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Interventions for the Treatment of Obstructive Sleep Apnea in Adults: Recommendations

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Abbreviations

AHI	apnea-hypopnea index
CPAP	continuous positive airway pressure
EDS	excessive daytime sleepiness
GTA	genial tubercle advancement
HTA	health technology assessment
HTERP	Health Technology Expert Review Panel
MAD	mandibular advancement device
MMA	maxillomandibular advancement
OSA	obstructive sleep apnea
PAP	positive airway pressure
QALY	quality-adjusted life year
QoL	quality of life

Summary of Recommendations

Obstructive sleep apnea (OSA) is characterized by a narrowing and collapse of the upper airway during sleep.[1,2] The prevalence of OSA is reported to be 15% in males and 5% in females.[3,4] The major symptoms include snoring, unrefreshing sleep, excessive daytime sleepiness (EDS), lack of concentration, impaired memory, and lower quality of life.[5,6] Aging, the male sex, and obesity are the main risk factors for OSA.[7,8] Untreated OSA is associated with motor vehicle accidents, cardiovascular disease, stroke, hypertension, diabetes, cognitive dysfunction, and all-cause mortality.[1,6,9-11]

The goal of treatment of OSA is to reduce the apnea-hypopnea index (AHI) — an index used to indicate the severity of sleep apnea — increase blood oxygen levels, and improve cardiorespiratory indicators. The AHI measures the number of apnea or hypopnea events per hour.[12] Although continuous positive airway pressure (CPAP) is the standard for treating OSA, between 29% and 83% of patients do not comply with regular device use.[13-15] Adherence with oral appliances, including mandibular advancement devices (MADs), is not as well documented, but is regarded as superior to CPAP adherence.[16,17] Surgical interventions for OSA treatment are invasive procedures for which evidence of effectiveness and safety is unclear.[12] For patients with mild or asymptomatic OSA, lifestyle interventions such as exercise programs, diet changes, and positional therapies may be an option for treatment before proceeding to other interventions.[18]

Across jurisdictions, OSA is associated with a substantial economic and societal burden.[7,8,19] Currently, public coverage for treatment of OSA varies widely across Canada, with some provinces supporting CPAP therapy for OSA patients, but the criteria and type of reimbursement varies.[2] No provincial programs reimburse oral appliance costs while some federal programs do reimburse eligible patients.

Given the range of clinical presentation, symptoms, and severity, recommending the most appropriate treatment for OSA patients can be challenging. To facilitate decision-making, CADTH conducted a health technology assessment (HTA) on the clinical effectiveness and cost-effectiveness of interventions for the treatment of OSA in adults. Patient perspectives and experiences, ethical and implementation issues, and environmental factors related to therapy selection for OSA in adults were also considered in an evaluation of the appropriate use of OSA interventions.[20]

1. **For patients with mild OSA who are overweight or obese, the Health Technology Expert Review Panel (HTERP) recommends lifestyle interventions. For patients with mild OSA who are not overweight or obese, HTERP does not recommend active treatment.**
2. **For patients with moderate or severe OSA, HTERP recommends continuous positive airway pressure (CPAP). For patients with moderate or severe OSA for whom CPAP is unacceptable, oral appliances are recommended.**
3. **HTERP does not recommend surgical maxillomandibular advancement in patients with OSA, unless other interventions have failed or are unacceptable to the patient.**

Technology

Treatment of obstructive sleep apnea (OSA) includes a wide range of options.[21]

Continuous positive airway pressure (CPAP) forces air into the upper airways to prevent soft tissues from collapsing and is considered the gold standard for the treatment of OSA.[12,21,22] Other positive airway pressure (PAP) technologies, such as autotitrating PAP and bilevel PAP, may be offered to patients with specific needs.[12,21] Another treatment option is nasal expiratory PAP valves, which are disposable devices that use a patient's own breathing to create positive end-expiratory pressure that prevents airway collapse.[23]

Oral appliances, including the mandibular advancement devices (MADs) and tongue-retaining devices (TRDs), can be offered as an alternative to CPAP.[12,24,25] For patients with mild or asymptomatic OSA, lifestyle interventions such as exercise programs, diet changes, and positional therapies may be proposed.[18]

Surgical maxillomandibular advancement (MMA) permanently pulls the lower jaw forward to create more space and prevent airway collapse.[26,27] Genial tubercle advancement (GTA) is a surgical intervention that removes bone tissue from the chin and pulls the base of the tongue forward to create more airway space, and can be performed in conjunction with MMA or other surgeries to potentially improve therapeutic success.[28,29]

Policy Question

What is the optimal use of PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle interventions for treatment of adults with OSA?

