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Optimal Use Report

CADTH

Optimizing Health System Use of Medical Isotopes and Other Imaging Modalities

Supporting Informed Decisions

Optimizing Health System Use of Medical Isotopes and Other Imaging Modalities

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Authorship

Michelle Mujoomdar, Erin Russell, François Dionne, and Kimberlee Lambe were responsible for planning, authoring, and reviewing the report. Michelle Mujoomdar led the project team and was the liaison between MIIMAC and CADTH. Erin Russell, Kristen Moulton, and Christine Murray were responsible for authoring and revising select research reports. Erin Russell was responsible for reviewing cost estimates for all reports. Sarah McGill performed literature searches and verified bibliographic references.

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Conflicts of Interest

None declared.

INTRODUCTION

Medical isotopes, specifically technetium-99m (^{99m}Tc), are used in a variety of diagnostic imaging procedures involving approximately 24,000 Canadians every week.[1] Molybdenum-99, the precursor to ^{99m}Tc, is produced primarily at five large commercial reactors located in Belgium, Canada, France, the Netherlands, and South Africa.[2] The five reactors, commissioned between 45 and 55 years ago,[3] collectively supply 90% to 95% of the world's molybdenum-99.[2] Due to their advancing age, the reactors are experiencing an increasing number of scheduled (for maintenance) and unscheduled shutdowns, thereby making the production of molybdenum-99 unreliable.

According to a report to the Minister of Health from the Ad Hoc Health Experts Working Group on Medical Isotopes — formed in the midst of the nearly month-long unexpected shutdown of the National Research Universal (NRU) reactor in Chalk River, Ontario, in November 2007 — there were "enormous variations in how well or poorly Canada's nuclear medicine facilities fared during the 2007 shutdown of the NRU reactor."[4] The majority of Canada's supply of ^{99m}Tc is sourced from the NRU reactor — between 80% and 85% when the NRU is operational.[1]

In December 2008, the NRU reactor was again shut down unexpectedly, three days before planned scheduled maintenance, returning to service one week later.[5] Most recently, and of most significance, was the May 2009 to August 2010 outage, when the NRU reactor was unexpectedly off-line due to a leak in the reactor vessel.[2] Throughout the May 2009 to August 2010 outage, the supply of ^{99m}Tc was greatly reduced — with weekly supplies fluctuating significantly, depending on the province, region, or supplier.

It was as a result of the extended 2009-2010 shutdown of the NRU reactor that medical isotope production made headlines as a high-profile issue affecting patient access and requiring national action. In response, the Canadian government established an Expert Review Panel on Medical Isotope Production to assess the most viable options for securing supplies of ^{99m}Tc for the Canadian health care system over the medium- and long-term, and to identify any actions that might be required by governments and others to facilitate the realization of these options.[6]

In November of 2009, the panel submitted to the Minister of Natural Resources a report that contained a series of recommendations including "achieve better use of ^{99m}Tc supply through advanced alternative medical imaging technologies."[3] Following that, the Government of Canada developed an action plan to increase the security of the medical isotope supply for Canadians.[6,7]

The Government of Canada announced in January 2011 that it was investing in four projects to develop new ways of producing ^{99m}Tc.[8] The Non-reactor-based Isotope Supply Contribution Program was designed to advance cyclotron and linear accelerator technologies to achieve a more diverse and secure supply of ^{99m}Tc, with less reliance on nuclear reactor–based production.

In addition to the four non–reactor-based isotope projects, it was also announced that Health Canada was providing funding to the Canadian Agency for Drugs and Technologies in Health (CADTH) to "investigate the optimal use of medical isotopes and alternatives" and develop national guidance on how to optimize the management and use of ^{99m}Tc, and consider appropriate alternative medical isotopes and medical imaging equipment.[8] In 2009, Health Canada released a document titled *Guidance for Maximizing Supply of Technetium-99m (Tc-99m) During a Shortage*.[9] The guidance document was based largely on a disruption plan developed by the Government of Ontario. The goal of the CADTH project was to build on this existing guidance.

Most medical isotopes, unlike some other medical supplies, cannot be stockpiled because of their relatively short half-lives (half-life refers to the time it takes for the product to lose half its radioactivity). The half-life of molybdenum-99 is 66 hours and the half-life of its decay product, ^{99m}Tc, is six hours. Because it cannot be stockpiled, when there is a disruption in the supply of ^{99m}Tc, health care providers are faced with rationing a reduced supply. A 2010 paper by Rosenthal[10] discussed allocation of ^{99m}Tc when its supply is reduced and concluded that allocation decisions should be made by multi-disciplinary committees, using an ethical and transparent approach.

Throughout the life of the project, CADTH was advised by the specially created Medical Isotopes and Imaging Modalities Advisory Committee (MIIMAC).[11] MIIMAC was a 23-member pan-Canadian, multi-disciplinary committee consisting of institutional and regional representatives from health professions (nuclear medicine physicians, diagnostic radiologists, medical radiation technologists, cardiologists with expertise in cardiac imaging, a medical oncologist, a radiopharmacist, and a medical ethicist), administrators from ministries of health, and members of the public, as well as experts in scientific research and methodology. The composition of MIIMAC was chosen carefully and deliberately to allow for multiple perspectives, inclusive discussion and debate, and transparency in process.

ISSUE

Technetium-99m is the most widely used medical isotope in nuclear medicine and its supply is susceptible to shortages. Following the most recent supply disruption, which occurred from May 2009 to August 2010, CADTH was asked to develop national guidance on the optimal use of ^{99m}Tc in times of supply disruption.

OBJECTIVES

The purpose of this project was to provide national guidance on the optimal use of ^{99m}Tc during a situation of reduced supply. To accomplish this, our objective at CADTH was:

- to develop, taking a national perspective, a priority ranking of the most common clinical uses of ^{99m}Tc for use by decision-makers at various levels of the health system (i.e., institution, health authority, or jurisdiction) during a period of reduced supply of the isotope.

Early in the project, CADTH and MIIMAC acknowledged that a priority ranking constructed taking a national perspective will not accurately reflect the local contexts of all jurisdictions in which it is meant to be used. Given this, our second objective was:

- to design a customizable, web-based prioritization tool that allows decision-makers the opportunity to create personalized priority lists specific to their institution, health authority, or jurisdiction for use during a period of reduced supply of the isotope.

METHODOLOGY

Medical Isotopes and Imaging Modalities Advisory Committee

At the outset of this project, CADTH recognized the need to seek input from, and engage, experts in both medical imaging and the methodologies being used for the project. We also wanted additional perspectives, such as those of the public, to be represented.

MIIMAC was a purpose-built, project-specific committee with a term of less than two years. We actively recruited members who had experience on previous initiatives related to the shortages of ^{99m}Tc (e.g., Health Canada's Ad Hoc Health Experts Working Group, Natural Resources Canada's Expert Review Panel, and the Federal/Provincial/Territorial Working Group on Medical Isotopes). We did this specifically to leverage the experience of these individuals and also to ensure that we were avoiding duplication of effort. The 23-member committee was co-chaired by a nuclear medicine physician and a pediatric diagnostic radiologist. A list of MIIMAC members is available in Appendix 1.

In recruiting MIIMAC members, we worked to ensure that the committee had the appropriate expertise while also having national, geographic representation. Eight of the 10 provinces that conduct nuclear medicine imaging were represented on MIIMAC; nuclear medicine is not practised in any of the three territories.[12]

A professional facilitator was used for all committee meetings, which allowed the co-chairs to be full participants. Including the orientation meeting (held in October 2010), MIIMAC met four times (January 2011, April 2011, and January 2012). In addition, CADTH convened Working Groups (WG) — sub-groups comprising different MIIMAC

members who worked with the project team between meetings of the full MIIMAC. Three WG meetings took place (December 2010, March 2011, and November 2011). During the project period, the co-chairs and the project lead met 12 times via teleconference or web conference. One original MIIMAC member did not finish his term, leaving a 23-member committee for most of the term of the project. MIIMAC members were asked to declare any conflicts of interest before each full committee meeting. Any changes to declarations were reviewed by CADTH and by the co-chairs.

In lieu of voting, MIIMAC relied on debate and dialogue to ensure that all members had a level of comfort with each step before checking for consensus and proceeding to the next step. For our purposes, consensus was defined not as "Do you agree with it?", but rather, "Can you live with it?". No decision was final until the project lead, or a designate, followed up with any members who were absent from meetings. MIIMAC members were asked to complete a survey following each full committee meeting. The results of the surveys indicated that the vast majority of MIIMAC members were "extremely satisfied" with how meeting objectives were met, as well as with pre- and post-meeting communication.

