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Clinical and Cost Effectiveness of CT and MRI for Selected Clinical Disorders: Results of Two Systematic Reviews

Technology
Computed tomography (CT) and magnetic resonance imaging (MRI)

Conditions
Coronary artery disease, peripheral vascular disease, renal artery stenosis, lung cancer screening, pulmonary embolism, carotid artery disease, cerebral aneurysms, headaches, head injuries, seizures, stroke, cerebral arteriovenous malformations (AVMs), and urolithiasis screening.

Issue
CT and MRI are accepted investigations for some clinical conditions, but uncertainty exists as to their value for others. The devices are costly to buy and to operate. Given the increasing demand for CT and MRI, their clinical and cost effectiveness should be established for the investigation of disorders where their use is controversial.

Methods and Results
In two literature searches, using well defined search strategies, 48 systematic reviews (SRs) of clinical effectiveness, and 21 complete economic evaluations met the inclusion criteria for analysis for 11 and eight of the clinical conditions respectively.

Implications for Decision Making
- Evidence for use of CT in investigation of stroke is promising. The most compelling evidence of clinical and cost effectiveness suggested that CT scanning within 48 hours of presentation for stroke patients has the potential to improve quality-adjusted life-years, and offset the costs of in-patient care.
- Some CT and MRI uses are still investigational. No economic evidence was found supporting use of these technologies in coronary artery disease, headaches, and seizures. No clinical or economic evidence was found for cerebral AVMs and urolithiasis screening.
- Less compelling evidence was found for other conditions. Decisions to use these technologies for the remaining clinical conditions appears to be based solely on demonstrated diagnostic performance or clinical opinion, not on published evidence.
- Evidenced-based decisions require an updated review. CT and MRI technologies have advanced rapidly. Findings from the identified SRs and economic evaluations may not be sufficiently contemporary in some instances to be useful to clinicians and decision makers.

1 Introduction

Computed tomography (CT) and magnetic resonance imaging (MRI) scanners allow detailed visualization of the internal organs. In CT, X-rays and computed analysis are used to produce cross-sectional images of slices of the body. A volume of the body is scanned as individual images that can be manipulated by a technologist or radiologist to produce two-dimensional (2D) and three-dimensional (3D) images. With helical (or spiral) CT, the X-ray tube rotates and scans continuously while the radiology table moves the patient along. With multi-slice CT [or multiple row detector CT (MDCT)], multiple slices are taken simultaneously, thus increasing scanning speed. In MRI scans, the molecular hydrogen in tissues, a large magnet, intermittent radio waves, and a computer are typically used to produce 2D and 3D images. Contrast media or other injected agents may be used to enhance the images.

In Canada, CT and MRI machines are approved and regulated by Health Canada’s Therapeutic Products Directorate using a four-class system, with class I being the most benign, and class IV being the least benign. CT scanners are classified as class III devices (considered potentially hazardous or could represent immediate danger if they fail), and MRI scanners are classified as class II devices.

Purchase costs for CT and MRI machines depend on the level of sophistication required, and the number of additional features installed. A 2000 report by the Canadian Association of Radiologists (CAR) estimated the average purchase cost of a CT machine to be $1,400,000, and that of an MRI machine to be $2,500,000.\(^1\) Operating and maintenance costs, updates to software and hardware, radiologists’ fees to provide scan interpretation, and building or renovating expenses to provide suitable space for the machines must also be considered. In 2000, the CAR estimated the life cycles to be eight years for CT machines and six years for MRI.\(^1\)

The indications for the use of CT and MRI scanners are not restricted through government regulation or licensing. Rather, clinical practice guidelines for diagnostic imaging have been developed in Canada, the US, Europe, and elsewhere. Although there are many clinical situations where the use of CT or MRI is accepted, in 2004, the CAR identified 13 clinical conditions where the effectiveness of using CT and MRI remained controversial: coronary artery disease, peripheral vascular disease, renal artery stenosis, lung cancer screening, pulmonary embolism, carotid artery disease, cerebral aneurysms, headaches, head injuries, seizures, stroke, cerebral arteriovenous malformations (AVMs), and urolithiasis screening.

Given the increasing demand for CT and MRI tests, and constrained resources, the tests’ clinical and cost effectiveness of these technologies must be established in the investigation of disorders where their application has been considered controversial.

