CT and MRI for Selected Clinical Disorders: A Systematic Review of Economic Evaluations
Until April 2006, the Canadian Agency for Drugs and Technologies in Health (CADTH) was known as the Canadian Coordinating Office for Health Technology Assessment (CCOHTA).


This report and the French version entitled Examen méthodique d’évaluations économiques sur la tomodensitométrie (TDM) et l’imagerie par résonance magnétique (IRM) dans certaines indications are available on CADTH’s web site.

Production of this report is made possible by financial contributions from Health Canada and the governments of Alberta, British Columbia, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Nunavut, Ontario, Prince Edward Island, Saskatchewan, and Yukon. The Canadian Agency for Drugs and Technologies in Health takes sole responsibility for the final form and content of this report. The views expressed herein do not necessarily represent the views of Health Canada or any provincial or territorial government.

Reproduction of this document for non-commercial purposes is permitted provided appropriate credit is given to CADTH.

CADTH is funded by Canadian federal, provincial, and territorial governments.

Legal Deposit - 2006
National Library of Canada
H0350-August, 2006

PUBLICATIONS MAIL AGREEMENT NO. 40026386
RETURN UNDELIVERABLE CANADIAN ADDRESSES TO
CANADIAN AGENCY FOR DRUGS AND TECHNOLOGIES IN HEALTH
600-865 CARLING AVENUE
OTTAWA ON K1S 5S8
CT and MRI for Selected Clinical Disorders:
A Systematic Review of Economic Evaluations

James Murtagh MHA CHE
Rebecca N. Warburton PhD
Vicki Foerster MD MSc
Brian C. Lentle MD FRCPC
Ronald J. Wood RTR
Shaila Mensinkai MA MLIS
Don Husereau BScPharm MSc

August 2006

1 ProMed Associates Ltd., Coquitlam BC
2 School of Public Administration, University of Victoria, Victoria BC
3 Canadian Agency for Drugs and Technologies in Health, Ottawa ON
Reviewers

These individuals kindly provided comments on this report.

External Reviewers

Douglas Angus, BCom MA  
Professor
School of Management  
University of Ottawa
Ottawa ON

AK Dixon, MD FRCR FRCS FMedSci  
Professor of Radiology  
University of Cambridge
United Kingdom

CADTH Scientific Advisory Panel Reviewers

David Hailey, MSc PhD Grad RIC  
Adjunct Professor  
Department of Community Health Services  
University of Calgary
Calgary AB

Craig Mitton, PhD  
Assistant Professor  
University of British Columbia
Okanagan
Kelowna BC

This report is a review of existing public literature, studies, materials and other information and documentation (collectively the “source documentation”) which are available to CADTH. The accuracy of the contents of the source documentation on which this report is based is not warranted, assured or represented in any way by CADTH, and CADTH does not assume responsibility for the quality, propriety, inaccuracies or reasonableness of any statements, information or conclusions contained in the source documentation.

CADTH takes sole responsibility for the final form and content of this report. The statements and conclusions in this report are those of CADTH and not of its Panel members or reviewers.

Authorship

James Murtagh was the lead author, and participated in developing the project protocol, the literature search strategy, and all team conference calls. He also developed inclusion criteria, and screened all literature for inclusion with Rebecca Warburton; reviewed included literature and populated evidence tables; acted as primary author for the report; assembled and edited the report before and after external review; and developed responses to external reviewers’ comments.

Rebecca Warburton discussed strategies for assessing levels of evidence, document search criteria, and document inclusion criteria. She also screened retrieved papers against criteria; resolved inconsistencies with other screeners; participated in conference calls; discussed format and content of evidence tables with James Murtagh; reviewed evidence tables that were drafted by James Murtagh and made joint revisions; discussed report structure and content with James Murtagh; reviewed draft report and made joint revisions; read reviewers’ comments; discussed responses with James Murtagh; and made joint revisions to the final report.
Vicki Foerster participated in the protocol development and commencement of the project. She reviewed the literature search to screen for clinically suitable articles. She also contributed sections of text from the clinical report, and responded to external review comments with edits to the report.

Brian C. Lentle collaborated in defining the project, provided data, and participated in the critical review.

Ronald J. Wood was the principal investigator of the project (he coordinated the overall project to meet goals and objectives, contributed to the literature search protocol, supported lead researchers as required, and participated in teleconference calls). He also reviewed drafts and provided input as required; reviewed comments from reviewers and the team’s response; and provided feedback.

Don Husereau made suggestions to the lead researcher on the content of drafts, and contributed to the design of the analysis.

Shaila Mensinkai participated in the protocol development, designed and executed the literature searches, wrote the methods section and the associated appendix on literature searches, reviewed drafts, and verified and formatted bibliographic references.

**Conflicts of Interest**

Don Husereau, Vicki Foerster, Shaila Mensinkai, James Murtagh, Rebecca Warburton, and Ronald J. Wood disclosed no conflicts of interest. Brian Lentle indicated that he was once paid by Proctor and Gamble to lecture on osteoporotic fracturing to the Canadian Association of Radiologists.
CT and MRI for Selected Clinical Disorders: A Systematic Review of Economic Evaluations

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

Disease
Coronary artery disease, peripheral vascular disease (PVD), renal artery stenosis, lung cancer screening, pulmonary embolism (PE), carotid artery disease, cerebral aneurysms, headaches, head injuries, seizures, stroke, arteriovenous malformations (AVMs), and urinary tract calculi screening

Issue
There is increasing demand for the use of CT and MRI techniques for a variety of clinical disorders. Because CT and MRI are costly to buy and to operate, cost-effectiveness should be established to optimize their use.

Methods and Results
Published economic evaluations (EE) were systematically identified by searching multiple databases using a defined strategy and selection criteria. Of 423 potentially relevant EE, 21 studies of eight clinical conditions were identified: PVD, renal artery stenosis, lung cancer screening, PE, carotid artery disease, cerebral aneurysms, head injuries, and stroke. No economic studies addressed coronary artery disease, headaches, seizures, AVMs, or urinary tract calculi screening.

Implications for Decision Making
- MRI angiography is of unproven advantage in terms of cost-effectiveness compared to duplex ultrasonography or digital subtraction angiography for patients with peripheral vascular disease.
- CT scanning within 48 hours for stroke patients can improve QALYs, but the cost-effectiveness of more rapid scanning is contingent on avoiding or shortening in-patient admissions, and capturing the associated savings.
- Limited evidence suggests that the preliminary imaging of medication-resistant renovascular hypertension with MRI is more cost-effective than with CT or conventional angiography compared to enhanced medical therapy. Additional evaluation is required.
- Limited evidence suggests that immediate CT for mild head injuries, and discharge home if the result is normal are cost-saving compared to in-patient observation. Better evidence of effectiveness is required to confirm this.
- The evidence is equivocal for a cost-effectiveness advantage versus standard care for CT and MRI used in lung cancer screening, PE, carotid artery disease, and cerebral aneurysms.

This summary is based on a comprehensive health technology assessment available from CADTH’s web site (www.cadth.ca): Murtagh J, Warburton RN, Foerster V, Lentle BC, Wood RJ, Mensinkai S, Husereau D. CT and MRI for selected clinical disorders: a systematic review of economic evaluations.
EXECUTIVE SUMMARY

The Issue
Computed tomography (CT) and magnetic resonance imaging (MRI) are medical imaging techniques used to investigate clinical disorders. They are costly to buy and to operate. For some clinical indications, CT and MRI are accepted investigations; for others, there is uncertainty and controversy about the value of their use. The clinical and economic performance of CT and MRI relative to one another or to alternative technologies is often unclear or poorly documented. Given the increasing demand for CT and MRI tests from patients and physicians, their cost-effectiveness in the investigation of disorders where their application is considered to be controversial, should be established.

Objective
The objective of this report is to summarize the available evidence of the cost-effectiveness of CT and MRI in investigating specific clinical conditions of the chest, cardiovascular, neurological, and urological systems.

Methods
The authors identified and retrieved published literature from 2000 to the present, using an extensive, well defined search strategy encompassing electronic databases and grey literature. References were considered to be eligible for inclusion if they were complete economic evaluations that covered the populations of interest [coronary artery disease, peripheral vascular disease (PVD), renal artery stenosis, lung cancer screening, pulmonary embolism (PE), carotid artery disease, cerebral aneurysms, headaches, head injuries, seizures, stroke, arteriovenous malformations (AVMs), and urinary tract calculi screening]; examined CT and MRI technologies for investigation of the identified conditions; published from 1999 to October 2005; and based on data from 1998 onward.

Two authors independently applied the selection criteria for screening. From the included references, information was extracted into evidence tables and analyzed. The quality of all included references was assessed using the Oxford Centre for Evidence-Based Medicine levels of evidence and grade of recommendation scale.

Results
From the electronic database search, 18 of 315 studies were selected for inclusion, with an additional three studies (of 108) added after review of the grey literature. These 21 studies covered eight clinical conditions: PVD, renal artery stenosis, lung cancer screening, PE, carotid artery disease, cerebral aneurysms, head injuries and stroke. No economic studies addressed coronary artery disease, headaches, seizures, AVMs, or urinary tract calculi screening.

The studies included in this review suggest that CT or MRI are effective for some conditions (especially PVD and stroke), but they are not necessarily more effective or cost-effective than traditional alternatives (for PVD). For other conditions, the evidence of cost-effectiveness appears positive but limited (renal artery stenosis and mild head injuries). The evidence for effectiveness or cost-effectiveness of CT or MRI for lung cancer screening, PE, carotid artery disease, and cerebral aneurysms is equivocal or conflicting.
This study has several limitations, including the quality of available literature, the absence of literature addressing the most current technology, and issues inherent to cost-effectiveness analysis, such as ignoring competing priorities and assuming that resources are available for deployment or redeployment.

**Conclusion**

The indications for CT and MRI, and their performance compared with earlier generations of the same technologies, are advancing faster than the available literature. As a result, this report may be dated in some areas. Years after CT and MRI techniques have been first advocated or come into use, it remains difficult to find high quality studies that address their use. For this report, no studies were found that addressed the cost-effectiveness of CT and MRI for coronary artery disease, headaches, seizures, AVMs, or urinary tract calculi screening.

The studies included in this report suggest that CT and MRI are cost-effective in the investigation of some controversial clinical conditions (especially PVD and stroke), but not necessarily more effective or cost-effective than traditional alternatives (for PVD). For other clinical conditions, there is evidence of cost-effectiveness, but it is limited (renal artery stenosis, mild head injuries). The evidence for cost-effectiveness of CT and MRI for lung cancer screening, PE, carotid artery disease, and cerebral aneurysms is equivocal or conflicting.

