Canada's Drug and Health Technology Agency

CDA-AMC Health Technology Review

RapidAI for Stroke Detection

Health Technology Expert Review Panel Recommendation

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Recommendation

Summary

What is the indication under review?

The indication under review is the detection, using artificial intelligence (AI) software, of large vessel occlusion (LVO; i.e., ischemic stroke) and intracranial hemorrhage (ICH; i.e., hemorrhagic stroke) for people of any age with a suspected acute stroke.

What is RapidAI?

RapidAI is an AI-enabled software platform that facilitates the viewing, processing, and analysis of CT images to aid clinicians in assessing patients, including those with suspected stroke. It builds upon the original RAPID software, initially developed to automate and expedite the post-processing of CT perfusion imaging. The platform currently also incorporates modules that perform AI-driven LVO and ICH detection, which were evaluated in the current review. RapidAI is intended to complement, rather than replace, clinician interpretation of CT images and is to be used as a supportive tool rather than a standalone diagnostic intervention.

How did Canada's Drug Agency (CDA-AMC) evaluate this technology?

To examine the value of implementing RapidAI for detecting LVO and ICH, CDA-AMC conducted an evidence review on RapidAI that identified, synthesized, and critically appraised literature evaluating RapidAI's effectiveness, accuracy, and cost-effectiveness. CDA-AMC highlighted and reflected on the ethical and equity implications of using RapidAI for stroke detection, engaged a patient contributor, sought feedback from knowledge users, and consulted an expert panel.

What else did CDA-AMC Do?

CDA-AMC applied Digital Technology Assessment Criteria (DTAC), a checklist currently used in the UK, to the health care context in Canada by determining whether we have equivalent or similar measures, strategies, and policies to implement digital health technologies safely. CDA-AMC also conducted a literature review to identify implementation guidance specific to AI-enabled medical device use and relevant to Canada to supplement DTAC. For this work, CDA-AMC integrated ethics and equity considerations, leveraged patient engagement activities conducted in the concurrent RapidAI review, sought feedback from knowledge users, and consulted an expert panel.

What is the Health Technology Expert Review Panel (HTERP) Recommendation for RapidAI?

In sites where RapidAI has already been implemented for use in detecting suspected LVO and ICH, HTERP recommends: (i) RapidAI is used only as indicated, alongside clinician interpretation of CT scans, to reduce the risk of incorrect results; and (ii) the generation of evidence to evaluate its value in health care systems, including its use in less-resourced centres with limited access to stroke specialists.

In sites considering the implementation of RapidAI, given the uncertainty and gaps in the evidence regarding clinical, economic, and equity value of RapidAI, HTERP cannot provide recommendations for or against its implementation.

What is the indication under review?

The indication under review is the detection, using artificial intelligence (AI) software, of large vessel occlusion (LVO; a finding that can support the decision to perform urgent mechanical thrombectomy in acute ischemic stroke) and intracranial hemorrhage (ICH; i.e., hemorrhagic stroke) for people of any age with a suspected acute stroke. Stroke is one of the leading causes of death and a major cause of disability in Canada. For patients with suspected stroke, prompt evaluation using CT imaging and other tests can help to determine the type of stroke, assess the severity of damage, and guide urgent treatment decisions.

What is RapidAI?

RapidAI (iSchemaView, Inc., Menlo Park, California) is an AI-enabled software platform that facilitates the viewing, processing, and analysis of CT images to aid clinicians in assessing patients, including those with suspected stroke. It builds upon the original RAPID software, which was initially developed to automate and expedite the post-processing of CT perfusion imaging and is widely implemented in some jurisdictions, such as Ontario.[1,2] More recently, the software platform has expanded its suite of products to include several static AI-derived algorithms for evaluating the brain's physiological status, such as Rapid ICH, Rapid ASPECTS, Rapid CTA, Rapid LVO, and Rapid HVS.[3,4] These algorithms are considered static because they remain fixed and unchanging after development through machine learning processes, performing their tasks based on pre-established rules and training data. While RapidAI has numerous features and functionalities, what is relevant for this report are the modules that perform AI-driven ICH and LVO detection to inform stroke diagnosis. RapidAI is intended to complement, rather than replace, clinician interpretation of CT images and is to be used as a supportive tool rather than a standalone diagnostic intervention.[5] As of March 2024 (i.e., when CDA-AMC checked its regulatory status), RapidAI (version 4.9.2.1) is licensed for sale in Canada as a Class III medical device.

How did CDA-AMC evaluate RapidAI?

To examine the value of RapidAI in stroke detection, CDA-AMC:

- identified, synthesized, and critically appraised literature evaluating the effectiveness, accuracy, and cost-effectiveness of RapidAI,
- used methods that were guided by the Scottish Health Technologies Group's health technology assessment framework,[6]
- highlighted and reflected on the ethical and equity implications of using RapidAI for stroke detection found in the clinical literature, integrating these considerations throughout the review,
- engaged 1 patient contributor who had experienced a hemorrhagic stroke,
- incorporated feedback from 3 peer reviewers (i.e., 1 clinical expert with expertise in stroke assessment, 1 clinical expert with expertise in AI radiology, and 1 ethics expert with expertise in AI), the manufacturer, and other interested parties, and
- consulted an expert panel to deliberate on unmet clinical need, clinical value, economic considerations, impacts to health systems, and distinct social and ethical considerations regarding RapidAI.

What else did CDA-AMC do?

