Canadian Agency for Drugs and Technologies in Health

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HTA
HEALTH TECHNOLOGY UPDATE

A newsletter on new and emerging health care technologies in Canada

Scanning the Horizon

Informing Decision-Makers About Emerging Medical Technologies, Policies, Practices, and Research

Welcome to the eleventh issue of *Health Technology* Update. This second newsletter of 2009 brings you information on a variety of medical technologies.

The issue's feature article addresses the current global crisis in isotope production in medical imaging. New and emerging technologies and practices are currently being identified that may play a role in providing alternative solutions to molybdenum-99, the medical isotope that is currently in short supply.

The solutions explored are those that could be adopted within a five to ten year time frame. We also bring you an update on the expanding distribution of positron emission tomography or PET scanners in Canada; PET imaging is one of several alternatives to isotope use.

Additionally, this issue provides a cross-section of emerging genetic tests, and we look at a group that supports the development and implementation of an evidence-based process for evaluating genomic applications.

In this issue

We want your feedback... Tell us what you think

Health Technology Update is a source of information for those involved in planning and providing health care in Canada. Did we hit the mark in our efforts to bring you information on medical technologies and issues in practice and policy, as well as the HTA research used to make decisions? Tell us what you think. Send your comments to Andra Morrison at andram@cadth.ca.

CADTH President and CEO Recognized Internationally

Dr. Jill M. Sanders, President and Chief Executive Officer of the Canadian Agency for Drugs and Technologies in Health, will contribute to the leadership of two renowned international Health Technology Assessment organizations.

Dr. Jill M. Sanders

Effective June 22, 2009, Dr. Sanders was elected as Vice-President of the Health Technology Assessment International (HTAi) board for a two-year term. HTAi is an international society for the promotion of health technology assessment. Dr. Sanders was a member of the HTAi Founding Board of Directors and served as a Director from 2003 to 2008. As Vice-President, she is positioned to become President of HTAi in 2011.

Effective June 23, 2009, Dr. Sanders was also elected as Chair of the International Network of Agencies for Health Technology Assessment (INAHTA) for a two-year term. A non-profit organization, INAHTA provides a forum for HTA agencies around the world to identify and pursue common interests. INAHTA has 50 member agencies from approximately 25 countries.

Find out more about these two organizations at their websites:

Health Technology Assessment International: http://www.htai.org/.

International Network of Agencies for Health Technology Assessment: http://www.inahta.org/.

Future Alternatives to Molybdenum-99 (Mo-99) Production for Medical Imaging

International governments and the nuclear imaging industry have focused their attention on the need for reliable contingency plans for medical isotope production.

There are current shortages in international supplies of technetium-99m (Tc-99m), the isotope used in more than 80% of diagnostic applications. The investigation into alternatives to Tc-99m has become a top priority. The repeated shutdown of Canada's aging Chalk River nuclear reactor that produces molybdenum-99 (Mo-99) — from which Tc-99m is derived — and the recent announcement of its permanent closure by 2016, has fuelled the need to find alternative solutions in medical imaging, as has the subsequent cancellation and delay of diagnostic testing throughout Canada and the US. Only five other reactors in the world produce Mo-99 and some of these are experiencing the same age-related problems as the Canadian facility.

Canada produces approximately half the world's supply of Mo-99[1] and the US imports approximately 50% to 80% of its supply from Canada. The derivative Tc-99m plays an important role in the diagnosis and treatment of conditions such as heart disease and cancer. Tc-99m has a half-life of approximately six hours, so it cannot be inventoried as a precautionary measure when reactors shut down.

Plans to develop alternative solutions that would ensure security of supply were initially halted because two new Canadian reactors were being built as dedicated suppliers of the entire global demand for Mo-99.[1] However, in early 2008, the construction of these reactors was discontinued. At that time, there were no facilities in the US that manufactured commercial quantities of Mo-99.[1]

Long-term solutions for the disruption to the continuous and reliable supplies of Tc-99m fall into three broad categories:

- the building of new, or the modification of existing, nuclear

reactors and accelerators to produce medical isotopes
- the development of alternative isotopes that do not rely on existing nuclear reactor and accelerator infrastructures
- a reliance on new and emerging medical imaging devices that bypass the need for Tc-99m.

Table 1 summarizes these technologies and their development status.

TABLE 1: Investigational, Emerging, and Available Technologies for Medical Imaging

Alternative	Technology Description	Status (Investigational[1]/ Emerging[2]/Available)
Nuclear reactor/ accelerator	Revive existing	Available
	Photo-fission accelerator	Investigational
	Aqueous homogeneous	Investigational
	Neutron beam	Investigational
	Neutron reactor	Investigational
Medical imaging	PET/CT	Available
	PET/MRI, SPECT/CT, PEM, D-SPECT	Emerging
	SPECT/MRI	Investigational
	Photo-acoustic	Emerging
	CT/MRI/3-D, image-guided cell therapy	Investigational
Alternative isotope tracers	SPECT tracers: I-123 MIBG, I-123 BMIPP for thyroid disease imaging	Emerging
	PET tracer: BMS747158	Emerging
	SPECT tracer: RAFT-RGD, radio-iodinated compounds	Investigational
	SPECT tracer: Tl-201 tracer. Replaces Tc-99m tetrofosmin (Myoview) and Tc-99m sestamibi for cardiac perfusion imaging	Available
	F-18 Fluorine PET tracer. Replaces Tc-99m MDP as bone-imaging agent	Available

BMIPP=p-iodophenyl-3-(R,S)-methylpentadecanoic acid (I-123 BMIPP); CT=computed tomography; MDP=Medronate; MIBG=metaiodobenzylguanidine; MRI=magnetic resonance imaging; PEM=positron emission mammography; PET=positron emission tomography; RAFT-RGD=regioselectively addressable functionalized template (arginine-glycine-aspartic acid); SPECT=single photon emission computed tomography

[1]Technology that is either at the conceptual stage, anticipated, or in early stages of development, through to a technology that is undergoing bench or laboratory testing.

[2] Technology that has not yet been adopted into the health care system, usually in phase 2 or 3 of clinical trials or pre-launch. The time horizon is 0 to 5 years before that introduction into the health care system.

Nuclear Reactors and Accelerators: New and Existing Facilities

Inspired by the ongoing and unscheduled disruption of the supply of medical isotopes, a number of international companies are setting up long-term contingency plans.

In April 2009, MDS Nordion — Canada's radioisotope production facility — and TRIUMF — Canada's national laboratory for particle and nuclear physics — announced a collaboration to study commercially viable and reliable supplies of Mo-99 using photo fission-based accelerator technology. More recently, MDS Nordion announced a partnership with the Moscow-based Karpov Institute of Physical Chemistry to supply reactor-based Mo-99.