2 Objective

The objective of the systematic reviews (SRs) was to summarize the evidence from clinical SRs and economic evaluations concerning the clinical and cost effectiveness of CT and MRI in the investigation of specific clinical conditions of the chest, and the cardiovascular, neurological, and urological systems.
3 Clinical and Economic Review Methods

Clinical Effectiveness Review Methods

A search of published literature was conducted on the MEDLINE®, EMBASE®, INSPEC®, BIOSIS Previews®, and PASCAL databases using the DIALOG® system. There was no language restriction. Parallel searches were performed and updated on LILACS, the Cochrane Library, and PubMed databases. Grey literature was retrieved by searching the web sites of health technology assessment and related agencies.

Articles were included if they were SRs published between 2000 and November 2004, examining the use of CT or MRI to investigate one of the 13 clinical conditions of interest.

The quality of the studies in the included articles was assessed using the Oxman and Guyatt tool,2-4 which consists of nine questions to evaluate study methods and their vulnerability to bias. A score of 7 is the best, scores of 4 to 5 indicate minor flaws and possibly major flaws, and scores of 0 to 3 suggest major flaws. Included studies were also subjected to the Fryback and Thornbury hierarchy tool5 to assess the highest level of diagnostic imaging efficacy that could be assigned. In increasing order of efficacy, the levels are 1 (measurement of technical quality), 2 (diagnostic accuracy), 3 (diagnostic thinking), 4 (patient management), 5 (patient outcome), and 6 (societal costs and benefits).

Economic Review Methods

All resources accessed for the clinical review were also searched for the economic review, as were the Health Economics Evaluations Database (HEED) and selected bibliographies. Subject experts were contacted for related information.

Included articles were required to be complete economic evaluations (complete with cost and effect data) in the form of primary studies, modelling exercises, meta-analyses, or SRs; based on clinical effect data from 1998 onward; published between 1999 and October 2005; and examining the use of CT and MRI to investigate one of the 13 clinical conditions of interest in the clinical review. The Oxford Centre for Evidence-based Medicine (CEBM) Levels of Excellence scale was used to assess the quality of studies.6 Levels of evidence (determined by study design), which are used to grade recommendations, range from the best at 1a (systematic review of randomized clinical trials) to the worst at 5 (expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”). Grades of recommendation in descending order of strength are A (consistent level 1 studies) to D (level 5 evidence or troublingly inconsistent or inconclusive studies of any level).

4 Results

The total number of included studies for both evaluations is provided in Table 1.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Number of Studies</th>
<th>Clinical Effectiveness</th>
<th>Cost Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular conditions</td>
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<td></td>
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<tr>
<td>Coronary artery disease</td>
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<tr>
<td>PVD</td>
<td>5</td>
<td>3</td>
<td></td>
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<tr>
<td>Renal artery stenosis</td>
<td>2</td>
<td>1</td>
<td></td>
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<tr>
<td>Chest conditions</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Lung cancer screening</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Neurological conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carotid artery disease</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cerebral aneurysms</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Headaches</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>Head injuries</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Seizures</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>AVMs</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Urological system</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urolithiasis screening</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>49*</td>
<td>22*</td>
<td></td>
</tr>
</tbody>
</table>

*One article* reported on two conditions, and is counted twice in the sum.

**Clinical Review**

Of the 947 articles identified, 71 fulfilled the inclusion criteria. Subsequently, 40 of these were excluded, primarily because they were not SRs or comprehensive reviews. The grey literature search identified 145 articles, of which 17 met the inclusion criteria. Therefore, a total of 48 articles were selected, reporting on 49 studies. No SRs were found for AVMs or urolithiasis screening.

Most studies in the included articles (72%) had Oxman and Guyatt scores of 4 or lower, indicating possible major flaws or worse. The balance had minor to minimal flaws. In addition, 42 studies (86%) graded using the Fryback and Thornbury scale were deemed to only be at level 2 (out of 6), defined as assessing the diagnostic accuracy, sensitivity, and specificity of the images only, rather than reporting on patient management or outcomes, or societal costs of the technologies.