Methods

CADTH conducted a HTA to assess the clinical effectiveness, cost-effectiveness, patient perspectives and experiences, ethical issues, implementation issues, and environmental impact of PAP devices, oral appliances, surgical interventions, and lifestyle interventions for the treatment of OSA in adults.[20] The Health Technology Expert Review Panel (HTERP) (Appendix 1) developed recommendations about interventions for the treatment of OSA based on the evidence presented in the HTA report. HTERP members reviewed the evidence, discussed all elements of the HTERP deliberative framework,[30] and developed a consensus-based recommendation through discussion and deliberation. See Appendix 2 for details.

Additional information on the HTERP process is found on the HTERP page of the CADTH website: https://www.cadth.ca/collaboration-and-outreach/advisory-bodies/health-technology-expert-review-panel.

Detailed Recommendations

The objective of these recommendations is to provide advice for Canadian health care decision-makers about the optimal use of interventions for the treatment of OSA of varying severity in adults. These recommendations are relevant for patients who were diagnosed with any severity of OSA and were either treatment-naive or previously treated, as measured objectively by polysomnography or portable monitoring.

1. For patients with mild OSA who are overweight or obese, HTERP recommends lifestyle interventions. For patients with mild OSA who are not overweight or obese, HTERP does not recommend active treatment.
2. For patients with moderate or severe OSA, HTERP recommends CPAP. For patients with moderate or severe OSA for whom CPAP is unacceptable, oral appliances are recommended.
3. HTERP does not recommend surgical MMA in patients with OSA, unless other interventions have failed or are unacceptable to the patient.

Rationale

The results of the clinical review indicate that, while various interventions may have similar and only marginal effects on improving sleepiness across mild-to-severe cases of OSA, CPAP may have the largest effect on improving OSA severity, if patients comply with the therapy. Further, the clinical and economic data indicate that patients with moderate OSA may benefit most from MADs, and those with severe OSA may benefit most from CPAP. More specifically, the results suggest that CPAP is more effective than MADs for EDS in adults with severe OSA. Although treatment is not

recommended in patients with mild OSA, the committee suggested that treatment may be considered in patients with mild OSA who are symptomatic.

Surgical MMA, with or without GTA, was the most clinically effective and cost-effective intervention at a willingness-to-pay threshold of $17,125 per quality-adjusted life-year (QALY) in patients with very severe OSA. Unlike other interventions for OSA, this is an invasive procedure. In addition, the findings on MMA, with or without GTA, were obtained from small, uncontrolled pre- and post-treatment studies of highly selected patients, and therefore MMA is not recommended for most patients with OSA.

There were no major adverse events reported for most OSA interventions.

Some of the evidence was deemed to be of high quality, but there are quality concerns for some studies due to their eligibility criteria, sample sizes, and uncontrolled study design.

Patient factors that influence whether people seek and commence OSA treatment are individualized and contextual. People with OSA usually perform a trade-off between the benefits of OSA treatment and their discomfort with the intervention. All treatments had some degree of discomfort, and this discomfort may change over time as patients become accustomed to the device. There is also a recovery time for surgery. For some patients, especially those with mild OSA, these feelings of discomfort were enough of a deterrent that therapy was discontinued. For others, the physical, mental, and social benefits experienced from using an intervention for OSA were motivation to continue treatments. For those using CPAP, the sense of embarrassment and perceived unattractive appearance while using the device might be a reason for nonadherence. Those with supportive partners may be able to persevere and continue with treatment, though not all spouses are supportive. OSA interventions affected patients and their partners, and decisions regarding treatment may be made within the context of their relationship, with a consideration of the impact of treatment on the spouse.

Although there are no ethical concerns inherent with the technologies used to treat OSA, it can be a challenge for some patients to access some of the necessary resources, such as sleep specialists and specialized sleep labs.