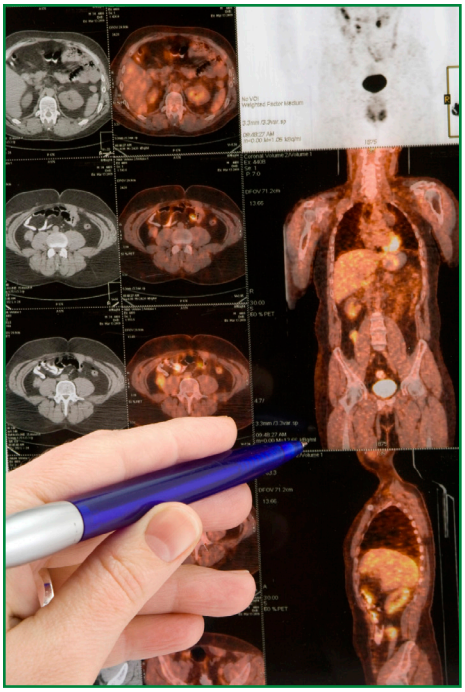
In June 2009, the Canadian government committed $22 million for infrastructural upgrades to a McMaster University nuclear reactor. The funding will help, in part, to increase Canadian production of medical isotopes. Production at this reactor could begin within 18 months.

Advanced Medical Isotope Corporation (AMIC), a US company, is working in collaboration with a number of universities toward launching compact generator systems and developing and implementing proprietary devices to produce short-lived, as well as longer-lived, isotopes. Over the next two to three years, AMIC plans to produce 13 different isotopes in regional facilities across the US.

In January 2009, AMIC and the US Department of Energy partnered on

a two-year project with the Kharkov Institute of Physics and Technology in the Ukraine to develop and market compact systems technology for producing medical isotopes.

Also in January 2009, Babcock & Wilcox, an energy technology supplier, signed an agreement with Covidien, a health care products company, to develop solution-based reactor technology for manufacturing Mo-99. Production will use aqueous homogenous reactor technology utilizing low-enriched uranium. This facility could potentially supply 50% of the US market and could be operational by 2012.



In May 2009, Positron Systems and the Idaho State University collaborated to manufacture Mo-99 with proprietary particle accelerator-based technology. Commercial Mo-99 production could start within two to three years at the site.

SNM, an international organization promoting nuclear medicine, recently set up a task force to look at potential domestic supply solutions to medical isotopes in the US. The task force examined the possibility of reviving domestic production of Mo-99 at facilities like the University of Missouri Research Reactor Center in Columbia, Missouri. Production of Mo–99 at this site could begin in 2012 and could potentially meet approximately 50% of the current market demand.

In 2008, URENCO, a manufacturer of enriched uranium, and the Delft University of Technology in the Netherlands collaborated to patent a new technique to produce Tc-99m that does not require a high neutron influx reactor.

Molecular Imaging Solutions

PET scans in Canada

Positron emission tomography or PET is a diagnostic imaging alternative that does not require Tc-99m. Instead, PET uses isotopes that are produced locally in cyclotrons. While there are publicly funded PET scanners across Canada, the necessary infrastructure is not currently sufficient for PET to replace the work of Tc-99m isotopes for heart ailments, and cancer diagnosis and staging. In addition, up until July 2009, PET was only accessible via clinical trials for specific cancers in Ontario or via individually approved access through the Ontario PET Registry Program. Ontario has now made PET scanning a publicly insured health service available to cancer and cardiac patients under conditions where PET scans have been proven to be clinically effective. The Ontario Ministry of Health and Long-Term Care has also committed a one-time funding of $1.4 million to produce an alternative PET isotope during the current isotope crisis.

As of July 2009, there were 28 centers performing publicly funded scans in seven Canadian provinces. Access to PET scans is greatest in Quebec, with a total of 11 PET/CT (computed tomography) scanners performing clinical scans in the province. Ontario also has 11 PET/CT which will start performing publicly insured scans in October 2009. Saskatchewan, Prince Edward Island, and Newfoundland and Labrador have no facilities and residents are expected to travel out of province for a PET scan. Newfoundland and Labrador, however, is expected to have a PET/CT scanner in operation within the next three to four years. The status of publicly funded Canadian PET scans and cyclotrons is shown in Table 2.

SPECT and PET hybrids and other molecular imaging solutions

Recent advances in technology have combined PET and single photon emission computed tomography (SPECT) with CT. The main benefit of these combined modalities is increased performance in resolution and sensitivity.

The development of hybrid imagers originated with PET/CT. While PET alone evolved slowly as an imaging tool relative to other imaging modalities, PET/CT has become the clinically preferred technology for PET imaging. None of the major manufacturers currently offer stand-alone PET scanners for commercial sale.[2]

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TABLE 2: Location of Publicly Funded PET Scanners and Cyclotrons in Canada (2009)*

Province	Hospital or Centre	City	Type (Number of Scanners)	Number of Cyclotrons	Additional Information
British Columbia	BC Cancer Agency	Vancouver	PET/CT (1)	1	TRIUMF cyclotron operates principally for research
				1 (anticipated)	New on-site cyclotron and radiopharmaceutical lab expected to be operational in November of 2009
Alberta	Cross Cancer Institute	Edmonton	PET (1; used for research only) PET/CT (1)	1	
	University of Alberta Hospital	Edmonton	PET/CT (1)		FDG obtained from Cross Cancer Institute
	Foothills Hospital	Calgary	PET/CT (1)		FDG obtained from Cross Cancer Institute
Manitoba	Health Sciences Centre	Winnipeg	PET/CT (1)	1 (anticipated)	New on-site cyclotron expected to be operational in the summer of 2009
Ontario	Hamilton Health Sciences	Hamilton	PET (1)	1	
	St. Joseph's Healthcare Hamilton	Hamilton	PET/CT (1)		
	The Ottawa Hospital	Ottawa	PET/CT (1)		
	University of Ottawa Heart Institute	Ottawa	PET/CT (1)	1	
	Centre for Addiction and Mental Health	Toronto	PET (1) PET/CT (1) (both scanners used for brain research, only)	1	
	Princess Margaret Hospital	Toronto	PET/CT (2) PET/CT (1) (used for research only)	1 (anticipated)	New on-site cyclotron expected to be operational in late 2009
	Sunnybrook Health Sciences Centre	Toronto	PET/CT (1)		
	St. Joseph's Health Care	London	PET/CT (1)	1 (anticipated)	New on-site cyclotron expected to be operational in the summer of 2009
	Hospital for Sick Children	Toronto	PET/CT (1)		
	Thunder Bay Regional Health Sciences Centre	Thunder Bay	PET/CT (1)		
Quebec†	McGill University Health Centre (Montreal General Hospital)	Montreal	PET/CT (1)		FDG obtained from cyclotrons at the Montreal Neurological Institute and Hospital, and Université de Sherbrooke Hospital
	Hôtel-Dieu Hospital (Centre hospitalier de l'Université de Montréal)	Montreal	PET/CT (1)		FDG obtained from privately owned cyclotron (Pharmalogic PET Services, Montreal)
	Hôtel-Dieu Hospital (Centre hospitalier universitaire de Québec)	Quebec City	PET/CT (1)		
	Université de Sherbrooke Hospital	Sherbrooke	PET/CT (1)	1	Current cyclotron operates principally for research. Second on-site cyclotron planned for 2010
	Jewish General Hospital	Montreal	PET/CT (1)		FDG obtained from Pharmalogic PET Services, Montreal
	Hôpital Maisonneuve-Rosemont	Montreal	PET/CT (1)		
	CHU Sainte-Justine Hospital	Montreal	PET/CT (1)		
	Centre hospitalier régional de Trois-Rivières	Trois-Rivières	PET/CT (1)		
	Centre de santé et de services sociaux de Rimouski-Neigette	Rimouski	PET/CT (1)		
	Centre de santé et de services sociaux de Chicoutimi	Chicoutimi	PET/CT (1)		
	Centre de santé et de services sociaux de Gatineau	Gatineau	PET/CT (1)		
New Brunswick	Saint John Regional Hospital	Saint John	PET/CT (1)	FDG supplied by Sherbrooke cyclotron	Another PET/CT scanner anticipated to be operating at the Dr. Georges-L. Dumont Regional Hospital in Moncton by late 2010 or early 2011
Newfoundland and Labrador			PET/CT (1)anticipated	1 (anticipated)	Expected to be operational by 2012 or 2013
Nova Scotia	Queen Elizabeth II Health Sciences Centre	Halifax	PET/CT (1)	1 (anticipated)	New on-site cyclotron anticipated to be operational in 2010