Regardless of the actual or perceived utility of CT and MRI, there remains a need to document their effectiveness and cost-effectiveness in specific areas of clinical practice.
## ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D</td>
<td>two-dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>three-dimensional</td>
</tr>
<tr>
<td>AHRQ</td>
<td>Agency for Healthcare Research and Quality (US)</td>
</tr>
<tr>
<td>AVM</td>
<td>arteriovenous malformation</td>
</tr>
<tr>
<td>CA</td>
<td>conventional angiography</td>
</tr>
<tr>
<td>CAR</td>
<td>Canadian Association of Radiologists</td>
</tr>
<tr>
<td>CEBM</td>
<td>Centre for Evidence-based Medicine</td>
</tr>
<tr>
<td>CE-MRA</td>
<td>contrast-enhanced MRA</td>
</tr>
<tr>
<td>CIHI</td>
<td>Canadian Institute for Health Information</td>
</tr>
<tr>
<td>CPG</td>
<td>clinical practice guideline</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
</tr>
<tr>
<td>CTA</td>
<td>CT angiography</td>
</tr>
<tr>
<td>DD</td>
<td>D-dimer assay</td>
</tr>
<tr>
<td>DSA</td>
<td>digital subtraction angiography</td>
</tr>
<tr>
<td>EBCT</td>
<td>electron beam computed tomography</td>
</tr>
<tr>
<td>HTA</td>
<td>health technology assessment</td>
</tr>
<tr>
<td>ICER</td>
<td>incremental cost-effectiveness ratio</td>
</tr>
<tr>
<td>MDCT</td>
<td>multi-detector row CT</td>
</tr>
<tr>
<td>MRA</td>
<td>magnetic resonance angiography</td>
</tr>
<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>NHS</td>
<td>National Health Service (UK)</td>
</tr>
<tr>
<td>NPV</td>
<td>negative predictive value</td>
</tr>
<tr>
<td>OECD</td>
<td>Organisation for Economic Co-operation and Development</td>
</tr>
<tr>
<td>PE</td>
<td>pulmonary embolism</td>
</tr>
<tr>
<td>PVD</td>
<td>peripheral vascular disease</td>
</tr>
<tr>
<td>QALY</td>
<td>quality-adjusted life-year</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>SR</td>
<td>systematic review</td>
</tr>
<tr>
<td>TOF</td>
<td>time of flight (MRA)</td>
</tr>
<tr>
<td>UK</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>US</td>
<td>ultrasound</td>
</tr>
<tr>
<td>VQ</td>
<td>ventilation-perfusion scintigraphy</td>
</tr>
</tbody>
</table>


**TABLE OF CONTENTS**

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXECUTIVE SUMMARY</td>
<td>iiiiv</td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td>vi</td>
</tr>
<tr>
<td>1 INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>1.1 Background</td>
<td>1</td>
</tr>
<tr>
<td>1.2 Overview of the Technology</td>
<td>2</td>
</tr>
<tr>
<td>1.2.1 Description of technology</td>
<td>2</td>
</tr>
<tr>
<td>1.2.2 Regulatory status in Canada</td>
<td>3</td>
</tr>
<tr>
<td>1.2.3 Clinical indications</td>
<td>3</td>
</tr>
<tr>
<td>1.2.4 Source of technology</td>
<td>3</td>
</tr>
<tr>
<td>1.2.5 Unit cost</td>
<td>3</td>
</tr>
<tr>
<td>1.2.6 Utilization and expenditure patterns</td>
<td>4</td>
</tr>
<tr>
<td>2 THE ISSUE</td>
<td>8</td>
</tr>
<tr>
<td>3 OBJECTIVE</td>
<td>8</td>
</tr>
<tr>
<td>4 CLINICAL REVIEW</td>
<td>9</td>
</tr>
<tr>
<td>5 ECONOMIC ANALYSIS</td>
<td>9</td>
</tr>
<tr>
<td>5.1 Methods</td>
<td>9</td>
</tr>
<tr>
<td>5.1.1 Literature search strategy</td>
<td>9</td>
</tr>
<tr>
<td>5.1.2 Selection criteria and method</td>
<td>10</td>
</tr>
<tr>
<td>5.1.3 Data extraction strategy</td>
<td>10</td>
</tr>
<tr>
<td>5.1.4 Quality assessment strategy</td>
<td>11</td>
</tr>
<tr>
<td>5.2 Results</td>
<td>11</td>
</tr>
<tr>
<td>5.2.1 Quantity of research available</td>
<td>11</td>
</tr>
<tr>
<td>5.2.2 Quality of research available</td>
<td>12</td>
</tr>
<tr>
<td>5.2.3 Characteristics of included studies</td>
<td>13</td>
</tr>
<tr>
<td>5.2.4 Summary of findings</td>
<td>14</td>
</tr>
<tr>
<td>6 HEALTH SERVICES IMPACT</td>
<td>21</td>
</tr>
<tr>
<td>7 DISCUSSION</td>
<td>22</td>
</tr>
<tr>
<td>7.1 Principal Findings</td>
<td>22</td>
</tr>
<tr>
<td>7.2 Study Limitations</td>
<td>24</td>
</tr>
<tr>
<td>7.3 Generalizability of Findings</td>
<td>25</td>
</tr>
<tr>
<td>7.3.1 Comparison to other studies</td>
<td>25</td>
</tr>
<tr>
<td>7.3.2 Other considerations with respect to generalizability</td>
<td>26</td>
</tr>
<tr>
<td>7.4 Knowledge Gaps</td>
<td>27</td>
</tr>
<tr>
<td>8 CONCLUSION</td>
<td>28</td>
</tr>
<tr>
<td>9 REFERENCES</td>
<td>29</td>
</tr>
</tbody>
</table>

APPENDICES - available from CADTH's web site www.cadth.ca
APPENDIX 1: Project Protocol
APPENDIX 2: Literature Search Strategy
APPENDIX 3: CEBM Scale: Grades of Recommendation
APPENDIX 4: Excluded Articles
APPENDIX 5: Evidence Tables
1 INTRODUCTION

1.1 Background

Computed tomography (CT) has been available in Canada since 1973, and magnetic resonance imaging (MRI) has been available in Canada since 1985. The first CT machines were limited by small apertures, and could only be used for images of the heads of adults or the bodies of small children. CT machines for the adult body became available and were widely used in Canada by the late 1970s to early 1980s. MRI emerged from a laboratory technology known as nuclear magnetic resonance spectroscopy, and initially provided more detailed images of the brain than were possible using CT, particularly the structures of the posterior fossa. MRI developments made it possible to create images of parts of the body that had been difficult to visualize, such as the spinal cord and musculoskeletal system.

CT and MRI are commonly used for several clinical situations. Physicians requisition one, the other, or both when they need clear anatomic images to show disease and its penetration, and to determine treatment. For example, CT is the imaging procedure of choice for detecting, staging, and monitoring of therapy in malignancies; investigations of the chest, abdomen, and cranium to show abnormal structures or tumours; pre-operative investigation of complex masses to assess treatment possibilities; and guidance for drainage procedures, biopsies, and nerve blocks. CT and MRI are thought to have equivalent abilities for some conditions, although MRI provides more information than CT for some disorders of the head and neck, and it is superior for imaging of the spine and musculoskeletal system. MRI is increasingly being used in oncology.

Advances in the technologies have made it possible to investigate more medical conditions. For example, the technology for CT scanning has advanced from single-slice to multi-slice (a concurrent capture of ≥64 slices), improving its diagnostic accuracy, and leading to its use in musculoskeletal applications, myelography (imaging the fluid space around the spinal cord), angiography (imaging blood vessels), cardiac scoring, evaluation of brain perfusion, acute chest pain and dyspnea (shortness of breath), with the aid of computed image reconstruction tools, and virtual endoscopy. Recent uses of MRI include breast and cardiac imaging, angiographic procedures, interventional techniques, and examination of brain function to map onto images of brain structure. The evolving advances in CT and MRI have spread their utility from investigative imaging to therapeutic modalities such as guidance of biopsies and other minimally invasive therapies.

Given the expanding indications for CT and MRI and the high cost of both technologies, the appropriate use and management of access are of concern. In many instances, the clinical and economic performance of CT and MRI compared with one another, or to other technologies, remains unclear.

The objective of this report is to provide a systematic review (SR) of the evidence that is available in economic evaluations of CT and MRI, as they relate to a defined set of clinical conditions. The report is intended to help decision makers and health care providers involved in the purchase and operation of CT and MRI equipment, or in patient management. Specific controversial clinical conditions that were targeted for review, were selected by an expert panel composed of Canadian Association of Radiologists (CAR) members. A companion SR addressing the clinical effectiveness of CT and MRI for the same list of clinical conditions has been published.
1.2 Overview of the Technology

1.2.1 Description of technology

CT and MRI machines acquire pictures of the inside of the human body through different mechanisms. CT scanning uses X-rays and computed analysis to produce cross-sectional images of slices of the body; whereas MRI usually uses the molecular hydrogen in tissues, a large magnet, intermittent radio waves, and a computer to produce two-dimensional (2D) or three-dimensional (3D) images. MRI scans avoid the use of ionizing radiation. The ability to process multiple images allows for the detailed visualization of internal organs. Contrast media or other injected agents may be used to enhance CT and MRI images.

CT and MRI scans are performed in dedicated suites, and specialized personnel are involved. Trained technologists perform the examinations, and obtain and process the images. Radiologists supervise the examinations, help determine the most appropriate imaging sequences for the particular clinical problems, and interpret the resulting images. Nurses may be needed if the patient requires contrast media or sedation. Physicists supply technical support to ensure image quality and radiation safety.

The technologies are continually changing, with newer machines allowing for increasingly detailed images and faster scanning. Image improvements are partly attributable to the decrease in time required to capture the images, so that artifacts caused by breathing or other movements are minimized, particularly for patients who are short of breath. In CT, advances in the technology include continuous image capture using helical (also known as spiral) data acquisition, rather than the capture of discrete “slices” of data as was typical of earlier generations of CT machines. Even more advanced are machines that build on helical or spiral scanning, and capture multiple images at once (“multi-slice” data acquisition or scanning). With these machines, a volume of the body is scanned and reconstructed as individual images afterwards. These machines provide detailed information that can be manipulated by a technologist to produce 2D and 3D images of the body.

The increasing speed of imaging, the improved detail, and the 3D capability facilitate new types of imaging such as CT and magnetic resonance angiography (MRA) and CT virtual endoscopy, now being investigated as alternatives to, and in some cases replacements for, more invasive techniques, such as catheter angiography, colonoscopy, and bronchoscopy.