Considerations

Reimbursement coverage for PAP treatments and oral devices differs across Canada, while surgery may be covered as a medical act. These variations in coverage can be a barrier to accessing effective treatments. Choosing an intervention for specific patients may need to consider the reimbursement criteria, OSA severity, and patient perspectives.

In the economic evaluation, the findings were relatively insensitive to the different reimbursement strategies explored. When oral appliances were expensed out of pocket, they were found to be the most likely cost-effective

intervention for mild-to-moderate OSA. However, a review of patient perspectives and experience and implementation has highlighted the financial burden from out-of-pocket costs as an important issue affecting adherence to treatment.

Trial periods for CPAP with the reuse of devices found to be unacceptable by others may help determine which patients would benefit the most from intervention, without an initial investment. Oral appliances and lifestyle interventions are feasible options for patients for whom CPAP is unacceptable, especially in less severe cases of OSA.[31-33] These alternatives may be appropriate for patients who do not have access to the necessary infrastructure (i.e., electricity, clean water, etc.) for specific treatments.

There was some evidence that the longer the study duration, the lower the effects of CPAP, MADs, and positional therapy, potentially due to discontinuation over time. It is also possible that the effects of CPAP and OAs first peak and then taper, which could also lead to discontinuation over time. In other words, the level of effect first rises and then falls. The authors of one study (retrieved after analysis) concluded that improved clinician communication skills can help support shared decision making and "motivate patients to try CPAP after the initial visit, and thereafter to improve long-term adherence".[34]

Surgical MMA is invasive and should only be considered if other treatment options have failed, are unacceptable, or are not affordable, and surgery is covered as a medical act. In practice, the appropriate surgical procedure for OSA depends on the site of the anatomical obstruction and a patient's anatomical features.

Many patients are nonadherent to therapy primarily for personal and contextual reasons. Patients experienced discomfort for all interventions, and this discomfort may change over time as they adjust to the device or recover from surgery. Patients require support from their health care providers and their partners and family. Receiving the right information about treatment choices or how to care for the devices they chose to use is an important component of supporting patients with OSA and their caregivers. Patients felt that it was important to interact with a health care professional following initiation of CPAP, and also expressed a desire for access to professional support and reassurance at night. Further, patients had to persevere with treatment, and the intervention had to become part of their routine for those who could tolerate it.

Although the diagnosis of OSA was beyond the scope of this report, diagnosis is required to access treatment, making access to publicly funded diagnostic testing an important consideration in the treatment of OSA.[35-37] A 2016 study reported that the AHI determined by a device for home diagnosis of sleep apnea was comparable with the results of standard polysomnography. This study suggests that patients may be able to reliably

diagnose sleep apnea at home, possibly increasing access to OSA diagnosis and subsequent treatment.[38]

In addition to differences in clinical presentation, such as sleepiness, fatigue, headache, or mood, men are more commonly reported to be diagnosed with OSA than women.[1] The patient perspectives and experiences review found that one reason for this could be that women are more likely than men to feel shame related to snoring and therefore less likely to seek diagnosis.[39] As well, women may not present with "classic" OSA symptoms,[40] and OSA symptoms do not always correlate with severity. Finally, women are more likely than men to encourage their spouses to be diagnosed, as opposed to the other way around.[41] These findings suggest that OSA could affect women more often than proposed by current diagnosis rates.

Background

Therapy selection for OSA is based on an assessment of the patient by lab-based polysomnography or home-based portable monitors.[36] An analysis of the clinical effectiveness and cost-effectiveness and a review of patient perspectives and experiences, ethical and implementation issues, and environmental factors were conducted to inform recommendations about the appropriate use of interventions for the treatment of OSA in adults.

The evidence on clinical and economic effectiveness, patient perspectives and experiences, ethical and implementation issues, and environmental factors used for developing this guidance was derived from the CADTH HTA: *Interventions for the Treatment of Obstructive Sleep Apnea in Adults*.[20]

Research questions

1. What are the clinical effectiveness, comparative clinical effectiveness, and safety concerns of PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle modifications for the treatment of OSA in adults?

    1a. What are the clinical effectiveness, comparative clinical effectiveness, and safety concerns of PAP devices, expiratory PAP valve, oral appliances, surgical interventions, and lifestyle for the treatment of adult patients with different OSA severity (i.e., mild, moderate, severe)?