**Economic Review**

The electronic search yielded 315 articles, and 88 articles were selected. After review, 70 were excluded, leaving 18 for inclusion. The grey literature search resulted in 108 articles, among which three were chosen. From the resultant total of 21, most (86%) received a CEBM grade C recommendation (reliance on level 4 studies or extrapolations from level 2 or 3 studies) with levels of evidence of 2b/3b (limited review of the evidence) or 2a/3a (SR of the evidence). Of the 13 clinical conditions of interest, no studies were found for five: coronary artery disease, headaches, seizures, AVMs, or urolithiasis screening.
5 Cardiovascular System

Coronary Artery Disease
Five SRs\textsuperscript{8-12} met the inclusion criteria for clinical evaluation; all used invasive angiography as the reference standard. Four\textsuperscript{9,11,12} examined the clinical effectiveness of MDCT or magnetic resonance angiography (MRA). Both MRA and MDCT scored high on sensitivity and specificity. Some arteries could not be evaluated using MDCT, and despite high sensitivity and specificity, the authors of one review\textsuperscript{12} concluded that 2D MRA was inferior to invasive angiography. They added that motion artifacts had to be reduced, and spatial resolution and contrast improved for 3D MRA. Investigators concluded that MRA and MDCT are promising, but are not yet superior to catheter angiography. No suitable economic analyses were located for this clinical condition.

PVD
The clinical effectiveness of PVD was addressed in five SRs\textsuperscript{7,13-16}. All investigated MRA, usually comparing it to invasive angiography. Investigators were positive about MRA and its potential to replace invasive angiography. They found gadolinium-enhanced 3D MRA to be superior to 2D technology in terms of examination time and accuracy.

Three papers\textsuperscript{7,17,18} met the inclusion criteria for economic evaluation. One\textsuperscript{7} compared the cost-utility of MRA and digital subtraction angiography (DSA). The authors found that MRA (2D, time-of-flight, and contrast enhanced) accurately identified occlusions and 50\% to 100\% stenoses. They noted almost no difference in the cost-utility of MRA and DSA. The second study\textsuperscript{17} compared MRA with duplex ultrasound (US), DSA, and no imaging work-up plus exercise. The authors concluded that the difference among imaging techniques was slight, and suggested that MRA and duplex US could replace DSA. The third study\textsuperscript{18} established target values for CT angiography (CTA) to be equivalent to MRA in terms of cost-utility. The authors indicated that multi-detector row CTA had the potential to be equivalent to MRA.

Renal Artery Stenosis
Two SRs\textsuperscript{19,20} compared the clinical efficacy of CTA and MRA with invasive angiography. In the first SR,\textsuperscript{19} the investigators concluded that MRA was highly sensitive and specific, and that MRA with gadolinium enhancement was superior to non-enhanced MRA. The second SR\textsuperscript{20} examined five technologies, including CTA (five studies) and MRA (14 studies). The authors of this review were also impressed with gadolinium-enhanced MRA, and concluded that CTA and MRA had better diagnostic accuracy than the other tests (ultrasound, captopril renal scintigraphy, and captopril test).

One study\textsuperscript{21} met the inclusion criteria for economic evaluation. The cost-utility of MRA, CTA, conventional angiography (CA), and enhanced medical therapy without preceding diagnostic testing were compared to the natural history of untreated hypertension resistant to medication. Results suggested that preliminary imaging followed by treatment (enhanced medical therapy or stenting) saved lives compared to enhanced medical therapy alone, and that MRA was the most cost-effective modality, followed by CA.
6 Respiratory System

Lung Cancer Screening
Eight SRs were identified;\textsuperscript{22-29} CT was the only imaging modality assessed. All investigators concluded that, compared with other means, CT could be used to detect small lung tumours at an earlier stage. They could not recommend CT for lung cancer screening, however, because of insufficient evidence, lack of data showing reduced mortality, low positive predictive values, high numbers of false positive results, high morbidity associated with post-CT follow-up procedures, and inconclusive results showing that benefits outweigh risks.

Five studies\textsuperscript{30-34} met the inclusion criteria for economic evaluation. Screening with CT was compared with no screening in four studies, and to alternative technology in one study. One study\textsuperscript{31} of hypothetical cohorts of current, quitting, and former smokers indicated that CT screening was unlikely to be cost-effective without significant mortality reductions, high rates of adherence, lower rates of over-diagnosis, and lower costs. A second study\textsuperscript{30} concluded that screening could be cost-effective, but only if CT screening could detect >50\% of cancers at a localized stage. Two studies\textsuperscript{32,34} suggested CT screening would be cost-effective, but one\textsuperscript{32} stated there was insufficient evidence to recommend routine population screening. The fifth study\textsuperscript{33} concluded that CT screening was cost-effective but presented little supporting evidence.