Following each MIIMAC and WG meeting, the project team held debriefing sessions with the co-chairs and the facilitator, with a focus on implementing any suggestions for improvement.

Multi-Criteria Decision Analysis (MCDA)

We used a multi-criteria–based approach for the project. Multi-criteria decision analysis (MCDA) methodology was used to organize information and assist in the development of the priority list. MCDA was chosen based on the understanding that users of ^{99m}Tc and decision-makers considered multiple factors, or criteria, when allocating the isotope during the last supply disruption. These criteria included the severity of the condition being treated and the availability of potential alternative medical imaging modalities for tests that use ^{99m}Tc.

In general, MCDA involves the assessment of all possible courses of action on the basis of a common set of criteria. Thus, the two key elements of the MCDA process are the possible courses of action and the criteria. The possible courses of action are the universe of possible (i.e., implementable) choices for the decision-maker. The criteria represent a measurement tool for all the relevant considerations in the decision-making process. Relevant criteria therefore depend on the decision-making context.[13] Once all possible choices have been evaluated on the basis of the selected criteria, they can be equitably compared and conclusions can be formulated.

MCDA is a transparent and explicit process that, for this project, involved four basic steps adapted from an established priority-setting process.[13]

The first step was to develop relevant evaluation criteria. Each criterion has four components: name, definition, weight, and a rating scale, with an explicit definition of each rating point on the scale. The objective, in the development of criteria, is to include all considerations relevant to the decision that has to be made and to provide sufficient clarity to ensure consistency in the translation of information into ratings.

The second step was to identify the clinical uses of ^{99m}Tc requiring prioritization. Information supporting each criterion was incorporated into a single research report for each clinical use.

The third step was to formally evaluate the clinical uses of ^{99m}Tc using the information presented in the research report. This was done by rating each clinical use on each criterion and, using the criteria weight, calculating a composite score (i.e., weighted score). Given that the same criteria were always used, the weighted scores were comparable across all of the clinical uses.

The fourth and final step had two parts: validation and ranking. First, the weighted score for each clinical use was validated by MIIMAC to ensure that no process errors took place. Once validation was complete, each clinical use was ranked in relation to all the others to generate the priority list.

Identifying the relevant criteria

Development and refinement

MIIMAC members began the process of identifying criteria at their first face-to-face meeting (October 4, 2010). CADTH presented 13 criteria, based on data collected at the orientation meeting and follow-up correspondence, to the committee in January 2011. After review and discussion by MIIMAC, 11 evaluation criteria were identified. The criteria fall into two domains: those related to the underlying condition (Table 1) and those comparing either health conditions or ^{99m}Tc-based imaging and alternative imaging modalities that could be used in place of a ^{99m}Tc-based test (Table 2).

The criteria were posted on the CADTH website from March 22 to April 6, 2011, for stakeholder feedback. The feedback was considered by the CADTH project team. Based on the feedback received, there were no changes to the list of criteria after this date; however, minor changes were made to some of the criteria definitions to add clarity.

Table 1: Criteria Related to the Underlying Health Condition

Criterion	Definition
Size of the affected population	The estimated size of the patient population that is affected by the underlying health condition and that may potentially undergo the test. The ideal measure is point prevalence, or information on how rare or common the health condition is.
Timeliness and urgency of test results in planning patient management	The timeliness and urgency of obtaining the test results in terms of their impact on the management of the condition and the effective use of health care resources.
Impact of not performing a diagnostic imaging test on mortality related to the underlying condition	Impact of not performing the test, in whatever way, on the expected mortality of the underlying condition. Measures could include survival curves showing survival over time, and/or survival at specific time intervals with and without the test.

Table 1: Criteria Related to the Underlying Health Condition	
Criterion	**Definition**
Impact of not performing a diagnostic imaging test on morbidity or quality of life related to the underlying condition	Impact of not performing the test, in whatever way, on the expected morbidity or on the quality of life reduction of the underlying condition. Measures of impact may include natural morbidity outcome measures such as events or disease severity, or might be expressed using generic or disease-specific quality of life rating scales with and without the test.

Table 2: Criteria Comparing ^{99m}Tc with an Alternative or Comparing between Clinical Uses	
Criterion	**Definition**
Relative impact on health disparities	Health disparities are defined as situations where there is a disproportionate burden (e.g., incidence, prevalence, morbidity, or mortality) amongst particular population groups (e.g., gender, age, ethnicity, geography, disability, sexual orientation, socio-economic status, and special health care needs). Impact on health disparities is assessed by estimating the proportion of current clients of the ^{99m}Tc-based test who are in population groups with disproportionate burdens. (Explanatory note: The implication of this definition is that, everything else being the same, it is preferable to prioritize those clinical uses that have the greatest proportion of clients in groups with disproportionate burdens.)
Relative acceptability of the test to patients	Acceptability of the ^{99m}Tc-based test from the patient's perspective compared with alternatives. Patient acceptability considerations include discomfort associated with the administration of the test, out-of-pocket expenses or travel costs, factors that may cause great inconvenience to patients, and other burdens. This criterion does not include risks of adverse events, but is about everything related to the experience of undergoing the test.
Relative diagnostic accuracy of the test	Ability of the test to correctly diagnose the patients who have the condition (sensitivity) and patients who do not have the condition (specificity) compared with alternatives.
Relative risks associated with the test	Risks associated with the test (e.g., radiation exposure, side effects, adverse events) compared with alternatives. Risks could include immediate safety concerns from a specific test or long-term cumulative safety concerns from repeat testing or exposure.
Relative availability of personnel with expertise and experience required for the test	Availability of personnel with the appropriate expertise and experience required to proficiently conduct the test and/or interpret the test findings compared with alternatives.
Accessibility of alternatives (equipment and wait times)	Availability (supply) of equipment and wait times for alternative tests within the geographic area. Includes consideration of the capacity of the system to accommodate increased demand for the alternatives. Excludes any limitation on accessibility related to human resources considerations.
Relative cost of the test	Operating cost of test (e.g., consumables, health care professional reimbursement) compared with alternatives.

^{99m}Tc = technetium-99m.

Identifying the clinical uses of ^{99m}Tc to be prioritized

Recognizing that ^{99m}Tc is involved in the imaging of a broad range of medical conditions, and acknowledging that we would not be able to evaluate all uses of ^{99m}Tc, our objective was to create a priority list for those uses that accounted for a large proportion of the work that is done at most Canadian institutions. We used filter criteria to select the clinical uses for evaluation and, ultimately, for prioritization.

For the purposes of facilitating refinement of the clinical uses, the comprehensive list of possible conditions requiring ^{99m}Tc-based imaging was divided into five groupings based on body systems: cardiovascular, renal, musculoskeletal, gastrointestinal, and other body systems. Working in small groups, MIIMAC members were asked to refine the list of uses and capture the filter criteria that were used in the process. The following filter criteria were used: the impact of a ^{99m}Tc-based test on the management of the patient, number of ^{99m}Tc-based tests performed (also expressed as number of patients undergoing the imaging test), quantity of ^{99m}Tc used for each test, and acceptability of alternative imaging modalities to patients.

Development and refinement

Using the filter criteria described, MIIMAC developed an initial list of 22 clinical uses of ^{99m}Tc and possible alternatives or comparators (i.e., other nuclear and non-nuclear imaging tests) for possible prioritization. Following refinement by the project team and feedback from MIIMAC, 21 clinical uses of ^{99m}Tc were selected for evaluation and prioritization. Several important assumptions were made at this time:

- X-ray would be used as a first-line investigational tool, if appropriate
- Uses of ^{99m}Tc for which there were no reliable alternatives would receive priority and would be excluded from the analysis
- Patients for whom alternatives to the ^{99m}Tc-based imaging test were contraindicated (e.g., computed tomography [CT] involving contrast for patients with an allergy to the contrast agent or magnetic resonance imaging [MRI] for patients with some types of implantable cardioverter-defibrillators [ICDs]) would be prioritized to receive ^{99m}Tc.