With respect to the CT and MRI discussed in this report, the studies used a variety of technologies:

- **Helical (or spiral) CT**: The CT X-ray tube rotates and scans continuously while the radiology table moves a patient through the scanner. This contrasts with earlier “step and shoot” CT technology, where an individual image was captured while the patient was stationary, the patient was then moved slightly with the machine turned off, and another image was captured, and so on.
- **Multi-slice CT** [(or multi-detector row CT (MDCT))]: Multiple slices are acquired simultaneously, thus increasing scanning speed. Initially, four slices were captured, but the newest technology allows for the capture of ≥64 slices.
- **CT and MR angiography (CTA and MRA)**: The imaging of blood vessel lumen is possible because of the fine detail and rapid scanning introduced with newer CT and MRI systems.
1.2.2 Regulatory status in Canada

Health Canada’s Therapeutic Products Directorate, which has a mandate to ensure that medical devices offered for sale in Canada are safe, effective, and of high quality, approves and regulates CT and MRI machines. To regulate medical devices, the directorate uses a four-class system modelled on a European classification scheme, with class I being the most benign and class IV being the least benign. CT machines require class III licences (devices in this class are considered to be potentially hazardous, or they present an immediate danger if they fail). MRI machines are class II.

1.2.3 Clinical indications

The government does not regulate or license CT and MRI machines for specific clinical indications. Rather, clinical practice guidelines (CPGs) or “referral guidelines” for diagnostic imaging have been developed in Europe, the United States, and other countries. Evidence-based CPGs aim to limit the use of medical investigations or interventions to those supported by good research that prove their clinical and cost-effectiveness.4

CT and MRI referral guidelines have been developed in Canada through local initiatives in several facilities or health regions, but until recently, no national guidelines existed. The CAR expressed a commitment to evidence-based guidelines, and has developed referral guidelines for diagnostic imaging procedures. The CAR subcommittee that was responsible for drafting the guidelines was interested in the appropriate use of the scanning technologies in clinical conditions where radiologists considered the use of these technologies to be controversial.

Radiology experts on the subcommittee identified and agreed on 13 clinical conditions in which the use of CT and MRI could be controversial.

- cardiovascular system: coronary artery disease; peripheral vascular disease (PVD); and renal artery stenosis
- chest: lung cancer (screening); and pulmonary embolism (PE)
- neurological system: carotid artery disease; cerebral aneurysms; headaches; head injuries; seizures or epilepsy (primary investigation); strokes; and arteriovenous malformations (AVMs)
- urological system: urinary tract calculi (screening)

1.2.4 Source of technology

Some of the principal manufacturers of CT equipment include GE Medical Systems (US), Phillips (the Netherlands), Siemens (Germany), Shimadzu (Japan), and Toshiba (Japan). The principal manufacturers of MRI equipment include all of the companies mentioned, and Hitachi (Japan), and ISOL Technology (Korea). The scanning equipment is generally bought as new installations with features and attachments, but there is a market for used equipment.5 In some cases, health regions may move their machines from tertiary sites to community hospitals as they acquire newer technology for the large teaching centres, and industrialized countries may sell or donate equipment to less developed countries.

1.2.5 Unit cost

The purchase costs for CT and MRI machines depend on the level of sophistication required, and the number of additional features installed. Documentation about costs is unavailable, but a 2000 CAR report estimated the average cost of a CT machine to be $1,400,000, and $2,500,000 for an MRI
A suitable space in a facility must be identified and renovated, or constructed. Yearly operating costs are considerable, as are maintenance contracts.

Because CT and MRI technology continues to advance, machines that are up-to-date at the time of purchase and installation are considered to be obsolete within a few years. Radiology staff may request upgrades of software and hardware annually, which can equate to hundreds of thousands of dollars per site.

In Canada, the fees paid to radiologists to provide professional interpretations of CT and MRI scans are set provincially and vary across jurisdictions, as does the method of counting scans. For example, the Ontario Health Insurance Plan 2003 Schedule of Benefits lists 25 fee codes that depend on the part of the body scanned (nine areas listed), the type of scan performed, and the use or lack of use of intravenous contrast media. Of the 25 fees established, compensation ranges from $34.60 for reviewing CT images used to guide a biopsy, to $109.35 for a CT of the spine, abdomen, or pelvis, with and without contrast media. Fees for MRI are similar, ranging from $31.75 to $109.85 (10 areas of the body, 23 fee codes).

For some examinations, several areas of the body may be scanned, and the number of sequences may vary; in some cases, the total professional fee paid will be the sum of the individual fee items. Overall, the fee structure is complex and continuously evolving. No single database collects fee information: some is collected provincially, and some nationally. The standardization of coding systems is a goal of interprovincial and federal bodies.

CT and MRI machines have limited life cycles. According to the CAR, outdated diagnostic imaging equipment is undesirable for several reasons:

- older machines may produce poorer quality images
- there is a higher rate of failure, which disrupts imaging services and may be dangerous for patients and staff
- parts may be difficult to obtain
- repairs may be costly
- the machines may be difficult or impossible to update or augment.

The life cycle of diagnostic imaging equipment varies, with no universally accepted standard. In 2000, the CAR published life cycles for diagnostic imaging technologies, stating that the life spans should be eight years for CT, and six years for MRI. In March 2003, the European Coordination Committee of the Radiological, Electromedical, and Medical IT Industries established general standards for electromedical equipment in Europe: 60% should be ≤5 years old, ≤30% should be from six to 10 years old, and ≤10% should be >10 years old. In Canada, as of January 2004, the proportion of machines <5 years old was 64% for CT, and 71% for MRI, according to a report by the Canadian Institute for Health Information (CIHI).

1.2.6 Utilization and expenditure patterns

In 1991, there were 200 CT machines and 22 MRI machines in Canada (all publicly funded). Since then, the growth in acquisition of this technology has been dramatic. In 2004, installations had expanded to 338 CT machines and 151 MRI machines (publicly and privately funded), for a growth rate of 70% for CT and almost 700% for MRI. The number of units per million people varies across jurisdictions (Table 1).
The number of CT and MRI machines as a rate per unit of population is often compared between provinces, and among countries. For example, the Organisation for Economic Co-operation and Development (OECD) tracks the numbers and rates of CT and MRI machines, and finds a significant variation in installations among countries (Figures 1 and 2). The importance of this variation is unclear as installation numbers do not correlate directly with the degree of use of the technology, access, or health outcomes for the population.10

In Canada, tracking the number of CT and MRI examinations (scans) performed is complex, and has not been accomplished nationally. Procedures are performed for in-patients and outpatients, in hospital and non-hospital settings, and in publicly and privately funded facilities.

For its 2004 report, *Medical Imaging in Canada*, the CIHI obtained fee-for-service CT billings by radiologists from New Brunswick, Newfoundland and Labrador, Ontario, Prince Edward Island, and Québec, for 1994 and 2001. The CIHI accessed several data sources to obtain the scan numbers, including ministries of health for New Brunswick, Newfoundland and Labrador, and Québec, and its National Physician Database for Ontario and Prince Edward Island.

The report presented rates of change in the number of CT scans performed in 1994 versus 2001, rather than raw numbers. As can be seen in Figure 3, the growth in numbers of scans ranged from 43% (Prince Edward Island) to 177% (Newfoundland and Labrador).9

This growth could be a result of the increasing number of machines installed, or an increasing use of existing machines. Data show that the number of machines installed is increasing, but it is unclear how much of the growth in the number of scans is attributable to the new machines versus increased use.
An illustration of the growth in the number of MRI scans being performed is provided in a report by the Institute for Clinical Evaluative Sciences (ICES) in Ontario. The report showed that the number of MRI scans performed in Ontario increased by nearly six times, from 25,406 scans in 1992 to 145,810 in 2001.
Figure 2: Diffusion of MRI units in 30 countries

Source: Diffusion of MRI units, 1990 to 2000, OECD HEALTH DATA 2005, © OECD 2005 All rights reserved
During this time, the cost to the Ontario Health Insurance Plan increased by almost 10 times, from about $3 million in 1992 to >$26 million in 2001. MRI scans for seven body areas were reported: abdomen, extremities, head, neck, pelvis, spine, and thorax. The head was the most common area scanned [39% of all scans in 2001 (57,106 of 145,810)], but the increase in abdominal scans was the greatest at 1,233% (394 in 1992; 4,858 in 2001).

2 THE ISSUE

CT and MRI machines are costly to buy, operate, and replace. Their findings may also generate additional investigations with further costs. The demand generated by patients and physicians outpaces supply, leading to issues of access. In parts of the country where access to CT and MRI machines has been limited, there is pent-up demand. Even when access is increased through the purchase of new machines or the extensions of operating hours, wait times may not shrink. Ideally, CT and MRI would only be used to investigate those clinical cases where there is compelling evidence from the medical literature that shows the results of the test will positively influence or expedite the management of the patient, or change his or her outcome. It is equally important that given constrained resources, clinically effective scans are cost-effective compared with recognized alternatives. The clinical and economic performance of CT and MRI relative to one another or to alternative technologies is often unclear or poorly documented.

3 OBJECTIVE

The objective of this report is to summarize the evidence available on the economic effectiveness of CT and MRI in the investigation of selected clinical conditions that have been identified by CAR experts as being controversial and of interest:
- cardiovascular system (coronary artery disease, PVD, and renal artery stenosis)
- chest [lung cancer (screening), and PE]
• neurological system [carotid artery disease, cerebral aneurysms, headaches, head injuries, seizures or epilepsy (primary investigation), strokes, and AVMs]
• urological system [urinary tract calculi (screening)].

This objective is accomplished by addressing the question: what is the evidence of cost-effectiveness from studies that examine CT or MRI for the investigation of the clinical conditions listed?

This report is intended to help decision makers who are involved in the purchase and operation of CT and MRI equipment and those involved in the investigation of patients who may be candidates for use of the technology.

4 CLINICAL REVIEW

A companion SR addresses the clinical effectiveness of CT and MRI for the same list of clinical conditions identified by the CAR.3 Key findings of the companion SR are summarized in section 7.3.1 of this Technology Report.

5 ECONOMIC ANALYSIS

5.1 Methods

A protocol for this project was written a priori and was followed throughout (Appendix 1). The protocol covered a review of clinical studies and a review of economic studies. At the outset, the plan was to combine these into one report. As the project progressed, it became apparent that the two topics would best be handled by splitting the material into two projects.

5.1.1 Literature search strategy

Published literature was retrieved by using a well defined search strategy, which is described in Appendix 2. On the DIALOG® system, MEDLINE®, EMBASE®, INSPEC, BIOSIS Previews® and PASCAL databases were cross-searched using the duplicate removal feature. The search strategy focused on the objectives of the review, and included descriptors and keywords for CT and MRI technologies in the cardiovascular, thoracic, neurological, and urological clinical areas determined to be controversial by the CAR.