    1b. What are the clinical effectiveness, comparative clinical effectiveness, and safety concerns of interventions for the treatment of adult OSA patients with or without comorbidities (e.g., obesity, hypertension, diabetes)?

2. What is the cost-effectiveness of PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle for the treatment of OSA in adults?

3. What are the experiences and perspectives of adult patients, their family members, and their caregivers regarding PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle for the treatment of OSA?
4. What ethical issues are raised by providing PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle to treat OSA in adults? How should these issues be addressed?
5. What are some of the implementation issues associated with PAP devices, expiratory PAP valve, oral appliances, surgical interventions, and lifestyle for the treatment of OSA in adults?
6. What are some potential environmental impacts associated with PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle for the treatment of OSA in adults?

Summary of The Evidence

Clinical Evidence

A systematic review of the literature was conducted, using MEDLINE, Embase, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, and PubMed, for an overview of systematic reviews, meta-analyses, and HTAs, supplemented by a review of primary studies for areas of gap. In total, 33 systematic reviews and 41 primary studies were included in the overview and review, respectively. Both involved adults with OSA who were treated with PAP devices, expiratory PAP valves, oral appliances, surgery, and lifestyle interventions and assessed on various outcomes, with EDS as the primary outcome.

CPAP, expiratory PAP, MADs, TRDs, MMA, GTA, weight loss programs, and positional therapy were all effective at reducing EDS (commonly measured by the Epworth sleepiness scale) compared with inactive controls or pre-treatment. Effect sizes were similar across the interventions, except for people with severe cases of OSA who may benefit more from CPAP than from MADs, although the difference may not be clinically significant. Based on an analysis using OSA severity as the outcome, commonly measured by AHI, effect sizes varied across the interventions, with CPAP showing the largest effect. For people with severe cases of OSA who are eligible for surgery, MMA with or without GTA may be effective at improving both EDS and OSA severity. However, the findings are mostly from small, uncontrolled pre- and post-treatment studies on highly selected patients and warrant caution, considering the invasiveness of the procedure and potential adverse events. Limited evidence was found on other outcomes, such as blood pressure, cardiovascular events, quality of life, and mortality. The 33 systematic reviews and 41 primary studies were assessed to generally be of high quality, using accepted quality assessment tools. But concerns were identified around the study eligibility criteria for the systematic reviews and small samples and uncontrolled pre- and post-treatment study designs for

the primary studies. The primary studies included in the 33 reviews ranged widely in their quality.

Economic Evidence

A Markov cohort model was constructed to evaluate the cost-effectiveness of various treatment strategies in adult patients diagnosed with OSA (i.e., 76.5% males, 55 years of age) over a patient's lifetime within a Canadian health care payer perspective. The effect of treatment in terms of change in AHI and blood pressure was determined from the clinical review and was translated to changes in the risk of cardiovascular events and motor vehicle accidents in the economic model. The primary outcome was cost per QALY gained in 2016 Canadian dollars. The base-case analysis compared a "no treatment" strategy against PAP therapy, MADs only, and surgery (i.e., MMA with or without GTA). A separate scenario analysis was conducted on obese or overweight patients, in which weight loss would be a suitable treatment strategy.

Cost-effectiveness of treatment strategies for OSA was found to be dependent on a patient's baseline disease severity, as measured by AHI (i.e., lower AHI equates to less severe OSA). At a willingness-to-pay threshold of $50,000 per QALY, the order in which interventions were considered cost-effective by increasing baseline disease severity was: no treatment (AHI < 15), MADs (15 ≤ AH I≤ 25), MMA with or without GTA (25 < AHI < 30), PAP therapy (30 ≤ AHI ≤ 32), and MMA with or without GTA (AHI > 32). Absolute gains in QALYs were found to follow a unimodal distribution and were a function of disease severity. Those with mild or more severe OSA had lower gains in QALYs, whereas the largest gains were observed in patients whose baseline severity reduced from severe (AHI ≥ 30) or moderate (15 < AHI < 30) to mild-to-moderate OSA (AHI < 30) or mild OSA (AHI < 15), respectively, due to the impact on subsequent morbidity and mortality risks. Incremental costs were largely driven by the costs of treatment and long-term maintenance costs, given the longer life expectancies of patients on treatment. The model was found to be most sensitive to changes in treatment adherence.

