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Transcatheter Aortic Valve Replacement

Environmental Scan

Context

Aortic stenosis, the most common valvular heart disease, occurs when there is a narrowing of the aortic valve opening. It is typically caused by age-related progressive build-up of calcium and scarring of the aortic valve, which creates obstructed blood flow out of the left ventricle to the rest of the body. Left untreated, aortic stenosis can lead to heart failure. Prognosis in the absence of treatment is poor; most patients will die within five years.[1] Currently, there are no effective medical therapies that can prevent the progression of aortic stenosis. Surgical aortic valve replacement (SAVR) is the only approach for severe aortic stenosis.[2] Transcatheter aortic valve replacement (TAVR) has emerged as a potential alternative for patients with severe aortic stenosis who are considered to be at high risk or who are ineligible for conventional SAVR due to age and comorbidities.

It is estimated that approximately 3% of the population older than 75 years of age, and 4% to 8% of people age 80 years and older have severe aortic stenosis.[2] Aortic stenosis is increasing in prevalence as the Canadian population shifts toward an aged demographic.

The two most used TAVR devices are the Edwards Sapien valve and the Medtronic CoreValve.[3] Since 2007, both the CoreValve and the Edwards Sapien valve have been available across Canada through a Special Access Program specifically for patients with symptomatic aortic valve stenosis who are not eligible for surgical valve replacement.[4] The Edwards Sapien valve (Edwards Lifesciences) was approved by Health Canada as a Class 4 device on June 22, 2011 (License number 86404) based on the results of the first 12 months of data from the PARTNER I trial. The CoreValve System (Medtronic) was licensed by Health Canada on August 1, 2012 (License number 89391). The device was recommended as a Class 4 medical device with a condition that the manufacturer provides ongoing evidence of safety and effectiveness from both clinical studies and marketing history for a period of five years post licensing.

Objectives

The purpose of this report is to identify new and emerging evidence on TAVR as an alternative treatment for patients with severe aortic stenosis. The following questions are addressed:

1. Have health technology assessments (HTAs) been published that compare TAVR with SAVR, and has new evidence emerged on TAVR effectiveness since the publication of those HTAs?
2. Are there randomized controlled trials (RCTs) currently in progress that compare TAVR with SAVR or standard therapy?
3. Are there newer TAVR technologies on the horizon?
4. To what extent is TAVR being used across Canada and how is the procedure funded?

Approach

This Environmental Scan is not intended to provide a comprehensive review of the topic. Results are based on a limited literature search of HTAs published between 2009 and 2012. Other publicly accessible information was used to identify new and emerging TAVR trials, guidelines, and devices. A survey was conducted to determine the use and funding of TAVR across Canada. This Environmental Scan does not include a systematic review or critical appraisal of the evidence.

Findings

1. Have HTAs been published that compare TAVR with SAVR, and has new evidence emerged on TAVR effectiveness since the HTA publication?

Health Technology Assessments

Ten HTAs have been published on the use of TAVR for patients with severe aortic valve stenosis (four of which are rapid reviews of the technology) between January 2009 and September 2012.[5-16] Most of these assessments were conducted after the results of the one-year follow-up PARTNER I trial was published.[5,7,9-12,16] The PARTNER I trial was the first, and to-date only, completed RCT of safety and effectiveness of TAVR in patients with severe symptomatic aortic stenosis who were considered to be at high risk for conventional surgery.[17,18] The comparator for one cohort (Cohort A; high surgical risk but operable patients) of the PARTNER I trial was SAVR. The comparator for the second cohort (Cohort B; high surgical risk but inoperable patients) of the PARTNER I trial was medical management and/or balloon aortic valvuloplasty (see Appendix A for further details of the study).

Seven HTAs included data from the PARTNER I RCT;[5,7,9-12,16] three exclusively,[9,11,12] and four incorporated additional levels of evidence, including other HTAs,[5,14-16] comparative non-randomized studies,[5,7,10] case series,[5,7,10] registry data,[10] and evidence-based guidelines.[16] Other notable characteristics of the 10 HTAs were that 4 were published in 2012,[5,7,9,10] 3 in 2011,[11,12,16] 2 in 2010,[14,15] and 1 in 2009.[13] Six were Canadian assessments.[9,10,13-16] Four assessments concluded that a multidisciplinary team of physicians including, for example, interventional cardiologists, cardiac surgeons, cardiac anesthesiologists and an expert in cardiac imaging should be involved in patient selection and risk determination for TAVR.[5,7,10,11]

Canada: Clinical Considerations

PARTNER trial data were included in three of the Canadian assessments: Health Quality Ontario (HQO),[9] Institut national d'excellence en santé et en services sociaux (INESSS),[10] and Canadian Agency for Drugs and Technologies in Health (CADTH) (2011).[16] These assessments compared TAVR with SAVR and/or medical treatment, and each assessment reported on one or two subgroups of patients: inoperable and operable but high risk.

The HQO[9] assessment compared TAVR with standard of care and SAVR. The SAVR comparator included two patient groups (TAVR compared with SAVR in patients for whom surgery is considered unsuitable, and TAVR compared with SAVR in patient for whom surgery is considered high risk). The INESSS[10] assessment included three comparators (SAVR, medical treatment, and balloon valvuloplasty) and two patient groups (patients for whom surgery is considered unsuitable, and patients for whom surgery is considered high risk). The CADTH[16] 2011 assessment compared TAVR with SAVR in

patients for whom surgery is considered unsuitable. Amongst the assessments that examined patients who were not surgical candidates, there was consensus that TAVR was either an adequate or effective alternative to SAVR.[9,10,16] Of the assessments that reported on patients for whom surgery is considered high risk,[9,10] there was support for the use of TAVR in this population. The HQO assessment[9] noted that in patients for whom surgery is considered high risk, TAVR has a mortality rate similar to SAVR, and was associated with significant adverse effects.