Pulmonary Embolism
For the evaluation of clinical effectiveness, CT or CTA were investigated in 10 SRs\textsuperscript{3,35-43} and MRA in two SRs\textsuperscript{44,45} (one analyzed both). The reference standards were pulmonary angiography (PA) or ventilation-perfusion scintigraphy (VQ). Investigators were cautious about the use of CT or MRA as the sole investigation in the diagnosis of pulmonary embolism; although many indicated that CT or MRA may have a place among traditional investigations. The authors of one review\textsuperscript{45} comparing gadolinium-enhanced MRA with PA stated that MRA may be a useful alternative for patients with risk factors that limit other investigative technologies.

Four studies\textsuperscript{36-49} met the inclusion criteria for the economic review. All studies compared CT with VQ scanning, D-dimer assay (DD) plus spiral CT, compression US, PA, or duplex US. Differences were seen in the results, but studies generally supported a role for CT in the diagnosis of pulmonary embolism, and suggested that PA could be replaced by CT or otherwise avoided.

7 Neurological System

Carotid Artery Disease
Six SRs examined CTA,\textsuperscript{50} MRA,\textsuperscript{7,51-53} and both CTA and MRA.\textsuperscript{54} DSA or surgical results were used as the reference standard. Conclusions from the one study examining only CTA were that it was a sensitive and specific imaging technique for identifying severe atherosclerotic stenosis and occlusion of the carotid arteries. Authors of the study examining both CTA and MRA were also positive about the technologies. Two of the four MRA studies had overlapping data;\textsuperscript{7,53} they supported the use of MRA for 70\% to 99\% stenosis, but not for 50\% to 99\% stenosis. The third MRA study\textsuperscript{51} found high sensitivity and specificity when 3D time-of-flight MRA was used to detect severe stenosis (>70\%).
The fourth study\textsuperscript{52} also supported the use of MRA, but recommended further examination of costs and effectiveness.

Three studies\textsuperscript{7,51,55} met the inclusion criteria for the economic review. It was impossible to draw any conclusions because the included studies did not address the same range of options, did not use the same reference standards, and did not all present incremental cost-effectiveness ratio (ICER) values. The first study\textsuperscript{7} suggested that MRA and DSA are equally cost-effective. The second study\textsuperscript{55} concluded duplex US alone is the most cost-effective approach. The final study\textsuperscript{51} suggested that at low prevalence rates, no imaging technology combined with standard medical therapy is most cost-effective.

**Cerebral Aneurysms**

All three included SRs\textsuperscript{43,56,57} reported on the use of imaging technologies for diagnosis, investigated the use of CTA (one\textsuperscript{57} also investigated MRA and Doppler US), and used DSA as the reference standard (one\textsuperscript{43} also used surgical findings as a reference). All investigators stated that CTA and MRA performed well, but were insufficient to replace traditional DSA.

Two studies\textsuperscript{58,59} met the inclusion criteria for economic review. Both estimated the cost-utility of using MRA to screen for asymptomatic cerebral aneurysms. In general, the studies suggested that screening is not cost-effective.

**Headaches**

One SR\textsuperscript{60} met the inclusion criteria for clinical review. It evaluated the effectiveness of using CT or MRI as investigative technologies in children with recurrent headaches. Results showed that all children with significant pathology on imaging also had abnormal neurological examinations. The investigators concluded that children with recurrent headaches do not benefit from CT or MRI if their neurological examinations are normal. No economic analyses were located for this clinical condition.

**Head Injuries**

Four SRs were identified. Two\textsuperscript{61,62} calculated the incidence of abnormal CT findings for patients presenting with head injuries, reporting values of 3\% to 14\%. A third SR\textsuperscript{63} reported that the use of CT was controversial, but presented clinical scenarios where it might be appropriate. In the fourth SR,\textsuperscript{64} the authors evaluated pediatric literature to compare CT and MRI to other imaging modalities. Overall, the SRs reported that the performance of CT and MRI were similar and superior to that of skull X-rays.

One study\textsuperscript{65} met the inclusion criteria for economic evaluation. The cost of CT examinations for mild head injury was compared with in-patient observation. Indirect evidence suggested that immediate CT and discharge home led to cost-savings compared with in-patient observation.