CDA-AMC conducted an additional review to assist health systems in Canada in preparing for the uptake of AI-enabled medical devices, as these technologies pose new challenges. CDA-AMC assessed whether the safeguards and assessment criteria captured by DTAC[7] and other AI-related resources are in place to inform decision-making around the digital infrastructure elements of implementation. To conduct the AI Implementation Review, CDA-AMC:

- applied Digital Technology Assessment Criteria (DTAC; a checklist used in the UK as an add-on component to HTAs)[7] to the health care context in Canada by determining whether we have equivalent or similar measures, strategies, and policies to implement digital health technologies safely,

- conducted a literature review to identify implementation guidance specific to AI-enabled medical device use and relevant to Canada to supplement DTAC,
- highlighted and reflected on the ethical and equity considerations,
- leveraged patient engagement activities conducted in the concurrent RapidAI review,
- incorporated feedback from 3 peer reviewers (i.e., same reviewers as RapidAI review) and other interested parties, and
- together with the concurrent RapidAI review, consulted an expert panel to deliberate on unmet clinical need, clinical value, economic considerations, impacts to health systems, and distinct social and ethical considerations.

Health Technology Expert Review Panel

The Health Technology Expert Review Panel (HTERP) is an advisory body to CDA-AMC that develops guidance and/or recommendations on non-drug health technologies to inform a range of decision-makers within health care systems in Canada.

HTERP is comprised of 7 core members to serve for all topics under consideration during their term of office: Chair, Ethicist, Health Economist, Patient Member, 2 Health Care Practitioners, and a Health Technology Assessment Specialist. In addition to the core members, HTERP will comprise up to five expert members appointed to provide their expertise on a specific topic. For this review, HTERP appointed 2 members with clinical expertise in stroke neurology and 1 member with expertise in neuroradiology and AI.

To make its recommendation, HTERP considered the following information:

- CDA-AMC's review of:
    - RapidAI, including:
        - 2 cohort studies and 11 diagnostic accuracy studies that assessed the effectiveness and accuracy of RapidAI for detecting stroke
        - ethics and equity considerations relevant to RapidAI, which were identified through published literature and patient, clinician, and other expert input
    - digital infrastructure elements of implementation considerations for digital health technologies, including ethics and equity considerations and additional considerations for using AI-enabled medical devices in Canada.

Using the available evidence, HTERP deliberated on and answered, "Should RapidAI be implemented to detect stroke in Canada, and how?"

Recommendation

In sites where RapidAI has already been implemented for use in detecting suspected intracranial hemorrhage and large vessel occlusion, HTERP recommends:

- RapidAI is used only as indicated, alongside clinician interpretation of CT scans, to reduce the risk of incorrect results
- The generation of evidence to evaluate its value in health care systems, including its use in less-resourced centres with limited access to stroke specialists

In sites considering the implementation of RapidAI, given the uncertainty and gaps in the evidence regarding clinical, economic, and equity value of RapidAI, HTERP cannot provide recommendations for or against its implementation.

Rationale for the Recommendation

HTERP recognized an unmet clinical need: stroke is a clinical condition associated with significant morbidity and mortality. There are effective treatments available for individuals experiencing acute stroke. These treatments require rapid clinical assessment and

imaging interpretation to select the most appropriate therapy. Still, timely access to these treatments varies within Canada (across jurisdictions, rural versus urban settings, hospitals with comprehensive stroke centres versus less-resourced centres).

Two cohort studies and 11 diagnostic accuracy studies that assessed the effectiveness and accuracy of RapidAI, a software platform that includes specific modules such as Rapid LVO for detecting LVO and Rapid ICH for detecting ICH, resulted in the following:

- Low certainty evidence suggests that evaluation of CT angiography images by Rapid LVO combined with clinician interpretation, compared to clinician interpretation alone, may result in clinically important reductions in radiology report turnaround time (i.e., the time it takes the radiologist to interpret the CT angiography images and provide a report or readback verification to the referring clinician) in patients with suspected stroke.
- The evidence is very uncertain about the effects of RapidAI on other time to intervention metrics, measures of physical and cognitive function, and response to therapy (e.g., reperfusion rates). CDA-AMC did not identify any evidence on the effects of RapidAI on many important clinical outcomes, including patient harms, mortality, health-related quality of life, length of hospital stay, and health care resource implications.
- From the diagnostic accuracy studies, low certainty evidence suggests that Rapid ICH combined with clinician interpretation, using neuroradiologist interpretation (board-certified or board eligible) as a reference standard, has a sensitivity of 92% (95% CI, 78 to 98%) and a specificity of 100% (95% CI, 98 to 100%) for detecting ICH. Estimates of sensitivity and specificity for detecting LVO varied, based on studies using different modules of RapidAI as a standalone intervention, providing only indirect accuracy data.

However, HTERP acknowledged the limitations of these studies given the current evidence is of limited certainty. It is not clear how the observed reductions in radiology report turnaround times in patients with suspected stroke translate into patient outcomes, or in which centres these reductions would be most useful.

HTERP emphasized the lack of cost information and cost-effectiveness evidence, which prevents any conclusions to be made on demonstrated value for money or budget impact.

HTERP underscored RapidAI, the health technology under review, is being assessed for implementation within a complex system with many situational factors that require consideration. Given the available evidence, the committee could not produce a strong recommendation for or against the implementation of RapidAI. The committee provides elaboration and rationale for each component of the recommendation, described in Table 1, to add further context to the main recommendation.

Table 1. Recommendation Elaboration and Rationale

Component of Recommendation	Elaboration and Rationale	Examples of Related Implementation Considerations from DTAC[7] and Other Resources Applicable to Canada's Health Care Context
Unable to provide recommendations for or against RapidAI regarding new investments and implementation or to recommend disinvestment	The current evidence is of limited certainty, making it insufficient to support recommendations regarding new investments and the implementation of stroke detection add-in functionalities to existing imaging platforms. Similarly, there is insufficient evidence to recommend disinvestment in centres in which RapidAI is already in use.	
Where already in use, RapidAI to be used only alongside clinician interpretation	The evidence to date reflects the use of RapidAI in combination with clinician interpretation. There is no	• Monitoring, maintenance, and sustainability; e.g., monitoring for automation bias (when a user's conclusion is overly reliant on the