Three Canadian assessments were published before the release of the PARTNER I trial data. These assessments were based on data from comparative non-randomized studies, case series, and uncontrolled patient registries.[13-15] One assessment reported that in spite of a high-mortality risk, TAVR gave patients symptomatic relief and potential life extension;[13] another reported that TAVR was a feasible option, with the potential for symptomatic relief, for patients who were considered to be inoperable.[15] The safety and efficacy of TAVR relative to SAVR, medical management, or valvuloplasty in the other assessment were reported to be unknown (see appendix A for more details).[14]

Canada: Cost Considerations

The HQO[9] assessment conducted an economic analysis to evaluate the cost-effectiveness of TAVR compared with standard of care in inoperable patients, and TAVR compared with SAVR in operable patients. The assessment reported the cost of a valve to be $37,606. The cost per life-year of TAVR compared with standard therapy in inoperable patients was $33,141. The cost per life-year of TAVR compared with SAVR in operable patients was $870,143. The assessment concluded that TAVR may be cost-effective for inoperable patients, but it is not cost-effective for patients who are operable. These findings were, however, subject to considerable variation based on economic model assumptions regarding the cost of the long-term consequences of TAVR in the comparator interventions. In particular, the assumption regarding the impact on long-term mortality and quality of life was important. The INESSS[10] assessment concluded that adequate and dedicated funding is necessary to ensure the sustainability of TAVR programs in different centres. It also recommended that funding should cover costs related to patient selection; the TAVR procedure, including the cost of the device; and short and long-term follow-up of TAVR patients. The McGill University Health Centre (MUHC)[13] assessment reported that the procedure could be carried out at the MUHC in inoperable patients at a net cost of $24,024 (2009 prices). The MUHC assessment was published before the publication of PARTNER I trial data and its findings are based on an older version of the Edwards Sapien valve that was approved by Health Canada. The CADTH rapid assessment[14] did not report on cost-effectiveness due to a lack of published data at the time.

More recent cost-effectiveness information from the manufacturer of the Edward Sapien transcatheter aortic valve states that the cost of the TAVR kit (including the device components provided by the company for the procedure) currently available in Canada, is in the range of $24,000. Future cost-effectiveness analysis would have to consider the most current price of the device along with other updated health care costs.

International: Clinical Considerations

Four international assessments reported on PARTNER I trial data.[5,7,11,12] The United Kingdom's (UK) National Institute for Health and Clinical Excellence (NICE) assessment[5] compared TAVR with SAVR in three patient groups: TAVR compared with SAVR in patients for whom surgery was suitable, but presented a high risk; TAVR compared with SAVR in patients for whom surgery was unsuitable; and TAVR compared with SAVR in patients for whom surgery was a suitable option, but does not pose a high risk.[5] The third patient group, patients for whom surgery was suitable, had not previously been reviewed. The assessment concluded that in patients for whom surgery was unsuitable, there was sufficient evidence to support the use of TAVR. There was inadequate evidence to support the use of TAVR in patients who were suitable for surgery but were considered high risk, and in patients suitable for surgery where SAVR did not present a high risk.

Two international assessments, one from the Scottish Health Technologies Group (SHTG)[11] and the other from the Belgium Health Care Knowledge Centre (KCE)[12] compared TAVR with SAVR (Cohort A), and standard of care (Cohort B).[11,12] The assessments reported that in patients not suitable for surgery , TAVR was an effective alternative to standard of care. In patients for whom surgery was considered to be high-risk, one assessment reported that TAVR was not inferior to surgery but was associated with a significantly higher incidence of vascular complications and neurological adverse events,[11] and the other assessment reported that TAVR might be considered as an alternative to surgery for high-risk patients who are willing to accept a higher risk of stroke. It was noted that from an economic perspective it is hard to defend TAVR reimbursement as an efficient use of resources.[12]

The California Technology Assessment Forum (CTAF) assessment[7] exclusively compared TAVR with the standard of care and reported that for patients not suitable for surgery, TAVR is a more effective alternative to standard therapy.[7]

A consistent finding across the four international assessments that included PARTNER RCT trial data was that for patients who were not surgical candidates, TAVR was, at minimum, considered to be an adequate alternative to either SAVR or standard care. Inconsistent findings were reported from the three assessments that evaluated TAVR in patients for whom surgery was considered high risk (see Appendix A for further details).[5,11,12]

International: Cost Considerations

Three international assessments considered the cost implications of TAVR.[8,11,12] The CTAF[8] assessment evaluated two cost evaluations for TAVR that were based on the analyses of the PARTNER Cohort B trial. One of these studies estimated the cost of the valve to be US$30,000 with an estimated incremental cost-effectiveness ratio of US$50,200 per year of life saved and US$61,889 per quality-adjusted life-year. The second study estimated the incremental cost-effectiveness ratio to be £16,100 per quality-adjusted life-year. Neither study incorporated the capital costs required to build and operate the hybrid operating room/cardiac catheterization laboratory that is typically used with this procedure. The costs varied depending on the exact specifications of the hybrid operating room, but were estimated to be approximately US$3 million. The KCE[12] assessment concluded that TAVR should be reimbursed for patients who are considered to be inoperable due to anatomical factors. Patients who are considered inoperable due to medical factors are not eligible for reimbursement. The SHTG[11] assessment did

not report on cost-effectiveness due to a lack of published data at the time.

New Evidence

Since the publication of the HTAs described above, three new studies have been published on TAVR in severe aortic stenosis patients.[19-21] The Kodali et al. RCT,[19] a two year follow-up to the PARTNER study (Cohort A), compared TAVR with SAVR in 699 high-risk patients who had severe aortic stenosis. The author concluded that after two years, the two treatments were associated with similar rates of mortality, reduction in symptoms, and improved valve hemodynamics, but paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality.

The Makkar et al.[20] RCT, a two-year follow-up of the PARTNER (Cohort B) study, compared TAVR with standard therapy in 358 patients who were not suitable for surgery. The author concluded that in this population, TAVR reduced the rates of death and hospitalization, with an improvement in valve hemodynamics and a reduction in symptoms that were sustained at two years of follow-up.

Lange et al.,[21] conducted a multivariable analysis of data describing 420 patients with severe aortic stenosis who were considered to be at high surgical risk. The author concluded that the results of the study demonstrate an important paradigm shift toward the selection of lower surgical risk patients for TAVR and that significantly better clinical outcomes can be expected in lower than in higher surgical risk patients undergoing TAVR (see Appendix B for more details).

Another RCT,[22] the STACCATO trial, that compared TAVR with SAVR in operable patients, was prematurely halted due to complications associated with TAVR in this patient population.

Clinical Guidance

Two North American TAVR guidance documents have been published in 2012. The first is a position statement by the Canadian Cardiovascular Society.[23] This position statement presents the consensus of a representative group of cardiologists and cardiac surgeons, and is based on a literature review and an evaluation of the evidence using the GRADE approach.[24] The paper recommends that TAVR should be considered as a viable option in patients with aortic stenosis if the risk of open heart surgery is prohibitive or high. The paper also makes recommendations on valve-in-valve implantation, the evaluation process for TAVR candidates, TAVR programs, and for guidance for facilities and institutions.