The search was limited to 2000 onward, to retrieve literature on contemporary technologies. A language limit was not applied. A filter was used to limit the retrieval to economic studies. Regular database alerts were established on the MEDLINE®, BIOSIS®, EMBASE®, and INSPEC databases to capture new publications until November 2005. The Heath Economics Evaluations Database (HEED) was also searched. Parallel searches were performed and updated on LILACS, the Cochrane library, and PubMed databases to capture additional studies.

Grey literature was retrieved by searching the web sites of health technology assessment (HTA) and related agencies. These searches were supplemented by handsearching selected bibliographies,
meaning that the references thus obtained could be pre-2000. In addition, subject experts were contacted for related information.

Search results from all the databases were downloaded into a Reference Manager database, and duplicates were removed.

5.1.2 Selection criteria and method

a) Selection criteria

Inclusion criteria included:

- study design [complete economic evaluations (cost and effect data) in the form of primary studies, modelling exercises, and self-identified SRs or meta-analyses]
- population groups [cardiovascular (coronary artery disease, PVD, renal artery stenosis); chest (lung cancer screening, PE); neurological (seizures, headaches, head injuries, stroke, carotid artery disease, cerebral aneurysms, AVMs); and urological (screening for urinary tract calculi)]
- interventions [any investigative application of CT and MRI technologies, including CTA and MRA; articles were excluded that reported exclusively on electron beam CT (EBCT), a related technology not in use in Canada, and experiencing decreased use elsewhere]

b) Selection method

From the search of citations and abstracts (where available), two authors (VF and JM) independently applied the population groups criteria to determine clinical relevance. Two authors (JM and RNW) then proceeded to develop independent subsets of potentially relevant citations based on the remaining criteria. The two independent subsets were compared. Where both authors agreed on relevance, citations were accepted. Where both reviewers agreed on lack of relevance, citations were eliminated. Where there was initial disagreement, relevance was determined by consensus. When an abstract was unavailable but the material in the citation suggested potential relevance, this citation was included. A short list of potentially relevant citations was developed. These citations were requested in full text.

The full-text articles and their associated references were independently reviewed (JM and RNW) against the inclusion criteria. The two sets of included articles were compared and refined to one list, with the reviewers reaching agreement by consensus. A third author was available to assist if consensus could not be reached, but this additional intervention was not needed. Two authors (JM and RNW) independently organized and reviewed the grey literature. They later compared and refined their inclusion and exclusion lists to one list on the basis of consensus.

5.1.3 Data extraction strategy

A template for summary evidence tables was developed.
Ideally in an SR, two authors review each included study, and collaborate in data extraction and interpretation to reduce possible bias in reporting and interpretation. Two authors (JM and RNW) each assumed responsibility for populating specific cells in the evidence tables, then cross-checked each other’s work.

5.1.4 Quality assessment strategy

Reports of higher quality are believed to draw more reliable conclusions. For this report, the Oxford Centre for Evidence-based Medicine (CEBM) scale was used to assess the quality of selected studies. This scale has several advantages. It results in a quantitative indication of study quality, and it explicitly considers economic and decision analyses, and evaluates them in the context of the type of research underlying the parameter estimates contained in, for example, decision analyses (Appendix 3).

Two authors (JM and RNW) independently applied the CEBM scale to all included studies. The results were compared, and any differences resolved by consensus.

5.2 Results

5.2.1 Quantity of research available

a) Electronic search
The electronic search yielded 315 possibly relevant citations. Two researchers (JM and RNW) independently screened each citation and abstract (when available) using the criteria, resulting in the selection of 88 articles. These were requested in full text, and then independently reviewed by the same researchers. The second round of review excluded 70 of the 88 articles, leaving 18 (6%) for inclusion. See Figure 4 for a flow chart of article selection, and Appendix 4 for a bibliography of the articles excluded in the second round of selection, with the reasons for exclusion.

b) Grey literature search
The search of the grey literature resulted in the identification of 108 electronic documents. JM and RNW independently reviewed these for relevance by applying the criteria, and selected 18. They reviewed these items a second time, and after discussion, chose to include three documents (4%).

c) Clinical categories and number of studies
Combining the articles selected through the electronic search (18) with those selected from the grey literature search (3) resulted in a total of 21 articles. One of these reported on two of the included conditions, and was accounted for twice in the numbers of included studies.

The authors sought information on the use of CT or MRI for investigating 13 clinical conditions.

Studies meeting the inclusion criteria were located for eight clinical conditions: PVD, renal artery stenosis, lung cancer screening, PE, carotid artery disease, cerebral aneurysms, head injuries, and strokes. No studies were found for coronary artery disease, headaches, seizures, AVMs, and urinary tract calculi screening. Table 2 summarizes the number of studies included for each condition.
5.2.2 Quality of research available

a) **CEBM levels of evidence**

The levels of evidence and grade of recommendation results for the included studies are summarized in Table 3. It was difficult to assign most of the included studies to a specific level of evidence. As a result, most studies were assessed as falling into one or the other of two levels. Descriptions of the level and grade components of the CEBM are presented in Appendix 3.

b) **Funding source**

As shown in Table 4, no industry funding was reported, but a significant number of papers included no comment about the presence or absence of funding support. Of the 22 studies reported, 50% were funded by a government agency [e.g., the Agency for Healthcare Research & Quality (AHRQ)] in the
Table 2: Selected clinical conditions and number of studies

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular systems</td>
<td></td>
</tr>
<tr>
<td>• Coronary artery disease</td>
<td>0</td>
</tr>
<tr>
<td>• PVD</td>
<td>3</td>
</tr>
<tr>
<td>• Renal artery stenosis</td>
<td>1</td>
</tr>
<tr>
<td>Chest systems</td>
<td></td>
</tr>
<tr>
<td>• Lung cancer screening</td>
<td>5</td>
</tr>
<tr>
<td>• PE</td>
<td>4</td>
</tr>
<tr>
<td>Neurological systems</td>
<td></td>
</tr>
<tr>
<td>• Carotid artery disease</td>
<td>3</td>
</tr>
<tr>
<td>• Cerebral aneurysms</td>
<td>2</td>
</tr>
<tr>
<td>• Headaches</td>
<td>0</td>
</tr>
<tr>
<td>• Head injuries</td>
<td>1</td>
</tr>
<tr>
<td>• Seizures or epilepsy</td>
<td>0</td>
</tr>
<tr>
<td>• Stroke</td>
<td>3</td>
</tr>
<tr>
<td>• AVMs</td>
<td>0</td>
</tr>
<tr>
<td>Urological system</td>
<td></td>
</tr>
<tr>
<td>• Urinary tract calculi (screening)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>22</strong>*</td>
</tr>
</tbody>
</table>

*Number of included studies was 21: one reported on two conditions.

Table 3: Distribution of studies by level of evidence and grade of recommendation results

<table>
<thead>
<tr>
<th>Level/Grade</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b or 2b</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2a or 3a</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>2b</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2b or 3b</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

United States, and the National Health Service (NHS) in the United Kingdom (UK)]. Non-profit agencies in the United States funded 9% (e.g., the Robert Wood Johnson Foundation). No source of funding was reported for 36% of the studies.

5.2.3 Characteristics of included studies

a) General comments

Although all languages were considered, and the English citations and abstracts of non-English reports were examined during the first step of literature selection, there are no non-English papers among the final included studies.
Table 4: Sources of funding of included studies (n=22)

<table>
<thead>
<tr>
<th>Funding Source</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Government or government-funded agency</td>
<td>11</td>
</tr>
<tr>
<td>Non-profit agency</td>
<td>2</td>
</tr>
<tr>
<td>Not funded and explicitly stated</td>
<td>1</td>
</tr>
<tr>
<td>Unreported</td>
<td>8</td>
</tr>
</tbody>
</table>

Efforts were made to obtain English versions of non-English studies from the authors, and we were successful in one instance. Where it proved impossible to obtain a version of a non-English paper in a language read by one of the reviewers, the non-English papers were excluded. Some or all of these papers may have been screened out (based on the study inclusion criteria), if an English version had been available.

The included studies varied in scope, length, rigour, and quality, ranging from a couple of pages (e.g., Adams, 2001) to hundreds of pages (e.g., Wardlaw et al., 2004). They were conducted by teams varying from one person (e.g., Adams, 2001) to large groups (e.g., Meenan et al., 2002). In general, the reviews obtained through the electronic search were shorter and more focused than the grey literature pool, which included extensive reviews of several competitive technologies.

b) Country of origin
As shown in Table 5, authors in the United States led nearly a third of the studies (seven of 22). The UK was a strong contributor, as were Japan and the Netherlands. Several studies were conducted by teams of authors, and some were collaborations across countries.

5.2.4 Summary of findings
In total, 22 studies in eight clinical categories met the inclusion criteria, and the information from these studies was abstracted into eight evidence tables (Appendix 5). The format described in section 5.1.3 was used to record information. Each table will be discussed, with an emphasis on the base case results; more details about aspects such as study characteristics are contained in the tables, and in the original documents. Readers with an interest in a particular clinical condition should consult the relevant table and associated studies. Money values have been reported as stated in the original research. The currency references are primarily United States dollars, or pound sterling. One study uses C$. Differences in health systems, the relative price of health services, and the timeframes of the included studies make the conversion of foreign currencies into Canadian dollars problematic.

a) Peripheral vascular disease
Three studies addressing PVD met the inclusion criteria and are summarized in Appendix 5 Table 1.

Berry et al. used a decision model to compare the cost-utility of MRA and digital subtraction angiography (DSA) in the treatment of PVD. Parameter estimates for the model were based, wherever possible, on an SR of the literature.

The authors concluded that 2D, time-of-flight (TOF) MRA and contrast-enhanced MRA (CE-MRA) accurately identify occlusions and 50% to 100% stenoses, with their results suggesting that there is little difference in the cost-utility of MRA and DSA. In the base case scenario, MRA yielded 0.59
quality-adjusted life-years (QALYs) and one-year costs of £6,395, while DSA yielded 0.61 QALYs and costs of £6,396. If the performance of MRA is improved to reflect the sensitivity and specificity of CE-MRA, then the effectiveness remains similar, but the costs of MRA are lower by £6 to £55. Given such little difference, the choice of technology will largely be a matter of what is available and clinician preference.