CT=computed tomography; FDG= 2-Deoxy-2-[18F]fluoro-D-Glucose; PET=positron emission tomography
*The information provided here is based on communications with health care officials in corresponding jurisdictions.
† Quebec also funds PET scanners used for research purposes at the following centres: Montreal Neurological Institute (two PET scanners), Montreal's Notre-Dame Hospital (one PET/CT scanner), and Université de Sherbrooke Hospital (one PET/CT scanner).

Canada has experienced slower uptake of PET. This is believed to be because of the need to more thoroughly evaluate its suitability for particular clinical applications, given PET's high capital and operating costs.[3] PET/CT is gaining faster acceptance in Canada than stand-alone PET.

The most important application of PET and PET/CT is in oncology;[3] this is because whole body imaging is used to identify primary cancer sources and scan for metastatic disease. In comparison, SPECT is more focused on organ function.[3]

The most important application of SPECT and SPECT/CT is in cardiology. Approximately 60% of SPECT/CT procedures are in this field. However, orthopedics, oncology, and infection imaging are other areas that drive utilization of SPECT/CT.[4]

While PET is a rapidly growing area of nuclear medicine, SPECT still constitutes the majority of nuclear radiologists' workload; thus, the potential market for SPECT/CT could be larger than that for PET/CT. The equipment and pharmaceutical costs are lower with SPECT and SPECT/CT.[4]

Despite the rapid uptake of hybrid nuclear imaging, there are some drawbacks to the use of CT as a complementary anatomical imaging modality. First, CT exposes patients to ionizing radiation. Second, CT provides relatively poor soft tissue contrast in the absence of oral and intravenous iodinated contrast.[2] MRI, on the other hand, offers the potential to provide more structural detail than CT scans, especially when imaging soft tissue. MRI does not expose the patient to ionizing radiation,[5] and it can provide more progressive functionality, such as diffusion and perfusion imaging, as well as spectroscopy.[2]

PET/MRI technology combines the soft-tissue contrast, high specificity, and structural detail of MRI, together with PET's sensitivity in assessing physiological and metabolic status.[3] It is speculated that technological evolutions of PET/MRI may replace PET/CT as the molecular multimodality imaging platform of choice for cancer, neurologic, central nervous system, and metabolic disorders. In addition, PET/MRI could help verify the efficacy of certain drugs by enabling clinicians to observe how drugs travel through the body.

While the technology required to combine PET/MRI is still in development, PET/MRI will be ready for widespread clinical use within the next decade.[6] Due to advancements in solid-state gamma camera technology, SPECT/MRI is also on the horizon, but is still in its early stages of clinical development.[6]

D-SPECT is a novel SPECT system for nuclear cardiology. D-SPECT technology allows cross-sectional images of the heart using advanced solid state detectors.[7] D-SPECT has the potential to offer better energy resolution and higher sensitivity than conventional dual-headed SPECT cameras,[8] thereby decreasing radiation dose or imaging time, and open the door for the development of entirely new tracers.[8]

Positron Emission Mammography (PEM) — an organ-specific, high resolution PET scanner — is also on the horizon. PEM is affected neither by either breast density or a woman's hormonal status, two factors that limit the cancer detection effectiveness of both standard mammography and MRI.[9] This technology is in its infancy, but preliminary reports are promising for the detection of ductal carcinoma in situ (DCIS). No imaging device is currently able to accurately image DCIS, unless it happens to be associated with pleomorphic calcifications seen on mammography. In addition, further refinements, including combining PEM with tomographic acquisition (using rotating detectors), have the potential to improve its diagnostic capabilities compared with the technology based on stationary detectors. While further refinements to the technology are needed, it is believed that its potential to detect early breast cancer is significant.[10]

Photo-acoustic imaging

Photo-acoustic imaging is a hybrid imaging modality. A photo-acoustic image is formed by irradiating tissue with pulses of nanosecond laser light, which induces the transient thermoelastic expansion of the tissue. A wideband ultrasonic wave is emitted that can be detected by an ultrasonic receiver. These waves are then converted into high-resolution, 3-D images of tissue structure.

It is believed that photoacoustic imaging may be useful in a number of clinical settings, and could play an important role in the future of mammography as a mass screening alternative to current gold standards.[11,12]

Other hybrid imaging technologies

Canada's Lawson Health Research Institute is currently investigating the plausibility of combining prostate cancer images using CT, MRI, 3-D ultrasound, and nuclear medicine techniques to create

a single technological platform to predict the location of cancer within the prostate. This research is intended to advance patient care in prostate cancer diagnosis and it may have applications for many other types of cancer.[13]

The European Institute for Biomedical Imaging Research (EIBIR) is working on a project called ENCITE — the European Network for Cell Imaging and Tracking Expertise. This project is focused on in vivo image guidance for cell therapy and on the development and testing of new MRI imaging methods and biomarkers. Currently, there is no single imaging modality that meets the requirements of cell therapy. It is predicted that these technologies will eventually be used for the treatment of cancer, cardiovascular diseases, and diabetes.[14]

The Future of Radiopharmaceutical Tracers

There is ongoing interest in developing more easily available and cheaper isotopes. While alternatives to Tc-99m, SPECT's most important tracer, are sought because of continued disruptions in their supply, alternatives to FDG, PET's most important tracer, are also in demand because they are expensive and difficult to process.