A US paper[25] developed by expert consensus by the American College of Cardiology Foundation, the American Association of Thoracic Surgery, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons was also published in 2012. This document recommends TAVR in patients with severe symptomatic calcific stenosis of a trileaflet aortic valve where the valvular and aortic anatomy is suitable for TAVR and where survival is predicted to be more than twelve months in patients who have a prohibitive surgical risk. TAVR is also recommended in patients at high surgical risk. Additionally, recommendations are made for team-based approaches, TAVR screening, site selection, centre and physician experience, procedural performance, post-procedural care, and registries (see Appendix C for details).

2. Are there RCTs in progress that compare TAVR with SAVR or standard therapy?

There are currently five randomized clinical trials with the United States (US) National Institute of Health's clinical trial registry that are investigating the safety and efficacy of the Medtronic or Edwards Sapien transcatheter aortic valve devices for patients with severe aortic stenosis. These devices have either received Conformité Européenne (CE) Mark compliance in the European Union and/or approval from the Food and Drug Administration. Four of the studies are RCTs that compare TAVR with surgery,[26-29] either in patients at intermediate surgical risk[26,28,29] or patients at high or very high surgical risk.[27]

The PARTNER II multinational trial[28] will use the second generation Edwards Sapien XT heart valve and NovaFlex delivery system. This trial has two patient cohorts: Cohort A — patients who are at intermediate surgical risk for SAVR (operable) and, Cohort B — patients who are not suitable for aortic valve surgery (inoperable). Enrollment will include up to 2,000 patients in Cohort A, up to 500 patients in Cohort B, and up to 100 patients in each nested registry. Study patients will undergo clinical follow-up at discharge, 30 days, 6 months, 1 year, and then annually for a minimum of 5 years.

The CoreValve Surgical Replacement and Transcatheter Aortic Valve Implantation (SURTAVI)[29] trial received FDA conditional approval to begin evaluating the CoreValve System in approximately 2,500 patients at intermediate surgical risk for open heart aortic valve replacement. Currently, the Medtronic CoreValve System is available in the US for investigational use only.[30]

The CoreValve Pivotal trial will evaluate the safety and efficacy of the CoreValve system for use in the US in high or extremely high surgical risk patients.[27] The Trial is currently part of the US FDA's Continued Access Policy.[30]

The CHOICE trial[31] compares the Medtronic CoreValve with the newest Edwards Sapien XT device in high surgical risk patients.
A single group study evaluates the safety and efficacy of Medtronic CoreValve System in a very high surgical risk patient population.[32]

In the UK, the National Institute for Health Research has funded a randomized UK trial that will assess the clinical and cost utility of TAVR.[33] As well, a UK technology assessment on the cost-effectiveness of TAVR for aortic stenosis patients who cannot undergo surgery is expected to be published in 2013.[34] The UK established a TAVR registry in 2007. All hospitals in the UK must provide data for each patient who receives the TAVR procedure.[33]

3. Are there newer TAVR technologies on the horizon?

There is potential for the expansion of the TAVR patient population with severe aortic stenosis from inoperable or high-risk patients to patients who have intermediate to low surgical risk. The current patient population in which TAVR has been evaluated in the PARTNER trials represents a small subset, approximately 30%, of patients with severe aortic stenosis.[1] It is anticipated that improvements in TAVR technology will expand the use of TAVR to younger and healthier severe aortic stenosis patients.[35] Current challenges with TAVR devices, that second generation TAVR models are intended to address, include: steep learning curves for the surgical procedure, difficulties with placing the device with precision, difficulties

with repositioning the device for optimization, inability to atraumatically remove the device if necessary, and increased risk of perivalvular leakages, permanent pacemaker implants and stroke.[36]

There are at least eight next generation transcatheter aortic valves on the horizon. It is likely that data from ongoing trials of these devices will be used to support regulatory approvals.

Engager (Medtronic): In September 2011, Medtronic announced the start of the Engager European Pivotal Trial to pursue a CE Mark for the Engager Transcatheter Aortic Valve Implantation System.[37] The trial is a non-randomized, single-arm study that evaluates the safety and clinical performance of the new valve and delivery system in patients with severe aortic valve stenosis who are at high risk for surgical valve replacement.[38] Medtronic's Engager was formerly called the Ventor Embracer.[39]

Acurate TA (Symetis): CE Mark approval for the Acurate transapical (TA) TAVR system was received in September 2011 and the commercial launch of the device took place in October 2011. The CE Mark was granted using a composite of patients from two clinical trials involving 90 patients. A post-market surveillance study, the Symetis Aortic Valve Implantation Registry, for the continued safety monitoring of the Acurate TA is currently enrolling patients.[40] Symetis is also expected to start a study of its transfemoral system, the Acurte TF, by the end of 2012.[41]

Direct Flow Medical Aortic Valve (Direct Flow Medical): This European CE Mark trial is currently enrolling patients and should be completed by the end of 2012. The purpose of the study is to determine the safety and performance of the Direct Flow Medical study valve and delivery procedure.[42]

Sadra Medical Lotus (Boston Scientific): A prospective, single-arm feasibility study, REPRISE I, designed to evaluate the acute safety of the Sadra Medical Lotus valve in patients with severe aortic stenosis, was initiated in 2012. Enrollment in REPRISE II is anticipated to happen this year. The purpose of the study is to evaluate the safety and performance of the Lotus system in 120 patients in 15 sites in Australia and Europe.[43]

Portico THV (St. Jude Medical): In 2011, a Canadian, 10-patient feasibility study evaluated the technical feasibility, safety, and device deployment characteristics of the Portico valve and transfemoral delivery system in high risk patients with severe aortic stenosis. Results at 30 days showed no or minimal paravalvular regurgitation, and no device or procedural adverse events or death.[44] A multicentre observational cohort study is currently recruiting patients for the investigation of the safety and effectiveness of the valve in patients at high surgical risk.[45]

JenaValve (JenaValve): The JenaValve device received CE Mark approval in September 2011.[35] The CE Mark pivotal study was a multicentre, prospective, single-arm study of 67 patients who were at high risk for surgery. Results at 30 days showed that for successfully treated patients either no or minimal paravalvular regurgitation occurred.[46] A new observational cohort study is currently recruiting patients with severe aortic stenosis who are at an increased surgical risk for the evaluation of the long-term performance and safety of JenaValve.[47]

Sapien 3 and CENTERA (Edwards Lifescience): Edwards has conducted two first-in-human trials for these two second generation valves. Both are investigational devices that are not yet commercially available in any country.