Originally, two uses (Table 3) were identified that would be excluded from the prioritization process because there was no reliable imaging alternative to ^{99m}Tc. Therefore, in the event of a shortage of ^{99m}Tc, these clinical uses should be prioritized. The list of 21 clinical uses selected for evaluation was posted on the CADTH website from March 22 to April 6, 2011, for stakeholder feedback. The feedback was considered by the CADTH project team and no changes to the clinical uses were made based on the feedback received. However, subsequent to posting, and based on feedback from MIIMAC, several of the original 21 clinical uses were excluded from the prioritization process. These uses, and the reasons for exclusion, are tabulated (Table 3).

Table 3: Clinical Uses of ^{99m}Tc Excluded from the MCDA

Clinical Use	Reason for Exclusion	MIIMAC Recommendation
Evaluation of reflex sympathetic dystrophy	No reliable imaging alternative	Should be prioritized
Diagnosis of Meckel's diverticulum in pediatric	No reliable imaging alternative	Should be prioritized

Table 3: Clinical Uses of ^{99m}Tc Excluded from the MCDA		
Clinical Use	**Reason for Exclusion**	**MIIMAC Recommendation**
patients		
Imaging suspected cases of brain death	No reliable imaging alternative	Should be prioritized
Diagnosis of acute pyelonephritis in pediatric patients	Limited impact on management of condition; nuclear medicine is primarily used to assess scarring, not to diagnose pyelonephritis	Should not be prioritized
Evaluation of the limping child (excluding suspected cases of abuse)	Refers to various conditions accounted for elsewhere (i.e., osteomyelitis and fracture)	Should be considered in related reports (i.e., osteomyelitis and fracture)

MCDA = multi-criteria decision analysis; MIIMAC = Medical Isotopes and Imaging Modalities Advisory Committee; ^{99m}Tc = technetium-99m.

Summary of clinical uses, interventions, and comparators included in the MCDA

The final clinical uses included in the MCDA are listed in Table 4. Two of the clinical uses, evaluation of obstructive uropathy and diagnosis of osteomyelitis, were separated into distinct adult and pediatric patient populations. Three other clinical uses — diagnosis of fractures, imaging for metastatic disease, and evaluation of painful prosthesis — were subdivided: diagnosis of fractures was rated separately for osteoporotic fractures and stress fractures; imaging for metastatic disease was rated separately for cancers of the breast, lung, and prostate; and evaluation of painful prosthesis was rated separately for infection and for loosening. The final priority list includes 24 ranked clinical uses. These represent the greater part of the volume of the work that is done at most Canadian institutions and includes those procedures that are time sensitive.

Table 4: Clinical Uses, Interventions, and Comparators Included in the MCDA			
Body System	**Clinical Use**	**Intervention**	**Comparator(s)**
Cardiovascular	Detection of ischemia	Stress SPECT MPI	CTCA Stress Echo Stress MRI Stress PET Stress ^{201}TI-SPECT
	Assessment of prognosis post-myocardial infarction	Stress SPECT MPI	CTCA Stress Echo Stress MRI Stress PET Stress ^{201}TI-SPECT
	Preoperative assessment prior to vascular, non-cardiac surgery	Stress SPECT MPI	CTCA Stress Echo Stress MRI Stress PET Stress ^{201}TI-SPECT
	ICD decision-making	RNA	Echo MRI
	Assessment of drug-induced cardiotoxicity	RNA	Echo MRI

Table 4: Clinical Uses, Interventions, and Comparators Included in the MCDA			
Body System	**Clinical Use**	**Intervention**	**Comparator(s)**
Renal	Evaluation of renal function — post-transplant	Renal scintigraphy	U/S
	Evaluation of renal function — suspected obstructive uropathy (in children and adults)	Renal scintigraphy	MRU U/S
	Evaluation of renal function — renovascular hypertension	Renal scintigraphy	Catheter angiography CTA MRA U/S
Musculoskeletal	Diagnosis of acute osteomyelitis (in children and adults)	Bone scanning	CT ^{111}In-WBC MRI PET U/S
	Evaluation of painful prosthesis	Bone scanning	Arthrography PET ^{111}In-WBC
	Imaging for metastatic disease	Bone scanning	MRI PET
	Diagnosis of avascular necrosis	Bone scanning	MRI
	Diagnosis of fracture (osteoporotic and stress)	Bone scanning	CT MRI PET
Gastrointestinal	Detection of lower gastrointestinal bleeding	GI scintigraphy	Abdominal angiography
	Diagnosis of acute cholecystitis	Hepatobiliary scintigraphy	CT MRCP U/S
	Assessment of bile leak	Hepatobiliary scintigraphy	CT ERCP MRCP U/S
Other	Detection of pulmonary embolism	V/Q scan	CTPA
	Identification of the sentinel lymph node in patients with breast cancer	Radiopharmaceutical + blue dye	Blue dye alone ALND

ALND = axillary lymph node dissection; CT = computed tomography; CTA = computed tomography angiography; CTCA = computed tomography coronary angiography; CTPA = computed tomography pulmonary angiography; Echo = echocardiography; ERCP = endoscopic retrograde cholangiopancreatography; GI = gastrointestinal; ICD = implantable cardioverter-defibrillator; ^{111}In-WBC = indium-111–labelled white blood cells; MCDA = multi-criteria decision analysis; MPI = myocardial perfusion imaging; MRA = magnetic resonance angiography; MRCP = magnetic resonance cholangiopancreatography; MRI = magnetic resonance imaging; MRU = magnetic resonance urography; PET = positron emission tomography; RNA = radionuclide angiography; SPECT = single-photon emission computed tomography; ^{201}Tl = thallium-201; U/S = ultrasound; V/Q = ventilation/perfusion.

Generation of research reports to inform the MCDA process

A single research report was generated for each of the clinical uses. For the five clinical uses that were further refined (i.e., diagnosis of fracture, diagnosis of acute osteomyelitis, evaluation of painful prosthesis, imaging for metastatic disease, and suspected obstructive uropathy), the research reports were organized such that the information was presented separately for each population in a single report. Literature reviews were conducted for each of the clinical uses selected by MIIMAC. Each literature search was performed by an information specialist using a peer-reviewed search strategy.

Published literature was identified by searching MEDLINE with In-Process records via Ovid; The Cochrane Library; PubMed; and Canadian and major international health technology agencies, as well as focused Internet searches. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and diagnostic accuracy studies (primary studies of randomized and non-randomized design). Randomized controlled trials and non-randomized studies were also searched for all but two clinical uses (post-myocardial infarction and ischemia), due to the large volume of literature for these two clinical uses. The searches were limited to English-language documents. Regular alerts were established to update the search until October 2011. Search strategies are described in each research report (Appendix 2).

Targeted searches were done as required for the application of the criteria, using the databases listed above and Internet search engines. When no literature was identified addressing specific criteria, experts were consulted. All fee codes used to inform the cost criterion were verified by experts.
The research reports contained a summary of the evidence and information relating to each of the criteria. All of the reports were reviewed by one to three MIIMAC members.

Producing a ranking

Assigning criteria weights

Once the list of clinical uses to be prioritized had been created and the evaluation criteria generated, MIIMAC assigned weights to the 11 criteria, to reflect their relative importance in the process of prioritization in a time of reduced supply of ^{99m}Tc. At the April 2011 meeting, MIIMAC began the weighting process first by clustering the criteria into high, medium, and low relative importance, with three to four criteria in the high and low clusters. This work was done in a small-group format to encourage and maximize dialogue.

MIIMAC used a simple approach that involved the allocation of 100 points to the 11 criteria. As a starting point, each cluster was given a total weight range — high relative importance (40 to 60 points), medium relative importance (20 to 40 points), and low relative importance (10 to 20 points). Once the criteria were mapped to the appropriate level of relative importance, MIIMAC members were asked to rank the criteria within each cluster (Figure 1). Using the rankings from each cluster, final weights were assigned (Table 5)

Figure 1: Weighting of the criteria

Cluster A — High relative importance (order of importance):
- Impact on mortality (1)
- Impact on morbidity (2)
- Timeliness and urgency (3)
- Diagnostic accuracy (4)

Cluster B — Medium relative importance (order of importance):
- Size of affected population (1)
- Accessibility (2)
- Health disparity (3)

Cluster C — Low relative importance (order of importance):
- Availability of expertise (1)
- Patient acceptability (2)
- Risk (2)
- Cost (3)

Table 5: Relative Importance of Criteria

Criterion	Weight
Impact of not performing a diagnostic imaging test on mortality related to the underlying condition	16
Impact of not performing a diagnostic imaging test on morbidity or quality of life related to the underlying condition	15
Timeliness and urgency of test results in planning patient management	14
Relative diagnostic accuracy of the test	12
Size of the affected population	9
Accessibility of alternatives (equipment)	8
Relative impact on health disparities	7
Relative availability of expertise and experience required for the test (personnel)	6
Relative acceptability of test to patients	5
Relative risks associated with the test	5
Relative cost of the test	3

Determining a rating for criteria

The tool used to rate each of the clinical uses of ^{99m}Tc against the 11 criteria is included in Appendix 3. Briefly, those criteria related to the underlying condition were permitted only positive values (range: 0 to +3), while criteria comparing ^{99m}Tc with an alternative imaging modality had negative or positive values (range: –3 to +3). Positive values were indicative of a situation in which the ^{99m}Tc-based imaging test outperformed the alternative, whereas a negative score indicated that the alternative test outperformed the ^{99m}Tc-based test. A rating of 0 was interpreted to mean that, for that particular criterion, there was no difference between the alternative test and the ^{99m}Tc-based imaging test.