Clinical trials will soon be completed for two new I-123-labeled tracer agents. Metaiodobenzylguanidine (I-123 MIBG) is for imaging the sympathetic nervous system of the heart, and p-iodophenyl-3-(R,S)-methylpentadecanoic acid (I-123 BMIPP) for imaging fatty acid metabolism and for use in the emergency department as an evaluation tool for patients who present with episodes of chest pain. The latter tracer, I-123 BMIPP, is marketed as Zemiva™ and can directly link symptoms to true cardiac tissue ischemia.[15] The University of Ottawa's Heart Institute is working on tracer development, while MDS Nordion has helped fund a new lab to focus on early stage characterization of tracers.

MDS Nordion, TRIUMF, and the University of British Columbia recently announced a three-year research and development partnership to develop new diagnostic tracers. The technology will be based on combining select radiometals with newly developed chelates.

There now exists a new positron emission tomography (PET) Fl-18-labeled perfusion tracer, BMS747158. This is a mitochondrial complex 1 inhibitor, which may allow the use of exercise stress — which, up until now, has not been possible with existing PET perfusion tracers.[16]

RAFT-RGD or regioselectively addressable funtionalized template (arginine-glycine-aspartic acid) is another new tracer in development, intended to provide better information about tumour development. It is currently being evaluated for SPECT molecular imaging of new blood supply to tumours. Another new tracer agent for SPECT imaging of the noradrenaline and peripheral benzodiazepine receptors is also in development. This project involves radioiodinated compounds for SPECT imaging of neurological receptors that are implicated in a range of neurological disorders such as clinical depression, Parkinson's disease, Alzheimer's disease, anxiety, and stroke.

Thallium-201 is already being used for cardiac perfusion as a replacement SPECT tracer and F-18 fluorine, a PET tracer, is an alternative bone imaging agent to Tc-99m.

While the technologies identified here have the potential for future adoption, it is difficult to determine which products will have any real place in the future. There are a number of determinants that may influence their commercial viability. Even if a technology makes it to launch, there is no certainty that it will command mainstream clinical acceptance; especially if the technology is expensive, is not reimbursable, and is aimed at replacing established modalities where there is already capital, infrastructural, and technological investment. Unanticipated technological developments may also render these technologies obsolete.

Suggested reading:

The development of a PET/CT program in Newfoundland and Labrador. Newfoundland and Labrador Centre for Applied Health Research, 2009: http://www.nlcahr.mun.ca/research/chrsp/EIC_PetCT_full_report.pdf

PET scan primer: A guide to the implementation of positron emission tomography imaging in Ontario. Ontario Health Technology Advisory Committee; 2008: http://www.health.gov.on.ca/english/providers/program/ohtac/pdf/rep_petscan_02_20080925.pdf

References

1. *Making medical isotopes: Report of the Task Force on Alternatives for Medical-Isotope Production.* Vancouver (BC): TRIUMF; 2008. Available: http://admin.triumf.ca/facility/5yp/comm/Report-vPREPUB.pdf.

2. Hicks R, et al. *Biomed Imag Intervent J* 2007;3(3):49.
3. *Medical imaging in Canada*. Toronto: Canadian Institute for Health Information; 2008. Available: http://secure.cihi.ca/cihiweb/products/MIT_2007_e.pdf.
4. Schultz B. *Imaging Tech News* 2006.
5. New device - combination PET and MRI scanner. *News-Medical net* 2008.
6. Blamire AM. *Br J Radiol* 2008;81(968):601–17.
7. Higuchi T. *J Nucl Med* 2008;49(10):1715–22.
8. Harvey D. *Radiol Today* 2006;7(15):22.
9. New mammography technology effective in detecting breast cancer. *Sci Daily* 2008.
10. Tafra L. *Ann Surg Oncol* 2007;14:3–13.
11. van der Burg S. *Sci Eng Ethics* 2008.
12. Wang L. *Med Phys* 2008;35(12):5758–67.
13. New hybrid imaging technology may have big potential for improving diagnosis of prostate cancer. *Pharmalicensing com* 2009.
14. *EIBIR annual scientific report 2008*. Vienna (Austria): European Institute for Biomedical Imaging Research; 2009. Available: http://www.eibir.org/html/img/pool/eibir_annual_report_08_web.pdf.
15. SPECT imaging agent with 'ischemic memory' shows positive Phase 2 data. *HealthImaging com* 2009.
16. Cerqueira M. *Medscape* 2008.

Liquid-Based Techniques for Cervical Cancer Screening

The evolution of cervical cell collection techniques for the detection of cervical precursor lesions has opened up new possibilities for alternative cervical screening strategies.

The new technologies, liquid-based cytology (LBC) and tests for the presence of human papillomavirus or HPV, are intended to improve the detection of cervical precursor lesions and provide a platform for human papillomavirus testing. Until recently, the only option for cervical cancer screening was conventional cytology (CC) with an annual Pap smear.

In an effort to determine the health and economic implications of these newer technologies in comparison to CC, CADTH has published two comprehensive assessments on this topic: in November 2003 and, most recently, in February 2008. The latest assessment examined the diagnostic and cost-effectiveness of strategies based on these technologies compared with CC conducted annually. The report cites the following implications for decision-making:

- **LBC and CC perform similarly.** The clinical evidence suggests that LBC is similar to CC regarding sensitivity and specificity. LBC is probably more sensitive and less specific, and may have a lower rate of unsatisfactory specimens.
- **LBC strategies can be cost-effective, but they increase colposcopy referrals.** Model projections suggest that LBC with HPV triage every two years can be cost-saving compared to an annual screening strategy with CC alone.
- **HPV triage is cost-effective.** Direct comparison of all screening and triage strategies indicate that annual screening with CC or LBC is always more costly and less effective than when paired with HPV triage. Adding HPV triage to annual CC can reduce colposcopy referrals by 5%. Compared to annual CC with HPV triage, LBC with HPV every two years will reduce disease burden further by 0.0004 QALYs, while increasing costs ($52 per person, discounted) and colposcopy referrals by 72%.

The findings of this report have been considered by provincial and territorial health ministries. Indeed, the Public Health Agency of Canada

requested a presentation of the report findings to the Cervical Cancer Prevention and Control Network Steering Committee in May of 2009. CADTH has received positive feedback from decision-makers on the impact of this report.

CADTH's 2003 assessment on this topic was considered by key health professional groups and Health Canada at a workshop entitled "Building on Success: A Pan-Canadian Forum on Cervical Screening" in Ottawa in November of 2003. The CADTH findings from this report formed the basis of published evidence-based recommendations on the delivery of cervical cancer screening within the Canadian health system.

Liquid-based techniques for cervical cancer screening: Systematic review and cost-effectiveness analysis.

CADTH, 2008: http://www.cadth.ca/index.php/en/hta/reports-publications/search/publication/799.

Liquid-based cytology and human papillomavirus testing in cervical cancer screening. CCOHTA, 2003: http://www.cadth.ca/index.php/en/media-centre/?&news_id=29.

Report of the 2003 Pan-Canadian forum on cervical cancer prevention and control. J Obstet Gynaecol Can, 2004: http://cap-acp.org/cmsUploads/CAP/File/report_pan_canadian_forum.pdf.