Vitality and Vanguard: (ValveXchange): ValveXchange completed first-in-man clinical studies in 2011 for its Vitality valve, and will be pursuing clinical trials in Europe in 2012. ValveXchange is also developing the Vanguard series of valves for the non-surgical patient population.[48]

Heart Leaflet Technology valve (Bracco Diagnostic): In 2008, a non-randomized, single-arm study was initiated to confirm whether the dimensions of the Heart Leaflet valve are appropriate for patients with aortic valve stenosis.[49]

4. To what extent is TAVR being used across Canada and how is it funded?

To determine the extent of TAVR use and funding across Canada, CADTH distributed a survey to each province and territory. A total of 10 responses were received from 8 provinces (Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador), and the 3 territories (see Appendix D for more information on survey responses).

Based on responses from this survey, TAVR is provided in Alberta, Manitoba, Ontario, New Brunswick, and Nova Scotia. Alberta first introduced TAVR at the Edmonton Mazankowski Alberta Heart Institute in 2010. The Calgary Foothills Medical Centre performed its first TAVR procedure in 2011.[50] The device is funded by Alberta Health Services and physician fees are funded through the Schedule of Medical Benefits.

A TAVR program was introduced to Manitoba's St. Boniface hospital in Winnipeg in September 2012. Winnipeg's Regional Health Authority has redistributed funds within their global budgets to support this new program.

In Ontario, TAVR has been performed since 2008, where its use has increased from 40 cases in 2008-2009 to 221 cases in 2011-2012.[2] Currently, there are eight cardiac centres in Ontario (University Health Network, University of Ottawa Heart Institute, Hamilton Health Sciences Centre, St Michael's Hospital, London Health Sciences Centre, Sunnybrook Health Sciences Centre, Southlake Regional Health Centre, and Trillium Health Centre) that have collectively performed approximately 550 TAVRs since 2008.[2] Ontario's Cardiac Care Network has maintained a provincial registry of TAVR procedures performed in the eight centres since 2009. TAVR is funded as an insured service through ministry global hospital budgets. Patients are eligible for TAVR if they have severe aortic stenosis and are inoperable.

TAVR was first funded in New Brunswick in 2010 at the New Brunswick Heart Centre at the Saint John Regional Hospital.[51] TAVR is funded as an insured service through New Brunswick Medicare for patients who are inoperable or at prohibitively high surgical risk.[52] The fee is currently before the New Service Items Committee for consideration. In the meantime, it is being covered under the same fee code as an open surgical valve replacement.

Nova Scotia scheduled its first patient for TAVR in September 2012, in a tertiary care hospital in Halifax. Previously, patients deemed appropriate for this procedure received TAVR in St. John, New Brunswick. The Capital District Health Authority has redistributed funds within their global budget to support the new TAVR program. Currently, there is no specific fee code available to reimburse cardiologists or cardiac surgeons performing TAVR. To date, no request has been made to the Fee Schedule Advisory Committee for a new fee.

Three provinces (Saskatchewan, Prince Edward Island, and Newfoundland and Labrador) and the three territories (Yukon, Northwest Territories, and Nunavut) do not currently provide TAVR in their respective jurisdictions. Each of these jurisdictions offers a small number of out-of-province TAVR procedures that are typically funded through reciprocal billing agreements. Since 2009, Saskatchewan has referred seven patients who were not eligible for SAVR either to British Columbia or Alberta. The Saskatchewan health ministry funds the invoiced cost of the device. Prince Edward Island does not have a cardiovascular surgery program. Patients there who require TAVR are primarily referred to the Saint John facility in New Brunswick. Prince Edward Island publicly funds TAVR through a reciprocal billing agreement. For each case, the Health and Wellness Ministry pays approximately $23,000 for the valve and at least another $3,000 for other related costs. Approval of the payment is sought from the province before the procedure is performed. Patient selection criteria are applied by the centre performing the procedure. Newfoundland and Labrador funds the TAVR procedure out-of-province for a small number of patients through the reciprocal billing process. The Yukon refers patients to provinces that perform TAVR and publicly insures the service on a case-by-case basis. The Northwest Territories refer patients to Alberta. Patients sent out of the territory for aortic valve surgical treatment receive the surgical/interventional procedure at the discretion of the attending cardiovascular surgeon. The Northwest Territories has no established criteria for the use of TAVR and approves the procedure on a case-by-case basis. Nunavut refers patients to Alberta, Manitoba, or Ontario for TAVR. Nunavut funds TAVR performed out-of-province through the reciprocal billing process. Patient eligibility for the procedure is based on the criteria established by the province performing TAVR.

Based on information that is available in the public domain, it is known that Quebec[10] and British Columbia[53] perform TAVR. However, the extent of the practice in these provinces is not available. In Quebec, several institutions either have TAVR programs or are in the process of setting them up. The ministère de la Santé et des Services sociaux (MSSS) recommended that this procedure be used only for patients who cannot be treated by traditional surgical methods due to an excessive risk of complications, and that only 300 procedures be offered per year in the province.[10]

Conclusion

Ten HTAs have been published since January 2009 that compare TAVR with SAVR in patients with severe aortic stenosis. Since the publication of these HTAs, two, two-year follow-up RCTs have been published as well as a multivariable analysis. There are at least eight newer TAVR technologies that are currently being tested in clinical trials. The TAVR procedure is being performed in seven provinces. Jurisdictions not currently offering TAVR send a limited number of patients' out-of-province for the procedure where it is typically funded through reciprocal billing agreements.

