patients, families, and clinicians to prepare for the future, emotionally and pragmatically. Physicians emphasize the need for a high degree of certainty in making the diagnosis.
Value for money How efficient is the health technology likely to be?	Economic evaluation How efficient is the health technology/intervention likely to be?	Research Questions <ul style="list-style-type: none"> Which clinical prediction rule for structural imaging (CCC (2) versus image all) is most cost-effective for the diagnosis of suspected dementia? Where structural imaging is indicated, which modality (CT or MRI) is most cost-effective? <p>No relevant cost-effectiveness analyses were identified in the published literature. An original Markov model was developed with the aim of determining which prediction rule is most effective and cost-effective. Where neuroimaging is required, we also aimed to determine whether CT or MRI is most effective and cost-effective. Using estimates of diagnostic accuracy identified in the clinical EBA, the results of the model showed that imaging all patients with MRI results in the greatest number of correctly diagnosed cases of space-occupying lesions and vascular dementia. However, because these patients represent a small proportion of all those with mild to moderate dementia, the greatest gain in quality-adjusted life-years (QALY) is realized by correctly identifying those with Alzheimer disease. Therefore, the strategy with the greatest combined specificity (CCC with CT followed by MRI for suspected space-occupying lesions) results in the greatest number of QALYs and is the least costly. However, the results of the model are sensitive to the specificity of MRI for detecting vascular causes of dementia. At a specificity of 64%, the most effective strategy is CCC followed by MRI. At a specificity of 85%, the most effective strategy is to image all patients with MRI. Due to limitations in the clinical data and challenges in the interpretation of this evidence, the model should be considered a framework for assessing uncertainty in the evidence base rather than providing a definitive answer to the research questions.</p>
Feasibility of adoption into health system How feasible is it to adopt the health technology into the Ontario health care system?	Organizational feasibility How organizationally feasible is it to implement the health technology?	Experts indicate that current practice is to assess approximately according to CCC guidelines. It is unclear if or how practice change would be required. Scans are not currently acquired and reported in a standardized way in Ontario, which may have implications for quality assurance.

Abbreviations: CCC, 4th Canadian Consensus Conference on the Diagnosis and Treatment of Dementia; CT, computed tomography; MRI, magnetic resonance imaging; QALY, quality-adjusted life-year.

^aThe anticipated or assumed common ethical and societal values held in regard to the target condition, target population, and/or treatment options. Unless there is evidence from scientific sources to corroborate the true nature of the ethical and societal values, the expected values are considered.

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