Three iterations of ratings were done. First, the project team rated the reports (October 2011). Second, a two-day WG meeting was held in November 2011, at which the WG extensively reviewed the pre-ratings done by the project team. The WG, made up of six MIIMAC members, and the project team discussed each rating for all 24 clinical uses. There was an emphasis on ensuring consistency between like modalities across clinical

uses. For example, acceptability to patients of the ^{99m}Tc-based test versus MRI received the rating of –1 (i.e., the ^{99m}Tc-based test is minimally less acceptable than MRI); this rating was then repeated for other clinical uses that had similar patient populations. The project team made any necessary revisions to the reports based on feedback from the WG.

In addition to reviewing and revising the ratings and generating preliminary scores, the WG discussed the criterion of "relative impact on health disparities." For the purposes of this project, we considered the 24 underlying health conditions requiring ^{99m}Tc-based imaging and discussed possible health disparities for each condition.

Four factors that are associated with variations in health status include socio-economic status, Aboriginal identity, gender, and geographical location.[14] The WG discussed the criterion of relative health disparity extensively and concluded that this important criterion reflected extremely local issues. While it could be argued that this is also the case for other criteria, the WG suggested that to assess and rate health disparities at a national level would dilute any potential disparities at the local level. As such, the WG made the recommendation to the full MIIMAC that this criterion be rated only at the local level. We did, however, include any information identified in the literature review that addressed potential health disparities within each research report.

Finally, the full MIIMAC convened for two days in January 2012 in order to finalize the ratings and rankings of the clinical uses of ^{99m}Tc developed by the WG. MIIMAC members reviewed the reports prior to the meeting. The ratings proposed by the WG were mostly unchanged. Because each available alternative imaging modality had to be rated for each clinical use, a total of 482 ratings (i.e., a rating of 0 to 3 or –3 to +3 was selected for each criterion for each alternative modality to ^{99m}Tc-based imaging for all of the clinical uses) based on the evidence and information identified were finalized by MIIMAC. MIIMAC accepted the recommendation of the WG to score the health disparities criterion at the local level.

After the ratings for each criterion for all 24 clinical uses were finalized, those ratings were multiplied by the corresponding weight for the criterion to generate a weighted score. For each clinical use, the weighted scores (rating assigned to a diagnostic alternative modality for a particular criterion multiplied by the weight of the criterion decided by MIIMAC) for the 11 criteria were summed to calculate a composite weighted score for each alternative modality. A total of 63 composite weighted scores were calculated. The placement of the clinical use in the priority ranking was determined by selecting the alternative to the ^{99m}Tc-based test with the lowest weighted composite score for each use. The lowest score was selected because the closer a score is to 0, the more closely the alternative resembles the ^{99m}Tc-based imaging test on the basis of the 11 criteria used in the analysis and, therefore, the more appropriate it is to use the alternative if there is a shortage of ^{99m}Tc.

Achieving consensus

The final ranking, based on the ratings agreed to by MIIMAC, was shown to members. As part of the validation, the meeting facilitator asked each committee member, "Do you support the ranked list?" Permissible responses were: "I agree," "I am still undecided," or "I disagree."

RESULTS

A total of 18 clinical uses of ^{99m}Tc were selected to be prioritized. Five of the clinical uses were further refined (i.e., diagnosis of fracture, diagnosis of acute osteomyelitis, evaluation of painful prosthesis, imaging for metastatic disease, suspected obstructive uropathy), resulting in a priority ranking of 24 uses of the isotope. A final priority ranking was generated based on the best alternative test to the ^{99m}Tc-based test. The ranking reported in Table 6 represents a prioritization list developed using a national perspective, assuming the availability of the next best alternative. Should the next best alternative not be available, a complete list of alternatives (and their weighted scores) is presented in Appendix 4. It is important to note that many of the weighted composite scores between uses and, indeed, between alternatives for a single use were very close. A complete list of the ratings for all the alternatives is provided in Appendix 5. The cut-offs for distinct clusters were not obvious and a discussion between end-users of the priority ranking must take place to determine what constitutes a true difference in scores. This process is not intended to be used as a "calculator"; rather, the intent is to collect and organize information and summarize it in a consistent manner.

The results of the national analysis by MIIMAC indicate that, in the event of a disruption in the supply of ^{99m}Tc, clinical uses with high scores (e.g., detection of lower gastrointestinal bleeding) have relative high priority, while clinical uses with lower scores (e.g., detection of stress fracture) are of relative lower priority.

Table 6: Priority Ranking of Uses of ^{99m}Tc

Clinical Use	Score	Next Best Alternative (If Available)
Detection of lower GI bleeding	200	AA
Assessment of bile leak	139	U/S
Detection of pulmonary embolism	135	CTPA
Diagnosis of (osteoporotic) fracture	132	MRI
Diagnosis of acute osteomyelitis (children)	131	CT
Imaging for metastatic disease (breast)	125	^{18}F-PET
Imaging for metastatic disease (lung)	118	^{18}FDG-PET
Assessment of prognosis post-myocardial infarction	117	Echo
Detection of ischemia	117	Echo
Imaging for metastatic disease (prostate)	113	^{18}F-PET
Preoperative assessment prior to vascular, non-cardiac surgery	108	Echo
Evaluation of painful prosthesis (loosening)	101	Arthrography
ICD decision-making	99	Echo
Diagnosis of acute cholecystitis	96	U/S
Evaluation of renal function — post-transplant	90	U/S
Evaluation of painful prosthesis (infection)	85	^{111}In-WBC
Assessment of drug-induced cardiotoxicity	82	Echo
Diagnosis of acute osteomyelitis (adults)	72	MRI
Diagnosis of avascular necrosis	70	MRI
SLNB*	67	Blue dye
Suspected obstructive uropathy (adults and children)	64	U/S
Suspected obstructive uropathy (adults and children)	64	U/S
Evaluation of renal function — renovascular hypertension	62	U/S

Table 6: Priority Ranking of Uses of ^{99m}Tc		
Clinical Use	**Score**	**Next Best Alternative (If Available)**
Diagnosis of (stress) fracture	57	MRI

AA = abdominal angiography; CT = computed tomography; CTPA = computed tomography pulmonary angiography; Echo = echocardiography; ^{18}F = fluoride; ^{18}FDG = fluorodeoxyglucose; GI = gastrointestinal; ICD = implantable cardioverter-defibrillators; ^{111}In = indium-111; MRA = magnetic resonance angiography; MRI = magnetic resonance imaging; MRU = magnetic resonance urography; PET = positron emission tomography; SLNB = sentinel lymph node biopsy; ^{99m}Tc = technetium-99m; U/S = ultrasound; WBC = white blood cells.

* Assumes that using blue dye alone is a viable alternative.

DISCUSSION

Summary

The purpose of this project was to provide national guidance on the optimal use of ^{99m}Tc during a situation of reduced supply. While there are a number of ways that the supply of ^{99m}Tc could be optimized, the focus of this project was on prioritization. We developed a framework by which relevant factors to be considered when allocating ^{99m}Tc can be combined to create a priority ranking.

Technetium-99m is used in the diagnosis or management of a wide array of conditions — from cardiac imaging, to evaluation of renal function in patients who received kidney transplants, to detection of a fracture. We acknowledged that we would not be able to prioritize all uses of ^{99m}Tc; however, we wanted to select a group of uses that account for the majority of patients who would be seen at nuclear medicine departments within Canadian hospitals.