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APPENDIX A

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
National Institute for Health and Clinical Excellence (NICE) UK April 2011; March 2012[5,6]	What is the evidence on the efficacy and safety of TAVR?	**1 systematic review:** Coeytaux 2010 **1 RCT:** Smith 2011 (PARTNER trial — Cohort A) Leon 2010 (PARTNER trial — Cohort B) **1 comparative non-randomized:** Jahangiri 2011 **6 case series:** El Henawy 2011 Moat 2011 Khawaja 2011 Krane 2010 Gurvitch 2010 Thomas 2010, 2011	For patients with aortic stenosis who are considered to be unsuitable for SAVR, the evidence on the efficacy of TAVR is adequate. For these patients, TAVR may be used with normal arrangements for clinical governance, consent, and audit. Details of all patients should be entered into the UK Central Cardiac Audit Database. For patients with aortic stenosis for whom SAVR is considered suitable but to whom could pose a high risk, the evidence on the efficacy of TAVR is inadequate. For these patients, TAVR should only be used with special arrangements for clinical governance, consent, and data collection or research. NICE encourages clinicians to enter suitable patients into the UK TAVR trial. In addition, details of all patients should be entered into the UK Central Cardiac Audit Database. For patients with aortic stenosis for whom SAVR is considered suitable and not to pose a high risk, the evidence on the efficacy of TAVR is inadequate. For these patients TAVR should only be used in the context of research. NICE encourages clinicians to	This assessment is a rapid review. Literature search was from Nov. 2010 to April. 2011.

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
			enter suitable patients into the UK TAVR trial. In addition, details of all patients should be entered into the UK Central Cardiac Audit Database. Clinicians wishing to undertake TAVR for patients with aortic stenosis for whom SAVR is considered suitable, but to whom could pose a high risk, should take the following actions: • Inform the clinical governance leads in their trusts. • Ensure that patients understand the risk of stroke and death, and the uncertainty about the procedure's efficacy in the long-term. Provide them with clear written information. In addition, the use of NICE's information for patients (*Understanding NICE guidance*) is recommended.	
California Technology Assessment Forum (CTAF) US February 2012; May 2012[7,8]	What is the evidence of safety, effectiveness, and improvement in net health outcomes of TAVR when used for the treatment of patients with aortic stenosis who are not candidates for surgery?	**1 RCT:** Reynolds 2011 (PARTNER trial Cohort B) Leon 2010 (PARTNER trial Cohort B) **2 comparative non-randomized studies:** Rajani 2010 Kapadia 2009	For truly inoperable patients with severe aortic stenosis, TAVR is believed to be a more effective alternative to standard therapy. A multidisciplinary team that includes at a minimum one cardiac surgeon, a general cardiologist, and an interventional cardiologist should agree that a patient is inoperable before offering TAVR.	Literature searched was from 1945-Dec 2011. The Sapien Transcatheter Heart Valve with Retroflex3 Transfemoral System was utilized TAVI compared with standard of care

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
	What is the cost of the TAVR procedure?	**13 case series:** Moat 2011 Bosmans 2011 D'Onofrio 2011 Eltchaninoff 2011 Lefevre 2011 Tamburino 2011 Zahn 2011 Thomas 2010, 2011 Gurvitch 2010 Rodés-Cabau 2010 Webb 2009 Grube 2008 Piazza 2008	The retail cost of the Sapien Transcatheter Heart Valve with the Retroflex 3 Transfemoral System is US$32,500. Two cost analyses for TAVR, based on the analyses of the PARTNER Cohort B trial, have been published. The estimated cost for the valve in the first cost-effectiveness analysis was US$30,000. The same study estimated the incremental cost-effectiveness ratio to be US$50,200 per year of life saved and US$61,889 per quality-adjusted life-years. The second study estimated the incremental cost-effectiveness ratio to be £16,100 per quality adjusted life-years. Neither study incorporated the capital cost required to build and operate the hybrid operating room/cardiac catheterization laboratory that is typically used for the TAVR procedure. The cost will vary depending on the exact specifications of the hybrid operating room, but one recent example at an academic institution cost US$3 million.	
Health Quality Ontario Canada May 2012[9]	What is the safety, effectiveness, and cost-effectiveness of TAVR for the treatment of aortic valve	**1 RCT:** Smith 2011 (PARTNER trial Cohort A) Leon 2010	TAVR is a reasonable option in patients with severe aortic stenosis who are not candidates for open heart surgery.	Literature search was from 2007 to Sept. 2011

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
	stenosis in symptomatic older patients?	(PARTNER trial Cohort B)	Ontario Health Technology Advisory Committee does not recommend TAVR in patients with severe aortic stenosis who are candidates for surgery. This is based on the similar effectiveness, higher complication rates, and unfavourable cost-effectiveness of TAVR compared with SAVR.	
Institut national d'excellence en santé et en services sociaux Canada May 2012[10]	What is the evidence on effectiveness, safety, and economic issues related to TAVR for adult patients with severe, symptomatic aortic stenosis, with an emphasis on clinical results at one year? What are the main organizational aspects of delivering this procedure, including the selection of patients before implantation and key considerations concerning ethics and the patient's perspective?	**1 RCT:** Leon 2010 (PARTNER trial Cohort B) **4 comparative non-randomized studies:** Rajani 2010 Kapadia 2009 Zierer 2009 Otten 2008 **8 case series:** Walther 2011 Lefevre 2011 Rodés-Cabau 2010 Sinning 2010 Gurvitch 2010 Himbert 2009 Thielmann 2009 Grube 2008 **4 registries:** Bosmans 2011 SOURCE registry UK TAVI (transcatheter aortic valve implantation) registry Tamburino 2011	TAVR can be considered for patients with symptoms attributable to severe aortic stenosis and for whom valve replacement surgery is contraindicated or judged to be excessively risky. In addition, there must be a reasonable probability that quality of life (related to functional capacity, autonomy, and activities of daily living/domestic activities) would significantly improve following the procedure and be maintained for at least one year. A multidisciplinary team, including cardiologists and cardiac surgeons, must evaluate the overall state of each patient to decide whether to offer TAVR, after examining cognitive function, frailty and physical status, as well as all other relevant dimensions. The definition of inoperability and eligibility for TAVR should be standardized across different performing centres.	Literature search was from Jan. 2008 to Jan. 2011 No primary economic study was undertaken.