Component of Recommendation	Elaboration and Rationale	Examples of Related Implementation Considerations from DTAC[7] and Other Resources Applicable to Canada's Health Care Context
	evidence to support the safe or effective replacement of clinician judgement with RapidAI. RapidAI is intended to complement, rather than replace, clinician interpretation of CT images and should be used as a supportive tool rather than a standalone diagnostic intervention.[5] Users should be aware of the potential risk of overreliance on the AI system (e.g., automation bias).	device output while ignoring contrary data or conflicting human decisions).[8] • Ensuring responsibility and accountability in using AI-enabled medical devices; e.g., training, competency requirements, and guidelines are required to reduce the potential harm and liability for malpractice.[8] The use of RapidAI alongside clinician(s) can help mitigate the potential harms regarding false positives and false negatives (e.g., an inaccurate diagnosis by RapidAI can be corrected or reinterpreted by clinicians before making care decisions).
Where RapidAI is in use, continued collection of evidence and continued monitoring and evaluation	The available clinical evidence has high levels of uncertainty. There is an incomplete understanding of ethical and equity considerations, including patient data considering PROGRESS-Plus[9,10] criteria and location of health care setting (e.g., rural or remote). No cost information or cost-effectiveness evidence to inform decision-making (value for money, budget impact) was identified. AI-enabled medical devices require additional considerations for safe and successful implementation, including monitoring, maintenance and sustainability throughout the AI product lifecycle. Current use of RapidAI in clinical practice affords the opportunity for the generation of evidence to evaluate its value in health care systems. In particular, evidence regarding its use in less-resourced centres with limited access to stroke specialists would be important for identifying opportunities to improve equity in access to timely, high quality stroke care.	• Monitoring, maintenance, and sustainability to ensure its relevance, accuracy, efficacy, and safety.[11] For example, monitoring to validate their performance and manage risks of overfitting, unintended bias, or degradation of the model,[101-103] monitoring the risk of harm outcomes, such as technical failures in added time to diagnosis, delay in diagnosis. Additional collection of study data from clinical study participants and data sets that are representative of the intended population (continued collection of evidence within adopted centres and at new centres as they adopt the technology) • Inclusiveness, equity, and reducing bias. It is important to attend to relevant ethics and equity considerations, such as algorithmic bias, lack of representation, data ownership, transparency, explainability, alongside evaluations of effectiveness and accuracy. For example, mismatches between the study populations and target populations could lead to a risk that the performance of RapidAI may not be applicable in all clinical settings (i.e., spectrum bias).[12]

Component of Recommendation	Elaboration and Rationale	Examples of Related Implementation Considerations from DTAC[7] and Other Resources Applicable to Canada's Health Care Context
Value for locations with limited access to stroke care specialists (e.g., rural and community settings)	This could not be assessed due to lack of evidence. There is potential value added for hospitals with limited access to stroke care specialists for early triage to inform, rather than make, stroke management decisions (e.g., preventing missed cases, reducing interpretation delays by speeding up the detection of LVO to inform decision-making about transferring patients for endovascular therapy). Stroke imaging interpretations by general radiologists can vary in turnaround time and accuracy, and a tool like RapidAI may be helpful and may reduce inequities in access to timely, high-quality stroke care. However, demonstrated evidence in these settings is required. There may be less value added for hospitals with comprehensive stroke centres, which have established and timely stroke management processes in place.	• Compliance with all technical security obligations, with special consideration for implementation models where a shared server is used across multiple sites (e.g., hub and spoke model would require an external threat risk assessment by an external provider). • User buy-in and organizational readiness may be a challenge in certain settings; e.g., rural and community hospitals generally have fewer resources (e.g., funding, staff, capacity, and technical infrastructure).
Value for money or budget impact	This could not be assessed due to lack of evidence. There is a lack of both direct and indirect (such as technician staffing or training or data oversight) cost information and information about cost-effectiveness (e.g., cost per quality-adjusted life-year gained). Without these data, no conclusions can be made on budget impact or demonstrated value for money.	• User buy-in and organizational readiness considerations take into account certain economic factors (e.g., demonstrated value, budget allocation, return on investment).[11]

AI = artificial intelligence; CDA-AMC = Canada's Drug Agency – L'Agence des medicaments du Canada; DTAC = Digital Technology Assessment Criteria; HTA = health technology assessment.

Deliberation

Table 2 provides a detailed summary of the key discussion points raised during the meeting, organized by the applicable domains of value. The committee deliberated using the following 5 domains of value included in the CDA-AMC HTA Deliberative Framework:

- **Unmet Clinical Need:** Unmet clinical need refers to morbidity and/or mortality arising from a condition or symptom that is not addressed effectively by available treatments.
- **Clinical Value:** Clinical value is the value that patients derive from a health technology in terms of its effect on their health and health-related quality of life. The determination of the clinical value of a health technology requires the measurement of its clinical benefits and harms and an assessment of the impact of these effects on patients. Clinical benefits and harms are assessed against relevant comparators.
- **Economic Considerations:** Economic considerations refer to economic evidence to inform the financial, human or other resource implications associated with the technology under review, and whether it is reasonable to allocate resources to the technology under review given its expected clinical benefits. Considerations may include the potential resource or cost impacts of the technology under review versus relevant comparator(s) and/or the potential economic value of the technology under review versus relevant comparator(s).

- **Impacts to Health Systems:** This domain considers 2 distinct but interrelated components: organizational feasibility of adoption is the ease with which the health technology can be implemented in the health system while realizing its clinical value, while economic feasibility of adoption (affordability) considers how the adoption of a health technology will financially impact the payer or budget holder.
- **Distinct Social and Ethical Considerations:** This domain considers the distinct social and ethical implications of health technologies (including in their design, evaluation, and implementation) not already assessed in the other domains and how they affect patients, caregivers, populations, and the organization of health systems.