Patient Perspectives and Experiences Evidence

A systematic review and thematic synthesis of the literature relevant to the research question on patient experience and perspectives were conducted. Patient experience information was identified by searching the following databases: MEDLINE (1946–), Embase (1974–), and PsycINFO (1967–) via Ovid; CINAHL (1981–) via EBSCO; and PubMed. Studies were eligible if they presented the patient or non-clinical caregiver experience. Qualitative studies, surveys, studies with mixed methodology, or systematic reviews of descriptive studies were eligible. A maximum variation approach was used to identify articles for inclusion in the thematic synthesis from a list of eligible articles. A thematic synthesis was conducted, comprising three stages: coding, developing descriptive themes, and developing analytic themes.

Thirty-two studies were included in the thematic synthesis, the coding and analysis of which led to two analytic themes. The first theme described a range of characteristics and factors that influence whether people seek and initiate OSA treatment. Patients are influenced by the information they have on therapy, any disability they may have, whether they receive support for complying with the intervention, and their current life situation. The second analytic theme centred on the finding that interventions for OSA require adaptation to daily routines and relationships; some patients can integrate these interventions into their life and experience benefits, while others are unable to do so. Some patients are noncompliant to therapy for a variety of reasons, each of which is personal and contextual to the individual. Patients reported some degree of discomfort for all interventions, and this discomfort may change over time as patients become accustomed to the device, or recover from surgery.

Ethical Issues

A systematic review of the normative bioethics literature was conducted to identify literature relevant to the identification and analysis of the potential ethical issues on interventions for OSA (i.e., articles that explicitly and specifically raise ethical issues). Targeted literature searches were performed by a CADTH Information Specialist in MEDLINE, PubMed, and CINAHL from database inception to March 2016. Key terms for ethics concepts and related terms were used and combined with search terms for OSA. The search was limited to English- or French-language literature.

The literature search yielded 1,268 unique citations, none of which passed the first stage of screening because no articles on OSA treatment were found that explicitly mentioned ethical issues. However, in the second stage, the reviewers selected 142 potentially relevant articles that raised implicit ethical issues. Ethical issues relating to OSA were explored according to six key values that emerged from the literature review. The six key values were: respect individual autonomy, maximize benefits and minimize harm for patients, maximize benefits and minimize harms for others affected by OSA, maximize benefits and minimize harms for populations, distribute benefits and burdens of health care resources fairly, and steward scarce resources. In terms of whether universal treatments for OSA should be implemented, they have been shown to offer benefits to OSA patients and reduce overall costs, and so appear to live up to values of conferring a benefit at a population level and stewarding scarce resources. Further, optimizing interventions for OSA to minimize harmful outcomes on both an individual and at the population level is of great benefit, given variability in adherence based on patient behaviours and attitude. To maximize overall benefit, OSA treatment should be provided through an ongoing partnership between health care provider and patient, rather than through discrete events of diagnosis, decision, and intervention.

Implementation Issues

A narrative literature review was conducted to identify some of the implementation issues associated with the different interventions for the treatment of OSA in adults. Citations arising from the literature searches conducted to address the clinical and economic effectiveness, patient perspectives and experience, and ethical issues were screened independently and in duplicate for information related to implementation issues. Issues identified from relevant studies are organized by OSA intervention (i.e., PAP devices, expiratory PAP valves, oral appliances, surgical interventions, and lifestyle modifications) and further categorized by the level where the issue arises: individual, team, organization, or system or policy. This information was summarized narratively.

From the 27 included studies, one of the biggest implementation issues identified for OSA treatment is difficulty accessing sleep specialists and specialized sleep labs. Home-based portable diagnostic devices and treatment titration options with telehealth-based support are suggested solutions. Most of the implementation evidence focuses on CPAP devices. Barriers to CPAP use include cost and lack of funding as well as patient discomfort or use problems. Suggested CPAP supports include patient education and training, as well as providers and centres that are accredited for the treatment of OSA. Barriers to treatment with oral appliances include lack of physician knowledge and awareness, anatomical and dental health requirements, and the need for regular re-evaluations. Little evidence on implementation issues for OSA surgery or lifestyle interventions was found.