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
			Ideally, the opinion that a patient is at an excessively high risk for valve replacement surgery or that surgery is contraindicated should be based on the consensus of at least two cardiac surgeons.	
Scottish Health Technologies Group (SHTG) Scotland September 2011[11]	What is the clinical and cost-effectiveness of TAVR?	**1 RCT:** Smith 2011 (PARTNER trial Cohort A) Leon 2010 (PARTNER trial Cohort B)	In Cohort B of the PARTNER RCT, TAVR significantly reduced the risk of death from any cause after one year compared with medical management in patients who were unsuitable candidates for surgery. In Cohort A of the PARTNER RCT, TAVR was not inferior to SAVR with respect to death from any cause after one year in candidates for surgery who were at high risk of increased operative complications and death. In Cohort A and Cohort B of the PARTNER RCT, a significantly higher incidence of vascular complications and neurological adverse events occurred in the TAVR group. Patient selection for TAVR should be undertaken by a multidisciplinary team. There are currently no published evaluations of the cost-effectiveness of TAVR.	
Belgian Health Care Knowledge Centre Belgium	The aims of the report are as follows: To provide a critical analysis	**1 RCT:** Smith 2011 (PARTNER trial Cohort A) Leon 2010	Patients with a symptomatic severe aortic stenosis and severe medical comorbidities, in whom correction of the aortic stenosis is	This is an update to a 2008 report.

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
2011[12]	of the PARTNER study. To provide a health economic study of TAVR based on the PARTNER results and cost figures from Belgium.	(PARTNER trial Cohort B)	considered as possibly beneficial, should preferably be treated surgically and are not eligible for reimbursement of TAVR, even if the estimated mortality risk of the operation is high or very high. Patients with symptomatic severe aortic stenosis in whom correction of the aortic stenosis is considered as possibly beneficial, but who are considered to be inoperable due to anatomical factors (as determined by a heart surgeon who is independent of the heart team treating the patient) are eligible for treatment with and reimbursement of TAVR with the Sapien valve. Patients with symptomatic severe aortic stenosis and severe comorbidities who are considered inoperable due to medical factors are not eligible for reimbursement of TAVR. In order to guarantee a sufficient workflow, TAVR treatment should be limited to one or two Belgian centres. Additional regulatory measures and good registration are required in order to guarantee that patient selection is correct.	

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
			No opinion can be given on the reimbursement of transapical TAVR or the CoreValve prosthesis.	
McGill University Health Centre (MUHC) Canada December 2009[13]	What are the benefits and risks of using the Cribier-Edwards Sapien aortic valve?	**3 comparative non-randomized studies:** Kapadia 2009 Zierer 2009 Otten 2008 **14 case series:** Bleiziffer 2009 Covello 2009 Tamburino 2009 Ree 2009 Descoutures 2008 Spargias 2008 Rodés-Cabau 2008 Svensson 2008 Walther 2008 Piazza 2008 Webb 2007; 2009 Grube 2007 Berry 2007	In spite of a high mortality risk and uncertain long-term prognosis, TAVR is a feasible procedure that clearly gives survivors symptomatic relief and probably causes some overall extension of life. It can be carried out at MUHC at a net cost of approximately C$24,024 per patient. A registry should be maintained, including follow-up of all cases.	TAVR at MUHC took place between Dec. 2007 and Oct. 2009
CADTH Canada January 2010[14]	What is the clinical effectiveness of percutaneous heart valve replacement for the treatment of patients with valvular heart disease? What is the cost-effectiveness of percutaneous heart valve replacement for the treatment of patients with valvular heart disease? What are the guidelines for the use of percutaneous	**1 HTA:** Belgian Health Care Knowledge Centre 2008 **2 comparative non-randomized studies:** Zierer 2009 Otten 2008 **2 case series:** Descoutures 2008 Dewey 2008	Percutaneous valve replacement is an evolving technology with ongoing changes to the devices and the insertion techniques. The safety and efficacy of percutaneous valve replacement relative to surgical valve replacement, medical management, or valvuloplasty is unknown. Evidence available is limited to observational data, which has methodological limitations. Percutaneous pulmonary and aortic valve replacement is technically feasible based on data from a small number of published cases. The literature suggests that successful implantation improves functional status. Impact	This assessment is a rapid review. Literature search was from 2004 to Dec. 2009.

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
	heart valves for patients with valvular heart disease?		on health-related quality of life and longevity of the devices is not known. Studies report that the aortic valve replacement procedure is technically challenging and has the potential for major complications including death. No information was available on the cost-effectiveness of percutaneous valve replacement at the time of publication of this report.	
CADTH Canada April 2010[15]	How does the MUHC HTA on TAVI align with findings from CADTH's percutaneous heart valve Rapid Response report?	**2 HTAs:** MUHC 2009 CADTH's January 2010 Rapid Response report	Despite addressing slightly different research questions and differences in the methodologies used in the two reports (the MUHC TAVI report was a systematic review while the CADTH report was a rapid review), the conclusions about the use of TAVI to treat patients with severe aortic stenosis who would not otherwise be surgical candidates for aortic valve replacement are similar. Both reports described the procedure as feasible and recognized the risks associated with undergoing the procedure and the potential for symptomatic relief. No information on cost-effectiveness was identified by either report.	This assessment is a rapid review.
CADTH Canada October 2011[16]	What is the clinical effectiveness (including documented mortality reduction) of	**1 SR:** NICE 2011	TAVR represents a viable alternative for patients with severe aortic valve stenosis who are not eligible for standard surgery treatment, with statistically significant	This assessment is a rapid review. Literature search was from Jan. 2005 to

Agency, Country, Publication Year	Research Question(s)	Included Studies	Conclusions/ Recommendations	Comments
	TAVI in adult patients with aortic stenosis who are ineligible for cardiac surgery? What is the clinical evidence regarding different possible procedural access points for TAVI? What is the clinical evidence regarding long-term success and complication rates associated with TAVI? What are the evidence-based guidelines and criteria regarding selection of optimal candidates for TAVI?	**1 RCT:** Smith 2011 (PARTNER trial Cohort A) Leon 2010 (PARTNER trial Cohort B) **2 Evidence-based Guidelines:** SASCI 2011 NICE 2008	clinical benefits. However, long-term success and complication rates of the procedure are uncertain at the present time. No evidence that met the study inclusion criteria regarding procedural access points was identified. Existing guidelines and reviews suggested that strict patient selection and procedural considerations following consultation with a multidisciplinary team are vital to the success of TAVR.	Sept. 2011.

CADTH = Canadian Agency for Drugs and Technologies in Health; HTA = health technology assessment; RCT = randomized controlled trial; SAVR = surgical aortic valve replacement, TAVI = transcatheter aortic valve implantation; TAVR = transcatheter aortic valve replacement; UK = United Kingdom; US = United States.