Table 2: Summary of Deliberation

Overarching question(s)	Discussion point(s)
Unmet Clinical Need	
Is there significant clinical need arising from the condition despite available treatments?	• HTERP recognized that stroke is a clinical condition of relatively high incidence that is associated with significant morbidity and mortality. HTERP discussed that while there are effective treatments available for individuals experiencing acute stroke, access to these treatments requires timely, accurate identification of stroke. This access varies within Canada (e.g., across jurisdictions, rural versus urban settings, hospitals with comprehensive stroke centres versus centres with limited resources), and as such, there are some unmet clinical needs in the timely detection of stroke. For effective management of acute stroke, it is vital to get the correct diagnosis (e.g., LVO versus ICH) and the right treatment at the right time ("time is brain"), which may require access to higher levels of care and transfer to stroke centres. Timely stroke diagnosis and treatment may help improve functional outcomes for patients who have experienced a stroke (e.g., severity of neurologic impairment). • In Canada's hospitals without a comprehensive stroke centre, stroke imaging interpretations by general radiologists can vary in turnaround time and accuracy. For centres with limited access to stroke specialists, HTERP members discussed how RapidAI could meet the clinical need of reviewing CT scans for acute stroke alongside general radiologists (as a "double-check") in a time-sensitive manner. This clinical need for RapidAI is similar to how collision avoidance systems are now implemented in cars. However, with experienced drivers (i.e., neuroradiologists working in comprehensive stroke centres), a system such as RapidAI is probably unnecessary and can sometimes introduce dangerous noise. Therefore, identifying the exact settings of need for a tool like RapidAI (i.e., less-resourced centres with limited access to stroke specialists) is important.
Clinical Value	
Does the technology under review demonstrate acceptable clinical value versus relevant comparators in the Canadian setting?	• HTERP discussed the lack of rigour in the available evidence. For example, HTERP acknowledged evidence from the cohort studies, identified in the RapidAI review, was of low or very low certainty because of imprecision and critical risk of bias due to confounding. For detecting LVO, the diagnostic accuracy studies to date examined RapidAI as a standalone diagnostic tool, which limits their applicability to clinical practice, where RapidAI is to be used to assist clinicians in interpreting CT scans. For detecting ICH, the diagnostic accuracy study provided low certainty evidence due to risk of bias and imprecision. HTERP also noted the findings from these studies cannot be generalized to many settings in Canada, as the representativeness of the data used to train the algorithms is unknown, and the studies were conducted exclusively in centres with expertise in stroke management. HTERP recognized the difficulty in conducting high-quality studies in smaller stroke centres. The uncertainty of the evidence makes it difficult to make a strong recommendation either for adoption or disinvestment. • HTERP discussed that despite being limited and of low quality, the evidence available is encouraging, providing it translates into demonstratable clinical benefits (e.g., mortality, length of hospital stay, health-related quality of life, and patient harms). In hospitals

Overarching question(s)	Discussion point(s)
	without comprehensive stroke centres, in addition to clinical judgement, RapidAI may demonstrate added clinical value as high sensitivity and negative predictive value may improve the accuracy of early detection of stroke due to LVO or ICH and identify patients requiring transfer for timely treatment. Additional research is required to continue demonstrating high sensitivity, with subsequent human confirmation to rule in LVO or ICH diagnosis, given the critical nature of stroke diagnosis. • However, there are several caveats to acknowledge the number of uncertainties associated with this technology that might impact its realized value when implemented within the complex health care systems. HTERP acknowledged the need for more research to have confidence in RapidAI's place in care. HTERP discussed a need for more robust clinical evidence including the risk of harmful outcomes (e.g., technical failures in added time to diagnosis, delay in diagnosis), particularly those associated with false negatives (missed cases). • HTERP acknowledged that the potential added clinical value depends on existing installed resources, which vary across jurisdictions and regions. Conflicts may exist for centres in terms of weighing the potential for the highest utility and their ability to implement such technologies. Depending on the volume of stroke presentations and in-house imaging or clinical expertise, technologies such as RapidAI may offer higher utility for smaller regional or rural locations, but these sites often have resource constraints that may act as a barrier to acquiring, implementing, using, or monitoring these technologies. • For larger academic centres, there are more likely to be organizational structures, adequate scanners, good computer infrastructure, and technicians with the skills and availability to conduct the scans. In these centres, installing an additional technology (e.g., RapidAI) may be plausible and practicable. However, there may be lower utility in implementing the technology in these centres as adequate resources and expertise for the timely detection of stroke are likely already in place. • The available evidence was collected in comprehensive stroke centres, and its applicability has not been tested in smaller, remote locations that are less likely to have the volume of stroke cases and resources necessary to conduct studies. HTERP discussed the need for evidence on the performance of RapidAI and role in different clinical pathways to understand its utility in different locations (e.g., urban/larger centre vs. rural/smaller centres). Moreover, the HTERP discussed the comparator or reference standard for studies included in this RapidAI review was CT scan review by clinicians alone (e.g., assessment by a single radiologist, consensus obtained from a panel of neuroradiologists). The committee suggested the most relevant comparator in the Canadian setting is clinicians alone, but especially non-stroke physicians (e.g., emergency physicians, general internists, family physicians) to help understand RapidAI's potential added value in these smaller, remote locations.
Economic Considerations	
Are there economic considerations that are relevant to address when implementing the technology under review?	• HTERP recognized the lack of cost-effectiveness evidence. HTERP raised examples of how there could be potential for cost savings if RapidAI reduced missed cases or untimely patient transfers. However, the CDA-AMC report did not identify evidence to support this, which suggests there is a need for more research in this area.