Environmental Impact

Citations arising from the clinical literature search were screened for information relating to environmental considerations associated with obstructive sleep apnea.

One narrative review article identified the environmental implications associated with OSA. The article briefly examined the environmental considerations of the CPAP unit, including manufacturers adopting green shipping and production methods, creating more energy-efficient products, and using more recyclable materials.

Research Gaps

Additional research is needed to address patient characteristics that guide the selection of interventions. There is a dearth of evidence on comorbidities and outcomes of the interventions based on patient characteristics. Research on direct, head-to-head comparisons or network meta-analyses on the clinical effectiveness and safety of various treatments, and the impact of these interventions in subgroups of OSA patients who have hypertension or cardiovascular disease on the primary outcome and OSA severity, is also warranted.

Research on OSA treatment for several subgroups, including Indigenous populations, and populations with specific work occupations (e.g., military or law enforcers), is underrepresented in the literature. Further research on these subgroups may provide insight on the most effective treatments, given their living conditions and life situations. Studies on the diagnosis of OSA in women are necessary to assess whether OSA is underdiagnosed, less common, or misdiagnosed among the female population. For instance, there are differences in how men and women describe their symptoms, which may lead to misdiagnosis in women.

Education of primary care clinicians on all the available interventions is necessary, and research on adherence, especially its change with time and relationship with the effectiveness of various treatment interventions, comparative data across treatment interventions, and factors that influence it, is merited. There is also a need for work to evaluate shared decision-making and decision aids in OSA.

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Appendix 1: HTERP

HTERP consists of up to seven core members appointed to serve for all topics under consideration during their term of office, and up to five expert members appointed to provide their expertise for a specific topic. For this project, three expert members were appointed; their expertise included internal medicine, clinical chemistry, pathology, and family medicine. The core members include health care practitioners and other individuals with expertise and experience in evidence-based medicine, critical appraisal, health technology assessment, bioethics, and health economics. One public member is also appointed to the core panel to represent the broad public interest.

HTERP is an advisory body to CADTH and is convened to develop guidance or recommendations on non-drug health technologies to inform a range of stakeholders within the Canadian health care system. Further information regarding HTERP is available at www.cadth.ca/en/advisory-bodies/health-technology-expert-review-panel.

HTERP Core Members

Dr. Stirling Bryan (Chair)

Dr. Jenny Basran

Dr. Leslie Anne Campbell

Dr. Hilary Jaeger

Dr. Jeremy Petch

Dr. Lisa Schwartz

Ms. Tonya Somerton

Expert Members

Dr. Sachin Pendharkar

Dr. Najib Ayas

Dr. Jessica Otte

Conflict of Interest

No members declared any conflicts of interest. *Conflict of Interest Guidelines* are posted on the CADTH website.

Appendix 2: HTERP Deliberative Framework

Table 1: HTERP Deliberative Framework for Interventions for Obstructive Sleep Apnea

Framework Domain	Examples of Information and Element(s)	Possible HTERP Discussion Question(s)	Discussion Points
Background/Context	Audience; issue and policy question(s)	Who requested this assessment? Why?	• Need for evidence-informed selection of OSA intervention based on patient characteristics. • Identify considerations for prioritization of patients, when device supplies are limited. • Implementation of an efficient, respectful, and equitable OSA care pathway.
Need	Background on health condition Size of affected population	What condition does this health technology address? How many patients could potentially be affected?	• 3% of adult population is diagnosed with OSA; 17% to 25% are suspected to be or are at risk (i.e., age, male sex, obesity risk factors).
	Availability of alternatives	Are there existing therapeutic/diagnostic technologies that address the same problem?	• PAP reimbursement varies across jurisdictions (i.e., partial to complete coverage). • Dental devices coverage varies. • Surgery may be covered as a medical act.
Benefits	Efficacy Clinical effectiveness Impact on patient-centred outcomes Impact on clinical management Non-health benefits (e.g., patient autonomy, dignity)	Has the clinical effectiveness of the candidate technology been established? Compared with what? What improvements does this technology purport to offer over others? What types of evidence is this based on? Are we aware of any better-quality evidence likely to be produced in the near future?	• For severe OSA, CPAP more effective than MADs for excessive daytime sleepiness. • For severe OSA, MMA ± GTA most effective if PAP therapies failed (Note: outcomes were derived from small, uncontrolled studies). • For other OSA severities, all interventions similarly effective. • CPAC is superior for reducing OSA severity. • Limited evidence on blood pressure, cardiovascular events, QoL, mortality outcomes is available.