APPENDIX B

First Author, Publication Year, Country	Study Design, Patient Characteristics, Sample Size, Length of Follow-up	Intervention, Comparator	Outcomes measured
PARTNER Study Results			
Kodali et al. 2012[19] US	RCT 699 high-risk patients with severe aortic stenosis Follow-up: > 2 years	TAVR SAVR	▪ All-cause mortality at 2 years ▪ Cardiovascular mortality ▪ Stroke ▪ Repeat hospitalization ▪ Acute kidney injury ▪ Vascular complications ▪ Bleeding events ▪ New York Heart Association (NYHA) functional class
Author's conclusions: Two-year follow-up of patients in the PARTNER trial (Cohort A) supports the use of TAVR as an alternative to SAVR in high-risk patients with aortic stenosis. The two treatments were similar with respect to mortality, reduction in symptoms, and improved valve hemodynamics, but paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality.			
Other RCTs			
Makkar et al. 2012[20] US	RCT 358 patients with severe aortic stenosis not suitable for surgery Follow-up: > 2 years	TAVR Standard therapy	▪ All-cause mortality at 2 years ▪ Cardiac mortality ▪ Stroke ▪ Repeat hospitalization ▪ Survival ▪ Functional status ▪ Ischemic events ▪ Echocardiographic assessment of aortic valve gradients, aortic valve area, and paravalvular aortic regurgitation
Author's conclusions: In patients with severe aortic stenosis who are not suitable for surgery, TAVR reduced the rates of death and hospitalization, with an improvement in valve hemodynamics and a reduction in symptoms that were sustained at two years of follow-up.			
Other Study			
Lange et al. 2012[21] Germany	Multivariable analysis 420 patients with severe aortic stenosis considered to be at high surgical risk		Primary End Point: ▪ All-cause mortality within 30 days and 6 months follow-up Secondary End Points: ▪ Stroke/transient ischemic attack ▪ Vascular complications ▪ Need for a new permanent pacemaker within 14 days of TAVI ▪ Post-implantation aortic regurgitation
Author's conclusions: Significantly better clinical outcomes can be expected in lower surgical risk patients than in higher surgical risk patients undergoing TAVR.			

TAVI = transcatheter aortic valve implantation; TAVR = transcatheter aortic valve replacement; RCT = randomized controlled trial; SAVR = surgical aortic valve replacement.

APPENDIX C

Guideline Name, First Author, Publication Year, Country	Method of Assessment of Evidence	Key Statements/Recommendations, Quality of Evidence, Values and Preferences (if available)
Transcatheter Aortic Valve Implantation: A Canadian Cardiovascular Society Position Statement Webb et al.[23] Canada 2012	Representative group of cardiologists and cardiac surgeons reviewed the current literature, developed a consensus, and made recommendations using the GRADE system to evaluate the evidence and comment on the strength of the conclusion/recommendation.	1. Transfemoral TAVI is recommended in patients with aortic stenosis if the risk of open heart surgery is prohibitive and a significant improvement in duration or quality of life is likely and if life expectancy with treatment is likely to exceed one to two years. *(Strong Recommendation, High-Quality Evidence)* 2. For patients who are not candidates for open heart surgery or transfemoral TAVI, alternate access routes may be considered (e.g., transapical, transaxillary, or transaortic). *(Conditional Recommendation, Low-Quality Evidence)* **Values and Preferences:** Recommendation #2 places a high weight on positive outcomes from current registry experience using alternate access techniques to the transfemoral approach, and less weight on early feasibility studies. 1. TAVI is a reasonable alternative to SAVR for patients at high risk of major morbidity or mortality and duration and quality of life will likely be greatly improved by treatment; and treatment will elongate life expectancy by one to two years; and consensus is reached amongst a multidisciplinary team of cardiologists and surgeons. *(Strong Recommendation, High-Quality Evidence)* 2. For severe symptomatic aortic stenosis patients who are considered to be at low to intermediate surgical risk, SAVR is the best treatment option. *(Strong Recommendation, Moderate-Quality Evidence)* 3. In selected patients with severe symptomatic aortic stenosis who would otherwise be considered to be at low to intermediate risk of mortality, but where there is a consensus in the Cardiology team that the patient is at increased risk of morbidity or mortality due to extenuating circumstances (e.g., older patients, multivalve disease, etc.), TAVI may be offered to this group of patients.

Guideline Name, First Author, Publication Year, Country	Method of Assessment of Evidence	Key Statements/Recommendations, Quality of Evidence, Values and Preferences (if available)
		(Conditional Recommendation, Low-Quality Evidence) **Values and Preferences:** Recommendation #5 places greater weight on patient quality of life and morbidity, with less weight on yet unidentified possible differences in valve durability and patient mortality between transcatheter and surgical aortic valve replacement. Please refer to this publication [23] for recommendations on valve-in-valve implantation, the evaluation of TAVI candidates, TAVI programs and for guidance to facilities and institutions.
2012 ACCF/AATS/SCAI/STS Expert Consensus Document on Transcatheter Aortic Valve Replacement Holmes et al.[54] US 2012	Expert consensus	TAVR is recommended in patients with severe, symptomatic calcific stenosis of a trileaflet aortic valve where the valvular and aortic anatomy is suitable for TAVR; and where survival is predicted to be > 12 months; and who have a prohibitive surgical risk. TAVR is a reasonable alternative to SAVR in patients at high surgical risk. Please refer to this publication[54] for recommendations on a team-based approach, TAVR screening, site selection, centre and physician experience, procedural performance, post-procedural care and registries. Recommendations are also provided as to when SAVR, balloon aortic valvuloplasty, and medical therapy are suitable treatment options.

AATS = American Association for Thoracic Surgery; ACCF = American College of Cardiology Foundation; AS = aortic stenosis; GRADE = Grading of Recommendations Assessment and Development; SAVR: surgical aortic valve replacement; SCAI = Society for Cardiovascular Angiography; STS = Society of Thoracic Surgeons; TAVI = transcatheter aortic valve implantation; TAVR = transcatheter aortic valve replacement; US = United States.