Fetal Fibronectin Testing for Pre-Term Labour: Put to the Test in Canada's Arctic

In remote northern and Arctic communities of Canada, the birth of premature infants can be associated with considerable health problems.

Testing for fetal fibronectin (fFN) can be used to predict the onset of pre-term birth in women with symptoms of pre-term labour. The presence of fFN, a protein found in cervical secretions, is associated with pre-term labour. A negative result can avoid the unnecessary transfer of women not yet confirmed to have imminent delivery to hospitals in larger centres. This information provides additional value in rural and remote communities.

The use of fFN testing is associated with a reduction in negative health outcomes, hospital admissions, length of hospital stay, and hospital costs in the management of suspected pre-term labour.[1] In addition, significant social stresses for rural women and their families may also be avoided.

CADTH's Health Technology Inquiry Service (HTIS) has produced three assessments of the clinical-effectiveness of fFN testing to predict pre-term labour and reduce non-essential transport or hospital length of stay. These assessments have been produced in response to inquiries from the territory of Nunavut, which has since distributed the fFN test to all of its health care centers and hospitals. In addition to CADTH's HTIS assessments, Nunavut has also conducted a pilot study in 2004 involving 33 patients in the region.

For Canada's northern communities, the impact on health care costs is noteworthy. The reduction of medical travel costs to transport patients from their home communities to the capital city of Iqaluit or to a southern centre such as Winnipeg or Ottawa is a significant consideration when deciding to provide health services based on the use of this technology. By preventing unnecessary medical evacuations, the stress on pregnant women and their families is greatly reduced as a result. The fFN test is intended to be a useful tool in assisting health care providers with rapid clinical assessment of pre-term labour and related care.

What are your experiences with using CADTH reports? Write to us! We value your feedback on the utility of our services in supporting health care decisions throughout Canada. Contact: andram@cadth.ca.

References

1. Macdonald W. *Alaska Med Supp* 2007.

Eastern Health's Commitment to Implementing Evidence for the Use of Off-Label and Non-Formulary Medication

Eastern Health is the largest integrated regional health authority in Newfoundland and Labrador, serving a population of more than 290,000. Of growing concern to Eastern Health is the need for health care delivery to respond to the increasing use of medications outside their original mandate.

Eastern Health operates more than 80 hospitals, health care centers, long-term care facilities, and community health offices. As a single harmonized organization, this regional health authority provides a complete succession of health services, including community, acute, and long-term care. It is responsible for tertiary or high-level care for the entire jurisdiction.

The use of medications for off-label and non-formulary indications is a fairly common practice, occurring in an estimated 40% of adult and 90% of pediatric prescriptions. Off-label medications are considered to be medications that have not been approved by Health Canada for a particular condition or patient group, but have demonstrated success in treating another condition or group. Non-formulary medications are drugs that have been approved by Health Canada for use in specific diseases, but may not be approved yet, or have not been approved at all, by jurisdictional drug lists.

At Eastern Health, requests for the use of off-label and non-formulary medication were traditionally directed to the Vice-President of Medical Services or the Program Director for approval. Neither of these senior health care professionals felt equipped with the necessary knowledge to make decisions about potentially life-saving treatment decisions. Many of these medications are for last resort requests to treat illnesses that were unresponsive to conventional therapy.

Questions were raised over who should make these important decisions and whether or not these decisions were being informed by evidence. An action plan was developed to guide the decision-making process and a Rapid Response Committee was established in the summer of 2008 to respond to the growing requests for funding and support of off-label and non-formulary medication use in patient treatments.

The Rapid Response Committee is an interdisciplinary collaboration and partnership that connects clinical and administrative committees from within Eastern Health. The committee's membership consists of a broad spectrum of senior health care representatives from allied health professional practices, clinical programs, affiliated local university health care professional schools, and research centres.

The committee's first steps included developing a supporting decision process map and identifying resources to support decision-making. CADTH's Health Technology Inquiry Service (HTIS) was identified as a first port of call for all new requests received by the committee. Additional resources to support decision-making included conducting literature reviews, tapping into clinical expertise, and considering ethical issues. By utilizing resources within the organization and supported by evidence from CADTH, a framework was developed.

The framework was based on issues relating to patient safety, current threats to disease progression, informed consent for treatment, evidence to support the decision to treat, the risks and benefits of off-label treatment with the drug to the patient, and the appropriate use of resources. The guiding principles of the framework were applied to the decision-making process.

The committee then focused on developing a decision process map that would provide direction to the decision-making process. Committee members were required to respond to a series of questions that would help them assess and implement the use of appropriate technologies for each new request for non-formulary or off-label medication.

The questions included:

- Is this the approved use of the medication in Canada and for this disease process?
- What evidence is available to support the request for off-label use of this drug?
- Is this an exceptional case?
- What are the immediate and future financial costs?

The committee now ensures that each new request consistently adheres to the decision process map. Commitment to the map guarantees that evidence is being used to support decision-making.

Funding non-formulary/off-label medications: do we or don't we? Evidence, decisions, outcomes. Optimizing the use of drugs and health technologies. Templeton, J. Eastern Health. CADTH Syposium, April 2009: http://www.cadth.ca/media/symp-2009/presentations/CS-12/Janet%20Templeton%20-%20Funding%20Non-formulary_Off-label%20Mediations%20-%20Do%20We%20or%20Don_t%20We.pdf.

To P or Not to P

The exercise of hypothesis testing in experimental research has long been a fundamental practice, and is commonplace in publications of medical research.

Statistically speaking, the technical definition of a P-value confuses many researchers, and while its details are not discussed here, succinctly put, a P-value in a standard randomized controlled trial comparing two interventions A and B can be thought of as a probability value between 0 and 1 that one of two competing hypotheses is supported. These two competing hypotheses are the *null hypothesis* (which suggests there is no difference in the relative effectiveness of A versus B for some relevant clinical outcome of interest) and the *alternative hypothesis* (suggesting that some form of difference between A and B exists).

A classical approach to hypothesis testing would apply an appropriate statistical test to evaluate this pair of hypotheses. Such a test would return what is commonly known as a P-value, often used by researchers to interpret their findings. The exercise of hypothesis testing and the use

of P-values have long been topics of debate. Investigators often have a primary goal in mind of achieving *statistical significance* (which is typically considered to occur when a P-value is less than 0.05) rather than focusing on estimating the difference of interest, a practice that is problematic.

First, in regard to the standard exercise of hypothesis testing, asking the question of whether or not the level of response in groups of patients receiving A and B is exactly the same (as the null hypothesis suggests) is a question whose answer is virtually always known a priori: "no" is that answer, as the probability of being exactly the same is remarkably small.

A more relevant question, to the extent that it has important clinical implications, is whether or not the levels of response in groups A and B are sufficiently different. Regarding the latter issue of reliance on P-values, these measures suggest only whether or not the difference between A and B is non-zero; this information is less interesting than the estimation of the size of this difference, which is more helpful in clinical interpretation.