A total of 24 clinical uses were selected for the prioritization process. The 24 uses were evaluated against 11 criteria that were developed by CADTH and MIIMAC. The criteria represent factors that should be considered when allocating the isotope during a period of reduced supply and are reflective of the varied perspectives on MIIMAC. For each of the uses, a research report was generated. Each report provided a summary of evidence found relating to each of the 11 criteria. Overall, the amount and quality of the related evidence varied between criteria and between clinical uses. The use of MCDA allowed for the comparison of very different clinical uses using the same framework.

Importantly, MIIMAC discussed the implementation of a priority ranking in a real-world clinical setting. Practically, when the available supply of ^{99m}Tc is reduced, the isotope would be allocated according to the priority list — first to high-priority clinical uses. Any remaining isotope activity at day's end would be allocated in similar manner, recognizing that some uses may require more of the isotope than what is remaining. In this instance, that particular clinical use would be skipped and the residual isotope would be used for the next use in the priority ranking for which there is adequate activity.

The guidance[9] developed previously by Health Canada and based on a disruption plan produced by the Government of Canada provided a number of suggestions to maximize the use of the existing supply of ^{99m}Tc. These included using a lower dose of the isotope and scanning for a longer period of time, adjusting the scheduling of procedures to allow for more efficient use of the ^{99m}Tc generator, using alternative imaging procedures, and

prioritizing patients who will receive the isotope. An explanation of the methodology used to develop the existing guidance was not available.

With respect to prioritization, the Health Canada guidance focused largely on urgent medical need as a driver for priority. No rank-order was provided and the majority of the clinical uses listed as “Priority Needs for Tc-99m” are uses for which an alternative is either not available or is contraindicated. Clinical uses of ^{99m}Tc for which there was no alternative, or the alternative(s) were not appropriate for a particular patient population, were not included in our prioritization process. Indeed, our group concluded that such uses should receive priority allocation and our project addressed the use of ^{99m}Tc beyond these “must do” uses.

The one notable difference between our priority list and that distributed by Health Canada is the use of ^{99m}Tc-based imaging to identify the sentinel node, and thereby provide information related to stage, in patients newly diagnosed with breast cancer. It is important to note that our process identified two alternative approaches to identifying the sentinel node — the use of blue dye alone and removal of all axillary nodes (axillary lymph node dissection; ALND).

In our analysis, the blue dye alone was rated as a relatively strong alternative to the ^{99m}Tc-based test; however, we acknowledge that at some institutions, this may not be a viable alternative. In this circumstance, ALND would be the only alternative. Given that ALND was rated as a less favourable alternative to the ^{99m}Tc-based test, at these institutions, identification of the sentinel node would likely receive higher priority.

Web-based prioritization tool

While the primary objective of the project was to develop, using a national perspective, a priority ranking of the most common clinical uses of ^{99m}Tc for use during a period of reduced supply, we recognized that some criteria such as the availability of alternatives, and health disparities, as well as the relative importance of the criteria, will differ between jurisdictions in Canada.

To that end, we are creating a web-based prioritization tool. The web tool will enable decision-makers to identify, from the national ranked list, the clinical uses of ^{99m}Tc applicable at their institution, as well as the alternative imaging modalities available. The tool will also allow for the re-weighting of the criteria, making the evaluation reflective of their local environment.

The output of the tool will be a site-specific, ranked list of clinical uses requiring ^{99m}Tc that can be used to assist local prioritization during a supply disruption and that is consistent with the national ranked list. A ranked list of alternative medical imaging modalities for each clinical use that can be used in lieu of ^{99m}Tc-based imagining will also be generated. Once complete, organizations can review or revise their customized priority list at any time – most importantly when there are major changes (e.g., new equipment, new procedures, new information, etc.).

A key component of this project was the involvement of individuals who provided unique perspectives on not only the development of the criteria, but also regarding the relative importance of the criteria. While the process can be completed by one or more

individuals who share a similar perspective (e.g., physicians from one department or administrators within a health region), it is strongly encouraged that as many as possible of the perspectives from those either involved with or affected by the allocation of ^{99m}Tc be involved in the process. The intent is for users of the tool to work collaboratively with key decision-makers within hospitals, health authorities, and jurisdictions to create a customized priority ranking that is reflective of their local setting. The tool will be available on the CADTH website after the report is finalized.

Strengths and Weaknesses of this Assessment

To allow for optimal committee dynamics, we were cognisant of its size, ensuring the composition of MIIMAC was comprehensive, but not exhaustive. For example, non-academic hospitals were less represented, some groups of referring physicians were not represented, and expertise of an adult radiologist specializing in CT and MRI would have been beneficial.

MCDA provides a transparent and explicit basis for decision-making and a framework for combining decision-makers' values and preferences with researcher measurement of performance.[15] The use of MCDA methodology in this assessment represents an innovative approach to an allocation decision. To our knowledge, this is the first instance in which MCDA has been used to prioritize patient populations. This approach also promotes consistency — within hospitals and within health authorities or jurisdictions — in how patients are prioritized and ultimately, who receives a ^{99m}Tc-based test during shortage situations.

The criteria used to evaluate the selected clinical uses and their alternative imaging modalities were chosen after extensive dialogue between key members of the medical decision-making community — practitioners, patients, and hospital administrators. This should ensure that the report and its findings are relevant to the end-users of the final product. The criteria were weighted according to their importance in the decision-making process by MIIMAC members. Care was taken to ensure that all committee members had a high level of comfort with each step of the process before proceeding.

To ensure consistency in how the clinical uses and their alternatives were rated, the ratings were validated first by a WG and then by MIIMAC. The scarcity of data to inform some of the criteria is a limitation of the assessment. In addition, because of the timelines associated with the project, we limited inclusion of studies for those six criteria requiring comparison of the ^{99m}Tc-based test directly to an alternative imaging modality to studies making direct comparisons. This approach likely resulted in the exclusion of studies that may have further supported or contradicted our findings for a particular criterion. However, each report was reviewed by at least one clinical expert on MIIMAC.

Generalizability of Findings

The priority ranking presented in this report is from the national perspective, and thus should be considered somewhat generalizable across the country. MIIMAC consisted of representatives from eight different jurisdictions (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, and Newfoundland). We strove for representation from both academic and non-academic hospitals; however, the composition of the committee does favour those who work at larger centres.

CADTH and MIIMAC recognize that there is significant variation in, among other things, the availability of alternatives, the availability of expertise, and the impact on health disparities from one jurisdiction to another, making it difficult to produce a national report that is truly generalizable. For this reason, an output of our work is the accompanying web-based prioritization tool that was developed to allow decision-makers to conduct customized analyses at the local level. The results of the customized analysis should be appropriate to the population of interest.

Knowledge Gaps

The lack of high-quality evidence regarding the diagnostic imaging procedures assessed in this project was a significant challenge to the production of the research reports used to inform the MCDA process. Where evidence from peer-reviewed published sources or the grey literature was not identified, we relied on expert opinion. Given more time, certain data could likely have been acquired through survey methods. Select knowledge gaps are highlighted in Table 7.

Table 7: Evidence Base

Criterion	Knowledge Gaps
Size of the affected population	Surveillance is common in the realm of infectious disease, but point prevalence estimates were not available for the clinical conditions included in this report.
Impact on health disparities	While health disparity reduction has been a health sector priority for decades,[14] we struggled to find data for any of the population groups identified as having a disproportionate burden. In the absence of these data, no informed comment could be made as to whether a supply disruption would reduce or increase health disparities.
Relative acceptability of the test to patients	Few studies[16,17] have investigated the acceptability of ^{99m}Tc-based tests, compared with the alternatives, from the patient's perspective. The two referenced in the evidence reports prepared by CADTH included 41 patients and 63 patients, respectively.
Relative diagnostic accuracy of the test	The bulk of the evidence presented to MIIMAC was about the diagnostic accuracy of the various tests. However, the evidence base is not as robust as it is for other health technologies, such as pharmaceuticals.
Relative risks associated with the test	There were discrepancies in the reported radiation dose associated with the nuclear and non-nuclear diagnostic imaging procedures being evaluated.
Relative availability of expertise and experience required for the test	This criterion was informed primarily by expert opinion. While the NPS captures the number of physicians and specialists in Canada, expert judgment was required to estimate how many of a given specialty might have the expertise required to perform a given procedure. For select non-imaging alternatives, some published information was available regarding competency to perform the procedure.
Accessibility of alternatives	This criterion was informed primarily by expert opinion. While the number of devices across the country, province, and territory is made available by CIHI, expert judgment was required to estimate the capacity of the system to accommodate increased demand for the alternatives.