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>2</td>
</tr>
<tr>
<td>Japan</td>
<td>3</td>
</tr>
<tr>
<td>Netherlands</td>
<td>3</td>
</tr>
<tr>
<td>Sweden</td>
<td>1</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1</td>
</tr>
<tr>
<td>UK</td>
<td>5</td>
</tr>
<tr>
<td>US</td>
<td>7</td>
</tr>
</tbody>
</table>

Visser et al.\textsuperscript{19} used a decision model to compare the cost-utility of treatment for intermittent claudication based on MRA, duplex ultrasound (US), or DSA results, to a reference strategy of no imaging work-up combined with exercise. Assuming that a minimally invasive treatment strategy (angioplasty or exercise) is appropriate, MRA was more effective and less expensive than duplex US. MRA and DSA had incremental cost-effectiveness ratios (ICERs) of $35,000 per QALY and $471,000 per QALY respectively, compared with the reference strategy. Assuming that a more invasive treatment strategy (bypass surgery) is appropriate, duplex US and MRA were dominated by DSA, which had an ICER of $179,000 per QALY compared with the reference strategy. In absolute terms, the relative effectiveness (as measured by QALYs) of duplex US, MRA, and DSA varied by <1%, and relative costs varied by 2% to 4%. The authors concluded that the difference among the imaging techniques is slight, and suggested that this implies MRA and duplex US can replace DSA, especially in minimally invasive treatment.

A second paper by Visser,\textsuperscript{20} with a different group of co-authors, used a decision model to determine the target values for diagnostic accuracy that would make multi-detector row CTA equivalent to CE-MRA in terms of cost-utility in the treatment of intermittent claudication. The base case suggested that for minimally invasive treatment (angioplasty or exercise), and assuming a willingness-to-pay threshold of $100,000 per QALY, CTA would be equivalent to MRA in terms of cost-utility, if CTA cost $420, had a sensitivity of 90%, and 20% of patients needed additional work-up with DSA. In a more invasive treatment scenario (bypass surgery), CTA would be equivalent to MRA, if CTA cost $673, had a sensitivity of 95%, and 20% of patients required additional work-up with DSA. The authors concluded that multi-detector row CTA has the potential to be equivalent to MRA in the investigation of patients with intermittent claudication.

The paper by Berry et al.\textsuperscript{13} has a quality score of 2a or 3a, grade C recommendation. The paper appears to be a well executed SR, but the authors note that “…the doubtful validity of the studies included in the review means that some of the conclusions must be treated cautiously” (page 107). Both papers by Visser et al.\textsuperscript{19,20} received quality ratings of 2b or 3b, grade C recommendation. These papers were based on limited reviews of the evidence, the underlying quality of which was unaddressed, and sensitivity analyses that were limited to one-way analysis.
b) Renal artery stenosis

One study addressing renal artery stenosis met the inclusion criteria, and is summarized in Appendix 5.

Carlos et al. used a decision model to examine the cost-utility of MRA, CTA, or conventional angiography (CA) followed by enhanced medical therapy or stent placement versus enhanced medical therapy without preceding diagnostic testing. All of these treatment options were compared with the natural history of untreated hypertension that is resistant to medication. The authors’ results suggested that all of the strategies are more effective than natural history (i.e., they generate higher QALYs), albeit at higher cost. MRA and CA dominated other strategies, and had ICERs in the $6,000 to $7,000 per QALY range. Compared with enhanced medical therapy alone, the authors suggested that MRA and CTA dominated medical therapy, and CA remained cost-effective with an ICER in the $1,500 per QALY range. The authors concluded that preliminary imaging saved lives compared with enhanced medical therapy alone, and that MRA was the most cost-effective imaging modality. CA remained a cost-effective option too.

This paper received a quality score of 2b or 3b, grade C recommendation. The paper was based on a limited review of the evidence, the underlying quality of which was not assessed, and the sensitivity analysis was limited to one-way analysis.

c) Lung cancer screening

Five studies addressing lung cancer screening met the inclusion criteria, and are summarized in Appendix 5.

Chirikos et al. used a decision model to examine the potential cost-effectiveness of lung cancer screening with low dose helical CT versus no screening. Screening occurred annually for the first five years, and the hypothetical cohorts (screened and unscreened) were followed for 15 years. The base case scenario indicated that screening with yields of 30%, 50%, or 70% localized disease generates ICERs of $90,022, $48,357, and $33,557 per life-year saved respectively. The authors concluded that there is no cost-based reason (relative to the cost of other screening programs) to exclude definitive clinical trials, but noted that to be cost-effective, lung cancer screening would have to detect over 50% of cancers at a localized stage.

Mahadevia et al. used a decision model to assess the cost-utility of helical CT screening versus no screening in populations of current, quitting, and former smokers. The hypothetical cohorts were composed of 60-year-old patients (55% male) with a history of heavy smoking [>20 pack years (i.e., the equivalent of one pack of cigarettes a day for 20 years)]. Screening occurred annually from the age of 60 to 80 years, and patients were followed to the age of 100 years. Assuming a 50% stage shift, the base case results suggested that screening would result in an absolute mortality reduction of 553 per 100,000 (relative mortality reduction of 13%) among smokers, but would be accompanied by 1,186 false-positive results. The ICER associated with screening smokers was $116,300 per QALY. The incremental QALYs associated with screening never exceeded 0.039, and were lower for quitting and former smokers (0.008 and 0.002 respectively). As a result, the ICERs for screening quitting and former smokers were $558,600 per QALY and $2,322,700 per QALY respectively. The authors concluded that screening is unlikely to be cost-effective without significant mortality reductions, high rates of adherence, lower rates of over-diagnosis, and lower costs.
Marshall et al.\textsuperscript{24} used a decision model to examine the effectiveness and cost-effectiveness of low dose helical CT screening versus no screening. The hypothetical cohorts included 100,000 people 60 to 74 years old, who were followed for five years. The screening cohort was screened on a one-time basis (a prevalence screen). Base case results suggested that screening would generate 4,400 incremental life-years at a cost of $5,941 per life-year saved. The authors concluded that there is insufficient evidence to recommend routine population screening, but suggested that their findings indicate screening could be cost-effective.

Okamoto\textsuperscript{25} used a deterministic mathematical model to examine costs and effects for three screening alternatives including CT scanning. The author concluded that CT-based screening for lung cancer represents a future trend, because, although more expensive than chest X-ray, it is more effective.

Wisnivesky et al.\textsuperscript{26} used a decision model to evaluate the cost-effectiveness of screening with low dose CT versus no screening. The hypothetical cohorts included persons $\geq 60$ years old with a $\geq 10$ pack year smoking history. The screened group received a one-time CT scan (a prevalence screen), and it appears that the cohorts were followed for one year. The study indicated direct costs incurred in the first year after diagnosis were considered, and there was no evidence of discounting. Base case results suggested screening would generate 0.10 additional life-years, and have an ICER of $2,500 per life-year saved. The authors concluded screening for lung cancer using CT would be economically efficient, and that the ICER for lung cancer screening using CT compares positively to the ICER values for other screening programs.

The paper by Mahadevia et al.\textsuperscript{23} received a quality score of 2b, grade B recommendation. This was one of two included papers that appeared to satisfy the requirements to receive a 2b level of evidence score. It included the presence of a multi-way sensitivity analysis. The papers by Chirikos et al.,\textsuperscript{22} Marshall et al.,\textsuperscript{24} and Wisnivesky et al.\textsuperscript{26} all received quality scores of 2b or 3b, grade C recommendation. As was typical of all papers receiving such a score, these were based on a limited review of the evidence, the underlying quality of which was not assessed, and all relied on one-way sensitivity analyses. The paper by Okamoto received a quality score of 4, grade D recommendation, because no data sources were cited to support the assumptions made about model parameters.

d) Pulmonary embolism

Four studies\textsuperscript{15,18,27,28} addressing PE met the inclusion criteria, and are summarized in Appendix 5 Table 4.

Adams\textsuperscript{15} reported on two case series, and used the results to conduct a cost-minimization analysis comparing spiral CT, D-dimer assay (DD) plus spiral CT, and ventilation-perfusion (VQ) scanning. The calculations suggested that the effective cost to diagnose a PE using spiral CT, DD plus spiral CT, or VQ scanning alone is £295.41, £156.60, and £786.70 respectively. The author concluded that for reasons of clinical efficiency and cost, VQ scanning should be replaced by DD plus spiral CT.

Doyle et al.\textsuperscript{27} used a decision model to evaluate which of three test or treatment algorithms, combining compression US, VQ scanning, spiral CT, and pulmonary angiography for PE in pregnant women, was most cost-effective, and resulted in the fewest maternal deaths. In a hypothetical cohort of 100 pregnant women or women in the puerperium, the use of spiral CT as the primary diagnostic modality resulted in a cost per life saved of $17,208. Compression US±VQ scan±CT or pulmonary angiography cost $24,404 per life saved, while VQ scan±CT or pulmonary angiography cost $35,906
per life saved. The authors concluded that spiral CT is the preferred diagnostic modality for suspected PE in pregnant women.

Paterson et al.\textsuperscript{18} used a decision model to assess the impact on survival and costs of using spiral CT in the diagnosis of PE. Seven diagnostic algorithms combining VQ scanning, duplex US, spiral CT, and conventional pulmonary angiography were considered with VQ scan±duplex US±angiography being the reference standard. Two algorithms (CT±US, and CT±US±angiography) were associated with the highest expected survival rate (958.2 per 1,000), exceeding the reference standard by 4.5 per 1,000. The least expensive algorithm was VQ scan±US±CT, saving $25 per patient, but it also resulted in a survival decline of 0.30 per 1,000. Compared with the least expensive algorithm, the reference standard had an ICER of $83,333 per life saved while CT±US had an ICER of $70,833 per life saved. The latter algorithm had the most false positives, and the poorest positive predictive value. The authors supported the least expensive algorithm (VQ scan±US±CT), and concluded that CT can replace angiography after non-diagnostic VQ scans and negative US findings.

Perrier et al.\textsuperscript{28} used a decision model to examine the cost-utility of eight diagnostic algorithms. The algorithms combined CT, DD, US, VQ scan, and angiography with VQ scan±angiography being the reference standard. Base case results were presented for the low (10%), intermediate (37%), and high (69%) clinical probability of PE. With low probability, all algorithms were similar in survival (98.6% to 99.1%), but costs varied significantly. The most cost-effective algorithm was DD±US±VQ scan ($845) followed by DD±US±CT ($1,230), which compared with $1,728 for the reference standard. With intermediate probability, the survival ranged from 95.1% to 96.8%. The most cost-effective algorithm was DD±US±VQ scan±CT ($2,674). This algorithm allowed angiography to be avoided in all patients. DD±US±VQ scan±angiography ($2,832) was also cost-effective compared with the reference strategy ($3,164), and required angiograms in 29% of patients. With high probability, the survival ranged from 90.8% to 94.1%. DD±US±VQ scan±CT was the least expensive ($4,308), but was associated with a decline in survival of 0.47%. DD±US±VQ scan±angiography was cost-effective ($4,598) compared with the reference strategy ($4,866). Raising the sensitivity of CT to that of MDCT (>85%) would make DD±US±CT the most cost-effective approach for the intermediate and high probability scenarios, and eliminate the need for angiography. The authors concluded that combining CT with other diagnostic tests for PE can be highly cost-effective.