APPENDIX D

Province/ Territory	Is TAVI available to patients in your jurisdiction?	If so, how is TAVI funded/insured in your jurisdiction?
Alberta (Alta.)	Yes, TAVI is available. Tertiary centres in Edmonton and Calgary perform the procedure in selected patients. A minority of patients are from out of province.	The device is funded by Alberta Health Services. Physician fees are funded through the Schedule of Medical Benefits.
Saskatchewan (Sask.)	No. Patients are referred to Vancouver or Edmonton. The number of patients referred out of province is as follows: 2009-2010: 3 2010-2011: 1 2011-2012: 3	Sask. has an arrangement whereby Sask. pays the invoiced cost of the device. Patients referred are those that are not eligible for open valve replacement.
Manitoba (Man.)	The first TAVI procedures occurred in September 2012 at St. Boniface Hospital in Winnipeg. There is a multidisciplinary cardiac care team that recommends patients for this intervention.	The Winnipeg Regional Health Authority has redistributed funds within their global budget to support this new program. Appropriately triaging patients will be important to manage the number of cases and stay within the funding available through the global budget.
Ontario (Ont.)	Yes. Currently eight cardiac centres in Ontario perform TAVI procedures. The Cardiac Care Network of Ontario has established a TAVI Working Group and has implemented a cardiac registry of TAVI procedures performed at the eight cardiac centres (hospitals).	Until recently, TAVI has been provided through Health Canada's compassionate access approval. Hospitals have been able to develop and establish TAVI programs using various resources (e.g., funded through global budgets; research or foundation funds, etc.). With the relatively recent Health Canada approval of an aortic valve for transcutaneous implantation, the device is now marketed in Canada, eliminating the need for compassionate access. TAVI is funded as an insured service in Ont. hospitals through Ministry-provided global budgets. Based on the current available evidence, the Ontario Health Technology Advisory Committee (OHTAC) has the following recommendations (May 2012) regarding TAVI: • *" In patients with severe aortic valve stenosis who are candidates for surgery, in light of the high complication rates of TAVI, and similar effectiveness and unfavourable cost-effectiveness compared with surgery, OHTAC does not recommend using TAVI.* • *In patients with severe aortic valve stenosis who are not candidates for open heart surgery, TAVI is a reasonable option. However, given the high complication rates and uncertainty regarding short- and long-term effectiveness and cost-effectiveness of*

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		TAVI, OHTAC recommends close follow-up of patient resource use, quality-of-life preference information, and clinical outcome data as a coverage, with evidence development through Programs for Assessment of Technology in Health (PATH) and in collaboration with the Cardiac Care Network. A final decision regarding the use of this technology, including appropriate patient selection in Ontario, should be predicated on the outcomes from the coverage with evidence development. • *Given the complexity of this technology and significant complications associated with its use, OHTAC recommends in the interest of the highest quality of patient care that TAVI be restricted to institutions that have broad-based experience in its use with an appropriate volume of patients."*
Quebec (Que.) Information from INESSS assessment[10]	Currently in Que., several institutions either have already set up a TAVI program or are in the process of doing so. A narrative review of the literature up to 2009 and an analysis of the Que. experience was published in 2010 by a working group of the Réseau québécois de cardiologie tertiaire (RQCT).	Following release of the 2010 RQCT working group document, the Quebec Minister of Health and Social Services recommended that this procedure be used only for patients who cannot be treated by traditional surgical methods due to an excessive risk of complications, and be limited to 300 procedures per year to be offered only by university hospitals or institutions with experienced multidisciplinary teams (performing a minimum of 30 procedures a year). Procedures are covered under the province's health care program.
New Brunswick (NB)	Yes. The procedure is available through the NB Heart Centre at the Saint John Regional Hospital.	TAVR is funded as an insured service through NB Medicare. The fee is currently before the New Service Items Committee for consideration. In the meantime, it is being covered under the same fee as an open valve replacement. The clinicians decide on whether a patient meets the established criteria for TAVR or open heart surgery.
Nova Scotia (NS)	Previously (until this fall), NS patients deemed appropriate for this surgery had the procedure completed in St. John, NB, with NS paying a substantial fee for the valve, reciprocal billing, and transportation. The first patient is booked for this procedure in mid-September 2012 in Halifax. The procedure will only be available at the province's tertiary care hospital. There is a multidisciplinary cardiac care team that recommends	Capital District Health Authority has redistributed funds within their global budget to support this new program. Appropriately triaging patients will be important to manage the number of cases and stay within the funding available through the global budget. There is no specific fee code available to reimburse cardiologists or cardiac surgeons performing TAVI and to date no request has been made to the Fee Schedule Advisory Committee for a new fee code.

Province/ Territory	Is TAVI available to patients in your jurisdiction?	If so, how is TAVI funded/insured in your jurisdiction?
	patients who are unfit for open surgery for this intervention.	
Prince Edward Island (PEI)	PE does not have a cardiovascular surgery program. All patients are referred to Halifax or Saint John, NB. PEI patients who require TAVI are currently primarily referred to Saint John, NB.	The procedure is publicly funded by PEI for eligible PEI patients. For each case, PEI pays about $23,000 for the valve and at least another $3,000 for related costs. Billing would be under the reciprocal billing agreement. Prior approval of payment is sought from PEI before the procedure is performed; there are no specific criteria from PEI, but patient selection criteria are applied by the centre performing the TAVI procedure.
Newfoundland and Labrador (Nfld. and Lab.)	TAVI is not performed in Nfld. and Lab. A small number of patients (four since February 2012) has been referred to other provinces for the procedure on the recommendation of a cardiologist.	Nfld. and Lab.'s public health insurance covers TAVI performed out-of- province on patients referred by a cardiologist through reciprocal billing agreements.
Yukon Territory	TAVI is not available in the Yukon Territory; patients are referred out-of-territory.	Requests for territorial health insurance coverage for TAVI would be undertaken on a case-by-case basis, and if deemed appropriate the patient would be referred out-of-territory.
Northwest Territories (NWT)	No. The TAVI procedure is not available in the Northwest Territories. Patients are referred to Alberta.	Patients sent out-of-territory for aortic valve surgery receive the surgical/interventional procedure at the discretion of the attending cardiovascular surgeon in the respective jurisdiction. NWT has no established criteria for the use of this technology. If the procedure and device were not covered through reciprocal billing, then there would be a prior approval request for coverage sent to NWT Health Services Administration for consideration of approval on a case-by-case basis.
Nunavut	No. TAVI is not provided in Nunavut; patients are referred to Man., Alta., or Ont.	Through reciprocal billing, Nunavut public health funding covers TAVI procedures performed out-of-province. Patient criteria for the procedure would be as per the province where the TAVI is performed.

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CADTH takes sole responsibility for the final form and content of this environmental scan. The statements and conclusions in this environmental scan are those of CADTH.

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