**Seizures**

One SR\textsuperscript{66} met the inclusion criteria for clinical evaluation. The authors concluded that MRI is the standard of reference, with CT reserved for urgent assessments, or when MRI is contraindicated. Imaging for seizures is primarily for ruling out underlying pathology. No economic analyses were located for this clinical condition.
**Strokes**

Two SRs\(^ {67,68}\) reported on the use of CT and MRI. The first\(^ {67}\) examined two types of MRI examinations: diffusion-weighted imaging (DWI) and perfusion imaging (PI). Compared with conventional MRI or CT, DWI found more lesions and could distinguish new lesions from old. The authors indicated, however, that information was lacking to allow any conclusions to be drawn about the superiority of DWI or PI. In the second SR, \(^ {68}\) the investigators supported the use of CT and MRI for investigation of stroke, although data were lacking in some areas.

Three studies\(^ {68-70}\) met the inclusion criteria for economic evaluation. Results suggested that immediate CT scanning has the potential to reduce the cost of stroke care by shortening or avoiding hospital stays. It is unclear whether costs for non-hospital care were considered. In two papers\(^ {68,70}\) (reporting the same data), results suggested that early scanning is effective. The absolute difference between scanning immediately, within 24 hours, or within 48 hours was minimal.

### 8 Limitations

The quality of SRs included in the clinical review was generally poor, and did not address the impact of CT and MRI on patient management and outcomes, or societal impact. The papers included in the cost-effectiveness analysis lacked trial-based evaluations, and most authors emphasized cautious data interpretation. The need for further research in clinical and economic evaluations was indicated by many authors.

An additional reality is that advances in imaging technology occur rapidly, and the technologies reviewed in this report may not reflect those used currently. Therefore, clinicians and decision makers may perceive the findings in this report to be outdated with limited use for guiding current clinical decisions.

Inherent limitations in cost-effectiveness analyses have an impact on this review. In addition, the economic analyses were conducted in various jurisdictions at various times. Differences in health systems, unit costs, timeframes, and currency limit the application of results to the Canadian context.

Although the clinical conditions in this SR were identified by consensus in a group of experts, other relevant conditions may have been overlooked.

### 9 Health System Implications

Advances in computing power have combined to broaden the range of clinical applications for CT and MRI, while reducing the unit costs for examinations. Significant growth is likely in the demand for CT and MRI as front-line imaging modalities. The substitution of CT or MRI for other imaging technologies and expanding clinical indications suggest the need for additional capital spending and likely operational spending. With the expanding use of CT and MRI, the number of trained technologists must increase, physician training needs may be affected, and training to apply CT or MRI to new indications will be required. There may be training issues associated with the transfer of workload across specialties, or from tertiary to secondary centres.
10 Conclusions

CT and MRI show promising clinical SR evidence for the use of these investigative technologies in carotid artery disease, PVD, pulmonary embolism, renal artery stenosis, and stroke. Evidence is more cautious for their use in the investigation of cerebral aneurysms, coronary artery disease, and lung cancer screening; and sparse for headaches, head injuries, and seizures. No SR evidence was found for the use of CT and MRI in the investigation of cerebral AVMs or urolithiasis screening.

The review of economic evaluations suggested that CT and MRI are cost-effective for PVD and stroke, but not necessarily more cost-effective than traditional alternatives (as in the case for PVD). The evidence for cost-effectiveness was limited for renal artery stenosis and head injury, and equivocal for lung cancer screening, pulmonary embolism, carotid artery disease, and cerebral aneurysms.

There is a lack of high quality studies to address the clinical and cost effectiveness of CT and MRI for various conditions. Most studies suggested that more research is needed to investigate the benefits of CT and MRI as compared with technologies that are traditionally used. Policy makers, clinicians, and patients should be aware that decisions to use these technologies may be based solely on demonstrated diagnostic performance or clinical opinion, rather than scientific evidence in the form of rigorous SRs.

Although diagnostic imaging technologies may improve or expedite the diagnosis of disease, they do not necessarily change outcomes. Because diagnostic imaging investigation may occur early in the clinical timeline of a patient, many potential factors can affect progress from the time of the imaging test to ultimate patient outcome. To ensure the most effective use of these technologies, measurements of their influences on patient management and outcomes must be a goal of future studies.

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