Framework Domain	Examples of Information and Element(s)	Possible HTERP Discussion Question(s)	Discussion Points
		Are there any non-health benefits?	• Some literature is of high quality but there are concerns with regards to the eligibility criteria, small samples, and uncontrolled studies.
Harms	Safety	What is known about safety in absolute terms, and in comparison with existing technologies? What types of evidence is this based on?	• No major adverse events were reported, except MMA + GTA, with which all patients had complications caused by infections.
Patient Preferences	Acceptability of health technology by the patient	How will it potentially affect patients and what are their opinions about the technology? How acceptable is it to patients?	• Patient factors are individualized and contextual. • OSA affects bed partners. Patients perform a trade-off between the benefits of using interventions and their discomfort. • Elements of support and information are needed. • No evidence on patient experience with surgery was identified.
Economic Impact	Cost-effectiveness Infrastructure support costs Budget impact	What will the technology cost (including initial purchase price and consumables, maintenance, and training of personnel)? Is there evidence of value for money? How is value defined? What is the expected lifespan and total budget impact of the technology?	• PAP or MMA is the most cost-effective for severe OSA with a baseline AHI at a WTP of $50,000/QALY. • MAD or MMA is most cost-effective for moderate OSA. • No treatment is most cost-effective for mild OSA.
Implementation	Integration of technology into existing workflow Training/competency requirements Repair and maintenance	Have issues of implementation of the technology in a real-world health system been identified and addressed?	• One of the biggest implementation issues for OSA treatment is the difficulties in accessing sleep specialists and specialized sleep labs. • Most of the implementation evidence focuses on CPAP. • CPAP barriers include cost or lack of funding, patient discomfort or difficulties using the device.

Framework Domain	Examples of Information and Element(s)	Possible HTERP Discussion Question(s)	Discussion Points
			• CPAP enablers encompass patient education, training, or support accredited sleep centres or health care professionals, but there are no accepted guidelines. • OA barriers include lack of knowledge or awareness, anatomical and dental health. requirements, need for regular re-evaluations. • OA enablers encompass multidisciplinary sleep clinics. • Little evidence on implementation issues for OSA surgery or lifestyle interventions was found.
Legal	Legal impacts	Are there potential legal or regulatory aspects to the introduction and use of this technology?	• The legal issues associated with driving were discussed. For example, some jurisdictions can revoke a driver's licence if the person has severe OSA. • The Canada Health Act does not include dentists.
Ethics	Consistent with Canadian ethical values	Are there potential issues of equity (access by particular populations, for example) with respect to introducing this technology? Are there any other ethical issues to consider?	• Interventions for OSA do not appear to present ethical concerns that are inherent to the technologies. • Several values are relevant on how access to OSA interventions are organized and delivered. • Duties to act in ways that maximize benefits to patients or others, respect patient choice, and ensure reasonable access to resources are of core importance. • The capacity for patients to benefit from most OSA interventions relies heavily on the patient's behaviour, so patient context is perhaps unusually significant for these technologies.
Environmental Impact	Environmental impact of health technology	What is the potential impact on the environment of this technology?	• One review article examined the environmental considerations of the CPAP unit including: ○ Green shipping and production methods

Framework Domain	Examples of Information and Element(s)	Possible HTERP Discussion Question(s)	Discussion Points
			○ Creating more energy-efficient products ○ Using more recyclable materials.
Other		Are there particular questions with regards to professional fees that have been identified and addressed? Does this candidate technology raise some questions that are not addressed by the above set of questions?	• Compliance, adherence, and patient acceptability of the various treatment options. • Accurate diagnosis is necessary before appropriate treatment can be given.

AHI = apnea-hypopnea index; CPAP = continuous positive airway pressure; GTA = genial tubercle advancement; HTERP = Health Technology Expert Review Panel; MAD = mandibular advancement device;
MMA = maxillomandibular advancement; OA = oral appliance; OSA = obstructive sleep apnea; PAP = positive airway pressure; QALY = quality-adjusted life year; QoL = quality of life; WTP = willingness to pay.