Overarching question(s)	Discussion point(s)
Impacts to Health Systems	
Are there expected organizational impacts of implementing the technology that might affect health system sustainability? Does the magnitude of the expected budget impact of implementing the health technology or its uncertainty need to be addressed?	• While it was acknowledged that RapidAI is an add-on to existing RAPID systems which, if currently in place, is unlikely to lead to a significant budget impact, HTERP discussed the lack of available cost information, including expected budget impact, cost of implementation (e.g., training personnel or supporting IT infrastructure), and the need to balance costs and benefits given limited resources and opportunity costs (e.g., investing in a new technology or replacing an old existing machine), especially in small facilities that could benefit from this technology. • HTERP discussed considerations regarding the organizational feasibility of adoption. Even for well-resourced hospitals, there are difficulties in implementing software like RapidAI (e.g. requirement for local Information Technology department support) It is expected that there will be more challenges with rural/community hospitals. Depending on where RapidAI is implemented, it may require additional resources (e.g., infrastructure requirements, training, additional radiologist technicians). Of those sites in which the RapidAI system has already been installed, it is not clear how many use the AI functionality for the detection of ICH and LVO. There are opportunities for learning from existing sites using this technology to understand the feasibility of adoption (e.g., single-site "Hub" model versus "Hub and Spoke" model, where the hub and spoke implementation model would enable remote centres that do not have the resources that comprehensive stroke centres do to use and benefit from tools like RapidAI, including the ability to notify stroke centres and identify patients for transfer in a more timely way). • HTERP noted that the implementation of RapidAI may have implications for the use of other health services, such as emergency medical services and patient transport. For example, more accurate identification of patients requiring transfer to larger stroke centres could reduce the opportunity cost of ambulances unnecessarily travelling out of the communities they are meant to serve. • HTERP acknowledged that the RapidAI software does not adapt to real-world data collected during its use. The panel described the need for validation and monitoring of the underlying algorithms, especially in real-life settings and with software updates.
Distinct Social and Ethical Considerations	
Is there significant non-clinical need arising from the condition, despite available treatments, that would potentially be addressed by the technology under review? Are there any important measures that should be implemented to ensure that the use of the technology addresses relevant social and ethical implications?	• HTERP discussed the lack of evidence related to subgroup effects that consider PROGRESS-Plus[9,10] criteria. More information is needed to determine whether this technology will improve the outcomes of equity-deserving groups. • HTERP acknowledged that there are certain social and ethical considerations when considering the implementation of an AI-enabled medical device, such as the potential risk of bias in the stroke detection algorithms, human-machine interaction and the potential risk of overreliance on the AI system (e.g., automation bias). • HTERP discussed examples of guidance (e.g., DTAC) that could be useful as a resource for senior decision-makers when considering the implementation of AI health technologies, including RapidAI. The committee acknowledged CDA-AMC's findings that no checklist like DTAC exists in Canada. There is a potential need for a comprehensive checklist like DTAC for use in Canada to provide confidence that digital health tools used in Canada meet our clinical safety, data protection, technical security, interoperability and usability and accessibility standards. Like DTAC, the checklist would be designed for healthcare organizations to use to assess manufacturers at the point of procurement or as part of a due diligence process.[7] This checklist could be an adaptation of DTAC for the health care context in Canada and include additional implementation considerations for AI-enabled medical devices to ensure that these technologies meet the minimum baseline standards set out by DTAC and inform the next steps for the safe and successful implementation of AI-enabled medical devices in Canada.

AI = artificial intelligence; CDA-AMC = Canada's Drug Agency – L'Agence des medicaments du Canada; DTAC = Digital Technology Assessment Criteria; HTA = health technology assessment; HTERP = Health Technology Expert Review Panel; ICH = intracranial hemorrhage; LVO = large vessel occlusion; NPV = negative predictive value.

What did CDA-AMC find?

In this section, the CDA-AMC provides a summary of key findings from the CDA-AMC reviews, including:

- clinical, economic, and ethics and equity considerations identified from the RapidAI evidence review, and
- implementation considerations for digital health technologies described in the AI implementation review, including ethics and equity considerations and additional considerations identified for the use of AI-enabled medical devices in Canada.

To supplement the summary of HTERP's deliberation, CDA-AMC provides a summary of key findings and uncertainties from the reviews (refer to **Error! Reference source not found.**), organized by the HTA deliberative framework themes: unmet clinical need, clinical value, economic considerations, impacts to health systems, distinct social and ethical considerations.

RapidAI Review

Clinical Evidence

This review included 2 cohort studies and 11 diagnostic accuracy studies evaluating the effectiveness and accuracy of RapidAI for detecting stroke. Of these, 3 studies examined RapidAI as it is intended to be used in clinical practice (i.e., to complement clinician interpretation of CT images), while the remaining 10 studies assessed RapidAI as a standalone diagnostic tool. Twelve studies were specific to patients with suspected LVO, and 1 study included patients with suspected ICH.

The overall certainty of the evidence for all outcome-comparisons was assessed using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach. Outcomes for GRADE assessment were selected because they were important for those who might be affected by the intervention, including the patient contributor and experts who were engaged or consulted during this project.

Low certainty evidence suggests that using RapidAI to support clinician interpretation of CT angiography images may result in clinically important reductions in radiology report turnaround time for patients with suspected acute ischemic stroke. The evidence is very uncertain about the effect of RapidAI on other time to intervention metrics (e.g., time from door to intubation, time from door to revascularization). Additionally, the evidence was very uncertain regarding the effect of RapidAI on patient outcomes, including measures of neurological deficit, degree of functional neurological disability, and response to therapy (e.g., reperfusion rates).

For diagnostic accuracy, low certainty evidence suggests that when used alongside clinician interpretation (with neuroradiologist interpretation alone [board-certified or board eligible] as the reference standard), Rapid ICH has a sensitivity of 92% (95% CI, 78 to 98%) and a specificity of 100% (95% CI, 98 to 100%) for detecting ICH. When used as a standalone diagnostic tool, evidence from 10 diagnostic accuracy studies indicates that the sensitivity of RapidAI for detecting LVO ranges from 62% to 96%, with specificity ranging from 65% to 98%. Differences in the types of LVO assessed, the versions and modules of RapidAI used, the type of CT image analyzed (i.e., non-contrast CT or CT angiography), and the methods for determining reference standard diagnoses likely contributed to the variability in observed values for sensitivity and specificity. The certainty of the evidence for these findings was moderate, low, or very low, or there was insufficient information to judge certainty. These results have unclear applicability to clinical practice, as the accuracy of RapidAI as a standalone diagnostic tool does not directly answer how much it might improve the accuracy of a clinician reader.