CADTH = Canadian Agency for Drugs and Technologies in Health; CIHI = Canadian Institute of Health Information; MIIMAC = Medical Isotopes and Imaging Modalities Advisory Committee; NPS = National Physician Survey; ^{99m}Tc = technetium-99m.

CONCLUSIONS AND IMPLICATIONS FOR DECISION-MAKING

Recent global shortages in the supply of the medical isotope prompted Health Canada to request that CADTH produce national guidance on the optimal use of ^{99m}Tc. While there are a number of strategies that can be taken to optimize the use of the isotope — many of which were employed during the last supply disruption — the focus of our work is optimal allocation through prioritization in the event that the supply of ^{99m}Tc is scarce.

Working with a multi-disciplinary committee comprising experts in research methodology, health economics, institutional and regional representatives from health professions (nuclear medicine physicians, radiologists, technologists, cardiologists, a medical oncologist, a radiopharmacist, a medical ethicist), administrators from ministries of health, and members of the public, we developed a framework using a multi-criteria–based approach by which relevant factors to be considered when allocating ^{99m}Tc can be combined to create a priority ranking of clinical uses of the isotope.

The ultimate result of the process is a prioritized list of clinical uses of ^{99m}Tc that is backed by an explicit methodology that organizes all relevant information. Since the process is explicit, results can be explained, or adjusted to allow for changes in the relevant information (e.g., acquisition of new equipment or changes to wait times for imaging procedures). When the available supply of ^{99m}Tc is reduced, the isotope would be allocated first to high-priority clinical uses.

The list of clinical uses that require ^{99m}Tc-based imaging is not exhaustive. Its intent is to assist health care practitioners and decision-makers in managing a large proportion of the work they would see within their institution(s) during a time of reduced supply. Importantly, uses of ^{99m}Tc for which no reliable alternative exists were not formally included in the prioritization process because they should be allocated ^{99m}Tc, if available.

We strove to include the most relevant alternatives to ^{99m}Tc-based imaging, which typically included other radioisotopes, CT, MRI, PET, and U/S. We did not include modalities or approaches that were under investigation. In some jurisdictions, select alternative imaging modalities may be unavailable. In addition, wait times for imaging modalities in some jurisdictions may already be long, or there may be restrictions on the ordering of some of these modalities by family physicians. Institutions, health authorities, and jurisdictions may wish to consider measures to increase access to these imaging modalities, such as an extension to the hours the scanners are in operation or changes to ordering privileges.

The output of this project, the national guidance, has become the foundation for a flexible web-based tool that can be customized for local use. Ideally, users of the web-based tool will work collaboratively with key decision-makers at their level to create a customized priority ranking that is reflective of their local setting – be it a hospital, a health authority, or a jurisdiction, and consistent across the country.

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APPENDICES

Appendix 1: Members of the Medical Isotopes and Imaging Modalities Advisory Committee (MIIMAC) as of March 2012

Patrick Au
Dr. Robert Beanlands
Dr. Charles Butts
Gazira Chan
Susan Delaney
Dr. Sandor Demeter
Dr. Terry Ell
Dr. Dean Fergusson
Heather Gibson
Dawn-Marie King
Dr. Norman Laurin
Dr. Ted Lyons
Dr. Gilbert Matte
Dr. Sandy McEwan*
Dr. Craig Mitton
Christine Preece
Jean Pruneau
Dr. Martin Reed*
Dr. Terrence Ruddy
Rick Scanlan
Dr. Lisa Schwartz
Dr. Eric Turcotte
Dr. George Wells

*Indicates a position of co-chair.

Appendix 2: Research reports

Please refer to: http://www.cadth.ca/en/products/optimal-use/medical-isotopes-project/reports

Appendix 3: Rating Tool

Table A1: Domain 1 — Criteria Related to the Underlying Health Condition								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
#1: Size of the affected population	The estimated size of the patient population that is affected by the underlying health condition and that may potentially undergo the test. The ideal measure is point prevalence, or information on how rare or common the health condition is.	N/A	N/A	N/A	≤ 1 in 10,000 (0.01%)	> 1 in 10,000 (0.01%) and ≤ 1 in 1,000 (0.1%)	> 1 in 1,000 (0.1%) and ≤ 1 in 100 (1%)	> 1 in 100 (1%)
#2: Timeliness and urgency of test results in planning patient management	The timeliness and urgency of obtaining the test results in terms of their impact on the management of the condition and the effective use of health care resources.	N/A	N/A	N/A	Situations that would score 0 include: a) when the target time frame for performing the ^{99m}Tc-based test is > 30 days, or obtaining the test results in the appropriate	Situations that would score 1 include: a) when the target time frame for performing the ^{99m}Tc-based test is between 8 and 30 days and obtaining the test results in the appropriate	Situations that would score 2 include: a) when the target time frame for performing the ^{99m}Tc-based test is between 8 and 30 days and obtaining the test results in the appropriate timely	Situations that would score 3 include: a) when the target time frame for performing the test is in 24 hours or less and obtaining the test results in the appropriate timely

Table A1: Domain 1 — Criteria Related to the Underlying Health Condition								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
					timely manner for the underlying condition has no impact on the management of the condition or the effective use of health care resources b) target time frame for performing the ^{99m}Tc-based test is between 8 and 30 days and obtaining the test results in the appropriate timely manner for the underlying condition has minimal	timely manner for the underlying condition has moderate impact on the management of the condition or the effective use of health care resources b) target time frame for performing the test is between 2 and 7 days and obtaining the ^{99m}Tc-based test results in the appropriate timely manner for the underlying condition has minimal impact on the management of the condition or the effective	manner for the underlying condition has significant impact on the management of the condition or the effective use of health care resources b) target time frame for performing the test is between 2 and 7 days and obtaining the ^{99m}Tc-based test results in the appropriate timely manner for the underlying condition has moderate impact on the management of the condition or the effective use of health care resources c) target time	manner for the underlying condition has moderate to significant impact on the management of the condition or the effective use of health care resources b) when the target time frame for performing the test is in 2 to 7 days and obtaining the ^{99m}Tc-based test results in the appropriate timely manner for the underlying condition has significant impact on

Table A1: Domain 1 — Criteria Related to the Underlying Health Condition								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
					impact on the management of the condition or the effective use of health care resources	use of health care resources	frame for performing the test is in 24 hours or less and obtaining the ^{99m}Tc-based test results in the appropriate timely manner for the underlying condition has minimal impact on the management of the condition or the effective use of health care resources	the management of the condition or the effective use of health care resources
#3: Impact of not performing a diagnostic imaging test on mortality related to the underlying condition	Impact of not performing a diagnostic imaging test, in whatever way, on the expected mortality from the underlying condition. Measures could include survival curves showing survival over time and/or	N/A	N/A	N/A	Diagnostic imaging test results have no impact on mortality	Diagnostic imaging test results can have minimal impact on mortality	Diagnostic imaging test results can have moderate impact on mortality	Diagnostic imaging test results can have significant impact on mortality

Table A1: Domain 1 — Criteria Related to the Underlying Health Condition								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
	survival at specific time intervals with and without the test.							
#4: Impact of not performing a diagnostic imaging test on morbidity or quality of life related to the underlying condition	Impact of not performing the diagnostic imaging test, in whatever way, on the expected morbidity, or on the quality of life reduction of the underlying condition. Measures of impact may include natural morbidity outcome measures, like events or disease severity, or might be expressed using generic or disease-specific quality of life rating scales, with and without the test.	N/A	N/A	N/A	Diagnostic imaging test results have no impact on morbidity or quality of life	Diagnostic imaging test results can have minimal impact on morbidity or quality of life	Diagnostic imaging test results can have moderate impact on morbidity or quality of life	Diagnostic imaging test results can have significant impact on morbidity or quality of life