The paper by Adams\textsuperscript{15} received a quality score of 4, grade C recommendation. This paper, compared with others, addressed a limited number of options, and relied on data from case series. As a cost-minimization study, the paper implicitly assumed that the diagnostic options were equally effective but at different costs. The papers by Doyle et al.\textsuperscript{27} and Perrier et al.\textsuperscript{28} received quality scores of 2b or 3b, grade C recommendation. These studies were based on a limited review of the evidence, the underlying quality of which was not assessed, and relied on one-way sensitivity analyses. The study by Paterson et al.\textsuperscript{18} was the second of two papers to receive a quality score of 2b, grade B recommendation.

**e) Carotid artery disease**

Three studies\textsuperscript{13,14,17} addressing carotid artery disease met the inclusion criteria, and are summarized in Appendix 5.

Berry et al.\textsuperscript{13} used a decision analysis to examine the cost-utility of MRA versus DSA. Parameter estimates for the model were based, wherever possible, on an SR of the literature. The authors concluded that 2D TOF MRA and 3D TOF MRA accurately identify occlusions, and 70% to 99%
stenoses, but not 50% to 99% stenoses. The results suggested that there is little difference in the cost-utility of MRA and DSA. In the base case scenario, MRA yielded 6.89 QALYs and 10-year costs of £5,679.14, while DSA yielded 6.90 QALYs and costs of £5,873.33. While MRA appears to be equally effective at lower cost, the model assumes that the DSA examination costs of £204 include £144 for an in-patient stay. If the procedure can be accomplished without an in-patient stay, then DSA examination costs would be reduced to slightly above 50% of MRA costs.

Buskens et al.\(^\text{14}\) used a decision model to assess the cost-utility of 62 examination or treatment strategies in patients who had had a transient ischemic attack or minor stroke, and were suspected of having significant carotid artery disease. The model was an extension of a published 350-patient, blinded multi-centre prospective consecutive cohort study comparing the accuracy of US and MRA to DSA. The authors concluded that duplex US alone is cost-effective in choosing patients for endarterectomy, and that DSA should not be routinely performed. In the base case, assuming a 50% stenosis threshold for surgery, duplex US cost $2,683 per QALY, and dominated nearly all other strategies. Combining MRA with duplex US was more effective, but prohibitively expensive with an ICER of $1,665,000 per QALY. Assuming a 70% stenosis threshold for surgery, duplex US dominated all other strategies.

Meenan et al.\(^\text{17}\) used a decision model to assess the cost-utility of combinations of MRA, US, and DSA in the evaluation and treatment of newly diagnosed anterior circulation (carotid territory) ischemic strokes. The reference standard was no imaging combined with standard medical therapy including antiplatelet therapy. Model parameters were drawn wherever possible from an SR of the literature. The hypothetical patient cohort was composed of 65-year-old males who had survived acute stroke treatment, and had no indication or contraindication to carotid endarterectomy. The cohort members were followed for their lifetime or 30 years. The base case results indicated that at severe stenosis (>70%) prevalences of ≤0.15, all strategies had ICERs >$250,000 per QALY, and were dominated by the reference strategy. Sensitivity analysis indicated that at prevalences of 0.20, US+DSA confirmation and MRA with direct referral to endarterectomy had ICERs in the $60,000 to $75,000 per QALY range respectively. The ICERs dropped below $50,000 per QALY at prevalence rates of 0.25 and 0.30. The authors concluded that, given the inconsistent results reported in the literature and the poor quality of available studies, it is difficult to determine the most cost-effective strategy for choosing patients for endarterectomy. High quality assessments of US, MRA, and DSA are required.

The papers by Berry et al.\(^\text{13}\) and Meenan et al.\(^\text{17}\) received quality scores of 2a or 3a, grade C recommendation. Well documented SRs were relied on where possible to determine the parameter values for decision models, but the papers were limited by the quality of available studies. The paper by Buskens et al.\(^\text{14}\) received a quality score of 2b or 3b, grade C recommendation. This study was based on a limited review of the evidence, the underlying quality of which was not assessed, and relied on one-way sensitivity analyses.

f) Cerebral aneurysms

Two studies\(^\text{29,30}\) addressing cerebral aneurysms met the inclusion criteria, and are summarized in Appendix 5.

Baba et al.\(^\text{29}\) used a decision model to compare the cost-effectiveness of screening for cerebral aneurysms using MRA versus no screening. Two hypothetical cohorts of one million people each were followed for three years; the frequency of screening was unclear. The prevalence was assumed
to be 2%. CA was performed when the MRA was positive, and in the base case, surgery was assumed to be indicated in 50% of cases. Base case results suggested 11.6 deaths and 346.8 neurologic complications from CA, and 202.4 deaths and 853.6 neurologic complications from surgery, for a total of 283.3 deaths and 1,234.9 neurologic complications in the screened group. There were 153 deaths and 76.5 neurologic complications in the unscreened group. Although the authors presented little in the way of cost data, they noted there is greater cost associated with the screened group. They concluded that screening is not cost-effective, but might become so if the accuracy of MRA were to match that of CA, and if the complications associated with CA and surgery were to decline.

Yoshimoto et al. used a decision model to determine the cost-utility of screening for asymptomatic cerebral aneurysms using MRA. Hypothetical cohorts of asymptomatic 50-year-old patients were followed until death; the frequency of screening was unclear. The prevalence was assumed to be 3%, and analyses were conducted for annual rupture rates of 0.02, 0.01, and 0.005. Surgery was assumed to follow a positive MRA without angiographic confirmation. Base case results indicated that screening produces additional QALYs of 0.0690 and 0.0210 at annual rupture rates of 0.02 and 0.01 respectively. ICERs at these rupture rates were $7,760 per QALY and $39,450 per QALY. At the 0.005 rupture rate, screening reduced QALYs (i.e., screening had a harmful effect). The authors concluded that screening might be cost-effective in populations with high rupture rates, but at low rates, screening could only be cost-effective in the presence of low surgical mortality and morbidity.

The papers by Baba et al. and Yoshimoto et al. received quality scores of 2b or 3b, grade C recommendation. These studies were based on a limited review of the evidence, the underlying quality of which was not assessed, and they relied on one-way sensitivity analyses.

g) Head injuries
One study in this category met the inclusion criteria, and is summarized in Appendix 5.

Af Geijerstam et al. used a decision model to evaluate the cost of CT examinations for mild head injuries, and undertook a cost minimization analysis comparing the results with in-patient observation. The base case results suggested that the cost of immediate CT for mild head injuries (Glasgow Coma Scale 15) is £300 compared with £470 for in-patient observation. The authors concluded that indirect evidence supports immediate CT versus in-patient observation, but noted that a prospective randomized trial is needed to get reliable information about management strategies for mild head injuries. The paper received a quality score of 1b or 2b, grade C recommendation. Although literature was lacking, this paper reflected the features of an SR, and information about aspects such as the search strategy was presented.

h) Acute stroke
Three studies addressing acute stroke met the inclusion criteria, and are summarized in Appendix 5.

Gleason et al. modelled the cost of immediate referral to CT (for a protocol comprising unenhanced CT+head and neck CTA+whole-brain CT perfusion) and non-acute treatment of lacunar or small vessel strokes to usual acute in-patient care. Although unstated, this appeared to be a cost minimization study, as the effectiveness of non-acute versus usual care was not modelled. The base case results suggested savings of $1,695 to $3,568 per case, with most stroke patients discharged...
from hospital one day sooner, and small vessel or lacunar stroke patients diverted to non-acute care. The authors concluded that the proposed CT protocol can have a positive effect.

Wardlaw et al.\cite{16} used a decision model to evaluate the cost-utility of CT scanning for all stroke patients within 48 hours of admission versus 12 alternative strategies (11 involving CT scanning within various time frames, and one no-scan scenario). Hypothetical cohorts of 1,000 70 to 74 year old patients were followed for 24 months. The no-scan option generated QALYs of 1,904.2 and costs of £10,544,000; the reference standard (scan all patients within 48 hours) generated QALYs of 1,982.3 and cost £10,279,728. The lowest cost alternative was to scan all patients immediately, which cost £9,993,676 and generated 1,982.4 QALYs. The lower costs evident in some alternatives were linked mainly to reduced lengths of stay in hospital. Accordingly, the results were sensitive to changes in in-patient per diems. If the cost per patient day fell >10%, then the scan-all-immediately strategy was similar to the reference strategy in terms of cost. The authors concluded that the most cost-effective strategy is immediate CT scanning. A second paper by Wardlaw et al.\cite{33} involved a different group of authors, but reported on the same data and analysis as mentioned.

The paper by Gleason et al.\cite{32} received a quality score of 2b or 3b, grade C recommendation. This study was based on a limited review of the evidence, the underlying quality of which was unassessed, and relied on one-way sensitivity analyses. The papers by Wardlaw et al.\cite{16,33} received a quality score of 2a or 3a, grade C recommendation, as both drew on a documented SR of the literature.

6 HEALTH SERVICES IMPACT

Summarizing the health services impact of the diagnostic interventions addressed in the included studies is challenging. The included studies address multiple technologies and eight clinical conditions. Many of the included economic evaluations produced inconclusive or conflicting results. Furthermore, detailed population level data about disease prevalence, diagnostic algorithms, and costs are lacking, making definitive comments about budget impact impossible. These difficulties aside, the included articles highlight some key trends that have implications for the organization and delivery of health services.

Some of the economic evaluations included in this study focused on new applications for CT and MRI (lung cancer screening, and cerebral aneurysm screening) or optimization of current applications (stroke), but most considered the potential for CT and MRI to replace existing technologies in the diagnosis of specific conditions. The force driving change in diagnostic practice for the conditions addressed in this report, and for many other unaddressed conditions, is the emergence of CT and MRI as first-line imaging modalities.