Overall, the evidence suggests that RapidAI has potential to improve acute stroke care by creating efficiencies in the diagnostic process. However, the impact of RapidAI on many outcomes, including those that are important to patients, is uncertain due to the limitations of the available evidence. To improve the certainty of findings and provide a better understanding of the potential benefits and harms of RapidAI, there is a need for evidence from robustly conducted studies at lower risk of bias that enroll diverse patient populations and measure outcomes that are important to patients, with improved reporting.

Economic Evidence

Cost and Cost-Effectiveness

CDA-AMC did not find any studies on the cost-effectiveness of RapidAI for detecting stroke that met the selection criteria for this review; therefore, the cost-effectiveness of RapidAI for stroke detection is currently unknown. CDA-AMC reached out to the manufacturer but were unable to obtain updated pricing information on this technology. From publicly-available sources, CDA-AMC identified resource considerations regarding the implementation of RAPID and a budget impact analysis by Ontario Health[13] and provided it as relevant economic information in the discussion of the conclusions and implications for decision-making.

Ethics and Equity Considerations

CDA-AMC primarily leveraged and adapted the WHO Guidance on Ethics and Governance of Artificial Intelligence for Health[14] to organize and reflect on these considerations and their implications. Additionally, CDA-AMC drew from the ethical considerations proposed by the AI Task Force of the Society of Nuclear Medicine and Molecular Imaging,[15] whose recommendations on the major ethical considerations during the deployment of AI-enabled medical devices are directly relevant to the use of AI in diagnostic workups. The review explored the ethical concerns that could arise in the development, design, testing and deployment of RapidAI or other AI-enabled digital health technologies. Considerations related to equity, autonomy, privacy, transparency and explainability of machine learning models can influence how, when, and for whom technologies such as RapidAI are leveraged by clinicians, patients, and health care institutions. These considerations should be addressed throughout the technology lifecycle to ensure fair and equitable decision making around the risks, benefits, and trade-offs for patients, caregivers, clinicians and health systems.

Patient Perspective

The patient contributor identified important outcomes for stroke care, including speed and accuracy of diagnosis, minimizing the damaging effects of stroke, and reducing mortality rates. She also highlighted ethical considerations regarding the use of AI in health care, such as data privacy, equitable access, and informing patients about the use of AI technologies in the care pathway.

AI Implementation Review

Apply DTAC to Health Care Context in Canada

CDA-AMC conducted this review to assist health systems in Canada in preparing for the uptake of AI-enabled medical devices. CDA-AMC assessed whether the safeguards and assessment criteria captured by DTAC and other AI-related resources are in place in Canada to inform decision-making around the digital infrastructure elements of implementation. Focusing on DTAC's core areas (i.e., clinical safety, data protection, technical security, interoperability, and usability and accessibility),[7] this review found many of DTAC's assessment criteria have equivalent or similar guidance for the health care context in Canada with some important caveats. Some exceptions derive from the differences in Canada's current governance and health care structure (e.g., the level of governance for Canada's privacy laws depends on the type of data and jurisdiction and, unlike the UK, Canada does not have electronic health records managed at the federal level). The review suggests further investigation to confirm if certain policies in Canada, such as clinical safety, provide sufficient coverage to fulfill DTAC's criteria.

AI Implementation Considerations

CDA-AMC identified additional considerations for implementing AI-enabled medical devices that health care decision-makers may consider for the safe and successful implementation of AI in health care in Canada. Much of the identified guidance has ethical and equity implications and emphasizes implementation considerations that apply to the AI system's life cycle. CDA-AMC identified **monitoring, maintenance, and sustainability throughout the AI product life cycle as a key consideration for DTAC's core assessment areas**. Additional considerations include:

- AI data governance and data protection,
- Multi-disciplinary data governance team throughout the AI product lifecycle,
- Technical infrastructure and integration,

- Transparency, explainability, and intelligibility,
- Inclusiveness, equity, and minimizing bias,
- Responsibility and accountability, and
- User buy-in and organizational readiness.

CDA-AMC suggests using the findings from this review for all AI-enabled medical devices alongside reviews of specific AI technologies, including the concurrent RapidAI review. The report will serve as a foundational report tailored to each AI topic and updated with the latest developments in the regulation and other aspects of managing AI in Canada.

Ethics and Equity Considerations

This review integrated ethics and equity considerations arising in DTAC,[7] augmented with key Ethics of AI tools and frameworks.[14,16-18] CDA-AMC noted that the ethical considerations for digital health technologies were found in the DTAC's data protection domain, which relates to data privacy, management, and ownership concepts. CDA-AMC described the equity considerations for digital health technologies were found under DTAC's usability and accessibility domain, which primarily relates to the involvement of relevant users in technology design, and whether their needs are incorporated into elements of technology design. CDA-AMC leveraged the World Health Organization's Ethics and Governance of AI for Health guidance that speaks to the fundamental ethical principles for AI use for health.[14] This guidance aligns with certain DTAC criteria,[7] but offers more specific considerations for ethical considerations inherent in AI technologies.[14]

Patient Perspective

Relevant to this review, the patient contributor engaged in the RapidAI review highlighted data protection and privacy considerations (e.g., informing the patient about using AI technologies as part of care provided) and accessibility and equity considerations (e.g., equitable access).