The use of P-values alone fails readers on several fronts: they do not provide insight as to the magnitude of difference in the clinical response of A versus B; they provide no indication of the direction of the difference between A and B; and they rely on a standard cut-off (typically 0.05) for determining "important" and "unimportant" results, a simplistic practice that can potentially lead to misinterpretations.

P-values are also highly influenced by the sample size of a study, and those with particularly large numbers of patients may return P-values indicating a statistically significant difference between A and B which, clinically, is negligible. Conversely, studies of limited sample size may identify clinically important differences, but fail to achieve statistical significance based on a P-value due to small sample size or other issues.

It has been suggested several times in prominent journals that dependence upon P-values in reporting of research findings be replaced by the utilization of confidence intervals. Confidence intervals focus on the concept of estimation mentioned earlier; they are accompanied by a "best guess" of the difference between A and B, and provide a range of plausible values amongst which the true value of A and B may lie.

This approach enables clinical interpretation and avoids the sacrifice of information relevant to readers. The direction of effect is immediately clear, and avoidance of an unnecessary "yes" or "no" decision as to importance of the finding is replaced with a more thoughtful consideration of the data. These advantages produce a more transparent presentation of clinical findings that is of greater value to interested medical professionals, and leads to an increasingly sensible interpretation of findings by the researchers involved.

Confidence intervals rather than P values: estimation rather than hypothesis testing. Gardner MJ, Altman DG. BMJ(1986); 292: 746–750.

Confidence interval or p-value? Du Prel JB, Hommel G, Rohrig B, Blettner M. Dtsch Arztebl Int 2009; 106(19): 335-9.

P values: what they are and what they are not. Schervish MJ. Am Stat 1996;50(3):203–6.

That confounded p-value. Lang JM, Rothman KJ, Cann CI. Epidemiology 1998;9(1):7–8.

Emerging Issues in Genetics Technology

Evaluation of Genomic Applications in Practice and Prevention Working Group

In an era of personalized medicine, the potential benefits and harms of genetic tests need to be rigorously scrutinized before they are used in clinical settings. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group provides an evidence-based mechanism to facilitate the evaluation of genetic tests that are transitioning from research to clinical and public health practice.

Launched in 2005, the EGAPP Working Group — which provides an unbiased, transparent, and systematic process for evidence-based assessments — was set up to develop recommendations based on the validity and utility of genetic tests. The group recently developed new approaches and optimized existing methods for collecting, analyzing, and grading evidence on analytic and clinical validity and clinical utility of genetic and genomic tests.

The evaluation of genomic applications in practice and prevention (EGAPP) initiative: methods of the EGAPP Working Group. Genetics Med 2009:11(1): http://journals.lww.com/geneticsinmedicine/Abstract/2009/01000/The_Evaluation_of_Genomic_Applications_in_Practice.2.aspx.

For more information on the EGAPP working group itself: http://www.egappreviews.org/default.htm.

New Gene Test for the Treatment of Breast Cancer

Breast cancer is the most common cancer among Canadian women. According to the Canadian Breast Cancer Foundation, approximately 22,700 women will be diagnosed with breast cancer in 2009, or one in every nine women.

Gene expression profiling that assesses the need for chemotherapy as an adjuvant to hormone therapy in women with early stage, node-negative breast cancer has recently been developed. While chemotherapy can reduce the risk of breast cancer recurrence by about 25%, treatment is associated with serious side effects and is very costly.

The genetic test is intended to determine the likelihood of breast cancers' recurrence and the anticipated benefit of chemotherapy. If there is a low likelihood that cancer will recur, chemotherapy can be avoided. The results of this test, in conjunction with other clinical information and laboratory tests, is intended to help clinicians and patients make more informed decisions about treatment management.

Impact of gene expression profiling tests on breast cancer outcomes. AHRQ, 2008: http://www.ahrq.gov/Clinic/tp/brcgenetp.htm.

Recommendations from the EGAPP Working Group: can tumor gene expression profiling improve outcomes in patients with breast cancer? Genetics Med 2009:11(1): http://www.egappreviews.org/docs/EGAPPWG-BrCaGEPRec.pdf.

Genetic Test for Future Risk of Blindness

Age-related macular degeneration (AMD) is the leading cause of visual impairment in Canada. It is a progressive retinal disease that, if left untreated, can lead to blindness. Early detection and treatment can significantly slow the progression of the disease.

A new genetic test has been produced that is designed to determine the risk of developing macular degeneration. It is believed that genetic inheritance plays an important role in the disease. The test will allow clinicians to diagnose AMD before symptoms are present.

Since there is currently no known cure for AMD, prevention is important. According to the Canadian National Institute for the Blind, lifestyle changes such as cigarette smoking, hypertension, overexposure in sunlight, and diet are modifiable factors that can play a role in reducing risk.

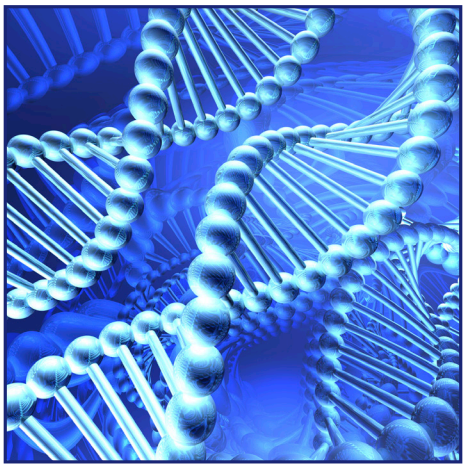
Genetic testing for macular degeneration. AMD Support Canada, 2008: http://www.amdsupport.ca/2008/07/23/genetic-testing-for-macular-degeneration/.

Predictive Gene Testing for Colon Cancer Treatment Options

A new genetic test, which scans for mutations in 12 genes expressed by colon tumours, has been developed for patients with stage II colon cancer. The test is designed to help predict which colon cancer patients are at a higher or lower risk of having their cancer return after surgery. Approximately 80% of stage II colon cancers are cured by surgery alone. However, there is no reliable way to predict who will require chemotherapy.

For patients in the low-risk group, the chance of recurrence three years post-surgery is believed to be approximately 8%. Patients in the high-risk group have a 21% chance of recurrence. Evidently, EGAPP believes "is currently insufficient to recommend for or against the routine use of UGT1A1 genotyping in patients with metastatic colorectal cancer who are to be treated with irinotecan".

Recommendations from the EGAPP Working Group: can UGT1A1 genotyping reduce morbidity and mortality in patients with metastatic colorectal cancer treated with irinotecan? Genetics Med 2009.



Type 2 Diabetes Gene Test

The detection of a gene variant that is almost twice as likely to be present in people with type 2 diabetes has paved the way toward the development of a genetic test for the prediction of type 2 diabetes. The test identifies the presence of two copies of the transcription factor 7-like 2 or TCF7L2 gene. The results of a positive test are believed to be of particular relevance to pre-diabetics who could reduce their risk of developing type 2 diabetes through weight loss and/or medication use.