Table A2: Domain 2 — Criteria Comparing a ^{99m}Tc-based Test with an Alternative								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
#5: Relative impact on health disparities	Health disparities are defined as situations where there is a disproportionate burden (e.g., incidence, prevalence, morbidity, or mortality) amongst particular population groups (e.g., gender, age, ethnicity, geography, disability, sexual orientation, socio-economic status, and special health care needs). Impact on health disparities is assessed by estimating the proportion of current clients of the ^{99m}Tc-based test who are in population groups with disproportionate burdens. Note: The implication of this	The size of the patient population belonging to one of more disadvantaged groups is > 10% lower than the average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is 6% to 10% lower than the average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is 1% to 5% lower than the average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is equal to average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is 1% to 5% higher than the average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is 6% to 10% higher than the average for all clinical uses of ^{99m}Tc	The size of the patient population belonging to one of more disadvantaged groups is > 10% higher than the average for all clinical uses of ^{99m}Tc

Table A2: Domain 2 — Criteria Comparing a ^{99m}Tc-based Test with an Alternative								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
	definition is that everything else being the same, it is preferable to prioritize those clinical uses that have the greatest proportion of clients in groups with disproportionate burdens).							
#6: Relative acceptability of the test to patients	Acceptability of the ^{99m}Tc-based test from the patient's perspective compared with alternatives. Patient acceptability considerations include discomfort associated with the administration of the test, out-of-pocket expenses or travel costs, factors that may cause great inconvenience to patients, and other burdens. This criterion does not include	^{99m}Tc-based test is significantly less acceptable to patients	^{99m}Tc-based test is moderately less acceptable to patients	^{99m}Tc-based test is minimally less acceptable to patients	^{99m}Tc-based test and alternative test are similarly acceptable to patients	^{99m}Tc-based test is minimally more acceptable to patients	^{99m}Tc-based test is moderately more acceptable to patients	^{99m}Tc-based test is significantly more acceptable to patients

Table A2: Domain 2 — Criteria Comparing a ^{99m}Tc-based Test with an Alternative								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
	risks of adverse events, but is about everything related to the experience of undergoing the test.							
#7: Relative diagnostic accuracy of the test	Ability of the ^{99m}Tc-based test to correctly diagnose the patients who have the condition (sensitivity) and patients who do not have the condition (specificity) compared with alternatives.	Diagnostic accuracy of the ^{99m}Tc-based test is significantly lower than alternative	Diagnostic accuracy of the ^{99m}Tc-based test is moderately lower than alternative	Diagnostic accuracy of the ^{99m}Tc-based test is minimally lower	^{99m}Tc-based test and alternative test have similar diagnostic accuracies	Diagnostic accuracy of the ^{99m}Tc-based test is minimally better than alternative	Diagnostic accuracy of the ^{99m}Tc-based test is moderately better than alternative	Diagnostic accuracy of the ^{99m}Tc-based test is significantly better than alternative
#8: Relative risks associated with the test	Risks associated with the test (e.g., radiation exposure, side effects, adverse events) compared with alternatives. Risks could	^{99m}Tc-based test is significantly less safe	^{99m}Tc-based test is moderately less safe	^{99m}Tc-based test is minimally less safe	^{99m}Tc-based test and alternative have similar safety profiles	^{99m}Tc-based test is minimally more safe	^{99m}Tc-based test is moderately more safe	^{99m}Tc-based test is significantly more safe

Table A2: Domain 2 — Criteria Comparing a ^{99m}Tc-based Test with an Alternative								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
	include immediate safety concerns from a specific test or long-term cumulative safety concerns from repeat testing or exposure.							
#9: Relative availability of personnel with expertise and experience required for the test	Availability of personnel with the appropriate expertise and experience required to proficiently conduct the test and/or interpret the test findings compared with alternatives.	N/A	N/A	N/A	> 95% of the procedures can be performed in a timely manner using the alternative, assuming the necessary equipment is available.	75% to 94% of the procedures can be performed in a timely manner using the alternative, assuming the necessary equipment is available.	25% to 74% of the procedures can be performed in a timely manner using the alternative, assuming the necessary equipment is available.	< 25% of the procedures can be performed in a timely manner using the alternative, assuming the necessary equipment is available.
#10: Accessibility of alternative tests (equipment and wait times)	Availability (supply) of equipment and wait times for alternative tests within the geographic area. Includes consideration of the capacity of the system to accommodate increased demand for the alternatives.	N/A	N/A	N/A	> 95% of the procedures can be performed in a timely manner using alternative, assuming that the necessary expertise is available.	75% to 94% of the procedures can be performed in a timely manner using alternative, assuming that the necessary expertise is available.	25% to 74% of the procedures can be performed in a timely manner using alternative, assuming that the necessary expertise is available.	< 25% of the procedures can be performed in a timely manner using alternative, assuming that the necessary expertise is available.

Table A2: Domain 2 — Criteria Comparing a ^{99m}Tc-based Test with an Alternative								
Criterion	**Definition**	**–3**	**–2**	**–1**	**0**	**1**	**2**	**3**
	Excludes any limitation on accessibility related to human resources considerations							
#11: Relative cost of the test	Operating cost of test (e.g., consumables, health care professional reimbursement fees) compared with alternatives.	Cost of the ^{99m}Tc-based test is significantly higher than alternative (i.e., incremental cost increase exceeds $501)	Cost of the ^{99m}Tc-based test is moderately higher than alternative (i.e., incremental cost increase is between $251 and $500)	Cost of the ^{99m}Tc-based test is minimally higher than alternative (i.e., incremental cost increase is between $26 and $250)	No difference in the cost of ^{99m}Tc-based test and alternative (i.e., incremental cost is between $0 and $25)	Cost of the ^{99m}Tc-based test is minimally lower than alternative (i.e., incremental cost decrease is between $26 and $250)	Cost of the ^{99m}Tc-based test is moderately lower than alternative (i.e., incremental cost decrease is between $251 and $500)	Cost of the ^{99m}Tc-based test is significantly lower than alternative (i.e., incremental cost decrease exceeds $501)

^{99m}Tc = technetium-99m.

Appendix 4: Weighted Composite Scores

Table A3: Final Ranking of Clinical Uses and Alternatives to ^{99m}Tc-based Imaging		
Clinical Use	**Weighted Composite Score**	**Alternative**
Detection of lower GI bleeding	**200**	**AA**
Assessment of bile leak	**139**	**U/S**
	152	MRCP
	165	CT
	177	ERCP
Detection of pulmonary embolism	**135**	**CTPA**
Diagnosis of (osteoporotic) fracture	**132**	**MRI**
	134	CT
	183	^{18}F-PET
Diagnosis of acute osteomyelitis (children)	**131**	**CT**
	137	U/S
	157	MRI
Imaging for metastatic disease (breast)	**125**	**^{18}F-PET**
	142	^{18}FDG-PET
Imaging for metastatic disease (lung)	**118**	**^{18}FDG-PET**
	125	^{18}F-PET
Assessment of prognosis post-myocardial infarction	**117**	**Echo**
	120	^{201}Tl-SPECT MPI
	130	PET
	135	MRI
	137	CTCA
Detection of ischemia	**117**	**Echo**
	120	^{201}Tl-SPECT MPI
	130	PET
	135	MRI
	137	CTCA
Imaging for metastatic disease (prostate)	**113**	**^{18}F-PET**
Preoperative assessment prior to vascular, non-cardiac surgery	**108**	**Echo**
	111	^{201}Tl-SPECT MPI
	121	PET
	126	MRI
	128	CTCA
Evaluation of painful prosthesis (loosening)	**101**	**Arthrography**
	145	^{18}F-PET
ICD decision-making	**99**	**Echo**
	124	MRI
Diagnosis of acute cholecystitis	**96**	**U/S**
	121	MRCP
	134	CT
Evaluation of renal function — post-transplant	**90**	**U/S**
Evaluation of painful prosthesis (infection)	**85**	**^{111}In-WBC**
	101	Arthrography
	169	^{18}FDG-PET
Assessment of drug-induced cardiotoxicity	**82**	**Echo**
	107	MRI
Diagnosis of acute osteomyelitis (adults)	**72**	**MRI**
	77	^{111}In-WBC

Table A3: Final Ranking of Clinical Uses and Alternatives to ^{99m}Tc-based Imaging		
Clinical Use	**Weighted Composite Score**	**Alternative**
	93	CT
	130	^{18}FDG-PET
Diagnosis of avascular necrosis	**70**	**MRI**
SLNB	**67**	**Blue Dye**
	119	ALND
Suspected obstructive uropathy (adults)	**64**	**U/S**
	107	MRU
Suspected obstructive uropathy (children)	**64**	**U/S**
	132	MRU
Evaluation of renal function — renovascular hypertension	**62**	**U/S**
	83	CT
	97	MRA
	115	RCA
Diagnosis of (stress) fracture	**57**	**MRI**
	59	CT
	108	^{18}F-PET

AA = abdominal angiography; ALND = axillary lymph node dissection; CT = computed tomography; CTCA = computed tomography coronary angiography; Echo = echocardiography; ^{18}F-PET = ^{18}F-labelled sodium fluoride positron emission tomography; ^{18}FDG-PET = ^{18}F-labelled fluorodeoxyglucose positron emission tomography; ^{111}In-WBC = indium-111–labelled white blood cell scan; MRA = magnetic resonance angiography; MRCP = magnetic resonance cholangiopancreatography; MRI = magnetic resonance imaging; MRU = magnetic resonance urography; PET = positron emission tomography; RCA = renal catheter angiography; ^{99m}Tc = technetium-99m; ^{201}Tl-SPECT MPI = thallium-201–labelled single-photon emission tomography myocardial perfusion imaging; U/S = ultrasound.