At one time, CT and MRI were seen as esoteric technologies with technical limitations and costs relegating them to second-line or third-line modalities with specific applications. Advances in computing power and speed have combined to broaden the range of clinical applications for CT and MRI, while reducing the unit costs for examinations. It is widely anticipated that CT and MRI will emerge as the front-line imaging modalities, while others, such as conventional radiography, will decline in use.\cite{34,35}

In terms of impact, it is likely there will be significant growth in demand for CT and MRI installations. At the same time, the indications for CT and MRI are likely to expand, and include new
screening initiatives that are focused on specific or multiple diseases. The substitution of CT or MRI for other imaging technologies and expanding clinical indications suggests the need for additional capital spending and likely operational spending. Operational spending requirements may be compounded in the transition period, when the clinical and cost-effectiveness of CT or MRI for specific clinical indications is unclear or are not better than existing modalities. In the case of screening programs, the non-invasive nature and apparent ease of use of CT and MRI could create challenges for decision makers.

Expanding roles for CT and MRI will have human resource implications. The number of technologists trained in CT and MRI will need to increase, and CT and MRI will have to assume a more central role in training programs. Physicians’ training needs may also be affected. Aside from the training needs associated with the application of CT or MRI to a new indication, there may be issues associated with the transfer of workload across specialties or subspecialties, and the transfer of workload from tertiary to secondary centres. In the latter case, volume and quality dynamics may become important.

7 DISCUSSION

7.1 Principal Findings

This review included 22 economic evaluations examining the use of CT and MRI for eight clinical conditions where the use of CT and MRI had been deemed to be controversial. No economic evaluations met the inclusion criteria for five additional conditions (coronary artery disease, headaches, seizures, AVMs, and urinary tract calculi screening).

- There were three studies on PVD. Two studies compared MRA and DSA (one included duplex US) to one another or to a reference strategy (no imaging work-up+exercise). The third study established target values necessary for CTA to be equivalent to MRA in terms of cost-utility. The studies comparing MRA and DSA found minimal differences in the cost-utility. This suggests that the choice of technologies will depend largely on local availability and clinicians’ preference. All three studies suggested that more clinical trials are required.

- There was one study on renal artery disease. This study addressed CTA, MRA, and CA. The results suggested that for patients with medication-resistant hypertension, MRA and CA are cost-effective. The absolute preference for MRA or CA is unclear. ICER calculations could not be replicated using the QALY and cost data presented. Recalculated ICERs vary from those presented in the study, but seem to support the conclusion that MRA is the most cost-effective imaging strategy, followed by CA.

- There were five studies on lung cancer screening. All of the studies compared CT screening with no screening or with an alternative technology. The conclusions reached by the authors varied significantly. One study stated that screening was unlikely to be cost-effective but left open the possibility that the cost per QALY could drop to $50,000 if a 91% stage shift occurred. A second study concluded that screening would likely be cost-effective only if it can detect >50% of cancers at a localized stage. The authors suggested that clinical trials are required. Two studies suggested that screening would be cost-effective, although one of them cautioned that there is insufficient evidence to recommend population-based screening. Both these studies based their conclusions on models that assumed only a prevalence screen occurs. These models were biased in favour of screening. The fifth study assumed that screening is cost-effective but
offered little evidence to support this presumption. All these studies incorporated unproven assumptions about the impact of screening and were the most hypothetical of the studies included in this review.

- There were four studies on PE. All the studies generally concluded that CT has a role in the diagnosis of PE, and all suggested that pulmonary angiography could be replaced by CT or otherwise avoided. Beyond this, the studies addressing PE displayed differences in their results. Two studies\textsuperscript{15,27} recommended CT in combination with DD, or alone. Another study\textsuperscript{28} concluded that CT alone was inadvisable, because it was consistently associated with lower survival. Two studies\textsuperscript{15,28} relied on DD as an initial diagnostic tool, whereas the other two excluded it as being inaccurate in a particular population (pregnant women)\textsuperscript{27}, or because its inclusion in any of the algorithms assessed would result in more deaths (10 per 1,000).\textsuperscript{18} Two studies\textsuperscript{18,28} stratified patients according to the probability of PE, but arrived at different conclusions about the recommended algorithm(s) (the appropriate tests and their sequencing).

- There were three studies on carotid artery disease. It is impossible to draw any conclusions based on the included studies. The first study\textsuperscript{13} suggested that MRA and DSA are equally cost-effective. The second study\textsuperscript{14} concluded that US alone is the most cost-effective approach. The final study suggested that cost-effectiveness partly depends on prevalence, and at low prevalence rates, no imaging combined with standard medical therapy is most cost-effective. The included studies did not uniformly address the same range of options, did not share common reference standards, and not all presented ICER values. Two studies\textsuperscript{13,17} were SRs that commented on the inconsistent and poor quality of available data.

- There were two studies on cerebral aneurysms. The included studies generally suggested that screening for asymptomatic cerebral aneurysms is not cost-effective. One of the studies\textsuperscript{29} presented little actual cost data, while the other\textsuperscript{30} suggested that cost-effectiveness is highly dependent on assumptions regarding the annual rupture rates for aneurysms, and that at rates of 0.02 and 0.01, screening could be cost-effective. The previous study suggested that screening was not cost-effective, even at high rupture rates. The divergence in results may reflect the fact that the first study stratified the probability of rupture according to aneurysm size, whereas the second appeared to assume uniform aneurysm characteristics and rupture rates.

- There was one study on head injuries. Good quality evidence regarding management strategies for mild head injuries was lacking. Indirect evidence suggested that immediate CT and discharge home in the case of a normal CT saves on costs compared with in-patient observation. Good quality randomized studies addressing the management of mild head injury are required.

- The three studies on stroke suggested that immediate CT scanning has the potential to reduce the cost of stroke care by shortening or avoiding hospital stays. This finding was sensitive to the cost of in-patient care, the availability of non-hospital stroke care, and the ability to capture saved patient-days. The conclusions about cost-effectiveness need to be interpreted cautiously, because it does not appear that the studies considered the costs for non-hospital care, despite the emphasis on avoiding or reducing hospital stays. Costs aside, two of the included articles (reporting the same data)\textsuperscript{36,33} suggested that early scanning is effective (QALYs were increased), but the absolute difference between scanning immediately, within 24 hours, or within 48 hours was minimal (QALY range of 1,982.3 to 1,982.4). The data behind these QALY calculations predated the licensing of thrombolysis in the jurisdiction in question. The absolute cost variation across the three scanning options was more significant at approximately 3%. 

---

CT and MRI for Selected Clinical Disorders: A Systematic Review of Economic Evaluations

---

23
7.2 Study Limitations

One strength of this report is that it involved a rigorous SR of the literature (from 2000 to October 2005) based on a well documented search process. The report focused on areas of interest defined by diagnostic imaging experts, and followed an SR addressing the clinical effectiveness of CT and MRI for the same list of clinical conditions.

The study also had several limitations.

- Three of the 22 included studies could be characterized as trial-based economic evaluations. Two others represented extensions of previous trials involving the same authors. All the studies relied on decision models, which may not accurately reflect reality. Buxton et al., who are experts in economic evaluation, noted that modelling is unavoidable, but the lack of trial-based economic evaluations, given the conditions and time frame of interest, was surprising. While the studies provide decision makers with valuable information, especially when the studies pertaining to a particular condition are viewed together, the lack of trial-based evaluations is a reason to proceed cautiously. Although the included studies often spoke authoritatively in terms of their conclusions, more than a third identified a need for more clinical trials to augment parameter estimates or confirm results.

- Assessing the quality of included studies was difficult, and likely overstated the quality. Five included studies were SRs, and all expressed reservations about the quality of available data. For example, Wardlaw et al. criticized the imaging literature as poor and biased. It seems unlikely that non-SRs would overcome such a challenge, but the balance of the included studies offered little information about how parameter estimates were identified, the characteristics of underlying studies, or the quality of those studies. This impeded definitive categorization of the included studies according to the levels of evidence in the CEBM scale. As a result, most studies were assessed as falling into one or the other of two levels of evidence, most often 2b or 3b (12 of 22 studies).

- The literature capture focused on 1999 onward to reflect current technology. This eliminated older studies, and might have contributed to the absence of studies on five conditions. It is questionable whether the included studies actually reflect current technology. Most of the studies relating to CT considered the older single detector machines, while one study mentioned MDCT only in the context of the sensitivity analysis. CE-MRA also received little attention.

- A small group of experts determined, by consensus, the clinical conditions identified as controversial. Other areas that are worthy of consideration may have been overlooked. The list of conditions considered was large. This served to limit the analysis associated with any one condition.

- There are inherent limitations in cost-effectiveness analyses that affected this review and its conclusions. By focusing on a specific question, cost-effectiveness analyses ignore the competing priorities confronting the health system. As a result, they ignore the opportunity costs associated with a particular course of action, by assuming that there is a pool of resources available for deployment or redeployment. In that sense, they may provide inappropriate guidance. Even where the guidance is appropriate, it may be incomplete, because most cost-effectiveness analyses will not define the budget impact of a change in practice at a regional or another level.

- The included cost-effectiveness analyses were prepared in varied jurisdictions, at varying times. Differences in health systems and unit costs may limit the utility of results, and when combined with dissimilar time frames, make the conversion of foreign currency amounts to Canadian dollars difficult or inaccurate.
7.3 Generalizability of Findings

If economic evaluations were designed to address specific problems for specific decision makers and jurisdictions, generalizability might not be an issue. Most studies included in this review made no comment on the generalizability of their findings. Conclusions were often presented in such a way as to suggest that the results have universal application. This perception is compounded when studies addressing a topic are read in isolation from one another. Many factors can raise concerns about the generalizability of findings.