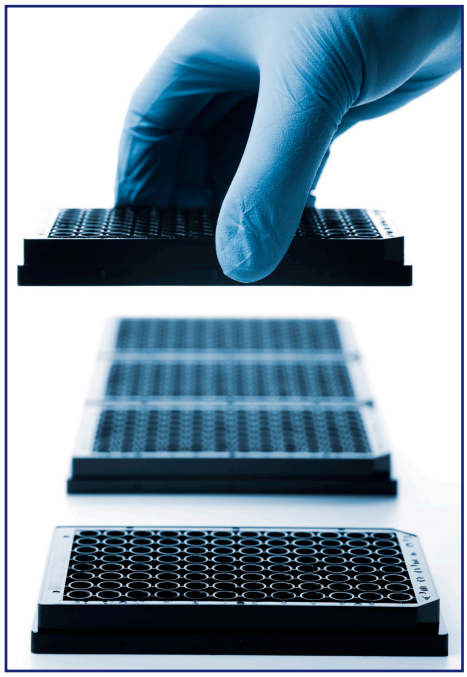
It is believed that the test's ability to predict a patient's genetic susceptibility to developing type 2 diabetes is currently no better than other predictors of risk.

Genotype score in addition to common risk factors for prediction of type 2 diabetes. NEJM, 2008: http://content.nejm.org/cgi/content/short/359/21/2208.

New Genetic Test for Down Syndrome

Advances in pre-natal testing are intended to make the process of diagnosing certain fetal anomalies technically easier, safer, and available earlier in pregnancy.

A new genetic test could prevent the need for invasive procedures such as amniocentesis, which requires inserting a needle into the uterus and is associated with an elevated risk of miscarriage. The new test involves taking a sample of the mother's blood, which contains DNA from the mother and her fetus. The test identifies genetic problems much earlier in gestation, around 12 weeks, than conventional tools.



The new method searches for abnormalities in the number of fetal chromosomes. Errors in chromosome numbers cause severe problems in physical and mental development. In addition to diagnosing Down Syndrome, this test also detects other chromosomal conditions, such as Edwards syndrome and Patau syndrome.

Current evidence using this technique is based on a small study of 18 pregnant women. A follow-up study evaluating the test in a larger population is underway.

A safer test for Down Syndrome: A noninvasive technique screens maternal blood for fetal DNA. Technology Review, 2008: http://www.technologyreview.com/biomedicine/21474/.

Genetic Predictors of IVF Success

A blood test is currently in development that could help in-vitro fertilization (IVF) decision-making.

Gene expression research has identified biomarkers in blood which can predict the likelihood of the successful implantation of an embryo. The gene analysis identified 128 genes that showed a more than two-fold difference in expression in early pregnancy compared with a non-pregnant state.

The research will also help to determine biomarkers that can identify events occurring at implantation, the maintenance of pregnancy, and a successful or unsuccessful pregnancy outcome.

The blood test could potentially spare couples the disappointment of repeated IVF failures and could save thousands of dollars in unnecessary IVF treatment.

Will IVF work for a particular patient? The answer may be found in her blood. Eurekalert, 2009: http://www.eurekalert.org/pub_releases/2009-07/esfh-wiw063009.php.

Suggested reading:

How will pharmacogenetics impact on pharmacy practice? Pharmacists' views and educational priorities. NHS Evidence, 2008: http://www.geneticseducation.nhs.uk/downloads/Pharmacogenetics.pdf.

Pharmacoeconomic evaluations of pharmacogenetic and genomic screening programmes: a systematic review on content and adherence to guidelines. Pharmacoeconomics. 2008; 26(7):569–87.

The evaluation of clinical validity and clinical utility of genetic tests. NHS Evidence, 2007: http://www.phgu.org.uk/file_gateway?link_ID=3932.

Genetic tests for cancer. AHRQ, 2006: http://www.ahrq.gov/clinic/ta/gentests/gentests.pdf.

Recent HTAs

These reports are available without cost at the websites below:

📖 **Anti-TNF-α Drugs for Refractory Inflammatory Bowel Disease: Clinical- and Cost-Effectiveness Analyses.** CADTH, July 2009: http://www.cadth.ca/media/pdf/H0479_Anti_TNF_a_Drugs_for_Refractory_Inflammatory_Bowel_Disease_tr_e.pdf

📖 **Dabigatran or Rivaroxaban Versus Other Anticoagulants for Thromboprophylaxis After Major Orthopedic Surgery: Systematic Review of Comparative Clinical-Effectiveness and Safety.** CADTH, May 2009: http://www.cadth.ca/media/pdf/M0006_Rivaroxaban_and_Dabigatran_L3_e.pdf

📖 **Cost-Effectiveness of Blood Glucose Test Strips in the Management of Adult Patients with Diabetes Mellitus:** http://www.cadth.ca/media/pdf/BGTS_SR_Report_of_Clinical_Outcomes.pdf and http://www.cadth.ca/media/pdf/BGTS_Consolidated_Economic_Report.pdf

📖 **Erythropoiesis-Stimulating Agents for Anemia of Cancer or of Chemotherapy: Systematic Review and Economic Evaluation.** CADTH, April 2009: http://www.cadth.ca/media/pdf/H0468_Erythropoiesis-stimulating_agents_tr_e.pdf

📖 **Recombinant Activated Factor VII in Treatment of Hemorrhage Unrelated to Hemophilia: A Systematic Review and Economic Evaluation.** CADTH, April 2009: http://www.cadth.ca/media/pdf/H0457A_Recombinant_Activated_Factor_VII_Hemorrhage_Hemophilia_tr_e.pdf

📖 **Dialectical Behaviour Therapy in Adolescents for Suicide Prevention: Systematic Review of Clinical-Effectiveness.** CADTH, April 2009: http://www.cadth.ca/media/pdf/M0005_Dialectical_Behaviour_Therapy_Adolescents_Suicide_Prevention%20_L3_e.pdf

📖 **Drugs for Pulmonary Arterial Hypertension: A Systematic Review of the Clinical-Effectiveness of Combination Therapy.** CADTH, April 2009: http://www.cadth.ca/media/pdf/M0004_Drugs_for_Pulmonary_Arterial_Hypertension_tr_e.pdf

📖 **Octaplas Compared With Fresh Frozen Plasma to Reduce the Risk of Transmitting Lipid-Enveloped Viruses: An Economic Analysis and Budget Impact Analysis.** CADTH, April 2009: http://www.cadth.ca/media/pdf/I4002_Octaplas%20versus%20FFP_L4_e_April%202009.pdf

📖 **Intravenous Immunoglobulin for Chronic Inflammatory Demyelinating Polyneuropathy: Clinial and Cost-Effectiveness Analysis.** CADTH, March 2009: http://www.cadth.ca/media/pdf/298_Intravenous_Immunoglobulin_CIPD_tr_e.pdf

📖 **Portable Ultrasonography in Small Emergency Departments: A Systematic Review of the Guidelines and Clinical-Effectiveness.** CADTH, March 2009: http://www.cadth.ca/media/pdf/M0003_Portable_Ultrasound_in_Small_Emergency_Departments_L3_e.pdf

HTAs From Other Organizations

📖 **Systematic Review of the Effects of Home Telemonitoring in the Context of Diabetes, Pulmonary Diseases, and Cardiovascular Diseases.** Aetmis, 2009: http://www.aetmis.gouv.qc.ca/site/phpwcms_filestorage/3b71f5915e1885970d1cf484d13e347e.pdf

📖 **Telemedicine and Radiation Oncology: State of the Evidence:** Aetmis, 2009.