Note: numbers in bold represent the best alternative to ^{99m}Tc-based imaging based on the criteria assessed.

Appendix 5: Criteria Ratings for All Clinical Uses

Table A4: Individual Ratings for Each Clinical Use of ^{99m}Tc

Clinical Use	Size of Affected Population	Timeliness and Urgency	Impact on Mortality	Impact on Morbidity	Alternative to ^{99m}Tc-Based Imaging Test	Health Disparities*	Acceptability to Patients	Diagnostic Accuracy	Risk	Personnel	Equipment	Cost
Detection of lower GI bleeding	1	3	1	2	AA	0	3	3	3	2	2	3
Assessment of bile leak	1	3	2	3	CT	0	1	2	1	0	0	1
					ERCP	0	3	–2	3	3	2	3
					MRCP	0	–1	0	–1	2	2	2
					U/S	0	–1	2	–1	0	0	–1
Detection of pulmonary embolism	2	3	3	2	CTPA	0	–1	0	1	0	0	–1
Diagnosis of (osteoporotic) fracture	2	3	2	3	CT	0	0	0	0	0	0	–1
					MRI	0	–1	–1	–1	1	1	1
					^{18}F-PET	0	–1	0	0	3	3	3
Diagnosis of acute osteomyelitis (children)	2	3	0	3	CT	0	1	2	0	0	0	–1
					MRI	0	2	1	1	1	2	1
					U/S	0	–1	3	–1	2	0	–2
Imaging for metastatic disease (breast)	2	2	0	3	^{18}FDG-PET	0	0	0	0	3	3	3
					^{18}F-PET	0	–1	–1	0	3	3	3
Imaging for metastatic disease (lung)	2	2	0	3	^{18}FDG-PET	0	0	–2	0	3	3	3
					^{18}F-PET	0	–1	–1	0	3	3	3
Assessment of prognosis post-myocardial infarction	2	2	2	2	CTCA	0	–1	1	0	2	2	–2
					Echo	0	–1	0	0	2	1	–2
					MRI	0	0	–1	0	3	3	–1
					PET	0	–1	–1	0	2	3	1
					^{201}TI-SPECT	0	0	1	0	0	0	0
Detection of ischemia	2	2	2	2	CTCA	0	–1	1	0	2	2	–2
					Echo	0	–1	0	0	2	1	–2

Table A4: Individual Ratings for Each Clinical Use of ^{99m}Tc												
Clinical Use	**Size of Affected Population**	**Timeliness and Urgency**	**Impact on Mortality**	**Impact on Morbidity**	**Alternative to ^{99m}Tc-Based Imaging Test**	**Health Disparities***	**Acceptability to Patients**	**Diagnostic Accuracy**	**Risk**	**Personnel**	**Equipment**	**Cost**
					MRI	0	0	–1	0	3	3	–1
					PET	0	–1	–1	0	2	3	1
					^{201}TI-SPECT	0	0	1	0	0	0	0
Imaging for metastatic disease (prostate)	2	2	0	3	^{18}FDG-PET	0	–1	–2	0	3	3	3
Preoperative assessment prior to vascular, non-cardiac surgery	1	2	2	2	CTCA	0	–1	1	0	2	2	–2
					Echo	0	–1	0	0	2	1	–2
					MRI	0	0	–1	0	3	3	–1
					PET	0	–1	–1	0	2	3	1
					^{201}TI-SPECT	0	0	1	0	0	0	0
Evaluation of painful prosthesis (loosening)	1	1	1	3	Arthrography	0	2	0	2	0	0	–1
					^{18}FDG-PET	0	1	0	1	3	3	3
ICD decision-making	1	2	3	1	Echo	0	–1	1	–1	0	0	–1
					MRI	0	–1	0	–1	2	2	2
Diagnosis of acute cholecystitis	1	3	1	2	CT	0	1	2	1	0	0	1
					MRCP	0	–1	0	–1	2	2	2
					U/S	0	–1	1	–1	0	0	1
Evaluation of renal function — post-transplant	0	3	1	3	U/S	0	–1	0	–1	0	0	–1
Evaluation of painful prosthesis (infection)	1	1	1	3	Arthrography	0	2	0	2	0	0	–1
					^{18}FDG-PET	0	1	2	1	3	3	3
					^{111}In-WBC	0	0	–2	1	1	1	2
Assessment of drug-induced cardiotoxicity	1	2	1	2	Echo	0	–1	1	–1	0	0	1
					MRI	0	–1	0	–1	2	2	2
Diagnosis of acute osteomyelitis	1	2	0	2	CT	0	1	2	0	0	0	–1

Table A4: Individual Ratings for Each Clinical Use of ^{99m}Tc												
Clinical Use	**Size of Affected Population**	**Timeliness and Urgency**	**Impact on Mortality**	**Impact on Morbidity**	**Alternative to ^{99m}Tc-Based Imaging Test**	**Health Disparities***	**Acceptability to Patients**	**Diagnostic Accuracy**	**Risk**	**Personnel**	**Equipment**	**Cost**
(adults)					^{18}FDG-PET	0	–1	1	1	3	3	3
					^{111}In-WBC	0	0	–1	1	1	1	1
					MRI	0	–1	0	–1	1	2	1
Diagnosis of avascular necrosis	1	2	0	2	MRI	0	–1	–1	–1	1	2	1
SLNB	1	3	0	3	ALND	0	3	0	1	0	0	1
	1	3	0	0	Blue dye alone	0	–1	1	0	2	0	–1
Suspected obstructive uropathy (adults)	1	1	0	2	MRU	0	–1	2	–1	3	2	2
					U/S	0	–1	2	–1	0	0	–1
Suspected obstructive uropathy (children)	1	1	0	2	MRU	0	2	2	1	3	2	2
					U/S	0	–1	2	–1	0	0	–1
Evaluation of renal function — renovascular hypertension	2	1	1	1	CTA	0	2	0	2	0	0	0
					MRA	0	–1	0	1	2	2	2
					RCA	0	3	–1	3	2	2	2
					U/S	0	–1	0	–1	2	0	–1
Diagnosis of (stress) fracture	2	1	0	2	CT	0	0	0	0	0	0	–1
					MRI	0	–1	–1	–1	1	1	1
					^{18}F-PET	0	–1	0	0	3	3	3

AA = abdominal angiography; ALND = axillary lymph node dissection; CT = computed tomography; CTCA = computed tomography coronary angiography; CTPA = computed tomography pulmonary angiography; Echo = echocardiography; ERCP = endoscopic retrograde cholangiopancreatography; ^{18}F-PET = ^{18}F-labelled sodium fluoride positron emission tomography; ^{18}FDG-PET = ^{18}F-labelled fluorodeoxyglucose positron emission tomography; GI = gastrointestinal; ICD = implantable cardioverter-defibrillator; ^{111}In-WBC = indium-111–labelled white blood cell scan; MRA = magnetic resonance angiography; MRCP = magnetic resonance cholangiopancreatography; MRI = magnetic resonance imaging; MRU = magnetic resonance urography; PET = positron emission tomography; RCA = renal catheter angiography; SLNB = sentinel lymph node biopsy; ^{99m}Tc = technetium-99m; ^{201}Tl-SPECT MPI = thallium-201–labelled single-photon emission tomography myocardial perfusion imaging; U/S = ultrasound.

*The relative impact of the health disparities criterion was not rated at the national level by MIIMAC; therefore, a rating of 0 was arbitrarily selected for scoring purposes.