Key Findings and Uncertainties

Table 3: Summary of Key Findings and Uncertainties

Section	Key Findings	Uncertainties
Unmet Clinical Need	Stroke, also known as cerebrovascular accident, is a life-threatening medical condition characterized by loss of neurological function. In Canada, stroke is 1 of the leading causes of death and a major cause of disability (e.g., limitations to physical functioning, sensory impairment),[19-21] with more than 100,000 stroke events resulting in hospital or emergency department presentations each year.[22] Stroke diagnosis and intervention is time sensitive. Accurately determining whether a stroke is ischemic or hemorrhagic with neuroimaging studies, often using CT scans, is crucial for selecting appropriate treatment options.[23] Misidentifying the type of stroke can lead to inappropriate treatments that may exacerbate the condition. Health care inequities exist in stroke incidence, prevalence, symptoms, quality of care, and outcomes across factors such as race, ethnicity, gender, sex, disability status, age, geographic location, and socioeconomic status.[24-31] For example, data from 2007 to 2011 indicate that rural hospitals in Canada have	Existing methods for diagnosing stroke, such as imaging and clinical assessments, are often effective, but the accuracy and speed of diagnosis can vary across health care settings due to differences in the availability of imaging equipment and access to stroke care specialists.

Section	Key Findings	Uncertainties
	significantly higher 30-day in-hospital mortality rates following stroke compared to urban academic hospitals and the national average.[32] RapidAI is an AI-enabled software that facilitates the viewing, processing, and analysis of CT images to aid clinicians in assessing patients with suspected stroke.	
Clinical Value	CDA-AMC reviewed evidence from 2 cohort studies and 11 diagnostic accuracy studies that assessed the effectiveness and accuracy of RapidAI for detecting stroke. RapidAI has the potential to improve acute stroke care by creating efficiencies in the diagnostic process. For detecting LVO: • Evaluation of CT angiography images by Rapid LVO combined with clinician interpretation, compared to clinician interpretation alone, may result in clinically important reductions in radiology report turnaround time in patients with suspected stroke (low certainty). • As a standalone diagnostic intervention, the sensitivity of RapidAI for detecting LVO ranges from 62% to 96%, while estimates of specificity range from 65% to 98% (moderate, low, or very low certainty, or there was insufficient information to judge certainty; results from 10 diagnostic accuracy studies). Heterogeneity in the types of LVO assessed, the versions or modules of RapidAI used, the type of CT image analyzed (i.e., non-contrast CT or CT angiography), and the methods for determining reference standard diagnoses likely contributed to the variability in these results. For detecting ICH: • Rapid ICH combined with clinician interpretation, using clinician interpretation as a reference standard, has a sensitivity of 92% (95% CI, 78 to 98%) and a specificity of 100% (95% CI, 98 to 100%) (low certainty; results from 1 diagnostic accuracy study). CDA-AMC investigated DTAC that captures the additional considerations for the implementation of DHTs not captured by traditional HTA to see if it could be applied to the health care context in Canada. With some caveats, they found that many of DTAC's assessment criteria have equivalent or similar guidance for the health care context in Canada. Moreover, they identified a need for a checklist like DTAC that senior decision-makers can use in Canada. This checklist could be an adaptation of DTAC and include additional implementation considerations for AI-enabled medical devices to ensure that these technologies meet the	The impact of RapidAI on many outcomes, including those that are important to patients, is uncertain due to the limitations of the available evidence. Clinical experts and the patient contributor identified key outcomes of interest: mortality, length of hospital stay, health-related quality of life, and patient harms (e.g., administration of harmful therapies or undertreatment due to inaccurate diagnosis). CDA-AMC did not identify any evidence on the effects of these outcomes as well as health care resource implications. One study examined the diagnostic accuracy of RapidAI as it would be used in clinical practice (i.e., as a tool to support the review of CT scans). More studies needed in order to form conclusions. The evidence is very uncertain about the effects of RapidAI on other time to intervention metrics, measures of physical and cognitive function, and response to therapy (e.g., reperfusion rates). For detecting LVO: • Evidence from the cohort studies was of low or very low certainty, primarily because of critical risk of bias due to confounding and imprecision. • Estimates of sensitivity and specificity for detecting LVO varied and were based on studies using different modules of RapidAI as a standalone intervention, providing only indirect accuracy data. For detecting ICH: • No evidence was found on the impact of RapidAI for detecting ICH on clinical outcomes, such as time to intervention or direct patient outcomes (e.g., functional status).

Section	Key Findings	Uncertainties
	minimum baseline standards set out by DTAC and inform the next steps for the safe and successful implementation of AI-enabled medical devices in Canada.	CDA-AMC highlighted that it is unclear if the potential time saved during stroke diagnosis with RapidAI will improve patient outcomes and access to care broadly. Other aspects of the health system infrastructure, including the availability of emergency medical services, stroke care specialists, operating rooms, imaging equipment, radiology technologists, and other emergency care resources may still limit the speed of treatment. The patient contributor highlighted the important stroke outcomes, including speed and accuracy of diagnosis, minimizing the damaging effects of stroke, and reducing mortality rates. CDA-AMC did not identify any evidence on the effects of these outcomes. CDA-AMC highlighted the importance of attending to relevant ethics and equity considerations, such as equitable access, accountability, algorithmic bias, and lack of representation, alongside evaluations of effectiveness and accuracy. Many ethical considerations related to AI in health care, as outlined by the Scottish Health Technology Group's HTA framework[6] and other foundational ethics of AI tools and frameworks, are often inadequately addressed in studies evaluating the effectiveness or accuracy of commercialized AI-enabled medical devices (i.e., the types of evidence included in the RapidAI review). CDC-AMC stated that further investigation is required to understand if certain policies in Canada provide sufficient coverage to fulfill DTAC's criteria (e.g., clinical safety).
Economic Considerations	No economic evaluations were identified to assess the economic value of RapidAI.	The acquisition cost of RapidAI is uncertain. The cost-effectiveness of RapidAI for stroke detection is currently unknown: CDA-AMC did not identify any studies that evaluated the cost-effectiveness of RapidAI (with or without clinician interpretation) to detect ICH or LVO.
Impacts to Health Systems	From publicly-available sources, CDA-AMC identified resource considerations regarding the implementation of RAPID. There are currently two approaches to	CDA-AMC was unable to address the potential budget impact of implementing RapidAI for stroke detection in Canada. It is