📖 **Assistive Reproductive Technologies: A Literature Review and Database Analysis.** Institute of Health Economics, 2009: http://www.ihe.ca/documents/Assistive_Reproductive_Technologies.pdf

📖 **Determinants and Prevention of Low Birth Weight: A Synopsis of the Evidence.** Institute of Health Economics, 2009: http://www.ihe.ca/documents/IHE%20Report%20LowBirthWeight%20final.pdf

📖 **Effectiveness of Organizational Interventions for the Prevention of Workplace Stress.** Institute of Health Economics, 2009: http://www.ihe.ca/documents/Interventions_for_prevention_of_workplace_stress.pdf

📖 **The Development of a PET/CT Program in Newfoundland and Labrador.** Newfoundland and Labrador Centre for Applied Health Research, CHRSP, 2009: http://www.nlcahr.mun.ca/research/chrsp/EIC_PetCT_full_report.pdf

📖 **Effective Non-Clinical Interventions to Prevent and Treat Childhood Overweight and Obesity in Newfoundland and Labrador.** Newfoundland and Labrador Centre for Applied Health Research, CHRSP, 2009: http://www.nlcahr.mun.ca/research/chrsp/EIC_Childhood_Obesity_Full_Report.pdf

📖 **Clopidogrel for the Treatment of Adult Patients Following Acute Coronary Syndrome.** Alberta Health Technology Assessment Coalition Therapeutics Initiative, 2009: http://ti.ubc.ca/node/446

📖 **Estradiol/Levonorgestrel (Seasonale) for Prevention of Pregnancy.** Alberta Health Technology Assessment Coalition Therapeutics Initiative, 2009: http://ti.ubc.ca/node/374

📖 **Imiquimod Cream for the Treatment of Adult Patients With Actinic Keratosis.** Alberta Health Technology Assessment Coalition Therapeutics Initiative, 2009: http://www.ti.ubc.ca/node/419

📖 **Calcipotriol/Betamethasone (Dovobet) Ointment for the Treatment of Adult Patients With Psoriasis Vulgaris.** Alberta Health Technology Assessment Coalition Therapeutics Initiative, 2009: http://www.ti.ubc.ca/node/417

📖 **Pressure Ulcer Prevention: An Evidence-Based Analysis.** Ontario Medical Advisory Secretariat, 2009: http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_pup_20090401.pdf

📖 **Intrastromal Corneal Ring Implants for Corneal Thinning Disorders.** Ontario Medical Advisory Secretariat, 2009: http://www.health.gov.on.ca/english/providers/program/mas/tech/reviews/pdf/rev_intacs_20090401.pdf

New Canadian Practice Guidelines

📖 **Canadian Cardiovascular Society consensus conference update on cardiac transplantation 2008: Executive Summary.** Can J Cardiol 2009:25(4): http://www.ccs.ca/download/consensus_conference/consensus_conference_archives/2009_CardiacTransplantationUpdate.pdf

📖 **The 2009 Canadian Hypertension Education Program Recommendations: An Annual Update.** Canadian Hypertension Education Program, 2009: http://hypertension.ca/chep/wp-content/uploads/2009/05/chep-recommendations-spiral-bookleten.pdf

📖 **Guideline for using point of care INR monitoring of Warfarin therapy.** Thrombosis Interest Group of Canada, 2009: http://www.tigc.org/pdf/PointOfCareWarfarinTherapy.pdf

📖 **The Use of Inhibitors of Angiogenesis in Patients With Inoperable Locally Advanced or Metastatic Renal Cell Cancer: Guideline Recommendations.** Cancer Care Ontario, 2009: http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=43557

📖 **The 'what, when, where, who and how?' of cardiac computed tomography in 2009: Guidelines for the clinician.** Can J Cardiol 2009:25(3).

📖 **Reporting adverse reactions to antiviral drugs during an influenza pandemic — guidelines for health professionals and consumers.** PHAC, 2009: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/2009_ar-ei_anti_guide-ldir-eng.pdf

📖 **H1N1 flu virus Interim Guidelines, June 15th, 2009.** PHAC, 2009: http://www.phac-aspc.gc.ca/ols-bsl/banhsl-abnhgp-eng.php

📖 **Use of antivirals to treat H1N1 flu virus (Human Swine Flu).** PHAC, 2009: http://www.phac-aspc.gc.ca/alert-alerte/swine-porcine/antiviral-antiviraux05–01–eng.php

📖 **Management guidelines for pregnant women and neonates born to women with suspected or confirmed H1N1 influenza A (human swine flu) — Interim Guidelines (draft).** British Columbia Perinatal Health Program, 2009: http://bcphp.ca//sites/bcrcp/files/spotlight/guideline_h1n1_interim_draft.pdf

📖 **Content of a complete routine second trimester obstetrical ultrasound examination and report.** SOGC, 2009: http://www.sogc.org/guidelines/documents/gui223CPG0903.pdf

📖 **Gastroscopy Following a Positive Fecal Occult Blood Test and Negative Colonoscopy: Guideline Recommendations.** Cancer Care Ontario, 2009: http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=43562

📖 **Gastroesophageal Reflux Disease — Clinical Approach in Adults.** BC Guidelines and Protocols Advisory Committee, 2009: http://www.bcguidelines.ca/gpac/pdf/gastro.pdf

📖 **Menopause and Osteoporosis Update 2009.** SOGC, 2009: http://www.sogc.org/guidelines/documents/Menopause_JOGC-Jan_09.pdf

📖 **Management of Meconium at Birth.** SOGC, 2009: http://www.sogc.org/guidelines/documents/gui224TU0904.pdf

📖 **Management Guidelines for Obstetric Patients and Neonates Born to Mothers With Suspected or Probable Severe Acute Respiratory Syndrome (SARS)**, SOGC, 2009: http://www.sogc.org/guidelines/documents/gui225CPG0904.pdf

📖 **Guideline for the Evidence-Informed Primary Care Management of Low Back Pain.** Towards Optimized Practice, Alberta, 2009: http://www.topalbertadoctors.org/PDF/complete%20set/Low%20Back%20Pain/backpain_guideline.pdf

📖 **Vision screening in infants, children and youth.** Canadian Paediatric Society, 2009: http://www.cps.ca/english/statements/CP/cp09-02.htm

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