7.3.1 Comparison to other studies

Few studies compared their findings to those of previous studies, although such a comparison could lend credence to study results. It is possible for this review to compare the results of included studies addressing a common condition (for those conditions where there was \(>1\) economic evaluation) and also to compare them with the results of the companion SR on the clinical effectiveness of CT and MRI. This latter comparison is constrained by the fact that most of the clinical SRs focused on intermediate endpoints associated with technological performance (e.g., sensitivity and specificity), whereas the studies included in this report tend to focus on outcomes. Also, the studies included in the two reviews did not necessarily address identical questions.

a) PVD
The clinical SR reflected favourably on MRA, especially gadolinium-enhanced 3D techniques, and suggested that MRA performed well in comparison to DSA. The studies in this review are generally consistent with the clinical SR results and with each other. The economic evaluations suggested, however, that there is a minimal difference between MRA and DSA in terms of cost-effectiveness.

b) Renal artery stenosis
The clinical SR suggested that the performance of gadolinium-enhanced MRA was impressive, but expressed concerns about cost-effectiveness. This review identified one relevant economic evaluation, and it suggested that MRA and DSA are cost-effective, with MRA being the most advantageous.

c) Lung cancer screening
The clinical SR acknowledged the capabilities of CT for detecting small lesions, but noted the lack of evidence supporting a link between early detection of lung cancer and reductions in mortality. Screening was unsupported on clinical grounds. The economic evaluations arrived at inconsistent conclusions. Three studies suggested that lung cancer screening would be cost-effective, although one concluded that it is too early to recommend routine population screening. Two other studies suggested that CT screening for lung cancer could be cost-effective, but that this probability was unlikely.

d) PE
The clinical SR was cautious, but suggested that CT and MRI could have a role in the work-up of patients who are suspected of having PE. The economic evaluations did not address MRA, but they endorsed a role for CT. The economic evaluations, however, were inconsistent in their assessment of the relative reliance to be placed on CT versus other technologies.

e) Carotid artery disease
The clinical SR suggested that MRA and CTA are effective in cases of severe stenosis (\(\geq 70\%\)), but expressed concerns about cost-effectiveness. None of the economic evaluations included in this review addressed CTA. Included studies were inconsistent in their results. One study supported the
clinical SR findings regarding MRA, but there was little difference in the cost-effectiveness of MRA versus DSA. The remaining studies suggested that other strategies might be more cost-effective than MRA or DSA.

f) **Cerebral aneurysms**
The clinical SR suggested that CTA and MRA performed well but could not replace angiography. The economic evaluations did not address CTA, and were inconsistent in their treatment of MRA. One model assumed that positive MRA results always required subsequent angiography, while the other assumed that only MRA was required.

g) **Head injuries (mild)**
The clinical SR generally confirmed the effectiveness of CT, but its routine use in the case of mild head injuries was controversial. The sole economic evaluation suggested that CT for mild head injury is cost-effective compared with in-patient observation.

h) **Stroke**
The clinical SR suggested that CT is effective. The economic evaluations generally supported this conclusion.

The comparisons of the clinical SR findings and the findings of this review are limited. The clinical SR provided full details about the included studies and their quality, and should be consulted if a comparison of results is desired. The greatest consistency between the clinical SR findings and the findings of this review seem to relate to the role of CT and MRI in the diagnosis and management of PVD and stroke. For other conditions, there is too little material for comparison (renal artery stenosis and head injuries), or there is too much variation in the findings of the included economic reviews (lung cancer screening, PE, carotid artery disease, and cerebral aneurysms). Hence, the opportunity for generalization of results appears limited, based on a comparison of studies.

### 7.3.2 Other considerations with respect to generalizability

In several included studies (addressing PVD, carotid artery disease, and stroke) concern was expressed about the quality of available data, and the impact that this might have on the validity of study results. A significant number of included studies (addressing PVD, lung cancer screening, carotid artery disease, head injuries, and stroke) identified a need for additional trials to augment data or confirm results. Two studies (addressing PVD and carotid artery disease) included caveats regarding imaging skills and experience. Berry et al. indicated that their results are valid only for high quality imaging studies and suggested that cost-effectiveness in regular practice will require practice guidelines, training, accreditation processes, and technical performance standards for equipment. Buskens et al. noted that trial-based estimates are generally better than those achieved in routine practice, and suggested that cost-effectiveness will be partly driven by local considerations about diagnostic and treatment strategies. Although statements about data quality, the need for trials, and caveats about local skill and experience imply caution in generalizing results, few studies addressed the issue.

Wardlaw et al. offered the most comprehensive comments regarding generalizability of results. They indicated that their cost data are transferable in the UK, with the possible exception of London. In their view, large portions of their stroke data should be relevant beyond the UK. Their outcome data, however, come from a centre with an organized stroke care program, and may not reflect routine experience. Four studies (addressing lung cancer screening, PE, carotid artery disease, and
stroke) noted that local and regional cost differences might affect results. One study tried to address this issue. Paterson et al. used Canadian costs in their base case analysis, but used United States figures as the upper limit for costs in their sensitivity analyses. Results were sensitive to the cost of diagnostic tests, and the cost relations between testing options that varied across the two jurisdictions (VQ scans were half the cost of CT in Canada but a third more expensive than the cost of CT in the United States).

Sculpher et al. developed checklists for assessing the generalizability of trial-based economic evaluations and model-based economic evaluations:

1. Are the decision problem, the relevant settings, and audiences (i.e., decision makers) specified?
2. Does the overall analytical approach incorporate the relevant perspectives (i.e., health service or societal) and relevant objective functions (i.e., maximizing health gain)?
3. Are the data used to populate the model relevant to the target audiences (i.e., decision makers) and settings?
4. Where data from different sources are pooled, is this done in such a way that the uncertainty relating to their precision and possible heterogeneity is adequately reflected?
5. If data from other settings are used, have these been assessed for relevance in the settings of interest?
6. Is uncertainty (i.e., parameter uncertainty and heterogeneity) adequately reflected in the model?
7. Are results reported in such a way that allows assessment of the appropriateness of each parameter input and each assumption in the target settings?

Most of the studies included in this review addressed a defined clinical condition, but were less clear about the setting and intended audience. The analytical approach was conventional and would be appropriate in most instances, provided decision makers are mainly interested in direct medical costs only. Some anomalies were noted regarding included costs and discounting (Appendix 5). With the exception of five SRs, most of the included studies apparently based their parameter estimates on limited literature reviews. The relevance of these estimates across settings was typically unaddressed. As noted by Sculpher et al., it seems that most studies “…made more effort to ensure that their cost inputs were specific to their target jurisdiction than their effectiveness parameters.” (page iii) All the studies included sensitivity analyses; two performed multi-way sensitivity analyses. Overall, the studies provided interesting information, but opportunities for generalization seem limited.

7.4 Knowledge Gaps

There is little evidence that the decision models in the included studies were subject to a validation process. While there may be debate as to how models can or should be validated, an apparent lack of validation combined with limited literature reviews is problematic for decision makers. Decision makers should look at the included studies, and consider how the results may vary if adjusted for local circumstances. There are knowledge gaps that make this difficult.

Two included studies were Canadian in origin with respect to the lead author, and one used Canadian costs. Paterson et al. used Canadian cost figures (from one hospital) in their base case analysis, and United States cost figures in their sensitivity analysis. Two issues flow from the lack of Canadian representation in the included studies, and from the costs presented by Paterson et al. What is the impact on study results if Canadian costs are used, and what is the true or full cost that should be used in analysis? The second question affects the first, and is more immediately problematic. Most of
the studies included in this review included direct medical costs and ignored other costs. One study did try to examine cost-effectiveness from the perspective of direct medical costs and societal costs.\textsuperscript{21}

The focus on direct medical costs would satisfy many decision makers, although presentation of a separate analysis using societal costs could prove informative. Presenting societal costs in a manner that is useful for decision makers remains difficult in light of the reliance on proxy measures. The study by Paterson \textit{et al.}\textsuperscript{18} highlights a credibility issue in relation to direct medical costs. While cost differences for diagnostic examinations might be expected across jurisdictions, the relative cost relationship between examinations would be expected to remain constant. For example, VQ scans and CT scans may be more expensive in the United States compared with scans in Canada, but which is cheaper would remain the same. Paterson \textit{et al.}\textsuperscript{18} found that this did not hold true for VQ scan and CT. In Canada, a VQ scan reportedly costs half of what a CT scan costs, whereas in the United States, a VQ scan costs a third more than a CT. Identifying true costs remains a problem area for cost-effectiveness analysis.

A related issue is the nature of costs (e.g., fixed, semi-fixed) and the implications this has, particularly for estimates of savings that are incorporated into cost-effectiveness analyses. There is a tendency to treat many costs as variable when they are semi-fixed. For instance, the studies addressing stroke partly relied on reductions in hospital stays, to arrive at conclusions about the cost-effectiveness of CT. Such “savings” are difficult to capture, and while their incorporation into cost-effectiveness models may be technically correct, it is operationally problematic. An understanding of local cost-functions is essential, but such information is difficult to acquire.

While researchers try to ensure that costs reflect the situation in a given jurisdiction, it is often assumed that other data (e.g., epidemiological, effectiveness) are universally applicable. Trial-based data, however, if applicable to the local population, may be different, at least in the short term, from routine practice. Local decision makers often face challenges in obtaining data that may provide basic information on clinical aspects such as the prevalence of disease and use of diagnostic algorithms. This makes it difficult to assess a model’s relevance.

A serious gap faced by some decision makers relates to the narrow perspective that cost-effective analyses provide, especially in light of constrained resources, and the fact that new techniques do not always fully replace older ones. A cost-effectiveness analysis comparing diagnostic imaging modalities is useful, but it ignores the presence of competing priorities. Ideally, decision makers could choose from opportunities that are known to be most effective. In practice, decision makers are typically forced to consider opportunities in isolation from other priorities.

8 CONCLUSION

The indications for CT and MRI, and their performance compared with earlier generations of the same technologies, are advancing faster than the available literature. As a result, this report may be dated in some areas. Years after CT and MRI techniques have been first advocated or come into use, it remains difficult to find high quality studies that address their use. For this report, no studies were found that addressed the cost-effectiveness of CT and MRI for coronary artery disease, headaches, seizures, AVMs, or urinary tract calculi screening.

The studies included in this report suggest that CT and MRI are cost-effective in the investigation of
some controversial clinical conditions (especially PVD and stroke), but not necessarily more
effective or cost-effective than traditional alternatives (for PVD). For other clinical conditions, there
is evidence of cost-effectiveness, but it is limited (renal artery stenosis, mild head injuries). The
evidence for cost-effectiveness of CT and MRI for lung cancer screening, PE, carotid artery disease,
and cerebral aneurysms is equivocal or conflicting.

Regardless of the actual or perceived utility of CT and MRI, there remains a need to document their
effectiveness and cost-effectiveness in specific areas of clinical practice.

9 REFERENCES

1. European Commission. Referral guidelines for imaging [Radiation protection 118].
   Jan 21).

   Multisection CT: scanning techniques and clinical applications. Radiographics

   selected clinical disorders: a systematic review of clinical systematic reviews [Technology
   report no 59]. Ottawa: Canadian Coordinating Office for Health Technology Assessment;

4. The AGREE Collaboration. Appraisal of guidelines for research & evaluation (AGREE)


6. Canadian Association of Radiologists. Outdated radiology equipment: a diagnostic crisis

7. Ontario Ministry of Health and Long-Term Care. Schedule of benefits: physician services
   Available:
   http://www.health.gov.on.ca/english/providers/program/ohip/sob/physserv/physserv_mn.html

8. Age profile of medical devices in Europe: the need for sustained investment! COCIR News
   24).


APPENDICES

Available from CADTH’s web site
www.cadth.ca