Section	Key Findings	Uncertainties
	implement RAPID. The first is a single site (hub) model that loads the application onto a server within the organisations firewall, so that the CT/MRI scanners at the site are connected to the system and the server allows the results to be processed for viewing and storage. The second approach is a multiple site model (hub and spoke) where the application is loaded on a server behind the firewall of one organisation, which can be shared across sites. The CT/MRI scanners at each site are configured to allow the results at the hub and spoke sites to be processed at the hub site and sent back to the originator site for viewing and storage. In terms of costs, there is a hub licensing fee, as well as server installation costs and training fees; the latter two of which would be shared across sites in the hub and spoke model. The 'hub and spoke' model has additional connection requirements (e.g., bandwidth and connection) and requires an external threat risk assessment conducted by an external provider. Furthermore, a data sharing agreement would need to be in place between hub and spoke sites.[2] In 2020, Ontario Health published a health technology assessment[13] on the use of automated CT perfusion imaging to aid in the selection of patients with acute ischemic stroke for mechanical thrombectomy. Their budget impact analysis stated the annual cost of a licence for the RAPID neuroimaging platform in 2019 was, depending on the number of connected scanners, between $27,500 (for 2 scanners) and $32,500 (for unlimited scanners) per hospital.[13] There was an added cost in the first year due to 1-time fees related to the initial implementation and optimization of Rapid, as well as for training staff ($12,350 for hospitals with 2 or more scanners).[13] It is estimated that publicly funding automated CT perfusion imaging across 42 hospitals in Ontario resulted in additional costs of $1.3 million in the first year and $0.9 million per year thereafter.[13] This costing information was for the full RAPID platform, which included several modules for conducting various cerebrovascular diagnostic procedures, in addition to automated CT perfusion.	unclear whether the results of the Ontario Health report could be generalized to other populations within Canada. CDA-AMC was unable to address RapidAI's capacity to inform treatment selection (e.g., selecting patients for reperfusion therapy). The patient contributor raised access concerns about the availability of AI technologies in hospitals outside urban stroke centres. She questioned whether AI-enabled stroke detection software would be available to all major hospitals for assisting in triaging and potentially transferring patients more quickly, or if its use would be restricted to certain facilities. CDA-AMC's report explains the budget, personnel, infrastructure and training requirements needed to implement RapidAI may limit its use to better resourced hospitals or health care centres, despite its potential to potentially improve some access to stroke care in rural and remote settings. CDA-AMC explains that even if there were data to suggest the performance of RapidAI is robust across diverse patient populations (i.e., low risk of bias in the algorithm's performance), limited access based on geographic location could exacerbate existing health inequities.[33]
Distinct Social and Ethical Considerations	CDA-AMC identified ethics and equity considerations relevant to RapidAI, which were found through published literature and patient, clinician, and expert input. Ethical and equity considerations related to patient autonomy, privacy, transparency, access, and algorithmic bias have implications across the technology lifecycle when using RapidAI for detecting stroke. In addition to the evidence on the effectiveness and accuracy of RapidAI for detecting stroke, the CDA-AMC RapidAI report suggests decision-makers may wish to	CDA-AMC highlighted that it is unclear if the potential time saved during stroke diagnosis with RapidAI will improve patient outcomes and access to care broadly. Other aspects of the health system infrastructure, including the availability of emergency medical services, stroke care specialists, operating rooms, imaging equipment, radiology technologists, and other emergency care resources may still limit the speed of treatment.

Section	Key Findings	Uncertainties
	reflect on the ethical and equity considerations that arise during the deployment of AI-enabled technologies, such as those related to autonomy, privacy, transparency and explainability of machine learning models, and the need for considerations related to equity and access in their design, development, and deployment. Relevant for both CDA-AMC reviews, the patient contributor engaged for the RapidAI review highlighted several relevant considerations (e.g., data protection and privacy and accessibility and equity). CDA-AMC identified several considerations for implementing AI-enabled medical devices, with many having underlying ethical and equity implications. Much of the identified guidance emphasizes implementation considerations that apply to the AI system's life cycle, such as ensuring AI-enabled medical devices are monitored, maintained, and sustainable. Other example considerations include AI data governance and data protection; transparency and explainability; and inclusiveness, equity, and minimizing bias.	CDA-AMC acknowledged the importance of additional ethical and equity considerations, but these considerations tend to be underreported in the identified evidence that is generally examined when evaluating the effectiveness and accuracy of interventions. CDA-AMC highlighted some of these gaps, such as: • Included studies did not provide details on the characteristics of study populations and did not conduct subgroup analyses based these criteria, preventing CDA-AMC from evaluating how RapidAI might perform across different groups. • Included studies did not describe the methods used to develop RapidAI's machine learning models, preventing CDA-AMC from assessing the representativeness and diversity of the training dataset and commenting on considerations related to inclusivity. • It is unclear if RapidAI has undergone bias assessment to determine if certain patient subgroups (e.g., based on age, gender, and ethnicity) are disproportionately affected by the model outputs, preventing CDA-AMC from commenting on the potential bias risks in the stroke detection algorithms.

AI = artificial intelligence; CDA-AMC = Canada's Drug Agency – L'Agence des medicaments du Canada; DTAC = Digital Technology Assessment Criteria; ICH = intracranial hemorrhage; LVO = large vessel occlusion.

HTERP Core Members

Leslie Anne Campbell – Chair, Nova Scotia

Louise Bird – Patient member, Saskatchewan

Brian Chan – Health economist, Ontario

Sandor Demeter – Health Care Practitioner, Manitoba

Lawrence Mbuagbaw – Health Technology Assessment Specialist, Ontario

Duncan Steele – Ethicist, Alberta

Note: As of January 2024, there is currently a committee seat vacancy for 1 Health Care Practitioner member.

Meeting date: September 12, 2024

Regrets: Lawrence Mbuagbaw – Health Technology Assessment Specialist, Ontario

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